March 2-7, 2024
Sheraton Waikiki Resort

Honolulu, HI

North American Neuro-Ophthalmology Society

1975-2024

North American Neuro-Ophthalmology Society

50th Annual Meeting

March 2-7, 2024; On Demand April 10 – August 31, 2024
Sheraton Waikiki, Honolulu, HI

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CME ACTIVITIES FACULTY AND PLANNER DISCLOSURE STATEMENTS

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INTERPROFESSIONAL CONTINUING EDUCATION

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STATEMENT OF NEED

The purpose of the North American Neuro-Ophthalmology Society's Continuing Medical Education (CME) program is to present neuro-ophthalmologists with quality lifelong learning opportunities to promote improvement and change in physician practices, performance, and competence needed to provide the best possible neuro-ophthalmic care for their patients.

EDUCATIONAL OBJECTIVES

After completing this activity, the participant should be better able to:

- Identify recent advances in the diagnosis and treatment of neuro-ophthalmic diseases.
- Identify advances in key areas of cutting-edge research and technology in neuro-ophthalmology.
- Apply skills and techniques from the educational sessions into their daily practice.

MISSION STATEMENT

The North American Neuro-Ophthalmology Society (NANOS) is dedicated to achieving inclusive excellence in the care of patients with neuro-ophthalmic diseases by the support and promotion of equitable education, research, and the practice of Neuro-Ophthalmology.

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Walsh Cases - Sunday, March 3rd

Host: Frank B. Walsh, University of Michigan
Lead Host: Lindsey De Lott, MD, MS

Host Committee Members:
Sangeeta Khanna, MD, Wayne Cornblath, MD, Tatiana Deveney, MD, Jonathan Trobe, MD
Expert Panel:
Neuroradiologist: Hemant Parmar, MBBS
Neuropathologist: Sandra Camelo-Piragua, MD

This session is designed to present complex neuro-ophthalmic cases that impact the visual pathways and ocular motor systems.
The format is a clinicopathologic conference. Clinical cases will be presented by neuro-ophthalmologists with comments by invited experts: a neuro-radiologist, a neuro-pathologist, and other selected experts. Neuroimaging, laboratory, and surgical pathology data will help illustrate clinical points. Cases will be discussed from clinical, anatomic, radiologic, and pathologic aspects with emphasis on diagnosis, pathophysiology, and management.

Upon completion of this session, participants should be able to: (1) Describe the varied clinical presentations of neuro-ophthalmic disease, (2) Formulate effective diagnostic testing strategies for complex neuro-ophthalmic cases including the use of new diagnostic tests, (3) Explain the value and limitations of neuropathology and neuroimaging, and (4) Identify newly described neuro-ophthalmic diseases in clinical practice.

Frank B. Walsh I [2.0 CME]

Moderators: Moderators: Wayne Cornblath, MD & Tatiana Deveney, MD

7:45 am – 8:05 am	**What Izit?** Michael Lee, MD
8:05 am – 8:25 am	**Orbitally Vexed**, Eliot Smolyansky, MD
8:25 am – 8:45 am	**It Can't Be Me, But … Maybe It's Both of Us?** George Park, MD
8:45 am – 9:05 am	**MY-OH-MY Just a Drop will Do**, Aurel Nagy, MD, PhD
9:05 am – 9:25 am	**Go Back to the House, M.D.,** Marc Bouffard, MD

Frank B. Walsh II [2.0 CME]

Moderators: Lulu Bursztyn, MD, Sangeeta Khanna, MD

10:00 am – 10:20 am	**Atypical Case of Optic Nerve Head Edema: Painful, Enhancing and Treacherous,** Samir Touma, MD
10:20 am – 10:40 am	**Headache and Visual Deficits: Ironing Out the Details**, Amalie Chen, MD
10:40 am – 11:00 am	**Double Double, Toil and Trouble**, Kevin Yan, MD
11:00 am – 11:20 am	**Anchora Sella**, Vanessa Dias Veloso, MD
11:20 am – 11:40 am	**(Don't) Blame it on Rio**, Avital Okrent, MD

Frank B. Walsh III [2.0 CME]

Moderators: Dane Breker, MD & Lindsey De Lott, MD, MS

3:00 pm – 3:20 pm	**Losing Vision, Losing Sleep**, Bart Chwalisz, MD
3:20 pm – 3:40 pm	**How to Get the Red Out**, Raghu Mudumbai, MD
3:40 pm – 4:00 pm	**The Path of Least Resistance: Over the Nose, Into the Orbit, and Around the Globe,** Sahar Noorani, MD
4:00 pm – 4:20 pm	**Devine Intervention,** Letitia Pirau, MD
4:20 pm – 4:40 pm	**A White Matter Riddle Encased in Mystery, Coiled Inside an Enigma**, Nathan Tagg, MD

"What Izit?"

Michael Lee [1], Casey Judge [2], Collin McClelland [1], Liam chen [1], Mehmet Gencturk [1], Andrew Venteicher [1]

[1] University of Minnesota, [2] Lehigh Valley Fleming Neuroscience Institute

History & Exam: A 67-year-old woman noted binocular double vision and right sided headache on 5/5/22. She was diagnosed at an outside facility with a right 3rd nerve palsy. Lab testing showed ESR 63, CRP < 0.5, normal AchR ab. She was placed on gabapentin. Noncontrast brain MRI/MRA was read as normal. Her past medical history included diabetes, hypertension, hypercholesterolemia, and breast cancer (2005) in remission status post mastectomy, radiation, and chemotherapy in 2015. Her medications were glipizide, metformin, lisinopril, chlorthalidone, simvastatin, anastrozole, and diclofenac. Her ROS was negative for GCA, she was a former smoker with occasional alcohol use, and she worked at a community center. Her mother went blind for an unknown reason at age 46. On 6/3/22, her pinhole acuities were 20/30 and 20/25. Her pupils and color vision were normal. She had mild cataracts and background diabetic retinopathy. There was ptosis of the right upper eyelid and incomplete omnidirectional ophthalmoplegia RE with severe painful eye movements. There was allodynia in the right V1/V2 distribution. Normal testing included ESR, CRP, ACE, ANA, ANCA, RPR, Quantiferon, Lyme and CT chest/abdomen/pelvis. Brain MRI with contrast demonstrated an enhancing lesion in the right cavernous sinus. She was placed on prednisone 80 mg/day with 2-week follow-up. She returned 9/27/22 on 60 mg of daily prednisone with a persistent right 3rd and 6th nerve palsy and facial numbness/pain. The pain had become intolerable. Her acuities were 20/60 RE and 20/40 LE. Her color vision dropped to 9/11 right eye. She had a 1+ RAPD RE. Repeat MRI showed interval progression into the right orbital apex, Meckel's cave, and right tentorium. She underwent a craniotomy on 11/3/22 and there was a dense, adherent, tan mass that was difficult to remove.

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“What Izit?”

Answer

Final Diagnosis: Cavernous sinus and orbital apex syndrome secondary to primary C. acnes infection

Summary of Case: There were 8 pathologic samples (middle fossa, foramen ovale x2), V3 dura, V2/V3 triangle, Meckel’s cave, tentorium x2) that showed fibrous tissue with and without chronic inflammation. There was no evidence of neoplasm or metastatic disease. Rare IgG4 positive cells were seen. Cultures were ordered but not performed. The patient complained of severe and progressive postoperative pain in the right V1 and V2 distribution unmitigated by opioids. Next generation sequencing (NGS) bacterial DNA 16 S Ribosomal test showed C. acnes on the permanent sections on 11/28/22. She saw Infectious disease on 12/7/22, who doubted the diagnosis but started the patient on oral penicillin 500 mg TID. By 12/11/22, the pain began to subside and resolved by 12/14/22. On 2/13/23, her pinhole acuities were 20/50 RE and 20/30 LE with normal color vision and normal pupils. Eye movements showed some minimal abduction and elevation deficits of the right eye. She only noted diplopia in extreme gazes. Repeat MRI on 2/14/23 showed resolution of the previous lesion (neurosurgery described diagnostic biopsies only). Penicillin was stopped on 3/7/23. She developed pain, itching, swelling and tenderness around the incision on 4/5/23. She resumed oral penicillin on 4/20/23 with resolution of signs and symptoms within 2 months. References: 1. Adesina OOO, et al. Optic neuropathy caused by Propionibacterium acnes pachymeningitis. J Neuroophthalmol 2014;34:264-7. 2. Fernandez-Rodrigez D, et al. Next-generation sequencing results require higher inoculum for cutibacterium acnes detection than conventional anaerobic culture. Clin Orthop Relat Res 2023 Jun 21. 3. Smith JL, et al. Spontaneous Propionibacterium acnes abscess with intraventricular rupture in an immunocompetent adult without prior neurosurgical intervention. Clin Case Rep 2022 Jan;10:e05216. 4. Odunukan OW, et al. Propionibacterium acnes abscess in an immunocompetent man in the absence of prior neurosurgery. S D Med 2016 Feb;69:71-3.

Struggle/Dilemma of the Clinical Presentation Description: The patient did not have prior neurosurgery, cultures were not performed, and C. acnes is a common contaminant in neurosurgery. The patient’s 16S testing was positive for C. acnes. Primary C. acnes CNS infection has been reported. The following occurred on penicillin alone: 1. Progressively worsening and intolerable pain for seven months resolved within a week 2. MRI lesion resolved within 2 months 3. Ophthalmoplegia improved almost completely.

Keywords: 3rd nerve palsy, 6th nerve palsy, Cavernous sinus syndrome, Complications of infections, Facial pain

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"Orbitally Vexed."

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History & Exam: An 84-year-old independent retiree presented with a three-day history of a painful, red, watery eye associated with horizontal binocular diplopia. His ocular history included bilateral intraocular lens replacement several years prior. Examination revealed mild left proptosis with marked periorbital oedema, chemosis and conjunctival injection. A small left esotropia was seen at primary with significant limitation of left ductions in all directions. The remainder of the anterior and posterior examination was normal with no afferent visual defect, nor additional cranial neuropathy observed. He remained systemically well without an intercurrent infective illness or constitutional symptoms. A mild pancytopenia was seen, though serum inflammatory makers were within normal limits and an extensive infective screen was unrevealing. A B-scan demonstrated left posterior globe thickening and a positive 'T-sign', while an MRI of the brain and orbits revealed a diffusely thickened left optic nerve sheath with enhancement from the orbital apex to the posterior globe, lacking extension into the optic canal or chiasm. Investigation into his background revealed an 8-year history of relapsing polychondritis associated with mild cytopenias, fevers, joint pain and one previous episode of periorbital oedema. His regular medication included tocilizumab and oral prednisolone. A bone marrow biopsy taken a year earlier demonstrated moderately hypercellular marrow with dysplastic tri-lineage haematopoiesis and prominent vacuolation of both erythroid and myeloid precursors. A diagnostic test had been performed on his biopsy to confirm the cause of his relapsing condition with management of his current presentation guided by this result.

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

“Orbitally Vexed.”

Answer

Final Diagnosis: Acute orbital manifestations of an underlying haematoinflammatory disorder, VEXAS syndrome.

Summary of Case: Genetic testing had revealed a Mel41Val missense mutation in a gene located in the UBA1 gene on the X-chromosome, in keeping with a diagnosis of VEXAS syndrome. Pulsed intravenous methylprednisolone resulted in rapid improvement of symptoms with only mild abduction restriction, temporal conjunctival injection and subtle inferior chemosis persisting after 48 hours and complete resolution observed by day four post treatment. VEXAS syndrome (vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic) is a newly characterised title for a group of adult-onset, treatment-refractory multi-system inflammatory diseases with haematological abnormalities. First reported in 2020, VEXAS occurs through recurrent and inactivating somatic mutations in the ubiquitin activating enzyme 1 (UBA1) gene in haematopoietic progenitor stem cells. Though phenotypical heterogeneity exists, VEXAS is recognised as a progressive and fatal systemic disease that mimics a number of rheumatological conditions and results in bone marrow failure and haematological malignancy. Missense mutations involving methionine at codon-41 on the X-chromosome are common, though additional mutations have been reported. True prevalence of the disease is likely under-appreciated due to clinical variability though population prevalence has been estimated as 1:4269 in men aged greater than 50 years . A history of relapsing polychondritis with macrocytosis or thrombocytopenia is thought to predict a risk of VEXAS with 100% sensitivity and 96% specificity. Common manifestations include recurrent fevers and fatigue, relapsing polychondritis, neutrophilic dermatosis, pulmonary infiltrations and various forms vasculitis [6]. Ocular involvement has been described in up to 40% of cases, with episcleritis, uveitis and scleritis the most frequently reported. Orbital myositis, superior orbital fissure syndrome and optic perineuritis have also been rarely identified in individual case reports. Corticosteroids are temporarising and used to obtain initial disease control, however patients typically become therapy refractory over time and considerable morbidity and mortality exists through myeloid-driven autoinflammation, progressive bone marrow failure or infective complications.

Struggle/Dilemma of the Clinical Presentation Description: The management of this patient was complicated due to the paucity of knowledge and literature on this recently characterised systemic haematoinflammatory disorder. The case resulted in management uncertainty due to the difficulty in differentiating an infective or inflammatory cause due to the clinical presentation, degree of background immunosuppression and the limited reports of ocular and orbital manifestations.

Keywords: Optic perineuritis, 3rd nerve palsy, 4th nerve palsy, 6th nerve palsy, Chemosis

References: 1. Grayson P, Patel BA, Young NS. ‘VEXAS syndrome’. Blood. Jul 2021. doi: 10.1182/blood.2021011455 2. Beck et al. ‘Somatic mutations in UBA1 and severe adult-onset autoinflammatory disease’. NEJM. Dec 2020. doi: 10.1056/NEJMoa2026834. 3. Ferrada et al. ‘Somatic mutations in UBA1 define a distinct subset of relapsing polychondritis patients with VEXAS’. Arthritis and Rheumatology. Oct 2021. doi: 10.1002/art.41743. 4. Kucharz EJ. ‘VEXAS syndrome: A newly discovered systemic rheumatic disorder’. Reumatologia. 2023. doi: 10.5114/reum/163090 5. Beck et al. ’Estimated prevalence and clinical manifestations of UBA1 variants associated with VEXAS syndrome in a clinical population’. JAMA. 2023. doi: 10.1001/jama.2022.24836

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"It Can't Be Me, But … Maybe It's Both of Us?"

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History & Exam: A 53-year-old male chef with extensive travel for work, history of T2DM (A1c 6.8%) developed positional headaches and diplopia over one month. Exam showed absent abduction of the left eye. MRI without gadolinium showed an infiltrative left petroclival lesion extending into the cavernous sinus. Endoscopic biopsy showed inflammatory infiltrates and he was treated for a sinus infection. Headaches worsened one week later. Infectious workup, including repeat endoscopic biopsy, showed no active infection but elevated serum IgG4. He was discharged on a steroid taper for suspected inflammatory/infiltrative process. He returned one month later with worsening headaches, left facial weakness and hearing loss. MRI showed increased soft tissue fullness around the left cerebellopontine angle extending into the left pons and midbrain. He had an episode of emesis and sudden lethargy. CT head showed acute hydrocephalus; an EVD was placed and converted to a shunt. He received 5 days of IV steroids for suspected IgG4-RD. Brain biopsy performed showed a dense population of histiocytes and non-caseating granulomas. Pathology sent to an outside institution confirmed non-necrotizing granulomatous inflammation including well-formed giant cells. Auramine stain highlighted rare mycobacterium. He was started on RIPE + azithromycin for suspected mycobacterial infection. Extensive workup, including LPs, serial imaging and serum studies revealed no alternative etiology. Samples were sent to two outside institutions for metagenomic next generation sequencing (mNGS). At follow-up outpatient visit, he was found to have new dysarthria, left facial numbness, left eye supraduction deficit with new vertical diplopia, persistent hiccupping and gait imbalance. He was readmitted and MRI showed interval enlargement of heterogeneous multifocal cystic enhancing lesions centered in the left petrous apex with extension into the cerebellopontine angle, pons and cerebellar peduncle. Lethargy progressed, ultimately requiring intubation. Cerebellar biopsy showed friable, inflamed tissue. Despite aggressive broad treatment with antimicrobials, antiparasitics and antifungals, patient ultimately died.

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Grant Support: None.

“It Can’t Be Me, But … Maybe It’s Both of Us?”

Answer

Final Diagnosis: After extensive evaluation with broad serum and CSF investigations, multiple cultures and several biopsies, the patient was ultimately diagnosed with Acanthamoebic granulomatous meningoencephalitis combined with mycobacterial meningoencephalitis.

Summary of Case: The patient presented with progressive positional headaches, likely related to presumed increased intracranial pressure, along with a left 6th nerve palsy. The process was likely related to local inflammation/compression with initial imaging showing a left petroclival lesion with extension into the cavernous sinus (petrous apicitis). He had extensive serum and CSF infectious and inflammatory workup, including a total of four endonasal and brain biopsies that were largely inconclusive until mycobacterium was found on auramine stain. Despite anti-mycobacterial therapy, this process eventually progressed intra-axially to involve multiple different cranial nerve distributions with imaging showing a heterogeneous cystic enhancing lesion extending into the brainstem. Eventually acanthamoeba returned positive on mNGS studies performed at an outside institution. Immediately afterwards the appropriate treatment was initiated for acanthamoeba however after several months of continued care in the Neuro ICU, patient ultimately expired. The aggressive nature of the clinical course heightened suspicion for an atypical infectious organism; this prompted further investigation. Additionally, the patient’s immune status was unclear given his history of T2DM and prolonged course of steroids, adding to the overall unclear nature of his immunological status. One important question raised by this case is how early mNGS studies should be sent for undiagnosed skull base lesions with suspected inflammatory or infectious etiology.

Struggle/Dilemma of the Clinical Presentation Description: There was diagnostic uncertainty throughout our patient’s course, making treatment decisions challenging. Initially, due to unrevealing extensive evaluations of serum, CSF and tissue, an inflammatory/infiltrative process such as IgG4RD was considered. Brain biopsy ultimately revealed AFB on auramine stain. The patient’s condition continued to deteriorate despite aggressive coverage for mycobacterium. Ultimately the diagnosis of acanthamoeba was made with mGCS testing. Both acanthamoeba and mycobacterium likely played a role in this patient’s progressive course.

Keywords: Infectious disease, Abscess, Diplopia, 6th nerve palsy, Brain stem syndromes

References: Bunsuwansakul C, Mahboob et al. Acanthamoeba in Southeast Asia - Overview and Challenges. Korean J Parasitol. 2019 Aug;57(4):341-357. doi: 10.3347/kjp.2019.57.4.341. Epub 2019 Aug 31. PMID: 31533401; PMCID: PMC6753290. Haston JC and Cope JR. Amebic encephalitis and meningoencephalitis: an update on epidemiology, diagnostic methods, and treatment. Curr Opin Infect Dis. 2023 Jun 1;36(3):186-191. doi: 10.1097/QCO.0000000000000923. Epub 2023 Apr 10. PMID: 37093056. Kalra SK, et al. Acanthamoeba and its pathogenic role in granulomatous amebic encephalitis. Exp Parasitol. 2020 Jan;208:107788. doi: 10.1016/j.exppara.2019.107788. Epub 2019 Oct 21. PMID: 31647916. Lau HL, et al. Granulomatous amoebic encephalitis caused by Acanthamoeba in a patient with AIDS: a challenging diagnosis. Acta Clin Belg. 2021 Apr;76(2):127-131. doi: 10.1080/17843286.2019.1660023. Epub 2019 Aug 27. PMID: 31455179.

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"MY-OH-MY Just a Drop will Do"

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History & Exam: A 45-year-old man presented with progressive loss of vision. Six months prior, he underwent cataract surgery in both eyes with subsequent development of refractory inflammation and intraocular pressures greater than 40 mmHg despite maximal medical therapy. He underwent bilateral trabeculectomies, scarring secondary to persistent inflammation and necessitating the placement of ahmed valves bilaterally. His intraocular inflammation was managed with topical and oral steroids and he was referred to uveitis who began an extensive work-up for this refractory inflammation. The patient endorsed headaches, depression, forgetfulness, low libido and weight loss. His medical history was unremarkable except for undercooked pork consumption monthly and travel to Mexico 5 years prior. On examination, the patient was somnolent and responded slowly. He had continuous hiccups and chewing movements of his mouth. His visual acuity was 20/80 OD and count fingers at 1 foot OS. Pupils were fixed and poorly reactive. His eye movements had partial limitation in all directions of gaze and extremely slow saccades. Anterior segment examination demonstrated moderate keratic precipitates bilaterally and diffuse anterior segment inflammation (Figure 1). Posterior segment examination demonstrated vitreous cell bilaterally with significant cupping and pallor of his optic nerves and scattered macular exudates. (Figure 2). Cranial nerve, motor and sensory examinations were normal. Optical coherence tomography of the retina demonstrated preretinal precipitates (Figure 3). MRI revealed bilateral optic nerve atrophy and an 8-mm enhancing hypothalamic/infundibular nodule with infiltration along the inferior aspect of the optic chiasm (Figure 4). Endocrine serology was notable for a slightly elevated prolactin (46.2 µg/L [normal range, 2.0 to 18.0 µg/L]). Serologic interferon-ɣ, Lyme antibody, treponemal antibody, and rapid plasma reagin were all negative. Chest radiography was normal. Cerebrospinal fluid analysis demonstrated normal (4) white cells with 10% neutrophils, protein, glucose and no oligoclonal banding and negative cultures. A diagnostic test was then performed.

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Grant Support: None

“MY-OH-MY Just a Drop will Do”

Answer

Final Diagnosis: Whipple's disease resulting in diffuse bilateral uveitis and detected by metagenomic sequencing of the aqueous humor.

Summary of Case: The patient initially presented with progressive intraocular inflammation and uveitic glaucoma. He reported headaches, weight loss, depression and changes in his libido. Upon examination, the patient’s mental status was altered, being somnolent, slow to answer questions, with continuous hiccups and masticatory myorrhythmia. Initial serologic and cerebrospinal fluid cultures were unremarkable. Repeat MRI redemonstrated the 8-mm hypothalamic/infundibular nodule with stable infiltration of the chiasm without other abnormalities. Neurosurgical biopsy was considered as the finding was felt to be consistent with granulomatous or neoplastic processes but was delayed due to urgent glaucoma intervention. A diagnostic pars-plana vitrectomy was performed with negative bacterial, fungal, viral, and toxoplasma, and flow cytometry. Cytopathology demonstrated histiocytes with rare mature-appearing lymphocytes (Figure 5). Aqueous PCR was negative for HSV/VZV/CMV/toxoplasma were all negative. At this time a previously submitted aqueous humor diagnostic study resulted demonstrating the presence of Tropheryma whipplei. Repeat cytopathologic, serologic, and CSF studies were obtained and confirmed the diagnosis of Whipple’s Disease. Ocular manifestations of Whipple's disease are extremely rare. In the absence of more traditional symptoms including gastrointestinal abnormalities and arthralgia, time to diagnosis can be significantly delayed with progression of the disease. This patient was enrolled in an IRB-approved clinical study for the detection of infectious pathogens by metagenomic next-generation sequencing. This approach identified T. Whipplei DNA in the otherwise negative aqueous humor sample (Figure 6). As directed molecular diagnostics for T. whipplei do not exist for ocular tissues outside of research laboratories, this case represents an exciting demonstration of the power and utility of this approach for the diagnosis of culture-negative ocular inflammation. Other features in his presentation that assisted with the diagnosis were the masticatory myorhythmia and the presence of periodic acid-Schiff staining histiocytes in the vitreous humor which are highly suggestive of Whipple’s disease (Figure 7).

Struggle/Dilemma of the Clinical Presentation Description: The patient’s chronic uveitis remained undiagnosed for a prolonged period and progressed despite high dose topical and oral steroid therapy resulting in progressive vision loss and neurologic decline. As ocular manifestations of Whipple disease are rare, this patient’s highly atypical presentation without gastrointestinal or rheumatological symptoms delayed diagnosis. Additionally, the oculomasticatory myorrhythmia was difficult to identify as the patient's ophthalmoplegia limited the eye movement component.

Keywords: Whipple’s disease, Uveitis, Oculomasticatory myorhythmia (Whipple''s)

References: Gonzales J, Doan T, VanZante A, Stewart JM, Sura A, Reddy A, Rasool N. Detection of Tropheryma whipplei Genome From the Aqueous Humor by Metagenomic Sequencing. Ann Intern Med. 174(9): 1329-1330. Lagier JC, Lepidi H, Raoult D, Fenollar F. Clinical Presentation of 142 Patients With Infections Diagnosed or Confirmed in a Reference Center. Medicine. 89(5): 337-345. Doan T, Sahoo MK, Ruder K, Huang CH, Zhong L, Chen C, Hinterwirth A, Lin C, Gonzales J, Pinsky BA, Acharya NR.Comprehensive pathogen detection for ocular infections. J Clin Virol. 136. 2021.

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“Go Back to the House, M.D.”

Marc Bouffard [1]

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History & Exam: A 72-year-old man presented to the emergency department with dysarthria and a left facial droop. He was in his usual state of health prior to the day of presentation. His social worker described him as being at his baseline on the morning of presentation, only to find him immobile with a facial droop, dysarthria, and incontinence several hours later. His medical history included hypertension, hyperlipidemia, and aspiration pneumonia complicated by delirium. Medications included lisinopril, furosemide, aspirin, carvedilol, and atorvastatin. No allergies were known. His family history was unclear. He was previously undomiciled but more recently lodged in state-sponsored housing with other previously homeless individuals. His substance use history was unknown. The initial examination, conducted by a neurology resident in the emergency department, revealed a disheveled patient with insect bites on his appendages. He answered simple questions but seemed inattentive (e.g., calling out for water). The cranial nerve examination revealed complete, non-supranuclear ophthalmoparesis OU but was otherwise normal, including reactive pupils and visual fields which were full to finger counting. His face appeared symmetric. The motor examination was limited but revealed symmetric anti-gravity movement throughout. Light touch was intact throughout. Reflexes, coordination, and gait were not assessed. Aspiration pneumonia was identified and he was started on antibiotics and IV thiamine. After admission, systolic blood pressures increased to the 200s. The neurology attending examination revealed preserved ability to follow commands despite an inability to open eyes. Blink to threat was absent. Pupils reacted from 3.5-3 on hospital day 2 but were fixed by hospital day 3 at 4.5mm. Eyes were conjugate with complete ophthalmoplegia and absent vestibulo-ocular reflexes in all directions. Corneal reflexes were very weak and cough was absent. No movement was noted proximally, though he could weakly squeeze hands and wiggle toes symmetrically. Tone was low. Reflexes were absent.

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

“Go Back to the House, M.D.”

Answer

Final Diagnosis: Foodborne botulism

Summary of Case: CSF examination revealed 0 WBC, 1 RBC, protein 78, and a glucose of 96. MRI brain revealed FLAIR hyperintensities in the brainstem, basal ganglia, and subcortical white matter without abnormal post-contrast enhancement or diffusion restriction. The history was revisited with a painstaking “yes/no” interview involving hand squeezing. The patient denied an antecedent diarrheal illness, recreational drug use, or alcohol use. He endorsed consumption of bulging, dented, and expired canned goods in the setting of food insecurity. Social work investigated his home and found multiple damaged canned goods. Botulinum antitoxin was requested from the CDC and administered in parallel with IVIg for possible Miller-Fisher. EMG subsequently revealed "severe motor process without signs of denervation.” GQ1b was < 1:100. The ganglioside panel, porphyrins, Mayo autoimmune encephalopathy panel from serum and CSF, Ma/Ta, and C.botulinum culture from stool returned negative. A serum assay for Clostridium botulinum toxin (Type A) returned positive from the CDC, establishing a diagnosis of foodborne botulism. On hospital day 19, a meeting was held with his estranged family who reported that he would not want to be intubated for any reason for any duration of time. He was terminally extubated and died. This patient’s presentation was classic for botulism, involving multiple cranial nerve palsies (featuring mydriasis and ophthalmoplegia), descending paralysis, and parasympathetic failure (hypertension, thirst) 1. Botulism is a rare cause of multiple cranial neuropathies2. Wernicke’s and an evolving brainstem infarct (near locked-in) were considered given the patient’s acute decline, but after MRI brain was unrevealing and his status worsened despite IV thiamine, Miller-Fisher/Bickerstaff, botulism, Lambert-Eaton, and brainstem encephalitides were promptly considered. Revisiting the history, despite the inherent difficulty in doing so, clarified the diagnosis. 1. Penas SC, et al. Ophthalmic manifestations in 18 patients with botulism. J Neuro-Ophth 2005;25:262-267. 2. Keane JR. Multiple cranial nerve palsies. Arch Neurol 2005;62(11):1714-1717.

Struggle/Dilemma of the Clinical Presentation Description: There were three dilemmas in this case: diagnostic, therapeutic, and ethical. The diagnostic dilemma revolved around differentiating between botulism and MFS/Bickerstaff spectrum (also, Wernicke’s, locked-in syndrome, Lambert-Eaton, and autoimmune encephalitides). The therapeutic dilemma arose from concern that administration of IVIg could opsonize the botulism antitoxin; MFS was statistically likelier, yet botulism fit more neatly making co-administration ideal. The ethical dilemma revolved around his family’s decision to terminally extubate a patient who would have likely recovered.

Keywords: Botulism, Pupil, Ptosis, Diplopia, Autonomic failure

References: None provided.

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"Atypical Case of Optic Nerve Head Edema: Painful, Enhancing and Treacherous"

Samir Touma [1], Katie Luneau [1], Jacinthe Rouleau [1]

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History & Exam: A 42-year-old female patient was referred to our neuro-ophthalmology clinic for unilateral gradual decrease of vision in her right eye over two weeks. She also reported light pain on extraocular movements as well as daily headaches. She did not have any focal neurological deficit on history and no fever, chills, or night sweats. She had received the second dose of her COVID-19 vaccine two days before the onset of symptoms and had a history of gonorrhea treated 2 months prior. Her visual acuity was 20/50 in the right eye and 20/20 in the left one. She did have a right relative afferent pupillary defect (RAPD), graded as 1+. Extraocular movements were full in both eyes, including normal saccades and pursuit. Color vision was decreased in her right eye with a score of 7/11 on HRR compared to 11/11 in her left eye. She did not have proptosis on Hertel examination. On slit lamp exam, her anterior segment was unremarkable, including a calm anterior chamber. She had severe right optic nerve edema graded as 5+. The disc was elevated over 360 degrees and all major vessels were obscured. She exhibited peripapillary hemorrhages as well as cotton wool spots. There was some subretinal fluid under the papillomacular bundle, but no macular star. Posterior pole and periphery showed some dot-blot and flame-shaped hemorrhages in the right eye only. No cells were visible in the vitreous. The left optic nerve was completely normal with clear margins and a cup-to-disc ratio of 0.3 Optical coherence tomography showed diffuse elevation of the retinal nerve fiber layer (rNFL) in the right eye (199 versus 98 µm). Ganglion cell complex was atrophied (54 versus 87 µm). Visual field testing (SITA 24-2) showed a cecocentral scotoma as well as inferior arcuate defect. Left eye had a complete visual field.

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

“Atypical Case of Optic Nerve Head Edema: Painful, Enhancing and Treacherous”

Answer

Final Diagnosis: After discussion with the multidisciplinary team, we decided to organise a DOTATATE PET scan. This special type of PET scan is a novel imaging technique that targets somatostatin receptor 2 (SSTR2), which is highly expressed in meningiomas. This technique improves the detection and delineation of the lesion. The DOTATATE PET scan revealed a circumferential lesion around the optic nerve with high concentration of somatostatin receptors, which suggested an ONSM or other neurogenic tumors. A transcranial biopsy was performed by the neuro-surgery team a few days later confirming the diagnosis of meningioma (transitional grade 1). Following the biopsy, the patient’s vision unfortunately decreased to no light perception. The team’s decision was to go forward with radiotherapy (30 fractions of 180 cGy). Nevertheless, she did not recover any vision. Our patient had a very atypical presentation for an ONSM as she exhibited none of the three most common presenting complaints: painless proptosis, optic nerve pallor and strabismus. Instead, she presented with rapid decrease in vision, pain on eye movements and significant optic nerve edema, causing CRVO and secondary macular edema. In conclusion, although rare, ONSM can present acutely with pain and important optic disc edema. Routine workup should still be completed to rule out more common diagnoses. However, when MRI cannot clearly differentiate perineuritis from ONSM, then a DOTATATE PET scan can be very helpful in making the right diagnosis and guide management.

Summary of Case: A cerebral MRI was done showing impressive enhancement of the intraorbital portion of the right optic nerve sheath with diffuse swelling of the optic nerve suggestive of optic neuritis. There was no extension to the optic chiasm and no infiltrative or demyelinating lesion. A retinal angiography revealed venous sheathing in the posterior pole as well as a few leaking veins in the macular region. These findings were compatible with a central retinal vein occlusion (CRVO), which could be secondary to the impressive optic nerve swelling. Blood work for NMO, MOG, sarcoidosis, IgG4 and inflammatory markers (ESR, CRP) were normal. Infectious workup including syphilis, tuberculosis, CMV, HIV, toxoplasmosis, Bartonella, and Lyme was negative. She also had a normal pulmonary radiography. The patient underwent a lumbar puncture with normal opening pressure and composition, no oligoclonal bands and negative cultures. We decided to treat the patient with intravenous cortisone after infectious etiologies were ruled out. She received three days of intravenous methylprednisolone (1g) followed by a two-week taper of prednisone PO (starting dose of 50 mg DIE). No improvement was noted regarding vision or pain following treatment. An orbital MRI was performed and revealed a thickening as well as a circumferential enhancement of the optic nerve sheath suggestive of a perineuritis or an atypical optic nerve sheath meningioma (ONSM). To complete the evaluation, she had a spine MRI and a whole-body PET scan with both being normal. A sudden decrease of vision occurred within 3 weeks following her initial visit with visual acuity reaching 20/400. Optic nerve head edema was slightly worse, while macular subretinal and intraretinal fluid had markedly increased. She underwent anti-VEGF injection with minor improvement. However, a gradual deterioration of the visual field, color vision and RAPD had occurred since the first evaluation.

Struggle/Dilemma of the Clinical Presentation Description: This patient’s case is atypical on multiple facets. Orbital imaging was suggestive of perineuritis, but inflammatory, infectious, and neoplastic workup was negative. Also, no improvement was noted with corticosteroids. ONSM was also considered based on imaging, but the rapid deterioration of vision (20/50 to 20/400 in less than 3 weeks) and pain on extraocular movements were atypical for this diagnosis. Given the onset of symptoms two days following COVID vaccine, an unreported complication was possible.

Keywords: Optic nerve tumors, Optic perineuritis, PET

References: None provided.

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"Headache and Visual Deficits: Ironing Out the Details"

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History & Exam: A 67-year-old woman with hypertension, hyperlipidemia, and diabetes developed posterior-predominant, non-positional headaches associated with nausea and vomiting. Two weeks after headache onset, she developed significant visual hallucinations. She described seeing "graphics," consisting of formed and unformed images and words coming and going throughout her field of vision. She noticed that faces looked distorted, but she did not have difficulty recognizing familiar people. She could not read the time on a clock or use her phone despite being able to see both. She had difficulty navigating unfamiliar settings, needing to hold onto walls or furniture to get around. She denied frank vision loss or double vision. She denied recent fever, rash, insect bites, unintentional weight loss, night sweats, or fatigue. Examination demonstrated normal level of arousal, comprehension, fluency of speech, repetition, reading, and writing. Visual acuity and color vision were normal. Visual field testing demonstrated a dense, congruous, left homonymous hemianopsia. She had impaired visual search within the intact field, but naming of visually presented objects was normal. On the Navon figure, she described the local elements but not the global form. She did not demonstrate left-sided neglect for tactile stimuli or with line cancellation testing. Pupils were equal and briskly reactive, with no relative afferent pupillary defect. Slit lamp and funduscopic exam were unremarkable. Efferent exam was normal. Cranial nerve, motor, sensory, cerebellar and gait exams were normal. Reflexes were 2+ and symmetric throughout, except the left plantar response was extensor.

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

"Headache and Visual Deficits: Ironing Out the Details"

Answer

Final Diagnosis: Leptomeningeal-predominant cerebral amyloid angiopathy-related inflammation causing headache, homonymous hemianopia, visual processing deficits, and seizures.

Summary of Case: MRI brain with gadolinium contrast revealed diffuse leptomeningeal enhancement, most prominently in the bilateral temporal parieto-occipital and left frontal sulci (Fig.1), with associated T2/FLAIR sulcal hyperintensity (Fig.2). T2-weighted images showed enlarged perivascular spaces (i.e. Virchow-Robin spaces) in the centrum semiovale (Fig.3). There were no other significant parenchymal T2-FLAIR abnormalities. Susceptibility-weighted imaging (SWI) lacked cortical superficial siderosis or microhemorrhages (Fig.4). CSF showed RBC 0 cells/mL, 4 WBC cells/mL, protein 78 mg/dL, glucose 89 mg/dL, and was negative for xanthochromia, malignant cells, infection, or autoimmune antibodies. Body PET/CT was normal. ESR and CRP were normal. ANA was negative and other serum autoimmune markers including ACE were normal. The patient had a witnessed generalized tonic-clonic seizure captured on EEG, which demonstrated a right temporal-onset seizure with generalization, as well as independent left temporal spike-wave discharges. She was initiated on levetiracetam and had no further seizures. Before the initiation of corticosteroids or other empiric therapies, she underwent a right occipital craniotomy with open biopsy that revealed thickened small and medium vessels within the leptomeninges and superficial neocortex with amorphous eosinophilic deposits in the vessel wall (Fig.5). Congo red stain of these deposits demonstrated apple-green birefringence under polarized light (Fig.6). Beta-amyloid immunostaining showed extensive amyloid deposition in the leptomeningeal and superficial cortical vessels, with scattered intraparenchymal amyloid plaques (Fig.7). Tau immunohistochemistry was negative. Additionally, a prominent perivascular lymphoid infiltrate was identified in the leptomeninges (Fig.8) without significant parenchymal inflammation. There were no microhemorrhages or hemosiderin deposits noted. Leptomeningeal-predominant cerebral amyloid angiopathy – related inflammation (CAA-ri) was diagnosed. She was treated with IV methylprednisolone with prompt significant improvement in her headaches and visual deficits. She has been continued on a prednisone taper and transitioned to mycophenolate mofetil immunotherapy without further relapse to date.

Struggle/Dilemma of the Clinical Presentation Description: The diagnosis of leptomeningeal-predominant CAA-ri relied on biopsy and could not have been made with imaging and CSF biomarkers alone. The differential diagnosis for diffuse leptomeningeal enhancement includes malignancy, infection, and less likely, inflammatory processes such as sarcoidosis. In this case, SWI MRI sequences did not demonstrate cortical microhemorrhages or superficial siderosis, and there were no parenchymal T2/FLAIR hyperintensities. Therefore, this case did not meet current radiographic criteria for probable CAA-ri (1).

Keywords: Cerebral amyloid angiopathy, Vision field loss, Balint syndrome, Seizure

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"Double Double, Toil and Trouble"

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History & Exam: Our patient initially presented in 2013 (age 66 years) with progressive subacute blurry vision, that progressed to double vision. She has history notable for remote breast cancer status post chemoradiation, in remission since 2001. She reported binocular double vision, worsened when looking left or down, included both horizontal and diagonal components, and generally worse with distance. She did not have headache or other neurologic symptoms. Neurologic examination showed mild left exophthalmos and deficits consistent with left trochlear and abducens nerve palsies. Brain MRI with and without contrast (Image 1) showed an enhancing left cavernous sinus mass, which was thought to be a meningioma. Biopsy was deferred due to concern for neurologic morbidity, and she underwent empiric radiation with improvement. In 2018 she reported jaw numbness. Brain MRI showed progression of the previously described lesion in the left cavernous sinus (Image 2). She was again treated with radiation and her symptoms improved. In late 2022, she reported horizontal double vision and lower motor neuron pattern left facial weakness. Imaging showed significant disease progression compared to 2018 with multiple new lesions and interval development of pachymeningeal enhancement (old lesion Image 3; new lesions 4, 5, 6); spinal imaging showed epidural enhancement and a L5 osseus lesion (Image 7). Extensive evaluation for malignancy (CT chest/abdomen/pelvis, PET scan, bone scan, serologic studies including flow cytometry) was completed without evidence of systemic illness. The patient had two biopsies in 2022 and early 2023 of the two peripheral lesions, which were read as having chronic inflammatory changes without clear disease. Throughout this time, the patient has continued to experience symptoms and morbidity related primarily to her double vision.

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Grant Support: None.

“Double Double, Toil and Trouble”

Answer

Final Diagnosis: Progressive unilateral cranial nerve palsies from a skull base lesion that was ultimately identified as Rosai-Dorfman syndrome.

Summary of Case: The patient’s symptoms are all related to her multiple intracranial lesions, with the left cavernous sinus lesion being the most symptomatic and resulting double vision and jaw numbness. The lower motor neuron pattern left facial weakness is likely attributable to posterior extension of the lesion along the skull base to involve the facial nerve in the internal auditory canal. The crux of this case was figuring out why she had multiple slow-growing intracranial masses. It was also challenging to differentiate disease progression from possible adverse effects of radiotherapy. A final biopsy performed by otolaryngology of the left inferior fossa tumor was performed (see Pathology images). This was notable for histiocytosis with emperipolesis. Notably, a large majority of these histiocytes stained positive for S100 protein. Stains for other diseases, including IgG4 disease, were negative. The patient was diagnosed with an underlying histiocytic disorder, Rosai-Dorfman syndrome. Once the diagnosis was made, the patient consulted with a hematologist/oncologist and was prescribed a prolonged course of systemic corticosteroid. Rosai-Dorfman syndrome (originally reported as sinus histiocytosis with massive lymphadenopathy, also known as Rosai-Dorfman-Destombes disease), first described in 1969, is a histiocytosis that occurs due to excessive histiocyte production in the lymph nodes, causing accumulation in other parts of the body, most commonly the cervical lymph nodes, but 40% of patients will have disease involvement outside the lymph nodes. This is typically a slow progressing disorder that is typically benign, and most cases undergo spontaneous remission. Treatment is reserved for symptomatic cases only and is usually limited to corticosteroids.

Struggle/Dilemma of the Clinical Presentation Description: This was a particularly difficult case because the most obvious diagnosis (meningioma) was appropriately treated several times with disease recurrence. Obtaining a tissue sample at the onset may have resulted in permanent neurologic disability due to the location of the lesion. Finally, the diagnosis was challenging as it is a somewhat unusual presentation of a rare disorder. It was necessary to obtain several different tissue samples before a final diagnosis was obtained.

Keywords: Diplopia, Cavernous sinus syndrome

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“Anchora Sella”

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History & Exam: A now 75-year-old man was evaluated in October 2018 for fatigue, decreased libido, and decreased vision in the left eye. Visual fields showed bitemporal hemianopia, worse in the left eye. Brain imaging showed a large (3.6 cm) sellar mass which was resected in October 2019 and was histopathologically confirmed to be meningioma (WHO Grade 1, Ki-67 1%). Visual function improved. He defaulted on follow up in the context of the coronavirus pandemic. In June 2023 he experienced double vision, along with headache and epistaxis. Brain MRI on June 14, 2023 showed a 2.5 x 3.2 x 4.1 cm sellar mass. Eye examination on June 17, 2023, showed visual acuities of 20/25 in the right eye and 20/30 in the left eye; there was a complete aBduction defect of the left eye. Initial neuro-ophthalmology examination on June 28, 2023 was remarkable for visual acuities of 20/25 in the right eye and 20/200 in the left eye, a left relative afferent pupillary defect and aBduction defect of the left eye. Automated perimetry showed mild superior temporal defect in the right eye and dense depression in the left eye. Repeat brain MRI on July 28, 2023 showed increased size of sellar mass, now 4.0 x 3.1 x 5.4 cm.

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

“Anchora Sella”

Answer

Final Diagnosis: Locally advanced poorly differentiated sinonasal cancer, SMARCB1 deficient.

Summary of Case: On August 3, 2023, endoscopic endonasal resection of the sellar mass revealed a soft hemorrhagic mass within the sphenoid sinus, sellar and suprasellar spaces. Gross appearance of the mass was atypical for meningioma while frozen section revealed malignant, metastatic appearance. Final pathology revealed a densely cellular lesion and composed of poorly differentiated/undifferentiated pleomorphic cells with high mitotic activity and complete loss of SMARCB1(INI1) immunohistochemical expression. Neuro-ophthalmology examination on August 22, 2023 showed visual acuity of 20/60 in the right eye and no light perception in the left eye. Pupils were sluggishly reactive, with a dense left relative afferent pupillary defect. There was aBduction defect of both eyes and pallor of both optic discs, worse in the left eye. Automated perimetry showed inferior altitudinal and superior temporal defect in the right eye with sparing of the superior nasal quadrant. Treatment plan is for induction chemotherapy with paclitaxel and carboplatin followed by radiotherapy for consolidation. SMARCB1-deficient carcinoma is a rare subset of sinonasal carcinomas that harbors inactivating alterations of the SMARCB1 tumor suppressor gene. SMARCB1 is located at 22q11.2 and is a component of the chromatin remodeling complex SWI/SNF, but its function is largely unknown (1). In a large case-series study, 39 patients with ages ranging from 19 to 89 (median 52) years old presented with locally advanced disease (T3 and T4 stages) often showing extensive involvement of the paranasal sinuses, nasal cavity and skull base (2). Grossly, these tumors exhibit infiltrative borders and a variable exophytic papillary surface component. SMARCB1-deficient sinonasal carcinomas have an aggressive clinical course. The prognosis is heterogeneous with more than half of the patients dying of their disease within two years. Platinum-based chemotherapy which has shown good response for SMARCA4-deficient non–small cell lung carcinoma has also been suggested for SMARCB1-deficient sinonasal carcinomas. (3)

Struggle/Dilemma of the Clinical Presentation Description: It was incorrectly assumed that re-growth of a sellar mass, at the exact same location of a previously resected meningioma, represented a recurrence of this tumor. This demonstrates premature closure bias (dropping the anchor too early!); As the patient was lost to follow-up during the coronavirus pandemic, it is unclear how tumor progression and symptom development occurred during this time. Timing of surgical intervention was accelerated by the rapid decline in afferent visual function.

Keywords: Skull base tumors, 6th nerve palsy, Intracranial tumors

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Contact Information: None provided.

“(Don't) Blame It on Rio”

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History & Exam: A 43-year-old woman experienced blurred vision and pulsatile tinnitus after gaining 20 lbs. Six months later, optometric evaluation showed normal vision and bilateral optic nerve swelling. MRI brain with and without contrast was reportedly normal. One month later, she underwent a "Brazilian butt lift" surgery, with worsening headache and vision loss right eye. Neuro-ophthalmology consultation was requested to see if the surgical procedure was related to the vision loss. Examination showed visual acuity 20/500 RE and 20/25 LE, right RAPD, mild bilateral abduction deficits and severe papilledema. She was admitted for therapy with high dose acetazolamide and lumbar drain for presumed fulminant IIH. MRI brain and orbits showed leptomeningeal enhancement involving bilateral cerebellum, concerning for meningitis. CSF opening pressure was 25 cm water with normal WBC (1), low glucose (14) and high protein (58). CSF and blood testing were negative for infectious and auto-immune etiologies except for low titer MOG-IgG in blood (1:20). CSF cytopathology and flow cytometry were negative. Repeat lumbar puncture showed CSF WBC 47, low glucose (20) and elevated protein (115) with negative cytology and flow cytometry. MRI spine showed subtle enhancement of the cauda equina nerve roots. Extensive workup for underling malignancy was negative. She was discharged after 4 days with improved vision (20/60; 20/20) and optic disc appearance. She did well for 3 months before returning with worse vision in both eyes (20/100; 20/50) and recurrence of papilledema. MRI brain and orbits with and without contrast showed worsening leptomeningeal disease with bilateral multifocal, supra and infratentorial cortical and leptomeningeal enhancing lesions, with increased thickness and subtle bilateral prechiasmatic optic nerve enhancement. Lumbar puncture showed opening pressure 51cmH20, WBC 7, protein 124, glucose 14, with negative microbiology, cytopathology and flow studies. Acetazolamide was increased to 1500mg. A procedure was performed 6 weeks later.

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Grant Support: None.

“(Don't) Blame It on Rio”

Answer

Final Diagnosis: Diffuse midline glioma, H3 K27-altered, WHO-CNS grade 4 with leptomeningeal and optic nerve infiltration.

Summary of Case: Brain biopsy was performed via right temporal craniotomy. Histopathology showed a high-grade glioma involving the leptomeninges along with evident infiltration of sampled cortical parenchyma. The tumor in the leptomeninges consisted of tightly packed spindle-shaped cells with a glial appearance and high-grade features including palisading necrosis. The tumor infiltrating the adjacent brain demonstrated a conventional astrocytic morphology. Immunohistochemistry showed positivity for GFAP, OLIG2, synaptophysin, and H3K27M in the tumor cells with loss of nuclear expression of ATRX and reduced nuclear expression of H3K27Me3. Methylation-based profiling performed at the NIH placed this tumor in the group designated "diffuse midline glioma, H3K27-altered." Based on the unusual morphological and molecular profile, tumor board recommended a treatment plan of temozolomide with concurrent craniospinal radiation. Despite therapy vision loss progressed rapidly (NLP; LP). Repeat MRI brain and orbits showed multifocal nodular leptomeningeal lesions and bilateral optic nerve sheath enhancement, non-enhancing left optic nerve edema, compatible with extension of leptomeningeal disease. 1 month later she was found unresponsive at home and admitted with acute hypoxemic respiratory failure secondary to COVID-19. Continuous EEG demonstrated status epilepticus. With no other therapeutic options available, she was transitioned to hospice and passed 2 weeks later (within 1 year of symptom onset). Gliomatosis cerebri can arise de novo or in association with another primary lesion with an infiltrative pattern. The majority are astrocytomas and are rapidly fatal with no proven effective therapy. H3K27 mutated glioma are more common in children occurring as infiltrative midline gliomas in the brainstem, cerebral midline, or spinal cord. In adults, these mutations are seen in bilateral thalamic tumors and have poor prognosis. Tumors of this type originating outside of the midline are exceedingly rare, with case reports of optic nerve or leptomeningeal infiltration.

Struggle/Dilemma of the Clinical Presentation Description: After initial normal MRI, patient was diagnosed to have “IIH”, advised weight loss and lost to follow up for 6 months before she returned with severe vision loss which was attributed to “Brazilian Butt Lift” surgery and later presumed “fulminant IIH”. Diagnosis remained elusive until brain biopsy showed an unusual and rare clinical, morphological and molecular form of malignant glioma likely originating in the leptomeningeal tissue with optic nerve infiltration.

Keywords: Papilledema, Tumor, Perineural invasion, Optic nerve tumors

References: None provided.

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"Losing Vision, Losing Sleep"

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History & Exam: A fifty-one-year-old man in good health presented with painless, right-sided visual deficits described as green-brown blotches, progressing to blurry vision and wavy lines in bilateral visual fields. Visual acuities were 20/50 OD, 20/25 OS. Ishihara plate scores were 5/8 OD and 8/8 OS. Automated perimetry demonstrated bilateral inferior arcuate visual field defects. Slit-lamp exam demonstrated anterior vitreous cells bilaterally. Funduscopy showed bilateral optic disc edema with telangiectasias. There was capillary leakage in both optic discs on fluorescein angiography. MRI of brain and orbits showed contrast enhancement of both optic nerve heads. The patient was initiated on IV methylprednisolone 1000 mg/day for 3 days, with partial visual improvement. He was discharged on high-dose oral steroids (60 mg daily) with taper, but self-discontinued due to side effects after 2 weeks, resulting in symptom recurrence three weeks later. Visual deficits worsened to involve bilateral lower quadrants. The patient reported symptoms of disabling orthostatic dizziness. He had mild sleep apnea, but began experiencing nighttime insomnia, daytime somnolence and sleep-related twitching movements in his extremities. Slit-lamp exam continued to show vitreous cells. Funduscopy demonstrated largely resolved optic nerve edema, with interval left temporal pallor development, with telangiectatic vessels extending off the left optic nerve. OCT showed bilateral ganglion cell thinning. Neurological exam demonstrated new subtle torsional nystagmus in down and right gaze, diffuse hyperreflexia and ataxic and abnormal tandem gait. Serological testing was negative/normal for ANA, ACE, SSA/B, RF, ANCA, hepatitis B & C, HIV, Lyme, tuberculosis, syphilis, aquaporin-4 and MOG antibodies. CSF evaluation demonstrated normal opening pressure, 4 nucleated cells with lymphocytic predominance and elevated protein of 82 mg/dl, without oligoclonal bands. CSF cytology and infectious screens were negative. Whole-body PET-CT was unrevealing. Left testicular ultrasound demonstrated hyperechogenic foci suggestive of burned-out tumor or a prior inflammatory process. Orchiectomy did not demonstrate malignant tissue.

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Grant Support: None.

"Losing Vision, Losing Sleep"

Answer

Final Diagnosis: The final diagnosis is IgLON5-associated optic neuritis. MRI contrast enhancement of optic nerve heads, vitreous cellularity, and capillary leakage of optic discs demonstrated an intra-ocular optic neuritis/papillitis, implying retinal-blood barrier breakdown. Initial optic disc involvement progressed within a few weeks to nystagmus, suggesting rapid progression towards more typical brainstem involvement. Spontaneous and gaze-evoked nystagmus is associated with anti-IgLON5 disease occurring with or without gaze palsy, square-wave jerks, and saccadic intrusions, particularly in PSP-like IgLON-5 disease. Initial reports noted no CSF or MRI abnormalities, and inconsistent immunotherapy responsiveness, especially in patients with longstanding disease. However, outcomes appear to be different for patients diagnosed early, with reported inflammatory CSF and MRI findings and immunotherapy responsiveness. Therefore, early initiation of therapy may potentially prevent progression to neurodegeneration. In our patient, early cessation of immunosuppressive therapy caused symptom recurrence, suggesting an inflammatory process. Combination and longer duration of immunotherapy, and aggressive second-line therapies, have improved outcomes in patients, including ours. Our report expands the neurological associations with IgLON5-antibody mediated disease to include bilateral intraocular optic neuritis, which is considered an inflammatory rather than a neurodegenerative syndrome. Our patient responded to immunosuppressive therapy. Neuronal cell-surface antigen directed antibodies may or may not be associated with malignancy. To date, there are no paraneoplastic syndromes associated with IgLON5 disease. Our patient had a testicular mass, suggestive of a burnt-out tumor or prior inflammatory insult, similar to regressed testicular germ-cell tumors reported in patients with Kelch11 and LUZP4 autoantibodies. More cases are needed to characterize possible paraneoplastic associations with this disease. As pathophysiological mechanisms of the disease are still being investigated, our case report supports IgLON5 disease being an autoimmune (possibly paraneoplastic) phenomenon, particularly early on in its course. A low threshold for diagnostic suspicion is emphasized, as treatment may prevent irreversible neuronal damage and subsequent neurodegeneration.

Summary of Case: CSF indirect immunofluorescence assay was positive for IgLON5 (Immunoglobulin-like cell adhesion molecule-5) antibodies at 1:8 titer, confirmed by cell-based assay. After completion of a subsequent steroid taper, given symptomatic progression, the patient's treatment regimen was escalated to monthly intravenous cyclophosphamide infusions (750 mg/m2 body surface area) for 6 doses, followed by maintenance on mycophenolate mofetil (1000 mg twice daily). The patient subsequently experienced improvement in neurologic and ophthalmologic symptoms, with stable exam. IgLON5 is a neuronal cell-surface antigen. Neuropathologic examination of brains from patients with IgLON5-targeted antibodies demonstrated neuronal loss and gliosis, with accumulation of hyperphosphorylated tau in the hypothalamus and brainstem tegmentum, up to the upper cervical cord. MRI T2 hyperintensities in the same areas early in the disease course suggest IgLON5-mediated inflammation in these regions. There is mounting evidence that while IgLON5-related disease in the subacute period resembles other autoimmune CNS neurologic disorders, if left untreated, it appears to develop into a tauopathy-predominant neurodegenerative condition. IgLON5 autoantibodies possibly interfere with the internal cytoskeletal network, leading to neuronal dysfunction and neurodegeneration. Thus far, the reported clinical spectrum includes sleep disorders with parasomnia and sleep breathing difficulties, a bulbar syndrome including dysphagia, sialorrhea, stridor/acute respiratory insufficiency, gait and movement disorders including hyperkinesis, chorea and a syndrome resembling progressive supranuclear palsy. Per our knowledge, there is no prior report of IgLON-5 antibody positivity accompanied by bilateral optic neuritis or a testicular mass. However, in recent conversations with colleagues at the Mayo clinic, an as-yet unpublished series of these patients has been identified. The current case would therefore represent the index case of an emerging neuroimmunologic condition of neuro-ophthalmic interest.

Struggle/Dilemma of the Clinical Presentation Description: Optic neuritis is a common condition in Neuro-ophthalmology. However, it behooves the neuro-ophthalmologist to identify when optic neuritis is atypical in its demographics, clinical presentation or imaging findings. In those cases, it may be appropriate to pursue a much more exhaustive workup than is typically done. This may include a search for antibodies for autoimmune and/or paraneoplastic neuroimmunologic conditions, which is best done as part of a panel, with an open mind towards novel associations.

Keywords: Optic neuritis, Uveitis, Eye movements, Autoimmune diseases, Paraneoplastic syndromes

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“How To Get the Red Out”

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History & Exam: A 56 year old male presented for evaluation of chronic redness of the left eye for the past 2 years. It was associated with pain, proptosis, engorged conjunctival vessels, and intraocular pressure elevation. Work up for possible scleritis, infection, uveitis, was negative. The patient also had a course of oral steroids for possible idiopathic orbital inflammation which did not lead to improvement. Exam showed normal vision, 2 mm of proptosis os, boggy, engorged conjunctival and episcleral vessels on the left side. EOMS were full. There was no APD and IOP was 16 mmHg OD and 29 mm OS. Fundus exam did not reveal significant abnormalities aside from left glaucoma cupping

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Grant Support: Research To Prevent Blindness

“How To Get the Red Out”

Answer

Final Diagnosis: Orbital and Ocular Amyloidosis

Summary of Case: Prior testing included C3, C4 normal, RF neg, ANA neg, MPO/PR3/ANCA neg HLA b27 neg, CCP neg, Hsv1 igG positive, Hga1c 6.3, ACE normal, HIV negative. An angiogram to evaluate for C-C fistula which was negative. MRI of the Orbits indicated Nodular enhancement along the left optic nerve with repeat imaging showing the same as well as the orbital roof. Biopsy of the optic nerve sheath indicated Amyloidosis with fibrosis with diffuse involvement of the orbital fat and optic nerve sheath with Amyloid. There was also amyloid identified in vessel wall. Liquid chromatography tandem mass spectrometry (LC MS/MS) indicated AL-Kappa. Workup for systemic amyloidosis was negative. The patient received orbital radiation with improvement of proptosis and the engorged conjunctival vessels.

Struggle/Dilemma of the Clinical Presentation Description: Orbital Amyloid may present in a manner similar to Carotid-Cavernous Fistula and Idiopathic Orbital Inflammation. Properly interpreting the imaging lead to removing from the differential diagnosis more common disorders like carotid-cavernous fistula and idiopathic orbital pseudo-tumor and utilizing an orbital biopsy to determine the more rare diagnosis of Orbital and Ocular Amyloidosis.

Keywords: Amyloidosis, Carotid cavernous fistula, IgG4 related disease

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"The Path of Least Resistance: Over the Nose, Into the Orbit, and Around the Globe"

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History & Exam: A 45 year-old man presented emergently with progressively worsening blurred vision, oblique binocular diplopia, photophobia, and dyschromatopsia in the left eye for 4 months. He reported swelling around the left eye, unintentional weight loss of 25 pounds, and presence of cervical lymph nodes for several months. Medical history included hypertension, diabetes, asthma with recent exacerbations, and seasonal allergies. He was seen by ophthalmology whose examination of the left eye revealed 3+ rAPD, slight proptosis, -4 abduction deficit, normal color vision via Ishihara color plate testing, and Frisen-like grade 3 disc edema with mild temporal peripapillary atrophy. Contrasted MRI brain & orbits showed enlargement and contrast enhancement of the left lateral rectus muscle, optic nerve sheath, and cavernous sinus. Serum studies were largely unremarkable including TSH, ANCA, ACE, lysozyme, IL2, IL6, MOG/NMO antibodies, thyroid antibodies, immunoglobulins, SPEP, syphilis, Lyme, and TB. ANA was positive with titer 1:320. CSF studies showed normal protein, cell count, and RBCs; elevated glucose (consistent with hyperglycemia); and unremarkable IgG index, ACE, VDRL, and fungal studies. He was started on prednisone 1 mg/kg daily with significant improvement in his ocular symptoms including resolution of blurred vision with acuity of 20/20-2, 1+ rAPD, and -1 abduction and supraduction deficits causing residual diplopia on extreme left gaze. There was improvement of edema around the orbit and optic disc of the left eye. Repeat MRI brain & orbits showed disease improvement. A diagnostic procedure was performed.

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“The Path of Least Resistance: Over the Nose, Into the Orbit, and Around the Globe”

Answer

Final Diagnosis: Eosinophilic granulomatosis with polyangiitis involving the extraocular muscles

Summary of Case: To determine a definitive diagnosis, biopsy of the left lateral rectus muscle was planned. Given the improvement seen on imaging and to optimize biopsy yield, the patient was weaned off steroids. However, he deteriorated almost immediately after cessation of steroids and developed worsening diplopia, blurred vision, proptosis, ophthalmoplegia, and optic disc edema. He also developed an enlarged left-sided lacrimal gland and pre-auricular and cervical lymph nodes. Due to concern for an infiltrative process, he was sent to the ER for expedited work up. Repeat contrasted MRI brain & orbits revealed worsening of his disease process. He underwent biopsy of the left lateral rectus muscle, orbital fat and lacrimal gland, and he was then restarted on prednisone 1 mg/kg. In the interim, CSF cytology was negative for malignancy. Biopsy results showed reactive lymphoid infiltrates with eosinophilia and no evidence of malignancy. It was then noted that while off prednisone, he had peripheral eosinophilia with an absolute eosinophil count of 1.99 (normal 0.00-0.70 x10(9)/L). He was seen by the Allergy and Immunology clinic, who determined he met criteria for eosinophilic granulomatosis with polyangiitis (EGPA).[1,2] He had asthma with recently worsening disease, peripheral eosinophilia >10%, paranasal sinus disease, and extravascular eosinophilia on biopsy. He was ANCA-negative, which can occur in 60-70% of patients with EGPA and is associated with increased cardiac and pulmonary involvement.[2,3] It is not typical for EGPA to present with ocular manifestations, which can be subdivided into idiopathic ocular inflammation and ischemic vasculitis.[3] The patient was started on mepolizumab, an anti-IL5 monoclonal antibody.[4] Presently, his symptoms have nearly resolved, and his neuro-ophthalmic exam shows near-complete resolution of optic disc edema in the left eye, though he has a persistent abduction deficit. He continues mepolizumab and is gradually tapering prednisone.

Struggle/Dilemma of the Clinical Presentation Description: The patient's case was difficult to diagnose due to its unique presentation of predominantly ocular symptoms, which are not common in EGPA. The patient had dramatic visual changes that required steroids for symptomatic management. However, steroids masked the peripheral eosinophilia, which was not noted until after steroid cessation. Ultimately, the patient's care required balancing the need for steroids to prevent vision loss and decreasing steroid use to optimize biopsy yield for diagnostic purposes.

Keywords: Vasculitides, Extraocular muscles, Vision loss, Binocular diplopia, Magnetic resonance imaging (MRI)

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“Devine Intervention”

Letitia Pirau [1], Wayne Cornblath [1], Lindsey De Lott [1], Sangeeta Khanna [1], Tatiana Deveney [1]

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History & Exam: A 30 yo woman presented to the comprehensive ophthalmology clinic with bilateral decreased vision. She had no prior ocular history. Her medical history was notable for breast cancer (diagnosed 1 year prior), treated with radiation, chemotherapy, lumpectomy, and pembrolizumab (completed 8/9 planned infusions). She described progressive vision loss in both eyes over the 2 weeks with light sensitivity, pain with eye movements, and diminished color vision. Her best corrected visual acuity was 20/500 in the right eye and count fingers at 3’ in the left eye. No APD. Confrontation visual fields were notable for dense constriction in the right eye and temporal field loss in the left eye. The dilated funduscopic exam was normal. She was sent to the emergency department for an expedited work-up. MRI brain and orbits with and without contrast revealed T2 signal and enhancement along the optic chiasm, tracts, and prechiasmatic optic nerves (radiology images 1-4). There was no evidence of demyelinating lesions. Lumbar puncture and CT chest/abdomen/pelvis were unremarkable with no metastatic or systemic inflammatory process identified. A diagnostic procedure was performed.

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Grant Support: None.

"Devine Intervention"

Answer

Final Diagnosis: Neuromyelitis Optica Spectrum Disorder After Pembrolizumab Treatment (In The Setting of Breast Cancer)

Summary of Case: Our patient presented with a rare presentation of neuromyelitis optica spectrum disorder (NMOSD) induced by pembrolizumab treatment. Serum testing confirmed the diagnosis as initial serum AQP4 titer was 1:1000. While AQP-4 antibody testing was pending, she was treated with a 5-day course of methylprednisolone 1g IV daily and discontinued pembrolizumab. However, her visual acuity declined OD to hand motion. Therefore, plasmapheresis (PLEX) was pursued for 7 sessions. Three months post-treatment, her BCVA was 20/20 OU. Her follow-up titer 2 months post-treatment was 1:100. There are several possible explanations for her presentation: 1.) NMO disease unrelated to breast cancer or pembrolizumab, 2) Pembrolizumab induced optic neuritis with false positive NMO, 3) Paraneoplastic optic neuritis related to breast cancer, or 4) Pembrolizumab induced NMOSD. We suspect the last is the most likely explanation given significant recovery and improving titers correlating with the discontinuation of pembrolizumab. There have only been nine reported cases of NNMOSD triggered by an immune checkpoint inhibitor (ICI) (1, 6). ICI monoclonal antibodies target cytotoxic T-lymphocyte-associated protein-4 or programmed-cell-death receptor-1 to inhibit T lymphocytes (2, 3)-- possibly secondary to "unmasking of a predetermined paraneoplastic condition" related to the underlying cancer (2). Symptoms generally occur about 2-16 weeks after treatment but may occur as far out as 1 year (4). With a prednisone taper, she had a complete recovery after completing PLEX. In contrast, the previously reported cases in the Hirano et. al. review were associated with only partial recovery with steroids and PLEX (1). Based on prior literature on neurologic manifestations of ICI toxicity (meningitis, myasthenia gravis, myositis, peripheral neuropathy) guidelines suggest prompt discontinuation of the immunotherapy, as well as steroids (8). Case reports on pembrolizumab-induced optic neuropathy have documented the use of long-term treatments including rituximab, infliximab, IVIG, and mycophenolate (9).

Struggle/Dilemma of the Clinical Presentation Description: Given the rare incidence of NMOSD secondary to ICI, it was unknown what was the best long-term treatment strategy. Prior cases have used rituximab for further immunosuppression after high-dose corticosteroids. In this case, due to her improving AQ4+ titers and clinical recovery, the decision was made with neuro-immunology to observe after receiving plasmapheresis.

Keywords: Optic chiasm, Optic neuritis, Magnetic resonance imaging (MRI)

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"A White Matter Riddle Encased in Mystery, Coiled Inside an Enigma"

Nathan Tagg [1], Elizabeth Rooks [2], Vanessa Smith [1], Thomas Cummings [1]

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History & Exam: A 59-year-old woman was admitted for evaluation of progressive paranoia and was treated for bipolar disorder. An MRI during evaluation revealed a 10 x 7 x 7 mm right MCA aneurysm. She underwent stent-assisted coil embolization nine months later without immediate complications. Four months post-procedure she developed gradual onset left-sided weakness and a focal aware seizure involving the left side. An MRI without contrast revealed extensive right hemispheric vasogenic edema. She continued to progress over the ensuing months and eventually developed a left homonymous hemianopsia. Repeat MRI imaging showed multilobar right hemispheric T2 changes and nodular leptomeningeal and parenchymal enhancement with no significant findings in the left hemisphere (Figures 1, 2). Extensive serum and CSF evaluation was negative. She was treated empirically with high dose steroids with improvement in symptoms. Her symptoms recurred with each attempted steroid taper, necessitating repeat admissions and steroid courses. She transitioned to mycophenolate mofetil (MMF) in combination with steroids. Further diagnostic studies were deferred at patients request and her disease progressed requiring readmission and addition of rituximab. Additional imaging revealed non-small cell lung cancer and she was treated with localized radiation therapy. Three years after symptom onset she was referred to our service and reported fluctuating symptoms responsive to steroids superimposed on a course of gradual worsening. Exam revealed a left homonymous hemianopia, left hemi-motor and sensory deficit. Extensive serum and CSF testing was remarkable only for one IgG band unique to CSF. A paraneoplastic panel was negative. PET scan was negative for new malignancy. MR vessel wall imaging was negative for vasculitis. MRI brain revealed right hemispheric encephalomalacia with residual patchy nodular enhancement (Figures 3,4). With no clear diagnosis for her unremitting leukoencephalopathy and enhancing lesions, a diagnostic brain biopsy was performed.

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“A White Matter Riddle Encased in Mystery, Coiled Inside an Enigma”

Answer

Final Diagnosis: Final Diagnosis: Delayed onset leukoencephalopathy secondary to foreign body from vascular intracerebral stent or coil. A stereotactic parenchymal biopsy demonstrated multinucleated foreign body giant cells centered on nonpolarizable filamentous structures. Histological examination was most consistent with a foreign body granulomatous type reaction following intravascular stent & coil. This rare entity is though to be a consequence of either a hypersensitivity / allergic reaction to endovascular hardware or a foreign body reaction to hardware coating material (i.e. polymer).

Summary of Case: A 59 y/o woman who developed the gradual onset of left homonymous hemianopsia, hemiparesis, hemisensory loss four months after undergoing endovascular stent-assisted coiling of a R MCA aneurysm. MRI imaging showed a progressive leukoencephalopathy with features of inflammation limited to the right hemisphere. Symptoms partially responded to steroids but the steroid sparing agents mycophenolate mofetil and rituximab failed to control progression over a period of 3 years. A brain biopsy showed granulomatous foreign body giant cells centered on non-polarizable filamentous material.

Struggle/Dilemma of the Clinical Presentation Description: The main dilemmas of this exceedingly rare case involved both diagnosis and treatment. Diagnostic difficulties include: delayed onset of symptoms after stent-assisted coiling, negative serum and CSF testing, and apprehension of the patient for brain biopsy. The treatment difficulties center around the apparent steroid responsiveness without a definitive diagnostic abnormality to guide long-term immunosuppression.

Keywords: Homonymous hemianopsia, Magnetic resonance imaging (MRI), Aneurysm

References: Ridwan S, et al. Delayed Leukoencephalopathy and Foreign Body Reaction After Endovascular Treatment in Patients With Intracranial Aneurysms and Aneurysmal Subarachnoid Hemorrhage-A Systematic Review of the Literature. Front Surg. 2021 Dec 23 Ikemura A, et al. Leukoencephalopathy: A Rare Complication after Coiling of Cerebral Aneurysms. AJNR Am J Neuroradiol. 2020 Feb;41(2):286-292 Miyamoto S, et al. Reversible and multiphasic parenchymal changes in MRI after coil embolization for a ruptured cerebral aneurysm. Surg Neurol Int. 2023 Apr 21;14:147 Bakola E, et al. Delayed recurrent enhancing white matter lesions complicating coiling of intracranial aneurysm. Eur J Neurol. 2021 Jul;28(7):2388-2391 Bakola E, et al. Delayed Leukoencephalopathy as a Complication after Endovascular Therapy of Intracranial Aneurysms-A Case Series. J Clin Med. 2023 Jan 7;12(2):496

Contact Information: None provided.

Meet the Poster Author: Descriptive Studies I – Sunday, March 3rd

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3	Thyroid Cancer and Ipsilateral Horner's Syndrome	Farnaz Javadian	Pupillary Disorders
4	A case of complete corpus callosum agenesis in unilateral Peters anomaly	Florence Yan	Pediatric Neuro-Ophthalmology
5	ACHOO and Burn: Macular scars secondary to sun- and laser beam-staring to induce photic sneeze reflex	Reilly Coombs	Pediatric Neuro-Ophthalmology
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7	Don't "Batten" An Eye When It Comes To Diagnosing Rare Ophthalmologic Diseases	Jordan Petersen	Pediatric Neuro-Ophthalmology
8	Oculomotor Paresis With Cyclical Spasms; New Insights Into The Etiology And A New Case With Videography	Su Ann Lim	Pediatric Neuro-Ophthalmology
9	Opsoclonus in children: diagnosis and etiology of opsoclonus in a tertiary pediatric hospital	Melissa Yuan	Pediatric Neuro-Ophthalmology
10	Pediatric Tolosa-Hunt Syndrome with Facial Nerve Involvement and Contralateral Relapse	Florian Guillot	Pediatric Neuro-Ophthalmology
11	Progressive Nystagmus and Ataxia: A Novel Phenotype and Mutation of CACNA1A	Robert Goodrich	Pediatric Neuro-Ophthalmology
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13	A Case of Late-Onset Immune Checkpoint Inhibitor-Induced Orbital Inflammation	Chad Serels	Orbital and Eyelid Disorders
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16	Bisphosphonate-induced orbital apex syndrome	Kimberly Nguyen	Orbital and Eyelid Disorders
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18	Multifocal orbital intramuscular angioma	Patrick Hughes	Orbital and Eyelid Disorders

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20	Outcomes of Immunotherapy Using PD-1 Inhibitors without radiation in Patients with Periocular Squamous Cell Carcinoma with Perineural Spread with Orbital and Skull Base Involvement	Bita Esmaeli	Orbital and Eyelid Disorders
21	Reaching A Diagnosis Of Ocular Lymphoma After 41 Months Of Trial And Error	Mark Lindquist	Orbital and Eyelid Disorders
22	Sclerotherapy in Orbital Dermoid Cysts: A Promising Minimally Invasive Approach	Rachna Agarwal	Orbital and Eyelid Disorders
23	Sudden onset diplopia in a patient with a stable long standing orbital vascular malformation	Fatima Tun Nissa Raza	Orbital and Eyelid Disorders
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26	Unusual Cases Of Orbital Inflammation	Sally Al Hassan	Orbital and Eyelid Disorders
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33	An unusual case of Diffuse ophthalmoplegia and ptosis: Myasthenia, CPEO or Something Else?	Virender Sachdeva	Ocular Motility Disorders and Nystagmus
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58	A Service Evaluation of a University Hospital Birmingham Neuro-Ophthalmology Virtual Clinic	Ahmed Abdel-hay	Neuro-Ophthalmic Practice
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70	A case of optic neuropathy secondary to microscopic polyangiitis and giant cell arteritis in the same eye	Chee Fang Chin	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
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74	A Dural Mass In Disguise	Nada Mobayed	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
75	A Positive Temporal Artery Biopsy Ninety-One Days After Corticosteroid Initiation	Grant Goodfellow	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
76	A proposed treatment protocol for leukemic optic neuropathy	Sachin Patel	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
77	A Rare Cause of Diplopia	Mangayarkarasi Thandampalayam	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
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80	An Unusual Case Of Aberrant Regeneration Of The Oculomotor Nerve Following Coil Embolization Of A Carotid Cavernous Fistula	Vivian Paraskevi Douglas	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
81	An Unusual Presentation of West Nile Virus Infection: Isolated Orbital Inflammation with Radiological Findings	Stuart McFarland	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
82	Association of Race and Obesity in Myelin Oligodendrocyte Protein Antibody Disease (MOGAD) from a Single Institution in the Southwest United States.	Annah Baykal	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
83	Ataxia, deafness, optic neuropathy, aphonia associated with ANNA-1/ /"anti-Hu" and LUZP4 antibodies	Rani Priyanka Vasireddy	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
84	Attenuated phenotype in individuals diagnosed with mitochondrial complex I deficiency caused by homozygous NDUFAF8 c.195+271C>T variant	Neringa Jurkute	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
85	Beyond the Usual Suspects: A Rare Case of Germ Cell Tumor-Associated Optic Neuritis	Miguel Santiago	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
86	Bilateral Infiltrative Optic Neuritis as the Presenting Finding in Metastatic Gastric Leptomeningeal Carcinomatosis and its Dramatic Response to Nivolumab	Alicia Jiang	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
87	Bilateral Sequential Vision Loss From Multiple Progressive Fusiform Aneurysms With COL1A1 Genetic Variant With Vascular Ehlers-Danlos Syndrome Phenotype	Johanna Yun	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
88	Blind Spot in the Battle Against Giant Cell Arteritis	Madhura Shah	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
89	Calciphylaxis in a middle-aged Asian patient: An unusual cause of disc swelling	Kelvin Li	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
90	Case Series: Severe Pediatric Optic Neuritis with Significant Visual Recovery Despite Extensive Ganglion Cell Layer Loss	Lucy Li	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
91	Cemiplimab Induced Myasthenia Gravis, Painless Myositis, Myocarditis, and Hepatotoxicity with Initially Isolated Neuro-ophthalmological Findings	Abdulaziz Al Abdulghani	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
92	Central Nervous System Recurrence of Diffuse Large B-Cell Lymphoma: Tissue Is The Issue	Daniela Vultorius	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
93	Central Vision Loss After Tick-Bite Induced Alpha-Gal Syndrome Leads to Nutritional Optic Neuropathy	Erin Lanzo	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
94	Concurrent Wernicke’s encephalopathy and posterior reversible encephalopathy syndrome following gastric sleeve surgery	Doowon Huh	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
95	Considering an unforeseen diagnosis for patients presenting with Cogan lid twitch sign	Sneha Gajarla	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases

96	Corneal Confocal Microscopy Assessment of Pediatric and Young Adult Diabetic Corneal Neuropathy.	Vinit Majmudar	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
97	Evaluation of peripapillary retinal nerve fiber layer thickness in intracranial atherosclerotic stenosis	Yuan Gao	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
98	Facial neuropathy in patients with recurrent painful ophthalmoplegic neuropathy	Jae-Myung Kim	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
99	Frontal Muscle flap advancement for Myogenic and Neurogenic ptosis	Kira Lin	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
100	Fulminant Idiopathic Intracranial Hypertension in Setting of Malignant Arterial Hypertension: Prompt Suspicion Matters	Bashaer Aldhahwani	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
101	GFAP Astrocytopathy masquerading as Idiopathic Intracranial Hypertension	Naga Pradyumna Kothapalli	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
102	Gnarly Carotid Arteries – Another “GCA” Emergency?	Meagan Shinbashi	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
103	High Grade Optic Pathway Glioma in Child with Neurofibromatosis-Noonan Syndrome	Kate Matsunaga	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
104	Homonymous hemianopsia and visual hallucination as a manifestation of Sturge-Weber syndrome without facial nevus	Hyun Ah Kim	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
105	Homonymous Hemianopsia as the Presenting Sign of Tumefactive Multiple Sclerosis	Savannah Schauer	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
106	Hypertrophic pachymeningitis with serpiginous-like choroiditis: a case report	Tzulun Huang	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
107	Idiopathic Granulomatous Optic Neuropathy in the Pediatric Patient: A Case Report	Casey Anthony	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
109	Immune Checkpoint Inhibitor Induced Myasthenia Gravis With Neuro-Ophthalmologic Findings	Margaret Shmunes	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
110	Large Sub-Hyaloid Hemorrhage Associated With Recurrent Optic Neuritis in Multiple Sclerosis	Ricardo Tochimani	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
111	Leber Hereditary Optic Neuropathy (LHON) Global Data Collection Program (DCP)	Malinda Marsh	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
112	Malignant Peripheral Nerve Sheath Tumor (MPNST) Presenting As A Progressive Unilateral Cranial Polyneuropathy	Jiemin Li	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
113	MALT Lymphoma Presenting as Symptomatic Optic Neuritis: A Case Report	Dan Tong Jia	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases

114	Metabolic Optic Neuropathy Secondary To Hyperbaric Oxygen Therapy: A Case Report	Carlos Torres-Quinones	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
115	Metastatic Adenocarcinoma Presenting as Orbital Apex Syndrome: Application of Immunohistochemistry in Diagnostic Ophthalmic Pathology	Farida Marcelle Vergara	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
116	More than Meets the Eye: Unmasking a Case of Dermatomyositis with Unilateral Periocular Edema	Thomas Lamson	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
118	Neuro-ophthalmological Findings of Increased Intracranial Pressure Due to HSV-II Meningitis	Abdulaziz Al Abdulghani	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
119	Optic neuropathy associated with acute motor axonal neuropathy in the post partum period	Alexis Kassotis	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
120	Orbital Apex Syndrome With Normal Imaging	Sari Yordi	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
121	OSPREY: An Open-label Study to Investigate Safety, Tolerability, and Exposure of the Antisense Oligonucleotide (ASO) STK-002 in Patients with OPA1 Autosomal Dominant Optic Atrophy (ADOA)	Patrick Yu-Wai-Man	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
122	Outer Retinal Tubulations in Boucher-Neuhäuser Syndrome	Joshua Kepler	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
123	PABPN1 Mutation in an Indigenous New Mexican Family Affected by Oculopharyngeal Muscular Dystrophy	Elise Ma	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
124	Papilledema in Setting of Newly Approved Drug for Amyotrophic Lateral Sclerosis	Azraa Chaudhury	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
125	Persistent Radiological Changes After Cryptococcal Meningoencephalitis In An Immunocompetent Patient With Bilateral Optic Atrophy	Elizabeth Akinsoji	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
126	Petrous Apicitis Complicated with Ophthalmoplegia and Death - A Case Report	Nancy Chen	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
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128	Rare case of Miller Fisher syndrome initially presented as bilateral Internuclear opthalmoplegia	Sanghyun Kim	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
129	Recurrent Diplopia Associated with Maxillary Sinusitis	Ileok Jung	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
130	Relapsing-Remitting Multiple Sclerosis and Intermediate Uveitis: A Consolidated Treatment Approach	Tamer Ghanayem	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases

131	Satralizumab Treatment In Adults With AQP4-IgG–Seropositive Neuromyelitis Optica Spectrum Disorder: A Retrospective Case Series	Michelle Gheen	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
132	Sequential vision loss in a patient with giant cell arteritis while on intravenous steroid therapy: a case report	Malshi Karunatilake	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
133	Taking One on the Chin: A Precautionary Case of Burkitt's Lymphoma and Radiation Induced Optic Neuropathy	Annah Baykal	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
134	The Unmasking of a Basilar Aneurysm by Masked Facies: Bilateral Eight-and-a-Half Syndrome due to Basilar Aneurysm	Sannah Vasaya	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
135	Trapped In My Head	Padmaja Sudhakar	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
136	Carotid-Cavernous Fistula Masquerading As Uveitis	Sophie Gu	Neuro-Imaging
137	Neurolymphomatosis Manifesting as Oculomotor Palsy in a 65-Year-Old Female with Diffuse Large B Cell Lymphoma	Andrew Silverman	Neuro-Imaging
138	Post-Operative Magnetic Resonance Imaging of the Inferior Oblique Muscle	Paul Micevych	Neuro-Imaging
139	Pupil-sparing oculomotor nerve palsy due to neurovascular compression by the posterior cerebral artery	Hyunsoo Kim	Neuro-Imaging
140	Retinal Ganglion Cell Organizational Changes Detected With Visible Light Optical Coherence Tomography in a Patient with Visual Field Improvement Despite Stable Ganglion Cell Layer Thinning	Avram Bar-Meir	Neuro-Imaging
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145	Isolated Lower Motor Neuron Facial Nerve Palsy as a presenting sign in COVID-19 associated Orbital Mucormycosis patients. A Retrospective Observational Study	Rachna Agarwal	Miscellaneous
146	It's Just a Twitch	Agni Kakouri	Miscellaneous
147	Non-neuro-otological positional vertigo-superior vena cava syndrome	Eunjin Kwon	Miscellaneous
148	Tacrolimus-Induced Intracranial Hypertension and Papilledema	Hamza Inayat	Miscellaneous

149	Tooth to brain: a case of multiple intracranial abscesses, retro-chiasmal pathway involvement, infectious optic neuropathy and infectious endocarditis after right lower wisdom tooth extraction	Somya Chowdhary	Miscellaneous
150	Why get a topography when you can get an MRI?	David Price	Miscellaneous
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152	Characterization and Visual Outcomes of Fulminant IIH: A Narrative Review	Jacqueline Shaia	Idiopathic Intracranial Hypertension (IIH)
153	Clinical Characteristics of Idiopathic Intracranial Hypertension in Chinese Patients	Carmen Chan	Idiopathic Intracranial Hypertension (IIH)
154	Clinical characteristics of patients with idiopathic intracranial hypertension in central China	Tian Tian	Idiopathic Intracranial Hypertension (IIH)
155	Combination of severe anemia and renal failure as the cause of atypical idiopathic intracranial hypertension	Xiaojun Zhang	Idiopathic Intracranial Hypertension (IIH)
156	Idiopathic Intracranial Hypertension and Ehlers Danlos Syndrome: Case Series	Isha Ingle	Idiopathic Intracranial Hypertension (IIH)
157	Idiopathic Intracranial Hypertension In A Specialist Eye Emergency Department: A Retrospective Audit Of Patient Presentations And Outcomes	Elliott Cope	Idiopathic Intracranial Hypertension (IIH)
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165	The Peripapillary Retina – A Common Juncture in Stargardt Disease and Idiopathic Intracranial Hypertension	Luke Oh	Idiopathic Intracranial Hypertension (IIH)
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168	What Is The Best Approach To Pediatric Idiopathic Intracranial Hypertension? - A Case Series	Elizabeth Colvin	Idiopathic Intracranial Hypertension (IIH)
169	A Rare Case of SMARCA4-Deficient Undifferentiated Thoracic Tumor Presenting with Headache and Hallucinations	Aishwarya Sriram	Disorders of the Posterior Visual Pathway and Visual Processing
170	Hyperglycemic hemianopia: A reversible complication of nonketotic hyperglycemia	Jun Shyan Caius Goh	Disorders of the Posterior Visual Pathway and Visual Processing
171	Right-sided representational neglect due to bilateral parietal lesions	Eek-Sung Lee	Disorders of the Posterior Visual Pathway and Visual Processing
172	“Dark Cherry-Red Spot” from Ophthalmic Artery Occlusion, a Possible Initial Manifestation of Active Tuberculosis	Ariel Axelbaum	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
173	Abrupt Vision Loss in DIDMOAD	Marc Bouffard	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
174	Amiodarone-Associated Simultaneous Bilateral Ischemic Optic Neuropathies	George Landim	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
175	Autosomal Recessive Leber's Hereditary Optic Neuropathy Triggered by Superior Mesenteric Artery Syndrome	Archeta Rajagopalan	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
176	Bilateral Sequential Non-arteritic Anterior Ischemic Optic Neuropathy Induced by Methamphetamine Abuse	Caroline Cotton	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
177	Bitemporal hemianopsia in a case of tilted optic nerves	Rikki Cunningham	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
178	Caffeine and Vodka Induced Paracentral Acute Middle Maculopathy	Obadah Moushmoush	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
179	Can Visual Electrophysiology be used to screen patients with normotension glaucoma	Clement Tan	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
180	Case Report Of Early Visual Symptoms Heralding Fludarabine Ocular Toxicity	Alexander Engelmann	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)

181	Case Series: Two Patients With Optic Neuropathy Associated With Guselkumab Initiation	Daniel Elefant	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
182	Chronique Optic Neuropathy due to Nd YAG capsulotomy induced by Acutes spikes of Intra Ocular Pressure	Fayçal MOKHTARI	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
183	Clinical Characteristics and Treatment of Optic Neuritis in Asians	Reuben Foo	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
184	CRAO + Pupil-Involved CN III Palsy after Nasal Embolization: Where's the lesion?	Kendall Chaffin	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
185	Diagnosis and Management of Radiation-Induced Optic Neuropathy following Proton Beam Therapy for Sphenoid Wing Meningioma	Elizabeth Ciociola	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
186	Exploring Nimodipine's Potential in NA-AION: A Preliminary Investigation	Mohammad Salim Alzureiqi	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
187	Feel nothing, see nothing.	Preston Kung	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
188	Glioblastoma (CNS WHO grade 4) masquerading as bilateral atypical optic neuritis	Kathleen Louis-Gray	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
189	Linezolid Induced Toxic Optic Neuropathy - A Case Series	Narayanamoorthy Jayasri	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
190	Myelin Oligodendrocyte Glycoprotein Antibody Disease Optic Neuritis Masquerading As Fulminant Idiopathic Intracranial Hypertension	Ray Cortez	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
191	Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease Presenting with Posterior Scleritis	Nisreen Al-Balushi	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
192	Navigating the Vascular Terrain of the Human Optic Nerve in 3D	Drenushe Krasniqi	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
193	No light perception following uneventful cataract surgery	Madhumita Gopal	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
194	Non-arteritic Anterior Ischaemic Optic Neuropathy In The Pachychoroid Disease Spectrum	Melissa Tien	Disorders of the Anterior Visual Pathway (Retina,

			Optic Nerve, and Chiasm)
195	Non-Small Cell Lung Cancer Metastases to the Optic Nerve leading to Vision Loss	Prerna Das	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
196	Optic Chiasmal Prolapse in Primary Empty Sella Syndrome : A Rare Presentation	Kunjal Gala	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
197	Optic nerve sheath meningioma in Chinese patients - A case series	Noel Chan	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
198	Optic Neuritis In COVID-19 Infected Patients	Rong Yan	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
199	Optic Neuritis Masquerade Syndrome	Emely Karam	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
200	Optic Neuropathy Associated with POLG Mutations: A Case Series	Jeremy Reitinger	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
201	Optic Neuropathy with Novel Triple Targeted Therapy for Anaplastic Thyroid Cancer: Case Series	Nagham Al-Zubidi	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
202	Pallid Disc Edema in Non-arteritic Anterior Ischemic Optic Neuropathy: Not Always Giant Cell Arteritis	Malcolm Kates	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
203	Paracentral Acute Middle Maculopathy: A Complication of Papillophlebitis	Venkatkrish Kasetty	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
204	Prevalence of Familial Optic Disc Drusen Using Optical Coherence Tomography	alvilda steensberg	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
205	Recurrent Popper Induced Non-Arteritic Anterior Ischemic Optic Neuropathy: A Novel Entity	Elisa D'Alessandro	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
207	The Natural History Of Optic Nerve Sheath Meningiomas In A Tertiary Referral Centre	Kenneth Gilmour	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
208	The Presence of Macular Edema In Optic Neuritis	Ashley Streseman	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)

209	The Relationship Between Visual Field Defects in the Setting of Chorioretinal Coloboma and Optic Disc Drusen	Whitney Sambhariya	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
210	The Spectrum of Isolated Retinal Artery Occlusion Secondary to Giant Cell Arteritis: A Systematic Review	Ji Yun Han	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
211	Vision loss from Tuberculous Optochiasmatic Arachnoiditis following Tuberculous Meningitis	Michael Curley	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
212	Weight loss to sight loss: A case of bilateral NAION in a young female after aggressive weight reduction and treatment of diabetes	Somya Chowdhary	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
213	Blindness, pain and swelling, Oh my!	David Waitzman	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
214	It's Always The Cancer	Kenneth Gilmour	Neuro-Ophthalmic Practice
215	Occam's Razor or Hickam's Dictum?	Chloe li	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
216	Postoperative Papilledema: Not sure if I'm a fan!	Hyun Jun Kim	Pediatric Neuro-Ophthalmology
217	Stop the treatment - methotrexate-associated diffuse large B-cell lymphoma	Gabriele Berman	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
218	To Do or Not To Do	Charissa Tan	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases

1

A Cord and a Pupil: Neck Paraganglioma Presenting as Horner Syndrome

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Introduction:
Paragangliomas are slow growing tumors that are derived from neural crest cells associated with autonomic ganglia. While extremely rare in the head and neck, these tumors can involve the vagus nerve and cervical sympathetic chain resulting in vocal cord paralysis and Horner Syndrome, respectively.

Description of Cases:
A 50-year-old man with a past medical history of presumed idiopathic left vocal cord paralysis status post medialization thyroplasty (3 years prior) was referred by his ophthalmologist to the Emergency Department (ED) due to a 1-week history of anisocoria and ptosis. In the ED, his ophthalmic exam was notable for a briskly reactive left miotic pupil and left upper lid ptosis, concerning for a left Horner Syndrome. Computed Tomography (CT) Angiography of the head and neck demonstrated a 2.4 x 2.0 x 4.7 cm enhancing mass of the left post styloid parapharyngeal space extending from the inferior aspect of the left jugular foramen to the C2 level, displacing the left internal carotid artery. Magnetic Resonance Imaging (MRI) re-demonstrated this enhancing mass with additional radiographic features of vascular flow voids and mixed T1 iso-hyperintensity, findings that are most consistent with jugular and vagal paragangliomas.

Conclusions, including unique features of the case:
Head and neck paragangliomas should be on the differential diagnosis with a presentation of vocal cord paralysis and/or Horner syndrome. Advanced neuroimaging is warranted to characterize these lesions, which may ultimately require multi-disciplinary surgical planning for resection.

References: None provided.

Keywords: Pupil, Neuroimaging, Tumors

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2

Tadpole Pupil Associated With Horner's Syndrome From Compression Of The Carotid Sheath

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Introduction:
Tadpole pupil is a rare phenomenon characterized by spontaneous segmental spasm of the iris dilator resulting in a temporarily peaked pupil shape. Pupillary distortion is usually unilateral, episodic, and can occur in any segment of the iris. Etiology of tadpole pupil is unclear but occurs most frequently in young women and is commonly associated with an ipsilateral Horner's Syndrome.

Description of Cases:
37-year-old Asian female presented with complaints of her right pupil episodically enlarging and taking on an oblong shape several times per month. Associated symptoms included unusual sensation of the ipsilateral face, severe headache, and disorientation. Visual acuity was 20/20 bilaterally, with no dyschromatopsia or relative afferent pupillary defect. Initial examination demonstrated anisocoria, right smaller than left, and round pupils bilaterally without segmental paresis. Photographic evidence of her pupil demonstrated a classic tadpole appearance. General neurologic exam was normal. Topical apraclonidine 0.5% demonstrated reversal of anisocoria with segmental dilation of the right pupil inferonasally, confirming right Horner's Syndrome. MRI/MRA demonstrated a nodule along the right carotid sheath in keeping with an enlarged lymph node as the etiology of her pupillary dysfunction and autonomic symptoms.

Conclusions, including unique features of the case:
We present a rare case of tadpole pupil associated with Horner's Syndrome due to an enlarged lymph node compressing the carotid sheath. Tadpole pupil is typically unilateral and can change shape with each occurrence. Treatment with topical alpha-1 antagonist has been proposed but is unclear if it would be effective in patients who already have a sympathetic defect. It is important to be aware that although tadpole pupil is benign, it is most commonly associated with an ipsilateral Horner's Syndrome which must be ruled out to prevent life-threatening complications.

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3
Thyroid Cancer and Ipsilateral Horner's Syndrome

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Introduction:
Horner's syndrome is a rare manifestation of a neck mass and can be linked to thyroid cancer by compression of the sympathetic plexus. There are less than 15 reported cases in the literature of a malignant thyroid mass causing Horner's syndrome.

Description of Cases:
A 71-year-old male followed for narrow angles was found to have an incidental finding of a left-sided Horner's syndrome. He was referred to neuro-ophthalmology for further evaluation. The patient noted the presence of left ptosis for several years but denied any other ocular concerns. He noted previous headaches that would occur daily, which resolved following sinus surgery two years prior. Examination revealed ptosis and miosis of the left eye, with reversal of the anisocoria with apraclonidine. The ophthalmologic exam was otherwise unremarkable. CT of the head and neck showed no evidence of an intracranial lesion, arterial stenosis, or dissection, but revealed an incidental finding of a left thyroid goiter. CT of the chest did not show a mass, but revealed incidental non-specific pulmonary nodules, stable with repeat imaging after 5 months. An ultrasound of the left thyroid nodule indicated a high suspicion for malignancy. He was referred to a head and neck surgeon, with fine needle aspiration of the left thyroid indicating suspicion for a follicular neoplasm.

Conclusions, including unique features of the case:
This case is unique in that the patient had no specific complaints but found to have an incidental finding of left-sided Horner's, with an additional incidental finding of a thyroid neoplasm through imaging. The left-sided thyroid neoplasm appeared to be compressing the sympathetic cervical chain, leading to an ipsilateral Horner's. This demonstrates the importance of a thorough assessment for detection of malignancies, including thyroid pathology, in determining the etiology of Horner's syndrome.

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Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Tumors, Pupil

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4

A case of complete corpus callosum agenesis in unilateral Peters anomaly

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Introduction:
Peters anomaly is an uncommon congenital disorder of the anterior segment of the eye, resulting in corneal opacity. It has also been associated with systemic manifestations including seizures, developmental delays, craniofacial abnormalities, and abnormal cortical development. We report the first confirmed case of an infant with unilateral Peters anomaly and complete agenesis of the corpus callosum.

Description of Cases:
A four-day-old male presented to Children's National for evaluation of left eye corneal opacity. At birth, an MRI of the brain without contrast confirmed complete agenesis of the corpus callosum, intraventricular hemorrhage, and left terminal matrix hemorrhage. On examination, portable slit lamp revealed unilateral corneal opacity of the left eye with central opacification. Right eye was normal.Ultrasound microscopy of the left eye showed anterior segment dysgenesis with shallow anterior chambers and anterior rotation of the ciliary body. Where there was clear cornea, no areas with anterior chamber overlaying the iris could be identified. Ultrasound (B-scan) of both eyes showed formed globes without vitritis, retinal tears, or retinal detachment. Given these imaging findings, a diagnosis of Peters Anomaly was made.

Conclusions, including unique features of the case:
To our knowledge, this is the fifth reported case of Peters anomaly associated with complete agenesis of the corpus callosum, and ours is the only unilateral case of Peters anomaly. While abnormal development of midline structures such as the corpus callosum have been reported, complete agenesis of the corpus callosum is rare in the literature. Complete agenesis has been suggested to be part of a broader syndrome that is not well studied. Our study reports the only confirmed case of unilateral Peters anomaly with complete agenesis of the corpus callosum, emphasizing the importance of ruling out systemic abnormalities in unilateral or less severe cases of Peters anomaly.

References: None provided.

Keywords: Pediatric neuro-ophthalmology

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5

ACHOO and Burn: Macular scars secondary to sun- and laser beam-staring to induce photic sneeze reflex

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Introduction:
Sun- and laser-staring can lead to significant maculopathy, typically with poor visual recovery. The photic sneeze reflex, also called Autosomal Dominant Compelling Helioophthalmic Outburst (ACHOO) Syndrome, is a fairly common involuntary sneezing reflex upon exposure to bright light, occurring in about 1 in 4 individuals. It is typically considered a mere annoyance, but potential hazards include sudden burst of sneezing while driving. Children with psychiatric disorders or behavioral health diagnoses may be at risk for self-inflicted injuries of the eyes. In our patient, the photic sneeze reflex resulted in permanent vision loss from curious experimentation of a young boy.

Description of Cases:
A 12-year-old boy presented with painless, bilateral vision loss for at least one year. Medical history was significant for conduct disorder and attention deficit with hyperactivity disorder. He had a strong photic sneeze reflex, and he stated that if he felt a tickle in his nose, he would look at the sun or a laser cat toy to induce sneezing. He reported numerous attempts to elicit sneezing over an 8-year period. His visual acuity was 20/30 and 20/40 in the right and left eyes, respectively. Slit lamp biomicroscopy and intraocular pressures were normal in each eye. Fundus examination revealed bilateral, well-circumscribed ovoid atrophic scars, each with central hyperpigmentation and a ring of hypopigmentation, in the foveal region. Optical coherence tomography of both eyes showed subfoveal focal disruption of the photoreceptor outer segments with absence of the interdigitation and ellipsoid zones; there was preservation of the retinal pigment epithelium/Bruch's complex and external limiting membrane.

Conclusions, including unique features of the case:
This report demonstrates that a child with ACHOO syndrome may experiment with trying to trigger sneezing. It also highlights the importance of eliciting history of sun- and laser-staring in patients with unexplained maculopathy and of uncovering the root cause of the behavior so that it can be prevented.

References: None provided.

Keywords: Pediatric neuro-ophthalmology, Miscellaneous

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6

Clinical Course And Visual Outcomes Of Papilledema In Pediatric Cerebral Venous Sinus Thrombosis

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Introduction:
We report on the natural history and visual outcomes of papilledema in pediatric patients with cerebral venous sinus thrombosis (CVST).

Description of Cases:
Methods: Manual chart review was performed on 35 patients with imaging confirmed CVST and ophthalmologic assessment from a single tertiary care center. Results: Patients were 9 ± 5 years old (mean ± standard deviation) at time of CVST diagnosis and 40% female. The most common risk factors for CVST were infection (69%), dehydration (26%), and hypercoagulability (23%). Fundoscopic examination identified papilledema in 31 out of 35 cases (89%). Of these 31 cases, 9 cases (29%) had progression of papilledema despite treatment, 17 cases (55%) did not have papilledema progression, while 5 cases (16%) lacked follow-up records. The initial Frisén grade among all cases was 2 ± 1, and cases with progression reached a maximum of 4 ± 1. 8 cases underwent optical coherence tomography imaging at initial presentation, which demonstrated an average retinal nerve fiber layer thickness of 178 ± 70 µm. Most patients (97%) were treated with anticoagulation and 100% required acetazolamide and/or lumbar puncture. Among 26 patients with follow-up, papilledema resolved in 107 ± 128 (between 20 and 704) days. At final follow-up, 31% of patients had neurologic sequelae and 54% of patients had either optic atrophy or deficits on visual field testing.

Conclusions, including unique features of the case:
This is the first study reporting on the course of papilledema in pediatric patients with CVST. Our results highlight the importance of ophthalmologic follow-up during the treatment course of these patients to prevent irreversible vision loss.

References: None provided.

Keywords: Pediatric neuro-ophthalmology, High intracranial pressure/headache

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7

Don't "Batten" An Eye When It Comes To Diagnosing Rare Ophthalmologic Diseases

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Introduction:
Juvenile Neuronal Ceroid Lipofuscinosis (JNCL), or Batten Disease, is a rare autosomal recessive neurodegenerative disorder characterized by progressive vision loss, seizures, cognitive decline, and a shortened lifespan. We present a case of a 6-year-old female referred for decreased vision and other associated symptoms, ultimately diagnosed with JNCL.

Description of Cases:
The patient's parents sought medical attention due to their child's decreased vision over the past year. The child reported difficulty seeing the whiteboard at school and exhibited poor night vision. Additionally, the parents noted that the child frequently "tripped on things," suggestive of poor peripheral vision. The father also reported the child as "a little clumsy" and raised concerns about the possibility of Attention Deficit Disorder (ADD). Notably, at the age of 3, the patient had been treated in the Emergency Department for a head injury related to a fall. Clinical examination revealed visual acuity of 20/100 in the right eye and 20/150 in the left eye. Pupillary reactions and extraocular movements were within normal limits, and anterior and posterior segment examinations were unremarkable, except for mild pigment mottling in both maculae and peripheral areas of relative hypopigmentation. An electronegative electroretinogram was also observed. Genetic testing confirmed a homozygous CLN3 mutation, identifying the patient with Juvenile Neuronal Ceroid Lipofuscinosis (type 3). JNCL is characterized by symptom onset between the ages of 4 and 10, leading to progressive neurodegeneration, visual impairment, and ultimately death in the late teens or early twenties. The prevalence of JNCL is rare, with an incidence of 1 in 100,000.

Conclusions, including unique features of the case:
This case highlights the importance of considering JNCL in children presenting with progressive vision loss, ataxia, and associated symptoms. Early diagnosis through genetic testing can aid in providing appropriate medical care, genetic counseling, and support for families facing this devastating neurodegenerative disease.

References: None provided.

Keywords: Pediatric neuro-ophthalmology, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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8

Oculomotor Paresis With Cyclical Spasms; New Insights Into The Etiology And A New Case With Videography

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Introduction:
Oculomotor paresis with cyclical spasm (OPCS) is a rare disorder first reported by Rampoldi in 1884(1). In 1975, Loewenfeld and Thompson(2) reported the largest review (45 cases) as well as a new theory regarding the etiology of this condition. Since then, a PubMed search revealed 2 additional reports (3,4). We report a case of a case of OPCS with minimal ptosis and elevation paresis (external ophthalmoplegia) and spasms involving only the pupillary sphincter. We also discuss the new developments in anatomy of the Edinger-Westphal Nucleus(5), as well as the new insights into the regulation of axonal responses to injury that may assist in our understanding of this condition(6).

Description of Cases:
Patient is a 48 Chinese female with a history of fall down a flight of stairs at age 10. She complained of intermittent diplopia since her teenage years in lateral and upgaze. Examination revealed mild ptosis (1mm) and elevation deficit in the right eye. She was orthophoric except in up gaze where she had a left hypertropia of 3 prism diopters. Her left pupil was normal but her right did not respond to light. Instead, it would go into cyclic spasm every 55s (spastic phase 15s, paretic phase 40s).

Conclusions, including unique features of the case:
The Edinger-Westphal nucleus is classically defined as preganglionic parasympathetic input to the ciliary ganglion, primarily based on studies in monkeys. In mammals, this nucleus also contains centrally projecting neurons involved in sympathetic, consumptive and stress-related functions. This knowledge may give insight into the supranuclear connections giving the cyclic spasms(5). In addition, Sudhheendra et al is studying the factors that affect genes that affect axonal regeneration in the central nervous system. We believe that these new insights may enable us to explain what Loewenfeld and Thomson postulated in 1975.

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Keywords: Pediatric neuro-ophthalmology, Pupil, Ocular motility

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Opsoclonus in children: diagnosis and etiology of opsoclonus in a tertiary pediatric hospital

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Introduction:
Opsoclonus is often associated with serious neurologic and paraneoplastic pathology and neurologic morbidity. Pediatric ophthalmologists play an important role in its diagnosis. We sought to better characterize patients presenting with opsoclonus.

Description of Cases:
A retrospective chart review of patients seen at a quaternary children's hospital for suspicion of opsoclonus. Patients with opsoclonus were identified and demographic, exam, diagnostic work up and outcome information was collected. 82 children were identified with opsoclonus, with 66 being excluded as mimics. 36(44%) had paraneoplastic opsoclonus-myoclonus-ataxia syndrome (OMAS), 32(39%) had non-paraneoplastic OMAS, 1(1.2%) had optic pathway glioma, 5(6.1%) had other neurologic diseases (hypoxic-ischemic encephalopathy, congenital abnormalities, or encephalitis), 2(2.4%) had hydrocephalus, 5(6.1%) had benign neonatal opsoclonus, and 1(1.2%) had opsoclonus of unknown etiology. 77(94%) patients received brain MRIs, of which 53(69%) were normal and 13(17%) identified pathology. Out of 57 MRI chest/abdomen/pelvis studies, 24 (42%) identified pathology (most frequently neuroblastoma). 57(80%) had urine catecholamine studies. 50 patients (61%) received CSF studies, of which 15(30%) were abnormal. Only 24 patients (29%) were seen by ophthalmology. Diagnoses of 66 excluded patients initially thought to have opsoclonus included ocular flutter, roving eye movements in the setting of poor vision, nystagmus, voluntary eye movements, seizures and an oculogyric reaction to medication use.

Conclusions, including unique features of the case:
Extensive workup is usually performed to rule out an underlying neoplastic pathology and includes MRI brain, neck, chest, and abdomen, and urine catecholamine studies. Pediatric ophthalmologists can help to rule opsoclonus in or out and spare children unnecessary testing if it is not needed.

References: Grossman SN, Rucker JC. Opsoclonus and Ocular Flutter: Evaluation and Management. Curr Opin Ophthalmol. 2023 Aug;10:97. Pranzatelli MR, Tate ED, McGee NR. Demographic, Clinical, and Immunologic Features of 389 Children with Opsoclonus-Myoclonus Syndrome: A Cross-Sectional Study. J AAPOS. 2017 Sep;21(5):468.

Keywords: Pediatric neuro-ophthalmology, Ocular motility, Paraneoplastic syndromes

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10

Pediatric Tolosa-Hunt Syndrome with Facial Nerve Involvement and Contralateral Relapse

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Introduction:
Tolosa-Hunt Syndrome (THS), with an estimated incidence of one per million per year (Iaconetta, 2005), describes a rare cause of painful ophthalmoplegia thought to be due to indolent inflammation of the cavernous sinus, superior orbital fissure, or orbital apex. Treatment is focused on the use of corticosteroids with no consensus regarding dosage, route, or length of administration. It is thus essential to report new cases and build additional evidence for the diagnosis and treatment of THS. Among the pediatric population, evidence for treatment protocols is even more scarce and primarily based on case reports. Notably, only three cases of pediatric THS preceded by facial nerve palsy have been reported (Cerisola, 2011; Tsirigotaki, 2019; Wiener, 2020). Moreover, only a handful of cases have reported radiographical evidence of contralateral relapse, typically in adult populations. We present a unique pediatric THS case preceded by facial nerve palsy with subsequent contralateral relapse.

Description of Cases:
An 11-year-old girl with a prior history of right-sided Bell's palsy presented with binocular horizontal diplopia, right-sided esotropia and a right-sided headache. Her vitals were significant for hypertension and tachycardia. Exam revealed right abducens nerve palsy. Extensive infectious, inflammatory, and neoplastic workup were negative, and the patient was diagnosed with THS as defined by the 2018 International Classification of Headache Disorders 3rd Edition. Corticosteroid therapy improved her symptoms both clinically and radiographically. She presented 4 months later with a left-sided headache and transient left-sided esotropia with radiographic evidence of new involvement of the left cavernous sinus. She continues to be monitored for full resolution of her imaging.

Conclusions, including unique features of the case:
This case demonstrates that THS can rarely involve the facial nerve in pediatric patients, and reinforces that contralateral relapse occurs. Our patient is the fourth reported child to present with THS preceded by facial nerve palsy and the first documented to experience a contralateral relapse.

References: Iaconetta, Stella, Esposito, Cappabianca; Tolosa-Hunt syndrome extending in the cerebello-pontine angle, Cephalalgia Int J Headache, 25, 746–750, 2005. Cerisola, González, Scavone; Tolosa-Hunt syndrome preceded by facial palsy in a child, Pediatr Neurol, 44, 61–64, 2011. Tsirigotaki, Ntoulios, Lioumpas, Voutoufianakis , Vorgia; Tolosa-Hunt Syndrome: Clinical Manifestations in Children, Pediatr Neurol, 99, 60–63, 2019. Wiener, Cron; Successful treatment of pediatric Tolosa-Hunt syndrome with adalimumab, Eur J Rheumatol, 7, S82–S84, 2020.

Keywords: Pediatric neuro-ophthalmology, Neuroimaging, Ocular motility, Miscellaneous

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Progressive Nystagmus and Ataxia: A Novel Phenotype and Mutation of CACNA1A

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Introduction:
Genetic disorders affecting the cerebellum are an uncommon but important cause of gaze-evoked nystagmus and ataxia in children and adolescents, including spinocerebellar ataxias (SCA), Friedreich ataxia, and episodic ataxias (EA). The CACNA1A gene has been associated with SCA6, EA2, and non-ataxic paroxysmal disorders such as familial hemiplegic migraine, epilepsy, and dystonia. The clinical phenotype of CACNA1A-associated disease is expanding, and there is no established genotype-phenotype correlation. We present a case of progressive tremors and ataxia in an adolescent with persistent nystagmus associated with a likely pathogenic in-frame deletion in CACNA1A.

Description of Cases:
A 17-year-old male presented to child neurology and neuroophthalmology for evaluation of two years of tremors worsened by activity and progressive clumsiness with frequent falls. Additionally, he described that he developed "shaky eyes" a few months before evaluation in the clinic. Exam was significant for gaze-dependent nystagmus in horizontal gaze, a "no-no" head tremor, bilateral extremity postural and kinetic tremor, appendicular and truncal ataxia, and difficulty with tandem gait. Fundi were normal, and optical coherence tomography of the retinal nerve fiber layer was unremarkable. MRI brain showed marked atrophy of the cerebellar vermis and, to a lesser extent, the cerebellar hemispheres. Genetic testing revealed a CACNA1A likely pathogenic variant (c.5110_5112del; p.F1704del) causing in-frame deletion of a single amino acid that has not been previously published. Repeat expansion testing was negative, ruling out SCA6. He has shown some improvement with PT and OT.

Conclusions, including unique features of the case:
There have been reports of patients with CACNA1A variants that display a wide variety of clinical symptoms beyond the classic episodic ataxia phenotype. This case expands this clinical and genotypic spectrum to include adolescent onset of progressive ataxia, tremors, persistent nystagmus, and midline cerebellar atrophy related to a novel in-frame deletion variant in CACNA1A.

References: Barros J, Damásio J, Tuna A, et al.; Cerebellar Ataxia, Hemiplegic Migraine, and Related Phenotypes Due to a CACNA1A Missense Mutation: 12-Year Follow-up of a Large Portuguese Family, JAMA Neurol.,70(2):235–240, 2013. Muro García I, Toribio-Díaz ME, Quintas S.; Ataxia episódica: 20 años de retraso diagnóstico, Neurología, 35:500–501, 2020. Indelicato E, and Boesch S; From Genotype to Phenotype: Expanding the Clinical Spectrum of CACNA1A Variants in the Era of Next Generation Sequencing, Front. Neurol, 12:639994, 2021. Choi KD, Choi JH; Episodic Ataxias: Clinical and Genetic Features, J Mov Disord, 9(3):129-35. 2016. Hassan A; Episodic Ataxias: Primary and Secondary Etiologies, Treatment, and Classification Approaches, Tremor Other Hyperkinet Mov (NY), 28;13:9, 2023.

Keywords: Genetic disease, Nystagmus, Pediatric neuro-ophthalmology, Neuroimaging

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The use of topological data analysis in detecting papilledema using oral fluorescein angiography in children

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Introduction:
Differentiating papilledema from psedopapilledema could be challenging, especially in the pediatric population. However, differentiating the two conditions is essential in avoiding unnecessary invasive procedures and testing. Multiple technologies have been used over time to improve accuracy. One easy and efficient technique that is gaining popularity is oral fluorescein angiography (FA). A previous study that used expert readers demonstrated lower than expected accuracy in diagnosing papilledema. This was due especially to lower specificity. On the other hand, intravenous FA was reported as being a valuable tool, but has the drawback of an invasive test poorly tolerated in children.

Description of Cases:
We are using a topological data analysis (TDA) to process the FA output. Topology-based analysis, particularly persistence and Morse-Smale complexes, simplifies complex images and focuses on features of interest. TDA can be used for automatic detection of papilledema in medical settings such as eye clinics or emergency rooms. It also has the advantage of producing simpler, easier to understand visualizations that can be a benefit for the teaching of medical professionals. We have obtained promising results on images published in the literature and are extending the study on 175 patients with anomalous optic nerves referred for papilledema to our tertiary eye care center, of which less than 25% had real papilledema.

Conclusions, including unique features of the case:
TDA is user friendly and unexpensive, easily used on any web browser and offering an additional tool for improving the accuracy of diagnosing papilledema and avoiding expensive testing in patients with pseudoedema. It has application both for patient care and for teaching.

References: None provided.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), High intracranial pressure/headache, Pediatric neuro-ophthalmology, Miscellaneous

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Contact Information: None provided.

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A Case of Late-Onset Immune Checkpoint Inhibitor-Induced Orbital Inflammation

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Introduction:
We report a case, with clinical and radiographic imaging, presenting with diplopia, proptosis, and ophthalmoplegia secondary to Immune checkpoint inhibitors (ICI) with symptom-onset 11 months after initiation of treatment who improved with medication cessation and oral steroids.

Description of Cases:
A 49-year-old male with a 10 pack-year smoking history and stage IV pulmonary adenocarcinoma status post 16 cycles of Ipilimumab (CTLA-4 inhibitor) and Nivolumab (PD-1 inhibitor) immunotherapy presented with one month of worsening binocular diplopia and headaches. Initial exam showed visual acuity of 20/20 in each eye, normal intraocular pressures, full color plates, and Hertel measurements of 25 and 27. There was a right hypertropia and left exotropia worse in right gaze with -2 adduction deficit in the left eye. Slit lamp exam showed a normal right eye and 1+ conjunctival injection and chemosis in the left eye which blanched with phenylephrine. Anterior chamber and dilated fundus exam were unremarkable. Workup including MRI head and orbits showed marked edema, thickening, and enhancement of the left lateral rectus, right medial rectus, and right superior oblique muscles with sparing of the myotendinous junction. Thyroid function testing was normal. CT chest, abdomen, and pelvis showed no residual evidence of right lung disease, lymphadenopathy, or new evidence of metastatic disease. Given the distribution and normal thyroid function testing, this was felt to represent ICI-induced myositis. Ipilimumab and Nivolumab were discontinued, and the patient started 60mg of prednisone with a prolonged taper. His symptoms gradually improved and a repeat MRI 5 months later showed complete resolution of the orbital inflammation.

Conclusions, including unique features of the case:
This case of orbital myositis in the setting of metastatic pulmonary adenocarcinoma treated with 16 cycles of Ipilimumab and Nivolumab adds to the growing literature of ICI-induced orbital inflammation and demonstrates that late onset can occur and be successfully managed with medication cessation and initiation of oral steroids.

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Keywords: Orbit/ocular pathology, Ocular motility, Paraneoplastic syndromes, Neuroimaging, Miscellaneous

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A Novel Gene Variant Resulting in a Phenotypic Chronic Progressive External Ophthalmoplegia

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Introduction:
Chronic progressive external ophthalmoplegia (CPEO) is characterized by progressive blepharoptosis and ophthalmoplegia. It is categorized as a mitochondrial encephalomyopathy and can be associated with additional systemic comorbidities or occur in isolation. Isolated CPEO is reported to be caused by primary mutations in mitochondrial DNA (mtDNA) but can also be the result of deletions in mtDNA from the primary nuclear DNA (nDNA). This case describes the diagnosis and management of CPEO as the likely clinical phenotype of TWNKc.1000C>G, p.(Arg334Gly), a heterozygous missense variant that has not yet been reported in the medical literature or on disease-related variation databases.

Description of Cases:
A 63-year-old man presents with progressive blepharoptosis that began during his late teens and infrequent binocular diplopia. He uses bilateral lid crutches that are fixed onto the frame of his glasses, which provide improvement of his ptosis. He has a negative history for cardiac disease, dyspnea, dysphagia, muscle weakness, or myotonia. He does have a family history of ptosis in his father and paternal grandfather. The clinical exam reveals maximum palpebral apertures of 4mm OD and 5mm OS, while fully engaging his frontalis muscle, and severely reduced ductions in all positions of gaze, greatest in supraduction and infraduction. Given the clinical testing and family history, genetic testing was pursued. The patient was found to be heterozygous for TWNK c.1000C>G, p.(Arg334Gly).

Conclusions, including unique features of the case:
To the best of our knowledge, TWNKc.1000C>G, p.(Arg334Gly) is a missense variant that has not been reported in the medical literature or genetic databases. This variant should be considered among other known TWNK variants in those who have a clinical presentation consistent with CPEO.

References: Bau, V., & Zierz, S; Update on chronic progressive external ophthalmoplegia, Strabismus, 13(3), 133–142, 2005. Goffart, S., Cooper, H. M., Tyynismaa, H., Wanrooij, S., Suomalainen, A., & Spelbrink, J. N.; Twinkle mutations associated with autosomal dominant progressive external ophthalmoplegia lead to impaired helicase function and in vivo mtDNA replication stalling, Human molecular genetics, 18(2), 328–340, 2009. Hirano, M., & Pitceathly, R. D. S.; Progressive external ophthalmoplegia. Handbook of clinical neurology, 194, 9–21, 2023. Kirkpatrick, C. A., Shriver, E. M., Clark, T. J. E., & Kardon, R. H.; Upper Eyelid Response to Topical 0.5% Apraclonidine. Ophthalmic plastic and reconstructive surgery, 34(1), 13–19, 2018. Slonim, C. B., Foster, S., Jaros, M., Kannarr, S. R., Korenfeld, M. S., Smyth-Medina, R., & Wirta, D. L.; Association of Oxymetazoline Hydrochloride, 0.1%, Solution Administration With Visual Field in Acquired Ptosis: A Pooled Analysis of 2 Randomized Clinical Trials. JAMA ophthalmology, 138(11), 1168–1175, 2020.

Keywords: Genetic disease, Ocular motility, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease

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A Rare Case of Recurrent Proptosis and Optic Neuropathy

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Introduction:
Madelung's disease is characterized by progressive and symmetrical adipose deposition in the cervicofacial region. Only a few cases of isolated orbital involvement have been reported.

Description of Cases:
A 52-year-old Black male presented with one year of painless, progressive left-eye vision loss. History includes type 2 diabetes, obesity, and two prior orbital decompression surgeries without biopsies of unknown etiology eight years before the current presentation. Ocular findings included bilateral proptosis with Hertel 30mm right side and 35 mm left side, visual acuity of 20/20 OD and 20/500 OS, inferior and central vision involving visual field defect in the left eye, a left relative afferent pupillary defect, and left optic disc pallor. Optical coherence tomography showed retinal nerve fiber layer and ganglion cell layer thinning in the left eye. Magnetic resonance imaging (MRI) of the orbits revealed extensive bilateral intra and extraconal fat involving both orbits with associated proptosis and thickening of the bilateral inferior, lateral, and superior rectus muscles. The left optic nerve and left aspect of the optic chiasm were atrophic without T2 change or gadolinium enhancement. Brain MRI, CT scans of the chest, abdomen, and pelvis were unremarkable and negative for other masses. Serological tests for thyroid eye disease, infectious, inflammatory, and other metabolic causes were negative. Orbital fat decompression with biopsy confirmed lipomatous hypertrophy without neoplasm. Vision remained stable at 6 months after surgery.

Conclusions, including unique features of the case:
The clinical presentation, imaging findings, and biopsy are consistent with the diagnosis of orbital lipomatosis. Although orbital involvement has been reported in Madelung's disease, this case displays isolated orbital involvement, a further rarity. It is presumed that his prior orbital decompression surgeries were due to the same cause, which is consistent with the recurrent nature of the disease. Early recognition, surgery, and serial monitoring are critical to prevent permanent vision loss.

References: None provided.

Keywords: Neuroimaging, Orbit/ocular pathology, Visual fields, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Optic neuropathy

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Contact Information: None provided.

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Bisphosphonate-induced orbital apex syndrome

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Introduction:
Bisphosphonates act on osteoclasts to decrease skeletal remodeling and resorption rates in the setting of osteoporosis and other skeletal conditions.1 Although typically well tolerated, bisphosphonates are rarely associated with ocular side effects. The proposed pathogenesis involves drug secretion from the lacrimal gland, resulting in mucous membrane irritation and subsequent release of inflammatory mediators.2 Ocular adverse effects include conjunctival injection and chemosis, sclerouveitis, and orbital inflammation.3 Rarely, orbital inflammation may cause orbital apex syndrome, leading to ophthalmoloplegia and optic neuropathy.4 To our knowledge, this is the first reported case of bisphosphonate-induced orbital apex syndrome in the ophthalmology literature.

Description of Cases:
A 72 year-old female with several week history of alendronate use presented with decreased vision in the right eye (OD) and diplopia. Examination was notable for visual acuity of 20/200 OD, trace relative afferent pupillary defect OD, dyschromatopsia OD, significantly restricted extraocular movements (EOMs) OD, and was unremarkable in the left eye (OS). Slit lamp examination revealed proptosis, chemosis, and mild conjunctival injection OD. Posterior examination was unremarkable. MRI of the brain and orbits revealed enhancement of the right orbital apex and optic nerve sheath with adjacent fat stranding. Laboratory testing was unremarkable. Alendronate was discontinued and she was treated with IV methylprednisolone for 3 days followed by an oral steroid taper. At 3 month follow up, her vision improved to 20/20 OD with return of full color vision, EOMs, and visual fields.

Conclusions, including unique features of the case:
Bisphosphonates are widely used in the setting of skeletal disease and are rarely associated with ocular complications, most commonly presenting within days of drug initiation. We report a unique cause of bisphosphonate-induced orbital apex syndrome that occurred 5 weeks after bisphosphonate initiation. It is important for clinicians to consider this rare and potentially irreversible complication when evaluating patients with orbital inflammation.

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Invasive Sinonasal Mucosal Melanoma Presenting as Painless Vision Loss

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Introduction:
Sinonasal mucosal melanoma (SNMM) is a rare, aggressive disease that often presents with nonspecific symptomatology, leading to delays in diagnosis. This report describes a case of SNMM invading the orbit and cranial fossa in a young, healthy woman who presented to the eye clinic with painless vision loss.

Description of Cases:
A 41-year-old Hispanic female presented with one month of right eye blurry vision. Examination revealed a visual acuity of 20/30 with a trace relative afferent pupillary defect (APD) and 5/8 color plates in the right eye. External exam revealed 6 mm of relative proptosis and increased resistance to retropulsion of the right eye (Figure 1A). Extraocular movements were full in all gazes. Anterior segment exam and fundoscopic exams were unremarkable. Magnetic resonance imaging (MRI) of the brain and orbits revealed an enhancing soft tissue mass centered in the right ethmoid sinus with extension into the right extraconal orbit and frontal lobe (Figure 1B). Histopathology was suggestive of mucosal melanoma (Figure 1C). Immunohistochemistry was positive for HMB-45 and CD56. Full-body imaging revealed retroperitoneal and pulmonary metastasis. The patient received palliative radiation therapy with a total dose of 3500 cGy to the right ethmoid sinus and orbit and will commence systemic immunotherapy in the coming weeks.

Conclusions, including unique features of the case:
Sinonasal mucosal melanoma (SNMM) accounts for less than 1% of head and neck cancers and is rarely diagnosed based on ophthalmic findings. It is typically advanced at presentation, with an average overall survival rate of about 35% at 5 years. The authors describe a case of SNMM that highlights the rapid progression and relatively subtle exam findings, even in advanced disease. There can be variability in the histopathology and immunohistochemistry among SNMM lesions, which underscores the need for further research to elucidate optimal, targeted management strategies for this aggressive malignancy.

References: None provided.

Keywords: Orbit/ocular pathology, Optic neuropathy, Orbit

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Contact Information: None provided.

18
Multifocal orbital intramuscular angioma

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Introduction:
We report the second published case of multifocal orbital intramuscular angioma (IMA) affecting multiple extraocular muscles at presentation. The case also highlights a new technological approach to surgery in the orbital apex.

Description of Cases:
A 62-year-old woman developed progressive visual loss of the right eye, a right rAPD, unilateral right superior-temporal visual field defect, OCT attenuation of the right retinal nerve fiber and ganglion cell layers, and right optic nerve pallor. Testing in the fellow eye was normal. Contrasted magnetic resonance imaging (MRI) revealed discrete multifocal intramuscular lesions affecting the lateral and superior recti, the larger in the lateral rectus measuring 0.51 cm x 1.4 cm x 0.85 cm in the mediolateral, anteroposterior, and craniocaudal dimensions, respectively. Both demonstrated decreased T1 and T2 signal with heterogenous and confluent enhancement with the most posterior component displacing the right optic nerve near the orbital apex. She underwent transcranial extradural lateral rectus biopsy at the orbital apex utilizing a new commercially available modification to image guided navigation (highlighted in a separate submission) which provides real-time intraoperative navigation, preoperative and intra-operative virtual planning, and anatomical projection of user-defined 3-dimensional features into the surgeon's view while navigating via the operative microscope. This case represents one of the first applications of this platform in orbital surgery and demonstrates the utility of this system for safe and efficient surgery in the orbital apex. Pathology of the biopsied tissue showed small to intermediate-sized vascular channels lined by bland endothelial cells infiltrating skeletal muscle, compatible with intramuscular angioma.

Conclusions, including unique features of the case:
This case represents the second biopsy-confirmed multifocal orbital IMA and the first to employ a novel surgical intraoperative virtual reality mapping platform to facilitate safe and efficient surgery in the orbital apex.

References: None provided.

Keywords: Orbit/ocular pathology, Optic neuropathy, Tumors, Neuroimaging

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Occult Transhemispheric Craniofacial Fibrous Dysplasia Manifesting As Contralateral Optic Neuropathy

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Introduction:
Craniofacial fibrous dysplasia (FD) involving the orbit is a rare disease whereby fibro-osseous proliferation can compress the optic nerve. We present a patient with right facial malformation who developed optic neuropathy in the opposite eye due to craniofacial FD.

Description of Cases:
A 38-year-old woman presented to the neuro-ophthalmology service with blurred vision in the left eye for three months. She had a right facial malformation since childhood with right hearing loss and headaches and she was considering reconstructive surgery. The right eye was normal. Left eye exam revealed 20/20-1 visual acuity, unreliable Humphrey visual fields with non-specific defects, left relative afferent pupillary defect, abnormal color vision, normal intraocular pressure, and full extraocular movements. There was left optic disc pallor and optical coherence tomography (OCT) showed severe retinal nerve fiber and ganglion cell complex thinning. Magnetic resonance imaging revealed a right extracranial bone mass extending intracranially across midline, sparing the right orbit, and compressing the left optic nerve within the optic canal. The patient underwent bilateral craniotomies for left optic nerve decompression and right skull mass resection. Pathology confirmed FD. Post-operative exams revealed a new inferior field defect OS with 20/30 vision, improved color vision, and stable OCTs at five months.

Conclusions, including unique features of the case:
Due to its slow-growing nature, 95% of FD cases with optic canal involvement remain asymptomatic with no intervention required. This report highlights craniofacial FD sparing the ipsilateral orbit but severely compressing the contralateral optic nerve, causing optic atrophy and decreased visual function, warranting surgery. Post-operatively, the vision worsened with a new visual field defect. Visual function can improve 6-12 months after decompression, and her OCT has remained stable, offering a possibility of recovery. It is also possible that vision loss was imminent regardless of decompression.

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Keywords: Optic neuropathy, Orbit, Skull base, Neuroimaging

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Contact Information: None provided.

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Outcomes of Immunotherapy Using PD-1 Inhibitors without radiation in Patients with Periocular Squamous Cell Carcinoma with Perineural Spread with Orbital and Skull Base Involvement

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Introduction:
Periocular squamous cell carcinoma (SCC) with perineural spread (PNS) and orbital and skull base involvement is challenging to treat. Historically palliative treatments with high dose radiation therapy to the orbit and skull base have been offered. Radiation therapy has a high risk of ocular toxicity. Immunotherapy (IMO) using PD-1 inhibitors is a new alternative treatment.

Description of Cases:
Methods: Eight patients with periocular SCC with PNS treated with PD-1 inhibitor therapy at a single tertiary cancer center were retrospectively reviewed. Patients who had radiation therapy concurrent with IMO were excluded. Clinical and radiologic data, duration of immunotherapy (PD-1 inhibitors), response to treatment, and follow up data were analyzed.
Results: Seven men and 1 woman, with a median age of 65 years, all had been previously heavily treated with Mohs surgery, radiation therapy, chemotherapy or a combination of these modalities prior to presenting to our center with recurrent disease in the orbit and skull base. In all 8 patients cranial nerve V1 was involved; in 2 patients the facial nerve was also involved. The PD-1 inhibitors, cemiplimab and pembrolizumab, were used in 6 patients and 2 patients, respectively. Treatment duration ranged from 2 months to 24 months (median= 12 months). In all patients measurable response on MRI was achieved. Radiation therapy was avoided in all 8 patients during the follow up period. With a median follow up time of 22 months, all patients remain without evidence of recurrence at last contact.

Conclusions, including unique features of the case:
Treatment with PD-1 Inhibitors can lead to meaningful responses in patients with periocular SCC with PNS into the orbit and skull base. The goal of treatment ideally would be avoidance of high dose radiation therapy with its inherent toxicity to the eye. Careful long-term follow up including serial imaging is needed to assess long term durability of response to PD-1 inhibitors.

References: None provided.

Keywords: Chemotherapy and radiation injury, Orbit, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Skull base, Neuroimaging

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Reaching A Diagnosis Of Ocular Lymphoma After 41 Months Of Trial And Error

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Introduction:
This case report is of an 84-year-old male who presented with suspected anterior uveitis in the left eye. Despite 41 months of exhaustive diagnostic, pharmacologic, and procedural efforts, his condition worsened and no definitive diagnosis was reached. 1,256 days after symptom onset, an unfortunate coincidental stroke prompted the critical diagnostic test to be obtained.

Description of Cases:
Initially, treatment with durezol and atropine for suspected anterior uveitis yielded limited improvement in visual acuity. TP-PA, ANA, rheumatoid factor, B27, ACE, and Lyme markers were all within normal limits. Despite further treatment with durezol, homatropine, Sub-tenon's Kenalog injection, Rituxan, IVIG for peripheral neuropathy, and Neomycin-Polymyxin B-dexamethasone, the patient's vision in his left eye continued to deteriorate. 15 months post-onset, he was seen by a retina specialist who diagnosed chronic anterior uveitis and age-related macular degeneration. Visual acuity in his left eye improved following cataract surgery, but complications arose. He was diagnosed with a central scotoma due to retained lens material. Subsequently, severe posterior segment issues developed in the left eye including disc edema, cystoid macular edema, subretinal hemorrhage, and creamy white infiltrates. CMV, VZV, HSV testing were negative. Despite various treatments including Avastin, Kenalog, Cosopt, Vigamox, Rituxan, and prednisone, the patient's condition worsened, culminating in a funnel retinal detachment in the left eye 39 months after symptom onset. Two months later, the pivotal event occurred when he suffered a stroke. A CT scan was obtained that revealed an ocular lymphoma mass behind the left eye.

Conclusions, including unique features of the case:
This case demonstrates the importance of considering a broad differential diagnosis in patients with persistent symptoms despite extensive therapeutic interventions. It highlights the potential benefits of earlier structural evaluations, such as CT scans, which could have led to a more favorable clinical outcome.

References: None provided.

Keywords: Tumors, Neuroimaging, Orbit/ocular pathology, Orbit

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Sclerotherapy in Orbital Dermoid Cysts: A Promising Minimally Invasive Approach

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Introduction:
Surgical excision has been the treatment of choice for orbital dermoid cysts but can be associated with complications and aesthetic concerns.We aim to study the efficacy and safety of sclerotherapy, a minimally invasive approach, in managing dermoid cysts.

Description of Cases:
Methods: Retrospective interventional study of 29 patients from 2019 to 2022 treated with Intralesional sclerotherapy with Sodium Tetradecyl Sulfate (STDS) 3% or neoadjuvant sclerotherapy with STDS 3% followed by surgical excision. Results: The mean age of presentation was 19.5 years. The cysts were located medial angular in 12 cases, lateral angular in 7 cases, lateral orbitotemporal in 4 cases, inferotemporal in 4 cases and inferiorly in 2 cases. Among 29 patients, 17 underwent Intralesional sclerotherapy with STDS 3% while 12 received neoadjuvant sclerotherapy with STDS followed by surgical excision. Out of 17 patients who received intralesional STDS, 13(77%) achieved complete resolution of the cyst after one cycle of treatment while 5 required two additional cycles to achieve complete resolution. Neoadjuvant sclerotherapy with STDS reduced the cyst size by a mean of 5.6mm facilitating complete excision during the surgery. At a mean follow-up of 14.6 months, all patients demonstrated complete cyst resolution was noted. No complications related to sclerotherapy were noted.

Conclusions, including unique features of the case:
Sclerotherapy represents a promising and effective minimally invasive approach in the management of orbital dermoid cysts.

References: None provided.

Keywords: Neuroimaging, Tumors, Orbit/ocular pathology, Orbit

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Grant Support: None.

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Sudden onset diplopia in a patient with a stable long standing orbital vascular malformation

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Introduction:
A 70 y/F with chronic stable lymphovenous malformations presents with sudden onset binocular vertical diplopia . Imaging shows venous malformation of the left anterior middle cranial fossa and left frontal intraosseous venous malformation.

Description of Cases:
A 70 y/F with PMH of CKD, HTN, and arthritis, presented with acute onset diplopia in the setting of a longstanding left orbital venous malformation, diagnosed in childhood. Upon waking up, on 9/8/2023 she noticed painless binocular diplopia in right superior gaze. She attributed this to taking 1mg Lorazepam the previous night. She visited the ER on 9/9/23 and presented to our clinic on 9/19, already noticing some improvement. On examination VA was 20/30 OD and 20/40 OS, both pinhole to 20/20. IOPs were normal , and colors were full . No APD. The external examination revealed pulsatile exophthalmos and a 3mm lid lag OS . EOMS were full with a 2-3 PD RHT in upgaze. Examination revealed +2 left conjunctival injection and a long standing vascular malformation nasally. Nerves were small crowded, cupless with sharp margins and temporal PPA OU. There were drusen and RPE changes OU, and venous tortuosity OS. Neurologic exam was non-focal. MRI shows multiple left-sided venous anomalies with prominent enhancing structures in the anterior left middle cranial fossa which may relate to venous malformation. Left frontal intra-osseous venous malformation, also involving the left orbit. MRV shows Focal hypoenhancement in the far lateral left transverse sinus and at the junction of the left sigmoid and transverse sinus. These likely relate to arachnoid granulations although focal thrombus is possible

Conclusions, including unique features of the case:
Diagnostic dilemma: The differential for this patient's diplopia includes her known longstanding orbital venous malformation, dural AVM, CCFistula, cavernous sinus thrombosis, microvascular cranial neuropathies, or decompensated phoria. Chronic long standing lesions can develop sudden onset symptoms

References: None provided.

Keywords: Adult strabismus with a focus on diplopia, Neuroimaging, Ocular motility

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Contact Information: None provided.

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Surgical Theatre as a 3D Virtual Imaging Real Time Navigation System in Orbito-Cranial Surgery

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Introduction:
Neuro-navigation systems provide intraoperative 3-dimensional localization correlated to MRI, CT, and angiographic imaging in the axial, coronal, and sagittal planes. Surface contours or designated anatomic points are registered in 3-dimensional space against a location detector fixed to a head immobilization frame. An infrared registered navigation probe drives localization of the surgical area of interest into X, Y and Z axis reference planes that correspond to axial, coronal, and sagittal neuroimages available on an external monitor. The use of traditional neuro-navigation can be time consuming, labor intensive, and may only offer limited utility in "straightforward" orbital surgery.

Description of Cases:
Case presentation and review of videos in four consecutive deep orbital, cranial, or orbito-cranial cases using images and video that highlight virtual imaging and navigational capability based on microscope plane of focus rather than secondary probe or instrument. Surgical Theatre is a modular "add-on component" which augments the capabilities of several modern, advanced commercially available navigation and operative microscope systems. The sequential case series demonstrates the components of the system and provides examples of (1) virtual real time operative planning and modeling capability, (2) real time navigation generated by the projected plane of focus of the operating microscope, and (3) virtual 3D real- time image projection of selected anatomical areas into the operating microscope binocular for surgeon reference. To our knowledge this represents the first described use of this platform in orbital surgery. Enhanced navigation and visualization features may be of particular value in a surgical education setting.

Conclusions, including unique features of the case:
Surgical videos demonstrate a consecutive four case series and an orbital surgeon's consecutive experience using an add on navigational platform in increasingly complex cases. The system provides the opportunity to increase operative safety, efficiency and outcomes in selected deep orbital and orbito-cranial cases and enhance surgical education in orbital surgery.

References: None provided.

Keywords: Orbit, Tumors, Neuroimaging

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Teprotumumab Induced Adrenal Insufficiency: A Case Report

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Introduction:
We report a case of adrenal insufficiency in a patient who had been receiving teprotumumab infusions for the treatment of thyroid eye disease. To our knowledge, this is the first case report of adrenal insufficiency as a side effect of teprotumumab.

Description of Cases:
A 70-year-old female patient presented to our clinic for evaluation and treatment of binocular diplopia due to thyroid eye disease. After teprotumumab was initiated, the patient experienced intractable nausea and vomiting leading to significant weight loss while receiving the treatment. The patient experienced a 49.2% decrease in weight from baseline. However, after completing her 8th session of teprotumumab, severe nausea and vomiting persisted up until 6 months after. Work up for causes of nausea and vomiting were unremarkable. Adrenal insufficiency was diagnosed after finding low morning cortisol levels and prednisone was subsequently prescribed. After taking PO prednisone, the patient reported improved symptoms. Ophthalmic exam showed improved symptoms and resolved diplopia which remained stable until her last follow up 1.5 years after initiation of the infusion.

Conclusions, including unique features of the case:
Ophthalmologists providing teprotumumab for treatment of thyroid eye disease should be aware of adrenal insufficiency as a possible side effect and provide steroid replacement as needed.

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Keywords: Graves' disease, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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26
Unusual Cases Of Orbital Inflammation

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Introduction:
Orbital inflammation represents 11% of orbital diseases and can affect individuals of all ages and genders (1, 2). It leads to a range of symptoms, including periorbital pain, proptosis, diplopia, palpable periorbital mass, eyelid ptosis, and more (3). Etiologies vary and can include inflammatory, infectious and neoplastic conditions. We present a case series of atypical causes of orbital and perineural inflammation.

Description of Cases:
Case 1: A 40-year-old female presented with blurry vision and right eye periorbital edema. Examination revealed reduced right eye elevation; MRI showed soft tissue thickening around the right superior rectus muscle. Biopsy indicated non-specific inflammation. Elevated TSH receptor autoantibodies (TRAB) led to a diagnosis of euthyroid Graves involving monocular superior rectus muscle. Case 2: A 12-year-old female experienced intermittent left eye swelling, pain, and tearing. Examination revealed impaired left eye adduction. Imaging confirmed posterior scleritis and optic perineuritis. CT chest was suggestive of sarcoidosis. Case 3: A 68-year-old woman with osteoporosis on alendronate presented with right eyelid edema, pain, blurry vision, and binocular diplopia. Examination revealed elevation and abduction deficits. Imaging showed proptosis and orbital inflammation. Exclusion of other causes led to the diagnosis of bisphosphonate-induced orbital inflammation. Case 4: A 58-year-old man had a seven-month history of right eye eyelid swelling, ptosis, and pain. Examination showed bilateral ptosis, periorbital edema, and proptosis of the right eye. Imaging revealed bilateral intraocular muscle enlargement. Biopsies confirmed eosinophilic orbital myositis.

Conclusions, including unique features of the case:
Orbital inflammation presents with a wide range of symptoms. A comprehensive review of medical history, thorough physical exams, specific tests, and imaging can help establish preliminary diagnoses. Biopsy is necessary for atypical presentations and inconclusive tests. A multidisciplinary approach is crucial for managing these complex cases.

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Keywords: Orbit, Neuroimaging, Orbit/ocular pathology, Graves' disease, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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Fenestrations and PHOMS – Acutely Changing the Shape in Time

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Introduction:

Optical coherence tomography (OCT) is a non-invasive imaging technique that can aid in assessing papilledema by identifying elevation of the optic nerve head, peripapillary retinal nerve fiber layer, and deflections of Bruch's Membrane (BM).1 Peripapillary hyper-reflective ovoid mass-like structures (PHOMS) are seen on OCT deflecting at least two overlying retinal layers at the edge of BM and are thought to represent axoplasmic stasis of the optic nerve.2 PHOMS has been associated with disc-edema in papilledema, NAION, ODD and anomalous discs, although its prevalence in the general population and clinical significance have yet to be determined.3,4 Patients with elevated ICP have up to an 80% prevalence of PHOMS.5 In those with PTC, weight loss and acetazolamide affect the size and location of PHOMS over time.6 Optic nerve sheath fenestration (ONSF) is a surgical intervention that acutely reduces perioptic ICP. Given the relationship of PHOMS with papilledema, we evaluated the presence and appearance of PHOMS after ONSF.

Description of Cases:

Thirty-five eyes of twenty-three patients were reviewed before and after ONSF. Clinical information, the ocular examination, Humphrey visual fields (HVF), and serial OCTs were obtained pre- and post-operatively. Blind evaluation of each OCT was performed by two evaluators trained in PHOMS imaging, with a third evaluator to resolve disagreements. PHOMS were detected in 15 eyes pre-operatively and 20 eyes post-operatively. Changes in morphology and location were seen post-operatively, with the nasal quadrant being the most common. The post-operative detection of PHOMS did not impact visual acuity, RNFL thickness, optic disc edema, or visual field mean deviation.

Conclusions, including unique features of the case:

Our findings suggest changes in PHOMS morphology post-ONSF appear to occur. PHOMS were detected post-fenestration when not clearly visible pre-operatively in patients with severe papilledema. While OCT aids in PHOMS detection, accurately identifying and quantifying their morphology and size over time remains a challenge.

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Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), High intracranial pressure/headache, Pseudotumor cerebri, Visual fields

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Contact Information: None provided.

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Fluorescein Angiography in Internal Carotid Artery Dissection

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Introduction:
Internal Carotid Artery Dissection is an important cause of ischemic stroke in young patients and must be recognized and managed promptly to prevent devastating complications. Ocular manifestations of carotid artery dissection include ischemic optic neuropathy, retinal vascular occlusions, cranial nerve palsies, Horner's syndrome, and ocular ischemic syndrome.

Description of Cases:
33-year-old Caucasian female presented with acute onset graying of vision in her left eye. She reported decreased color saturation and jaw and neck pain. Her visual acuity was 20/20 bilaterally, with no relative afferent pupillary defect or extraocular motility restriction. Her color plates were normal, but with 10% red desaturation in the left eye. Dilated eye examination was unremarkable with no evidence of optic nerve swelling or retinal hemorrhages. General neurologic exam and strabismus testing were normal. MRI/MRA revealed a left internal carotid artery dissection with near occlusion of the left carotid. Fluorescein Angiography demonstrated normal right eye perfusion. FA in the left eye demonstrated subtle patchy choroidal filling and significant late retinal vascular leakage and optic nerve leakage in the left eye. There was no significant delay in choroidal or retinal artery filling.

Conclusions, including unique features of the case:
We present a unique case of a patient with acute ocular ischemia from internal carotid artery dissection. Despite a normal funduscopic examination, the patient had evidence of diffuse late leakage on fluorescein angiography without significant delay in choroidal and retinal vascular perfusion. It is important for clinicians to be aware of the diverse presentation of acute fluorescein changes in the setting of acute carotid artery insufficiency in order to appropriately diagnose and manage these critical patients. These include not only delays in choroidal perfusion and prolonged retinal arteriovenous filling times but also may include isolated retinal vascular leakage in keeping with ischemic endothelial dysfunction with increased vascular permeability.

References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Orbit/ocular pathology, Retina, Vascular disorders

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Contact Information: None provided.

29
Positive Diffusion Weighted Imaging (DWI) of Optic Nerve

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Introduction:
Diffusion restriction of the optic nerve has been reported in cases of optic neuritis, infiltrative optic neuropathy, ischemic optic neuropathy due to giant cell arteritis, and perioperative ischemic optic neuropathy. We review the literature on positive DWI of the optic nerve and report a rare case of orbital infarction syndrome due to common carotid artery occlusion.

Description of Cases:
A 60-year-old with hyperlipidemia, remote deep venous thrombosis/pulmonary embolism, and multiple myeloma presents with acute vision loss OS. He denies preceding transient vision loss or diplopia. He reports 1 day of headaches, scalp tenderness and jaw claudication, with weight loss over the past year. He denies any fevers. Examination shows visual acuity of 20/25 OD and NLP OS. His right pupil is brisk and his left pupil is non-reactive to direct and consensual with a 4+ APD OS. Intraocular pressure is 12 mm Hg OD and 5 mm Hg OS. Motility is normal OD with diffuse ophthalmoplegia OS and 35 prism diopters of exotropia. He has 2 mm proptosis OS with lid edema and ptosis. He has left conjunctival injection, corneal edema, and anterior chamber cell. Posterior exam shows pallid disc edema OS and diffuse retinal whitening without cherry red spot with severe arteriolar attenuation. His ESR is 11 and CRP is 27 (elevated). Contrast MRI brain and orbits shows no orbital apex/sphenocavernous lesion and no optic nerve enhancement. The left optic nerve is bright on DWI and dark on ADC. Left temporal artery biopsy is negative. MRA head/neck show non-opacification of left common carotid artery from its origin.

Conclusions, including unique features of the case:
Common carotid artery occlusion is very rare but should be considered in setting of orbital infarction syndrome. Positive DWI of the optic nerve due to orbital ischemia can be present in absence of cerebral ischemia due to rich collateral supply through Circle of Willis.

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Keywords: Neuroimaging, Optic neuropathy, Orbit, Vascular disorders

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The Eye That Wandered: A Three-Decade Odyssey, A Case Study

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Introduction:
Optic nerve sheath meningiomas (ONSM) are rare, benign intracranial tumors that originate from the meninges surrounding the optic nerve. While ONSM's imaging hallmark is perineural enhancement and calcification, their clinical presentation can be variable, ranging from asymptomatic cases to progressive vision loss. Diagnosing ONSM remains challenging due to the diversity in symptoms, and at times they may mimic other orbital conditions.

Description of Cases:
A 48-year-old woman with a history of recurrent episodes of left-sided eye pain, ophthalmoplegia, and double vision over three decades was evaluated for another episode of her left-sided ocular symptoms. Past episodes had been variably diagnosed, with resolution of symptoms with steroids for presumed Idiopathic Orbital Syndrome. Presenting examination revealed visual acuity of 20/40 OD and 20/100 OS, a left afferent pupillary defect, slight proptosis OS, and impaired ocular motility OS. Fundus exam showed pallor of the left optic nerve but otherwise unremarkable. Labs revealed elevated WBC 18.44, glucose 219, and a slightly elevated IgG4 89.2 (lower than the threshold serum level for IgG4-related ophthalmic disease). CT and CTA of the head and neck demonstrated perineural calcification near the left optic nerve with a positive "tram-tracking" sign. Contrast enhanced MRI head and orbit displayed abnormal enhancement of the optic nerve sheath, suggestive of ONSM, though the episodic nature of symptoms remained an unusual feature. Initial treatment of high-dose IV steroids showed gradual improvement of symptoms and visual acuity over three days.

Conclusions, including unique features of the case:
This case emphasizes the complexities in diagnosing ONSM with atypical presentations. Despite certain indications towards Idiopathic Orbital Inflammation, the discovery of perineural contrast enhancement and calcifications of the optic nerve sheath suggested ONSM. Literature review revealed a similar case of ONSM imitating orbital inflammatory syndrome. This case serves as a reminder of the importance of a thorough investigation when confronted with unconventional symptom presentations in orbital diseases.

References: None provided.

Keywords: Tumors, Neuroimaging, Orbit/ocular pathology

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Grant Support: None.

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31

"Oscillopsia as a Diagnostic Clue in GAD Antibody Neurological Disorder: The Significance of Neuro-Ophthalmology in Unusual Presentations."

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Introduction:
Glutamic acid Decarboxylase (GAD) antibodies-related neurological disorders linked to presentations like stiff person syndrome, cerebral ataxia, and limbic encephalitis. [1] We report a patient with a recent diagnosis of seizures experiencing persistent oscillopsia with no cerebellar signs except nystagmus, which led to a diagnosis of GAD neurological disorder.

Description of Cases:
A 54-year-old woman who has a recent history of seizures and is taking levetiracetam has reported new symptoms of positional dizziness, oscillopsia, and nausea that have persisted for several weeks. She was previously healthy with no other medical or psychiatric history. Neuro-ophthalmic examination revealed a horizontal end point anticlockwise torsional nystagmus on the right gaze with an otherwise normal neurological exam. Contrasted brain magnetic resonance imaging was unremarkable. Vestibular testing did not reveal evidence of peripheral vestibular dysfunction. Extensive serological testing for infectious, nutritional, and abusive drug etiologies was negative. The serum autoimmune panel showed high antibody titers of anti-GAD65 (1789 nmol/L). Whole-body imaging showed no evidence of malignancy. She started experiencing memory problems and was noted to develop cognitive dysfunction. Immunotherapy was initiated with monthly combined intravenous immunoglobulin and methylprednisolone infusions for three cycles with noted symptomatic improvement and subsequently managed with Rituximab infusions and multiple antiseizure medications for refractory epilepsy.

Conclusions, including unique features of the case:
This case study illustrates a distinctive manifestation of anti-GAD antibody-related neurological disorder, highlighting the pivotal significance of a comprehensive neuro-ophthalmic examination. This examination is critical in facilitating early diagnosis, emphasizing the importance of proactive and aggressive management strategies to achieve favorable patient outcomes.

References: None provided.

Keywords: Nystagmus, Paraneoplastic syndromes, Nystagmus

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32
Acetazolamide-responsive daily episodic diplopia in the morning

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Introduction:
Diplopia, or double vision, arises from various etiologies. Acetazolamide-responsive ataxia typically presents with episodic ataxia, dysarthria, nausea/vomiting, and occasionally diplopia or tinnitus. In this report, we describe a patient who experienced daily episodes of diplopia every morning, which improved after acetazolamide administration.

Description of Cases:
A 32-year-old woman presented to the neurology department with daily episodes of vertical diplopia for approximately one year. The diplopia occurred every morning upon awakening, lasted for about two hours, and then gradually resolved. She reported no associated symptoms such as dysarthria, gait disturbance, headache, or nausea/vomiting during these episodes. It only manifested after a night's sleep. She had no notable medical or family history. A neurologic examination at 8 a.m. revealed left hypertropia in the primary position and underaction of the left superior oblique. Pupillary responses were normal, being isocoric and light-reactive. All other cranial nerve examinations were unremarkable. Sensory, motor, and cerebellar functions appeared normal. At 4 p.m., a neurologic examination revealed the improvement of her left hypertropia, with no diplopia observed across all nine cardinal positions. Brain MRI results were normal. Funduscopy revealed extorsion of the left eye (17.28') and the right eye (21.82'). Comprehensive blood tests were all within normal limits. Repeated nerve stimulation tests also showed no abnormalities. Trialing pyridostigmine (60mg thrice daily) did not alleviate the diplopia and caused abdominal discomfort. However, upon initiating acetazolamide (250mg twice daily), her diplopia resolved within two days. Discontinuing acetazolamide for three days led to the return of her morning diplopia. Ataxia next-generation sequencing (NGS) panel testing found no abnormalities.

Conclusions, including unique features of the case:
Administration of acetazolamide, a carbonic anhydrase inhibitor, results in decreased regional brain pH and altered electrolyte channel function. While the genetic background in this case remains undetermined, acetazolamide proved effective against episodic morning diplopia. Thus, for similar cases, acetazolamide presents a readily triable therapeutic option.

References: None provided.

Keywords: Ocular motility, Adult strabismus with a focus on diplopia, Miscellaneous

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33

An unusual case of Diffuse ophthalmoplegia and ptosis: Myasthenia, CPEO or Something Else?

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Introduction:
Diagnosis of diffuse ophthalmoplegia often involves localization and work up to rule out a broad differential diagnosis. This unusual case presents a patient with progressive ophthalmoparesis secondary to Oculo-pharyngo-distal myopathy (OPDM).

Description of Cases:
A 72-year-old female presented with gradually progressive ptosis in both eyes (BE) and bilateral diffuse limitation of eyes movements after using Primidone for essential tremor from few months prior. Medical history was significant for Diabetes and Hypothyroidism from 6 months prior. She did have mild ptosis in both eyes since adulthood, however it worsened recently. On external examination, she had severe ptosis with Marginal reflex distance (MRD1) of -3 in BE, frontalis overaction, chin elevation, and -4 limitation of all ductions in BE. Snellen visual acuity was 20/25 in BE and fundus examination was normal. Clinical examination showed positive fatigue test but Ice test was negative. A provisional diagnosis of Ocular myasthenia was considered. Serum Acetyl choline receptor antibodies were borderline positive (0.40) and repetitive nerve stimulation test were negative. Neostigmine test showed a worsening response. A therapeutic trial of oral steroids, pyridostigmine, and azathioprine did not show any improvement. A differential diagnosis of chronic progressive ophthalmoplegia and mitochondrial myopathy were considered. Genetic analysis for ophthalmoparesis panel was ordered and the patient was found to be positive for RILPL1 gene which is reported to cause Oculo-pharyngodistal myopathy (OPDM4) characterized by ptosis, ophthalmoparesis, facial atrophy, swallowing, speech difficulties, weakness of extremities and respiratory muscles. Later the patient described a similar history of late onset ptosis in the patients mother.

Conclusions, including unique features of the case:
This case describes a rare case of progressive ptosis, ophthalmoparesis, and tremors all of which have been reported with a rare disorder called oculopharyngodistal myopathy. There was diagnostic dilemma as the acetylcholine receptor antibodies were borderline and fatigue test was positive, but there was no response to myasthenia treatment

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Keywords: Genetic disease, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Myasthenia

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Artificial Intelligence Evaluation: Etiology of Third, Fourth, and Sixth Cranial Nerve Palsies

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Introduction:
The ability of artificial intelligence (AI) to provide accurate diagnoses is being tested throughout the medical field. AI is an innovative tool that has significant potential to improve patient care. ChatGPT is one such modality which allows a user to provide a text prompt and receive an output. Through this AI platform there is potential for improvement of medical diagnoses and treatment.

Description of Cases:
ChatGPT-3.5 and Neuro-Ophthalmology Virtual Education Library (NOVEL) were utilized. A prompt was inputted into ChatGPT. The prompt clarified the subject as a “Neuro-Ophthalmologist” and asked for the top three differentials in order of most to least likely for the entered case. Case report information was inputted into ChatGPT including neuroimaging reports with omission of finalized pathology and overall eventual diagnosis. Search terms used in NOVEL for each palsy were entered as such ("third nerve palsy" AND "case report") OR ("3rd nerve palsy" AND "case report"). Date range for cases was 1980-2023. Of the 12 cases of third nerve palsy the correct diagnosis was determined (6/12) with (5/12) being the 1st differential and (1/12) being the 2nd differential. Of the 10 cases of fourth nerve palsy, the correct diagnosis was determined (7/10) with (6/10) being the 1st differential and (1/10) being the 2nd differential. Lastly, of the 10 sixth nerve palsies (8/10) were diagnosed by ChatGPT, with (8/10) being the first differential.

Conclusions, including unique features of the case:
We sought to assess the diagnostic accuracy of ChatGPT in ocular nerve palsies. ChatGPT was able to predict as first differential diagnosis 42% of third nerve palsies, 60% of fourth nerve palsies, and 80% of sixth nerve palsies. ChatGPT and other AI software offers not only the Neuro-Ophthalmologist but also primary care providers another strategy to provide optimal patient care. Future projects are needed to test AI in real time encounters of suspected ocular nerve palsies.

References: None provided.

Keywords: Ocular motility, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Miscellaneous

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Benedikt Syndrome, A Case Report

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Introduction:
Although midbrain syndromes have been documented since their initial descriptions in the 19th century, very few cases have been described in the literature. Benedikt syndrome is a rare midbrain syndrome characterized by ipsilateral oculomotor palsy, contralateral hemiparesis and contralateral involuntary movements or tremor.

Description of Cases:
An 80-year-old man presented with a new sudden onset of horizontal diplopia. Neurological examination was significant for a sluggish left pupil, left exotropia and hypotropia in primary gaze, left upper-eyelid ptosis, and limited adduction, elevation, and depression of the left eye. There was mild right hemiparesis and mild ataxia of the right arm. The initial head CT without contrast was unremarkable. However, brain MRI with and without contrast revealed acute infarcts within the left medial midbrain and left frontal lobe periventricular white matter due to embolic breakthrough strokes in the setting of atrial fibrillation. The patient was restarted on apixaban 5 mg twice daily and other secondary stroke prevention. He was discharged to an acute rehabilitation facility, and three weeks later his right sided weakness had improved. However, his left 3rd cranial nerve palsy and right sided ataxia remained unchanged.

Conclusions, including unique features of the case:
Small changes in structural integrity may lead to a wide variety of clinical presentations, with some potentially presenting more subtly than others. Therefore, a thorough neurological examination is necessary to diagnose these syndromes.

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Keywords: Adult strabismus with a focus on diplopia, Ocular motility, Neuroimaging, Stroke

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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36

Bilateral ptosis, internuclear ophthalmoplegia, and trochlear palsy from midbrain stroke

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Introduction:
Bilateral ptosis is an uncommon clinical feature of stroke. The central caudal nucleus innervates both levator palpebrae superioris muscles. The oculomotor subnuclei to the superior rectus and medial rectus are located adjacent to the central caudal nucleus. This is clinically significant because the differential diagnosis for bilateral ptosis is broad, often including neurogenic conditions (such as myasthenia gravis), aponeuritic, myogenic, and congenital etiologies.

Description of Cases:
A 38-year-old woman presented to an outside emergency department with acute onset bilateral ptosis, vertigo, and constant binocular oblique diplopia. Her past medical history was notable for endometriosis on norethindrone, a prior miscarriage, and hypertension. She underwent a stroke work-up and was found to have a left medial midbrain ischemic infarction on her MRI. There was no large vessel occlusion seen on her imaging, so she did not receive thrombolytics. By her follow-up visit 3 months later, her ptosis had resolved, but she had right trochlear nerve palsy and a left internuclear ophthalmoplegia. These findings are in keeping with her lesion of the left trochlear nerve nucleus and medial longitudinal fasciculus (which are adjacent to one another in the midbrain).

Conclusions, including unique features of the case:
Although rare, bilateral ptosis can occur with a lesion of the oculomotor nucleus. In addition, my patient had an internuclear ophthalmoplegia and a contralateral trochlear nerve palsy. This latter finding is due to the decussation of the trochlear nerves within the brainstem.

References: 1. Vanooteghem P, Dehaene I, Van Zandycke M, Casselman J. Combined trochlear nerve palsy and internuclear ophthalmoplegia. Arch Neurol. 2006;49(1):108-9. 2. Saeki N, Yamaura A, Sunami K. Bilateral ptosis with pupil sparing because of a discrete midbrain lesion: magnetic resonance imaging evidence of topographic arrangement within the oculomotor nerve. J Neuroophthalmol. 2000;20(2):130-4. 3. James S, Thozhuthumparambil KP. Brainstem stroke presenting as isolated bilateral ptosis. BMJ Case Rep. 2021;14(7):e243220. 4. Xie N, Sun Q. Bilateral ptosis caused by patent foramen ovale. QJM. 2022;115(12):863-854.

Keywords: Stroke, Adult strabismus with a focus on diplopia, Ocular motility

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Cogan Lid Twitch sign in Miller Fisher Syndrome

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Introduction:
Cogan lid twitch sign is a transient upper eyelid overshooting, which is elicited by gazing downward for a few seconds and then returning to primary gaze. Since it has been proposed to be related to the initial fatigability, followed by rapid recovery of the levator muscle, the Cogan lid twitch sign has been considered characteristic sign of myasthenia gravis (MG). However, recent studies have reported Cogan lid twitch sign in association with other diseases, such as Miller-Fisher syndrome (MFS), myopathic disease, or dorsal midbrain lesions. We report a patient with MFS who presented with ophthalmoplegia and fatigable ptosis accompanied by Cogan lid twitch sign.

Description of Cases:
A 75-year-old man presented with an acute onset of diplopia, ptosis, and unsteadiness for 2 days. He had a history of upper respiratory infection one week ago. At admission, neuro-ophthalmological examinations revealed bilateral ophthalmoplegia and asymmetric bilateral ptosis, more on the right side. The ptosis showed a fatigability which deteriorated during upward gaze and improved at rest. After several seconds of downward gaze, right upper eyelid briefly twitched upward on returning to primary gaze. Other findings included dysarthria, bulbar palsy, areflexia, limb and truncal ataxia. The tests for MG such as pyridostigmine test, anti-acetylcholine antibody titer, and Jolly test were all negative. Brain MRIs were unremarkable. Cerebrospinal fluid was acellular with mildly increased protein concentration. Serum anti-GQ1b and GT1b antibodies were positive, supporting a diagnosis of MFS. He was treated with intravenous immunoglobulin for 5 days. At 2-month follow examination, the ptosis and unsteadiness gradually improved, but the ophthalmoplegia was still present.

Conclusions, including unique features of the case:
Our case demonstrated that Cogan lid twitch sign can be observed in MFS other than MG. Therefore, it is important not to jump into conclusion when diagnosing patients with Cogan lid twitch sign, and careful differential diagnosis is needed.

References: None provided.

Keywords: Ocular motility

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Diagnostic Workup of Oculomotor Nerve Schwannomas: A Case Series of Six Patients

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Introduction:
Oculomotor nerve schwannomas are a rare but important cause of persistent, recurrent, or atypical cranial nerve III (CN3) palsies (1,2). The goal of this case series is to describe the presentation, neuro-imaging findings, and workup of oculomotor nerve schwannomas.

Description of Cases:
Six patients with radiologically confirmed oculomotor schwannomas followed at two North American neuro-ophthalmology practices were included. Five patients were female and age ranged from 22 to 77; none had a history of neurofibromatosis. Two patients had recurrent episodes, occurring 4 and 7 times, respectively. Two patients had single defined episodes. Each episode lasted 1-4 weeks. Two patients had a persistent course. Five patients had ptosis, three had anisocoria, and all had motility disturbances. Patients underwent a plethora of imaging prior to final diagnosis, including a total of 6 unenhanced CTs, 5 CT angiograms, 8 MRIs, and 5 MR angiograms. In those with a recurrent course, there was a 14-15 year diagnostic delay. Mean time to diagnosis in the remaining patients was 4.6 months. Standard enhanced MRI brain/orbits was sufficient for diagnosis in all cases. Three schwannomas were purely cisternal, one was cisternal/intracavernous, and two were intracavernous/intraorbital. All but one of the schwannomas enhanced. Two patients were tested for acetylcholine receptor antibodies, one underwent sfEMG and edrophonium testing, and two were checked for giant cell arteritis, with one patient undergoing three temporal artery biopsies.

Conclusions, including unique features of the case:
A high level of suspicion must be maintained for oculomotor nerve schwannomas in patients presenting with CN3 palsy. After ruling out posterior communicating artery aneurysm, MRI brain/orbits with gadolinium should be ordered in every patient with recurrent, persistent, or atypical CN3 palsy (1,2,3). Based on our series of six patients, diagnostic delay is especially prominent (over a decade) in patients with recurrent presentations mistaken for myasthenia gravis, giant cell arteritis, or ophthalmoplegic migraine (1).

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Keywords: Tumors, Neuroimaging, Ocular motility

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Contact Information: None provided.

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Etiology and clinical features of oscillopsia:29 cases report.

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Introduction:
Although oscillopsia is a visual symptom, it is more caused by eye movement system, optokinetic system and vestibular system disease, which involves the intersection of neuro-ophthalmology and neuro-otology. It can be a sequelae or an isolated manifestation of a disease, but it affects the visual function and quality of life of patients.

Description of Cases:
A total of 29 patients with oscillopsia were collected in this study, with an average age of 45.8±13.4 years old. 89.7% (26/29) had persistent symptoms and 10.3% (3/29) had non-persistent symptoms. 79.3% (23/29) were caused by different types of nystagmus, among which downbeat nystagmus was the most common (17 cases, which was caused by craniocervical junction compression, medullary vascular malformation, SCA, GAD or idiopathic DBN), periodic alternating nystagmus (1 case was caused by trauma, no causes was found in the other two cases), acquired pendular nystagmus (caused by stroke or optic neuritis) and pendular seesaw nystagmus (caused by chiasmatic compression) were 3 cases, 2 cases and 1 case, respectively. 10.3% (3/29) were caused by saccadic intrusion, 6.9% (2/29) by bilateral vestibular loss, and 3.4% (1/29) by unilateral superior oblique myokymia. 48.3% (14/29) of the patients were improved by symptomatic treatment, such as gabapentin,baclofen, clonazepam or immunotherapy.

Conclusions, including unique features of the case:
The most common cause of oscillopsia is different types of acquired nystagmus, also seen in bilateral vestibular loss, saccadic intrusion, and superior oblique myokymia. The recognition of different types of eye movement abnormalities is helpful for the localization and differential diagnosis, and some patients can benefit from symptomatic treatment. This group of cases is presented from the perspective of the clinical symptom of Oscillopsia, which is helpful for clinicians to understand the differential diagnosis that leading to this symptom.

References: None provided.

Keywords: Demeylinating disease, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Nystagmus, Ocular manifestations of vestibular disorders, Ocular motility

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Eye Movement Characteristics of Congenital Myasthenic Syndromes

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Introduction:
Congenital myasthenic syndromes (CMS) are a group of inherited disorders caused by gene variants leading to impaired transmission at the neuromuscular junction.1, 2 The gene CHRNE encodes the subunit of the pentameric acetylcholine receptor and pathogenic variants commonly cause CMS.3, 4 While patients with CMS can present similarly to those with acquired myasthenia gravis (MG), including fatigable weakness and oculo-bulbar symptoms, CMS can also closely mimic congenital myopathies or congenital cranial dysinnervation disorders (CCDDs). Detailed ocular motor descriptions of CMS are rare. We describe the efferent findings in a patient with CMS.

Description of Cases:
A 38-year-old woman was initially referred for a possible CCDD since her mother had Duane syndrome. Her diagnosis was unclear, although CCDD was deemed unlikely. She re-presented 5 years later after she was found to have the homozygous pathogenic variant CHRNE c.1353dupG:p.(N452Efs*4). She had a history of childhood-onset ptosis, diplopia, and ophthalmoparesis, tending to move her head rather than eyes to survey the environment. Motility range was impaired in all gaze directions. Saccades were slow and hypometric in both horizontal and vertical directions clinically and by infrared-oculography (Eyelink 1000+, SR Research). Ptosis was present bilaterally (palpebral fissures 6mm R and 5mm L). Curtain sign and Cogan's lid twitch were present. Afferent exam was unremarkable.

Conclusions, including unique features of the case:
We highlight a key distinction between CMS and MG. Despite reduced range of motion, saccades in MG have similar or increased peak velocities compared to normal individuals.5, 6 Furthermore, horizontal saccades in MG tend to have late-course disconjugacy, in contrast to other motility disorders.7 Our patient with CMS had slowed saccades on examination and infrared-oculography. Our case highlights that saccade velocities may help differentiate between MG and CMS and emphasizes the importance of a detailed neuro-ophthalmologic examination including quantitative measurements of saccadic velocities in the evaluation of these disorders.

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Keywords: Genetic disease, Ocular motility

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Infantile Nystagmus Syndrome Phenotypic Variability In A Family With FRMD7 Mutation

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Introduction:
Infantile nystagmus syndrome (INS) is a genetically heterogeneous disorder. It may be associated with afferent visual disorders (e.g., ocular albinism) or neurologically/ophthalmologically isolated, idiopathic infantile nystagmus (IIN). Horizontal pendular nystagmus is classic, though jerk waveforms occur. FRMD7 (X-chromosome) causes approximately 50% of IIN. FRMD7 protein is expressed in developing ocular motor structures, including the cerebellum and vestibular nucleus. We describe a family with the FRMD7 C741+2 T>G mutation with phenotypic variability.

Description of Cases:
Patient 1: 38-year-old woman, nystagmus documented age 12. Exam: left-beat jerk nystagmus (LBN) centrally, high-amplitude/high-frequency right beat (RBN) in right gaze, and low-amplitude/high-frequency LBN in left gaze (pseudo-Bruns pattern). Eye-tracking revealed pseudojerk, pseudocycloid, pseudopendular waveforms and intermittent LBN centrally. Patient 2: 44-year-old woman, nystagmus documented age 30, patient 1's sister. Exam: trace RBN centrally, increased in right gaze with trace upbeat/LBN in left and vertical gaze, with minimal pendular vertical component. Nystagmus amplitude was much smaller than patient 1. Patient 3: 11-year-old boy, nystagmus documented age 2 months, patient 2's son. Exam: pendular horizontal nystagmus with foveating saccades in all gaze directions. In left gaze, LBN component. No patient had oscillopsia, a definite null point, or latent component.

Conclusions, including unique features of the case:
These patients demonstrate intra-family INS phenotypic variability from a single FRMD7 mutation. Patients 1 and 2 were diagnosed later than typical in INS. While pendular nystagmus is the most classic waveform, it was only noted in patient 3; the father of patient 1&2 had pendular nystagmus. Patient 1 exhibited a pseudo-Bruns pattern with no pendular component. Though absent oscillopsia suggests INS, nystagmus features could be mistaken for acquired nystagmus without proper history, eye tracking, and genetic testing. While intra-family differences in nystagmus phenotype are described, eye-tracking in our patients illustrates the striking differences in appearance of INS from the same mutation and highlights related waveform features.

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42

Like Clockwork: A Case Report on a Presumed 24-Hour Cyclic Esotropia

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Introduction:
Cyclic esotropia (CE) is a rare disorder characterized by periods of strabismic esotropia alternating with binocular alignment over a specific time interval. The cyclic pattern most often occurs over a 48-hour period but can also present over a 24-hour period. This phenomenon reportedly occurs in one of every 3,000 to 5,000 cases of strabismus. Proposed pathophysiology includes central nervous system dysregulation affecting oculomotor function and/or circadian fluctuation of a sixth nerve palsy.

Description of Cases:
An 8-year-old girl presents for her annual eye examination with a complaint of diplopia that occurs daily upon waking for the past four years. Her father reports that her eye turns inward towards her nose only in the mornings, but never in the afternoons or evenings. Several examinations and photo-documentation over various times of day confirm a pattern of 24-hour cyclic esotropia. Her esodeviation changes from a 55 pd esotropia in the morning to a 16 pd esophoria in the evening. Work up, including an MRI of the brain and orbits and labs for juvenile myasthenia gravis and thyroid dysfunction, is ordered to rule out secondary causes, after which surgical correction can be considered.

Conclusions, including unique features of the case:
Cyclic esotropia should be in the differential diagnosis for cases of intermittent diplopia. We approached the case with serial photographs and examinations of binocular status which aided in the diagnosis of a 24-hour cyclic esotropia. Prompt diagnosis and surgical management can preserve stereoscopic vision in children with this condition.

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Keywords: Ocular motility, Pediatric neuro-ophthalmology

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Lyme Neuroborreliosis Presenting As Isolated Horizontal Jerk Nystagmus

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Introduction:
Lyme neuroborreliosis (LNB) refers to central and peripheral nervous system infection by the spirochete Borrelia Burgdorferi. (1) LNB rarely presents as an eye movement disorder. (2-4) We present a case of horizontal nystagmus signifying the first manifestation of LNB in an adult.

Description of Cases:
A 50-year-old male presented with one day of acute-onset oscillopsia, nausea and vomiting, and difficulty ambulating. His ocular symptoms were worse in right gaze and improved in left gaze. He reported an antecedent 10-day episode of chills, fatigue, joint pain, and malaise one month prior to appearance. He disclosed recent travel to New England and previous treatment of presumed "tick" infection. On presentation, he was noted to have uncorrected visual acuity 20/60 in both eyes; there was no afferent pupillary defect. His extraocular motility was full in all gazes, and he was noted to have right-beating, horizontal jerk nystagmus, worse in right gaze and absent in left gaze. Slit lamp and dilated fundus examination were unremarkable. MRI imaging demonstrated enhancement of multiple cranial nerves. Cerebrospinal fluid (CSF) analysis yielded pleocytosis with lymphocytic predominance, and elevated protein. Serum B. Burgdorferi IgM and IgG antibodies were positive, and Lyme antibodies were detected in the CSF. The patient's nystagmus resolved, and the patient subsequently developed decreased right V2 and V3 sensation and right-sided facial nerve palsy. The patient was treated with intravenous ceftriaxone, with improvement in his symptoms.

Conclusions, including unique features of the case:
We report a case of LNB first presenting as horizontal jerk nystagmus, in specific, acute labyrinthitis. Clinicians should consider LNB as a cause of acute labyrinthitis in the appropriate clinical context.

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Keywords: Nystagmus, Lyme disease, Ocular manifestations of vestibular disorders, Neuroimaging, Vestibular disorders

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Macular ischemia associated with primary autoimmune cerebellar ataxia

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Introduction:
We describe subacute cerebellar ataxia in a 44-year-old woman who was finally found to have primary autoimmune cerebellar ataxia (PACA) and macular ischemia.

Description of Cases:
Even though she initially presented with subtle oscillopsia and gait difficulty, symptom progression and associated fever, weight loss, intractable vomiting, and meningismus led to a suspicion of vestibulopathy of an autoimmune etiology. Furthermore, positive head-impulse tests, impaired smooth pursuit and visually-enhanced vestibulo-ocular reflex, and later development of macular ischemia led to a final diagnosis of PACA. The patient's symptoms and neurotologic signs improved markedly after intravenous methylprednisolone and oral tacrolimus administration.

Conclusions, including unique features of the case:
Our patient again emphasizes the importance of detailed ocular motor evaluation for detection of cerebellar dysfunction, especially among those with bilateral peripheral vestibulopathy having a subacute onset and progressing course.

References: None provided.

Keywords: Ocular manifestations of vestibular disorders, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Nystagmus, Nystagmus, Retina

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Over-diagnosis of Ocular Myasthenia: Clinical Profile and Predictive factors

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Introduction:

Objective To determine the prevalence, predictive factors, and clinical profile of patients with overdiagnosis of myasthenia. Methodology We retrospectively reviewed records of patients seen at our institute from January 2020 to September 2023, with an initial diagnosis of ocular myasthenia, but were later on established to have another diagnosis. Data was collected regarding initial presentation, demographic characteristics, clinical features of myasthenia, serological reports, and final diagnosis.

Description of Cases:

Results: During this period, we saw a total of 149 patients with an initial diagnosis of ocular myasthenia. Of these, 11 patients (median age: 56 years, 8 men: 3 women) were later re-diagnosed to have another cause of ptosis/ ophthalmoparesis/ both, giving an occurrence rate of 7.4%. Most patients were referred by general ophthalmologists (54%) followed by neurologists. 9(82%) patients presented unilateral or bilateral ptosis; of these, only 3(33%) & 1(9%) of them reported diurnal variation and diplopia respectively. Only one patient reported systemic fatiguability. Fatigue test and neostigmine test were positive in 27% and 9% of patients respectively. None of the patients had a positive ice test, serology, or therapeutic response to pyridostigmine. Clinical examination showed increased lid crease distance in 73% of patients. Aponeurotic ptosis (54%) and decompensated strabismus (18%) were the common final diagnoses made with bilateral sixth nerve palsy, Duane syndrome, and orbital apex syndrome diagnosed in one each. It took an average of Eight (8) hospital visits and considerable cost per patient before establishing the final diagnosis.

Conclusions, including unique features of the case:

Conclusion Overdiagnosis of OMG is relatively common in clinical practice. Acquired Aponeurotic ptosis with positive fatigue test and decompensated squints were often over-diagnosed as myasthenia. General ophthalmologists were most likely to consider myasthenia as a diagnosis. Attention to simple details like increased lid crease distance in the absence of true fatigability could give clues to these patients.

References: None provided.

Keywords: Myasthenia, Ocular motility, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease

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Overdrainage in Hydrocephalus Therapy Causing Dorsal Midbrain Syndrome and Parkinsonism in a Chinese Female

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Introduction:
Ventriculoperitoneal shunt is a routine therapy for treating obstructive hydrocephalus, and sometimes for fulminant idiopathic intracranial hypertension. However, shunt malfunction can leading to Sylvian aqueduct syndrome and rostral midbrain dysfunction. We reported a Chinese patient presenting with dorsal midbrain syndrome, parkinsonism and mental disturbances after V-P shunt therapy for treating hydrocephalus.

Description of Cases:
A 51-year-old female presented with dysfunction of eye movement and slow movement, together with memory deterioration after V-P shunt 5 months for treating hydrocephalus. The neuro-ophthalmologic examination showed BCVA was 20/30 OD and 20/100 OS. A left RAPD was presented and the left optic disc showed slight pale under funduscopic examination. The eyelids showed slight retraction bilateral and ocular motility showed absent upgaze and limitation of lateral gaze. There was no light-near reflex dissociation. There is no convergence retraction nystagmus. The MMSE score tested 12 (normal illiteracy >10). Parkinson-like mask facial feature, increased muscle tone, and sluggish gait. The imaging was remarkable for slit lateral ventricle compared with enlarged prior surgery. The Sylvian aqueduct revealed stenosis and upward herniation of the midbrain. The patient was underwent third ventriculostomy and the symptoms improved.

Conclusions, including unique features of the case:
Overdrainage of cerebral spinal fluid in V-P shunt therapy for treating increased intracranial hypertension can leading to brain stem lesions as Parinaud syndrome, diplopia, parkinsonism, and ever mental dysfunction. Third ventriculostomy under endoscopic is appropriate manner for treating these complications.

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Keywords: High intracranial pressure/headache, Nystagmus

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Persistent horizontal nystagmus in delayed post-hypoxic leukoencephalopathy

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Introduction:
Abnormal eye movements observed in unconscious patients include ocular bobbing or dipping, reversed ocular bobbing or dipping, ping-pong gaze, periodic alternating gaze deviation, and vertical myoclonus. Rarely, horizontal nystagmus has been observed in unconscious patients with unilateral cerebral hemisphere lesions. This may be due to the asymmetry in horizontal smooth pursuit or to epileptic seizures. We report a unique case presenting spontaneous horizontal nystagmus with exponentially increasing slow phases in delayed post-hypoxic encephalopathy.

Description of Cases:
A 79-year-old male with a medical history of coronary heart disease and diabetes mellitus presented with spontaneous horizontal nystagmus two weeks following hypoxic-ischemic brain injury from sudden cardiac arrest. He had received rehabilitation treatment after surgeries for subdural hematoma with diffuse axonal injury and ruptured cervical disc caused by traffic collision. Neurological examination revealed that he was in a vegetative state with the eye and head fixedly tuned to the left, and had quadriplegia. Video-oculography showed mainly left-beating nystagmus with small downbeat and counterclockwise (from the patient's perspective) torsional components in light. The removal of visual fixation did not result in significant change. The nystagmus showed exponentially increasing slow phases, with an amplitude ranging from 3 to 9 degrees and a frequency of 0.5 Hz. Diffusion-weighted imaging of the brain revealed delayed post-hypoxic leukoencephalopathy affecting the bilateral subcortical white matter and basal ganglia. An electroencephalogram (EEG) did not show any epileptiform discharges.

Conclusions, including unique features of the case:
Our patient developed persistent horizontal nystagmus two weeks after hypoxic-ischemic injury. Brain MRI revealed characteristic findings of delayed post-hypoxic leukoencephalopathy, affecting the bilateral subcortical white matter and basal ganglia. Remarkably, the nystagmus showed impaired suppression in light, and had exponentially increasing slow phases. Accordingly, persistent horizontal nystagmus observed in our patient with delayed post-hypoxic leukoencephalopathy may be attributed to an unstable neural integrator, likely caused by disrupted cerebellar feedback mechanisms for horizontal gaze holding.

References: None provided.

Keywords: Nystagmus

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Recurrent ophthalmoplegic cranial neuropathy: a cornucopia of diplopia

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Introduction:
Ophthalmoplegic migraine is classically defined as recurrent episodes of head pain and ophthalmoplegia. The term ophthalmoplegic migraine is considered a misnomer to the condition and recently has been reclassified as recurrent painful ophthalmoplegic neuropathy (RPON) per International Classification of Headache Disorders (ICHD). Diagnostic criteria includes - 2 or more attacks of unilateral headache followed by a palsy or paresis of one, two or all three ocular motor cranial nerves within 1-2 weeks and imaging findings excluding lesion of orbital, parasellar or posterior fossa. The pathophysiology is not certain, but demyelinating or inflammatory etiology has been considered.

Description of Cases:
In this case, we discuss an interesting presentation of RPON that meets the diagnostic criteria, but the pattern of presentation challenges the normative presentation previously described in the literature. A 42-year-old male has been followed over four years during which he presented with a right sixth nerve palsy, a right third nerve palsy, a left sixth nerve palsy, and more recently right third nerve palsy; all of which were preceded by typical migraine characteristics, and all of which had negative MRI findings. In this poster, we delve into the clinical course and resolution, extensive laboratory and imaging workup, and postulated pathophysiology of this poorly understood entity. We hope to provide clinical pearls of this disease and expand awareness of this perplexing clinical diagnosis.

Conclusions, including unique features of the case:
1. Recurrent ophthalmoplegic cranial neuropathy is a poorly understood, rarely described clinical entity that can present in unique ways, including alternating neuropathies and degree of involvement in the setting of negative/positive MRI findings.
2. A robust workup and broad differential must be considered to rule out nefarious etiologies such as sinus thrombosis, neoplasia, demyelinating diseases, Tolosa-Hunt, myasthenia gravis, anti-Gq1b syndrome, and Miller Fisher syndrome, among others.

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Keywords: Ocular motility, Neuroimaging, High intracranial pressure/headache

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Remember GQ1b Syndromes in Acute Ophthalmoplegia!

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Introduction:
Acute ophthalmoparesis is the most localized variant of Miller Fisher syndrome (MFS), which itself is a forme fruste of Guillain-Barré syndrome.

Description of Cases:
We present a series of consecutive patients with raised anti GQ1b IgG, presenting almost exclusively with various patterns of ophthalmoplegia. A 42-year-old man presented with diffuse weakness of extra ocular muscles and lids for 3-4 days. On questioning, he reported only mild tingling in his fingers. He had normal deep tendon reflexes, and no weakness or ataxia. A 61-year-old lady developed acute right pupil sparing III and IV palsy over 2 days. She had no ataxia, areflexia or sensory deficits. A 62-year-old man complained of acute diplopia without ptosis, weakness, numbness or ataxia of limbs. Examination revealed limitation of left eye adduction, right eye abduction and reduced deep tendon reflexes. Pupils were normal. The 4th patient is a 27-year-old lady who developed headache left gaze and right abduction deficits after a febrile upper respiratory tract infection. She had no weakness, numbness or ataxia and deep tendon reflexes are normal. Brain MRI was also unremarkable. In addition, she had bilateral papilloedema and mild spinal fluid pleocytosis, reminiscent of Bickerstaff brainstem encephalitis, another MFS variant associated with GQ1b antibody.

Conclusions, including unique features of the case:
In a recent review of 97 patients with acute oculomotor cranial neuropathies at our institution, an ischemic etiology was the most common etiology, accounting for 78%. However, 9% had MFS/GBS. In conclusion, we advocate checking the highly specific anti GQ1b antibody for patients who developed acute diplopia, especially if complex.

References: None provided.

Keywords: Ocular motility, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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Slab-Off Prism for Symptomatic, Vertical Heterophoria in the Reading Position

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Introduction:
Slab-off prism has historically been used to treat diplopia associated with vertical prism imbalance induced when patients with anisometropic refractive error view through their bifocal segments. Less well-known is the concept that slab-off or reverse slab-off prism can also be used to successfully resolve diplopia associated with incomitant vertical heterophoria in downgaze or reading position, unrelated to anisometropia.

Description of Cases:
This study followed the principles outlined in the Declaration of Helsinki. It was reviewed by the Johns Hopkins Institutional Review Board and determined to be exempt. Five consecutive patients were identified by the author in the electronic medical record as having a chief complaint of diplopia in the reading position that was treated with slab-off prism correction determined by the author. Deidentified information collected for this study included the patients' chief complaint, visual acuity, spectacle correction, sensorimotor examination data that included stereoacuity, Worth 4-dot test, prism and alternate cover testing, and final prismatic spectacle correction prescribed. Follow-up ranged from 1 month to 18 months. Success of the slab-off spectacle prism correction was determined at the follow-up visit, and by phone call in one patient who had not returned to verify resolution or persistence of diplopia associated with reading. Five adult patients were identified, age range 55 to 75 years (mean age 65.6 years). All 5 patients complained of vertical diplopia at near during reading. The near vertical deviation ranged from 2-6 prism diopters (PD) (mean deviation 3. 8PD). Mean slab-off power prescribed was 2.5 PD (range 2-3 PD). Symptoms resolved with slab-off prism in all patients.

Conclusions, including unique features of the case:
Slab-off spectacle prism in non-digitally manufactured multifocal lens prescriptions is an effective non-surgical treatment option for vertical diplopia related to small-angle vertical strabismus in the reading position.

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Keywords: Adult strabismus with a focus on diplopia, Ocular motility

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Strabismus as the Initial Manifestation Leading to the Diagnosis of Linear Scleroderma

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Introduction:
Patients with fronto-parietal linear scleroderma, also known as En Coup De Sabre (ECDS) may have multiple ocular manifestations, including enophthalmos, eyelid abnormalities, refractive errors, anterior segment and retinal abnormalities, and strabismus.(1-4) Only a few case reports have been reported on strabismus.(1-4) We present two unusual cases of strabismus as the initial manifestation in patients with undiagnosed ECDS. Remarkably, each of these cases is believed to be caused by a different mechanism.

Description of Cases:
We present two women, aged 51 and 21, who developed progressive strabismus associated with ECDS. In both patients, worsening ocular misalignment prompted neuro-ophthalmic evaluation. Examination revealed bony depression and loss of eyelashes and eyebrows, ultimately leading to the diagnosis of ECDS. Neuroimaging showed nonspecific white matter changes and the blood workup was negative in both patients. However, the second patient subsequently developed radiologic findings within the pons that could potentially be consistent with cranial nerve IV. Her lumbar puncture was positive for oligoclonal bands. She received IV methylprednisolone, with improvement in her diplopia. Both patients underwent strabismus surgery, and both experienced recurrent diplopia years later. The first patient's, initial strabismus mechanism was considered restrictive. At, the second surgery, no signs of restriction were observed, suggesting the initial restriction was from contracture in the setting of a paralytic process affecting the antagonist. In the second patient, the mechanism was believed to be paralytic due to active white matter disease.

Conclusions, including unique features of the case:
Although ocular manifestations of ECDS are not uncommon, strabismus is a less frequent manifestation. Our cases suggest that ECDS-related strabismus may present long before the diagnosis is established, and can result from different mechanisms (restrictive, paralytic, or combination). Systemic involvement, including potential neurological manifestations, may necessitate neuroimaging and thorough evaluations by rheumatology and neurology. Early diagnosis and systemic treatment potentially avert irreversible damage and offer a favorable prognosis.

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Keywords: Adult strabismus with a focus on diplopia, Ocular motility, Neuroimaging

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Unidirectional Palsy of Torsional Saccades in Cerebellar Ataxia Associated with Anti-GAD Antibody

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Introduction:
Anti-GAD antibody is known to cause ocular motor findings highlighted by horizontal or downbeat nystagmus, and saccadic intrusions or oscillations. We report unilateral palsy of torsional saccades in a patient with anti-GAD antibody-associated ataxia.

Description of Cases:
A 67-year-old man presented with progressive dizziness and imbalance for 3 months. He had a history of distal gastrectomy for gastric cancer 20 years ago. On neurological examination, he showed limb dysmetria on both sides and instability during tandem gait. The eyes were orthotropic with normal eyelid and pupillary functions. Video-oculography showed spontaneous downbeat and counterclockwise (upper poles of the eyes beating toward the left ear) torsional nystagmus on primary gaze. The downbeat nystagmus increased during leftward and downward gazes. The torsional nystagmus increased during leftward gaze. Downward smooth pursuit was impaired. Horizontal and vertical saccades were normal. Geotropic nystagmus was induced on head turning to either side while supine. Video head impulse tests were normal for all six semicircular canals. During head oscillation in the roll plane, the clockwise (upper poles of the eyes beating toward the right ear) torsional quick phases were lost when the head was tilted rightward, showing a distinct asymmetry between the sides. Brain MRIs documented diffuse cerebellar atrophy. No tumor was detected on chest and abdomen CT. Paraneoplastic antibodies and genetic testing for spinocerebellar ataxia and dentatorubral-pallidoluysian atrophy were all negative. However, anti-GAD antibody was found to be elevated at 9.23 U/ml.

Conclusions, including unique features of the case:
Anti-GAD antibody may cause a torsional saccadic palsy in addition to cerebellar dysfunction by involving the rostral interstitial nucleus of the medial longitudinal fasciculus (riMLF) that is responsible for vertical and ipsiversive torsional saccades in the mesodiencephalic junction. Given the normal vertical saccades observed in our patient, a loss of ipsiversive torsional saccades may be a more sensitive sign than vertical saccadic slowing in lesions involving unilateral riMLF.

References: None provided.

Keywords: Nystagmus, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Ocular motility

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Vertical saccadic oscillation and positional ocular flutter in late-onset cerebellar ataxia

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Introduction:
Saccadic oscillations are continuous back-to-back saccades without an inter-saccadic interval. When saccadic oscillations are present in the horizontal plane only or all three planes, they are called ocular flutter or opsoclonus, respectively. They have been associated with brainstem and cerebellar lesions, and usually occurs spontaneously. We report a patient with late-onset cerebellar ataxia who presented with unusual combination of saccadic oscillations such as spontaneous vertical saccadic oscillations and positional ocular flutter.

Description of Cases:
A 55-year-old man presented with progressive gait disturbance, slurred speech and head-motion induced dizziness. He had also mild cognitive impairment and dysautonomia including urinary frequency, nocturia and orthostatic dizziness. On neurological examinations, he had dysarthria, bilateral dysmetria, and truncal ataxia. Eye movement recording using video-oculography showed no spontaneous nystagmus with or without visual fixation. However, spontaneous vertical saccadic oscillations were observed during transient vertigo attack, with a duration of 2~3 sec, a frequency of 6 Hz, and amplitudes of 0.8°~8.2°. In addition, when moving to a head-bending, -leaning, and –hanging positions, transient ocular flutter followed by continuous square-wave jerks and superimposed downbeat nystagmus were consistently observed, along with dizziness and nausea. The frequency and amplitude of ocular flutter were approximately 6 Hz and 1.5°~15°, respectively. The video head impulse test, ocular, and cervical vestibular myogenic evoked potentials were normal. MRI of the brain exhibited hot cross bun sign at the pons with cerebellar atrophy, and FDG PET-CT disclosed significantly cerebellar hypometabolism. He was treated with amantadine and taltirelin, but his neurological symptoms remain unchanged.

Conclusions, including unique features of the case:
Vertical saccadic oscillations in our patient may result from transient excitation of the burst neurons in the rostral interstitial nucleus of medial longitudinal fasciculus due to dysfunction of the fastigial nuclei and impaired omnipause neurons. In addition, an ephaptic transmission between the vestibular pathway and saccadic premotor regions may lead to ocular flutter during positioning.

References: None provided.

Keywords: Nystagmus

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Wrong-Way Nystagmus In Acute Vestibular Disorders

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Introduction:
Peripheral vestibular disorders classically present with contralesional (inhibitory) nystagmus (e.g., vestibular neuritis in the acute vestibular syndrome [AVS]), while ipsilesional (excitatory) nystagmus is less common (e.g., Ménière's in the episodic vestibular syndrome [EVS]1,2,3). However, ipsilesional nystagmus (IN) is rare in the peripheral AVS, and possible mechanisms have not been elucidated.

Description of Cases:
Methods: We describe three patients with IN. Evaluation included video head impulse testing (vHIT) and contrast-enhanced MRI. Results: Case 1: EVS - Ménière's syndrome Examined at 3.5 hours; left ear hearing loss and tinnitus; spontaneous IN unchanged with hyperventilation or head-shaking. Normal vHIT and MRI. Case 2: AVS – unilateral 7th and 8th cranial neuropathies Examined on day 4 (day 10 of facial palsy); no aural symptoms; spontaneous IN increased with hyperventilation and head-shaking. Normal vHIT. MRI IAC - ipsilateral 7th & 8th enhancement. Case 3: AVS - labyrinthitis from COVID infection Examined on day 1; left ear hearing loss and tinnitus; IN increased with head-shaking, unaffected by hyperventilation. Normal vHIT and MRI.

Conclusions, including unique features of the case:
In Ménière's, there is an initial excitatory (1st) phase, then a paralytic or inhibitory 2nd phase, then a recovery (3rd) phase (i.e., adaptive mechanisms and increased sensitivity of vestibular nuclei on the paretic side).1,4,5,6,7 In Case 2, spontaneous IN could result from excitatory inflammatory and/or (viral) infectious phenomena and/or incomplete vestibulopathy (normal vHIT) with partial adaptation 4 days after onset. The significant hyperventilation-induced IN may suggest increased conductivity across an injured or demyelinated segment of CN8 (akin to vestibular schwannoma or vestibular paroxysmia).1,7,8 In Case 3, possible mechanisms include excitation and/or incomplete vestibulopathy (normal vHIT) with adaptation. Ipsilesional nystagmus in the EVS and AVS probably results from excitatory and/or adaptive processes. The observation of IN in peripheral AVS confounds the bedside ocular motor and vestibular examination, but may shed light on the mechanism of injury and/or etiology.

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Keywords: Vestibular disorders, Nystagmus, Ocular manifestations of vestibular disorders

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Cerebral Venous Disorders - An Update from The Society of Neurointerventional Surgery Section for Cerebral Venous and CNS Disorders

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Introduction:
Cerebral Venous Disorders are increasingly recognized as a mechanism for multiple neurological symptoms. The past century has focused on arterial diseases. Very little attention has been spent on the exhaust system of organs. The SNIS Section for Cerebral Venous and CSF Disorders was established in 2022 to concentrate scientific efforts at categorizing and studying cerebral venous pathologies. We have submitted for a new ICD 10 code for this group of diseases, and hope for approval this month. Cerebral Venous disorder patients frequently have visual obscurations as described in the modern articulation of idiopathic intracranial hypertension, but the spectrum of disease and the associated venous pathologies continue to expand in scope and breadth.

Description of Cases:
We will review multiple cases of cerebral venous congestion of various mechanisms, reviewing the anatomy, treatment, and outcome. Key illustrative case: An athletic financial analyst in his 30s presents with repeat CSF leaks with history of headaches, migraines with aura, pulsatile tinnitus, visual blurriness, and occasional cognitive disturbances. After repeat CSF leak repair, venous evaluation revealed tight R IJV stenosis. Surgical resection of the C1 transverse process resulted in improvement of venous flow with reduction of intracranial venous pressure and resolution of the patients recurrent CSF leaks, headaches, visual obscurations, pulsatile tinnitus, photopsia and cognitive limitations. Previously, the patient was working 4 hours a day due to cognitive impairment. Post surgery, 10 hours a day and fully able to exercise.

Conclusions, including unique features of the case:
Focused study of venous outflow will yield new insights in disease states affected by impaired clearance of waste products and metabolites. Venous stasis is well associated with inflammation and dysfunction in many body parts. The brain, eyes, hearing apparatuses are unlikely to be immune to these effects.

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Keywords: Interventional neuroradiology, High intracranial pressure/headache, Pseudotumor cerebri, Neuroimaging, Vascular disorders

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Vision Recovery, Incomplete Function: The PERG Perspective on a Pituitary Tumor Resection

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Introduction:
Pattern electroretinogram (PERG) provides a sensitive and selective assessment of the retinal ganglion cell (RGC) function (1). We report the case of a patient with reversible loss of visual acuity (VA) and visual field (VF) but not RGC function measured with PERG after resection of a pituitary tumor.

Description of Cases:
A 65-year-old glaucoma suspect (by high IOP (intraocular pressure) and central corneal thickness) was serially tested with PERG, VF, IOP and OCT (optic coherence tomography) of retinal nerve fiber layer and ganglion cell complex every 6 months for 5 years. After one year, the patient experienced rapid deteriorating VA associated with bitemporal hemianopsia and bilateral PERG magnitude loss. Brain MRI revealed a pituitary mass compressing the optic chiasm that was surgically resected. One year after the resection, the patient had complete VA and VF recovery but further PERG worsening. OCTs and IOP remained stable over the entire follow up.

Conclusions, including unique features of the case:
While deterioration and recovery of VA and VF are consistent with presence and removal of the pituitary tumor interfering with orthograde eye-to-brain connectivity, progressive PERG loss suggests impairment of retrograde brain-to-eye signaling resulting in RGC dysfunction (2,3). This case shows that measurable RGC disfunction could occur by injuries in the visual pathways coming from the brain to the eye and might not be necessarily dependent on the signal going from the eye to the brain often evaluated with visual fields. While this patient was a glaucoma suspect, throughout the entire follow-up her OCT tests and IOP measurements remained stable. Further follow-up will establish if dysfunctional RGCs will eventually recover or die, potentially resulting in OCT loss and optic atrophy.

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Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Tumors, Optic neuropathy, Visual fields, Miscellaneous

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A Collaborative Approach to Chronic Dizziness or Persistent Postural-Perceptual Dizziness (3PD)—The Utah Chronic Dizziness Collaborative (UCDC) and Dizzy School

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Introduction:
Dizziness is a common complaint accounting for 5.6 million clinic visits in the U.S. yearly. Up to 30% of cases develop chronic dizziness or Persistent Postural-Perceptual Dizziness (3PD). 3PD is a medical condition defined by a persistent feeling of dizziness or unsteadiness following a triggering event. 3PD is associated with reduced quality of life. Although vestibular testing is often non-explanatory, there is growing definable pathophysiology related to maladaptation of central networks responsible for space/motion perception. Sufferers often see multiple physicians, undergo costly inconclusive tests, ineffective rehabilitation, and experience suboptimal outcomes. The Utah Chronic Dizziness Collaborative (UCDC) was established in 2021 to develop a multidisciplinary approach to evaluation and treatment.

Description of Cases:
The UCDC held monthly virtual meetings from 2021-2023 with vestibular therapists, audiologists, physicians, psychologists, and a wellness coach. UCDC consulted with experts in the field of dizziness and 3PD as invited speakers. The team methodically reviewed literature regarding chronic dizziness to determine how to effectively evaluate and treat patients. The literature review was synthesized into quality of evidence tables and best practice recommendations were made.

Conclusions, including unique features of the case:
The UCDC recommends that patients referred for chronic dizziness undergo screening for medical conditions by referring providers, and if indicated have evaluation with vestibular testing. Co-morbid vestibular and neurologic disorders are sought, including vestibular migraine. For 3PD, based on available evidence, treatments include (1) customized vestibular rehabilitation with physical therapists, (2) low dose serotonin-based medication, and (3) cognitive behavioral therapy. As education is critical to success we created the Dizzy School website for patient and provider information. The UCDC is currently working on dissemination of this approach through local, national, and international meetings and workshops.

References: None provided.

Keywords: Ocular manifestations of vestibular disorders

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A Service Evaluation of a University Hospital Birmingham Neuro-Ophthalmology Virtual Clinic

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Introduction:
The University Hospitals Birmingham (UHB) neuro-ophthalmology department serves a large patient base despite increasing service pressures. A growing patient group with stable neuro-ophthalmic disease require specialist review due to a risk of disease progression. An asynchronous, 'virtual' clinic has been running since December 2021 to serve this patient group more efficiently.

Description of Cases:
Methods: Patient data was extracted from virtual clinic appointments Dec ’21-Dec ’22 inclusive. Using electronic patient records systems (Medisoft and Clinical Portal), data for diagnosis, patient outcome, days since last neuro-ophthalmic review and co-morbidities was collected retrospectively. Data was analysed for diagnoses, outcomes, time to be seen and attendance rate. Inclusion criteria: Patients deemed suitable to be seen in the virtual clinic. Exclusion criteria: Patients reviewed by consultant for issues not related to the service.

Conclusions, including unique features of the case:
Pituitary lesions, IIH and meningiomas made up 73% of cases. Only 8% of clinic outcomes resulted in F2F appointments. The service was effective at stratifying patient risk and clearing patient backlog.

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Keywords: Miscellaneous

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An Unusual Clinical Presentation Of Cryptococcal Meningitis: The Importance Of A Detailed History And Physical

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Introduction:
This case report discusses a previously healthy 40-year-old female presenting with recurrent headaches following the death of her husband. She received reassurances from her primary care physician and a neurologist, who reported a normal MRI scan. Yet, her persistent symptoms prompted her to seek further consultation.

Description of Cases:
This patient denied visual disturbances and sought the help of an ophthalmologist to explore the benefit of a new glasses prescription. Upon initial evaluation, she was seated cross-legged and wearing sunglasses. On exam, her visual acuity, intraocular pressure and visual fields were within normal limit, though she displayed trace bilateral lateral rectus weakness. Further detailed-history was obtained, revealing photosensitivity, fever and pain on neck flexion. Notably, the patient recently traveled to Vancouver-island several weeks before the onset of her headaches. Given this constellation of symptoms and a suspected diagnosis of meningitis, a subsequent lumbar puncture was performed. This unveiled a markedly high opening pressure of 57 cm, despite no evidence of papilledema. Analysis of the cerebrospinal fluid (CSF) discovered numerous fungal elements consistent with cryptococcus that were later speciated as cryptococcus gattii, which is endemic to the Pacific Northwest. The meningeal irritation of the optic nerve sheaths and spinal cord meninges likely accounts for her initial posture and use of sunglasses. Regarding her absence of papilledema in the setting of elevated intracranial pressure, it is hypothesized that inflammation along the optic nerve sheaths prevented transmission through the optic nerves.

Conclusions, including unique features of the case:
While initial findings suggested migraines, the diagnosis was ultimately cryptococcal meningitis. This case highlights the critical role of comprehensive history-taking, clinical observation and maintaining a broad differential. Additionally, with growing populations in the Vancouver Island area, the risk of potential future cryptococcus infections warrants increased awareness in clinical practices.

References: None provided.

Keywords: High intracranial pressure/headache

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Check point inhibitor optic neuritis versus arteritic anterior ischemic optic neuropathy, a diagnostic challenge.

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Introduction:
Optic neuritis is one of the most common neuro-ophthalmic adverse effects of immune checkpoint inhibitor (ICI) treatment. 60% have been associated with ipilimumab[1]. Nearly all patients experience improved vision with discontinuation and resolution of the disc edema post-treatment with steroids. The main differential diagnosis is arteritic anterior ischemic optic neuropathy secondary to giant cell arteritis (GCA - AAION).

Description of Cases:
A 77-year-old male with metastatic clear-cell renal cell carcinoma, hypertension, and hyperlipidemia developed acute painless loss of vision with severe visual field constriction OS. 2 days prior he had 6 isolated episodes of monocular blurred vision resolving within a minute. He denied any systemic symptoms of GCA but reported 40 lb weight loss over past month. Vision was 20/100-2 OD and 20/150+1 OS. He had pallid optic disc edema with peripapillary hemorrhage OS and questionable disc edema OD (Figure 1). ESR and platelets were normal. His CRP was elevated. He was started on Solumedrol due to possible GCA. His ICI therapy was discontinued. Temporal artery biopsy (TAB) was inconclusive revealing intimal thickening and associated patchy mild chronic inflammation of the intima and surrounding adjacent smaller vessels. Giant cells were not identified. Contrast MRI head and orbits was unremarkable . His vision improved to 20/40+2 OD and 20/40-1 with visual field improvement on high dose corticosteroids within 2 weeks (Figure 2).

Conclusions, including unique features of the case:
Differentiating ICI optic neuritis and GCA – AAION can be challenging. Active oncologic disease may elevate inflammatory markers and TAB may be inconclusive or even show inflammation secondary to ICI. The main differentiating factors may be lack of improvement in patients with GCA (exceedingly rare beyond 2 weeks of steroid treatment) versus ICI optic neuritis.. ICI should be discontinued and steroid treatment initiated without delay to optimize chances of visual recovery.

References: Systematic Review. Eye Brain, 2020. 12: p. 139-167.

Keywords: Optic neuritis, Optic neuropathy

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Combined cilioretinal sparing CRAO and cilioretinal artery occlusion in the fellow eye concurrent with bilateral arteritic anterior ION preceded by binocular diplopia.

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Introduction:
Typically, vision loss in giant cell arteritis (GCA) is a result of an ischemic optic neuropathy (ION); however, in up to 10% of cases, is due to central retinal artery occlusion (CRAO)[1] . Cilioretinal arteries exist in 15–30% of patients, and cilioretinal artery sparing CRAO can result in preserved or decreased central visual acuity[2]. This is rarely seen in GCA, for which only three previous case reports exist[3-5].

Description of Cases:
A 79-year-old male with a history of coronary artery disease and hypertension developed acute loss of vision OS with severe visual field constriction OD. 1 month prior he had several 15-minute episodes of binocular diplopia. He endorsed a 2-week history of new headaches, neck pain and jaw claudication. He was initially diagnosed with migraines with visual auras and treated with common analgesics. His headaches partially improved. 2 weeks later he presented in the ED with worsening vision (NLP OD and CF OS). He had pallid optic disc edema with peripapillary hemorrhage OU as well as a ciliary artery occlusion OD and CRAO with cilioretinal artery sparing OS (Figure 1). ESR, CRP and platelets were elevated. He was started on Solumedrol for presumed GCA which was later confirmed with a temporal artery biopsy (TAB). His vision only partially improved OS to 20/200. He was continued on high dose oral steroids followed by a slow taper.

Conclusions, including unique features of the case:
This case represents a unique and extreme presentation of biopsy confirmed GCA with extensive ocular involvement. Combined cilioretinal sparing CRAO and cilioretinal artery occlusion in the fellow eye concurrent with bilateral arteritic anterior ION preceded by binocular diplopia translates involvement of short and long cilioretinal arteries as well as the central retinal artery. We believe this case is a beautiful illustration of the varied ocular manifestations of GCA all in one patient.

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Keywords: Optic neuropathy, Vascular disorders

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Efficacy Of Telemedicine In Neuro-Ophthalmology Channelled Through "Vision Centres" In South India

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Introduction:
Most ophthalmologists in India are based in urban areas, catering to 30-35% of the population. However, the rural population (65%) has very little or no access to tertiary eye care. Vision centres are primary eye care services situated in villages manned by trained ophthalmic technicians. These are connected to the base hospital through internet services, enabling direct patient consultation and interaction with the ophthalmologist, thus making ophthalmic services accessible and affordable by reducing travel cost and time for patients. Further evaluation and treatment are done at speciality clinics to those referred to the base hospital.

Description of Cases:
Aim: To study the effectiveness of vision centre mediated telemedicine in neuro-ophthalmology. Methods: Retrospective observational study from January 2021 to December 2022. Of the 126,217 patients seen at 13 vision centres, 255 (0.2%) were referred for neuro-ophthalmology opinion. Results: 38 (15%) were excluded as they were found to be non-neuro-ophthalmic cases. Of the remaining 217 cases, the major diagnoses were cranial nerve palsies 69 (32%), cerebral vascular accidents 28 (13%), papilledema 22 (10%), optic neuritis 17 (8%), non-arteritic anterior ischemic optic neuropathy 15 (7%), ocular myasthenia 11 (5%) and traumatic optic neuropathy 9 (4%).

Conclusions, including unique features of the case:
Telemedicine has proved to be a cost-effective, accurate and reliable method for screening and monitoring patients with diabetic retinopathy and retinopathy of prematurity. In neuro-ophthalmology, it is an excellent tool to triage and sensitize patients to seek immediate medical attention, who are otherwise reluctant to visit a hospital. It is useful in long term monitoring, especially Idiopathic intracranial hypertension, ischemic optic neuropathies, etc. and is an important alternative for the elderly, parkinsonism, immunocompromised or mobility- challenged patients. Our study shows that tele-ophthalmology helps in diagnosing neuro-ophthalmology patients remotely, who need urgent vision or life-saving intervention. It might play a pivotal role in universal health care delivery system in the future.

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Late-onset Leber's Hereditary Optic Neuropathy And Anti-androgen Therapy For Prostate Cancer: Is There A Causative Link?

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Introduction:
Leber's Hereditary Optic Neuropathy (LHON) usually affects young men within their thirties. Reduced prevalence in women is explained by protective role of estrogens. Late-onset cases are usually associated to toxic exposure such as prolonged tobacco smoke or drugs with mitochondrial toxicity.

Description of Cases:
We describe two cases of late-onset LHON, presenting visual loss after introduction of enzalutamide, an antagonist of androgens' receptor, used as prostate cancer treatment in association with leuprolide, a gonadotropin-releasing hormone (GhRH) analogue. Patient 1 is a non-smoker 61-year-old male belonging to a family with recurrence of LHON (mother and two nieces). He started for metastatic prostate cancer leuprolide once every 3 months and denosumab monthly 3 years ago and enzalutamide 160mg/die 24 months before visual loss. He reported subacute and painless loss of vision in OS in August 2023, followed by OD in one month with evidence of optic disk hyperemia and pseudoedema. Genetic diagnosis confirmed the presence of homoplasmic m.3460G>A/MT-ND1 mutation. BCVA 3 months after onset was 20/200 OD and 20/500 OS. Patient 2 is a non-smoker 77-year-old male in treatment with leuprolide every 3 months since 12 years. Enzalutamide 160mg/die was started 12 months before visual loss. He reported rapid bilateral and painless loss of central vision in April 2023, not responsive to high-dose steroids. Genetic testing disclosed the presence of m.14484T>C/MT-ND6 in homoplasmic form. BCVA 5 months after onset was CF OD and 20/2000 OS.

Conclusions, including unique features of the case:
These two LHON cases are remarkable for their late-onset in absence of classic toxic factors, both after introduction of anti-androgen therapy. We argue if, in a context of global reduction of both estrogens and testosterone levels due to concomitant GhRH analogue treatment, the association of the anti-androgen, increasing circulating levels of androgens due to the receptor block, could imbalance the ratio against estrogens, known for their protective role in LHON.

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Keywords: Genetic disease, Optic neuropathy

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Navigating Complexity: Referrals from Vitreoretinal Surgeons to Neuro-Ophthalmologists

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Introduction:
This preliminary study characterizes referrals from vitreoretinal surgeons to neuro-ophthalmologists focusing on referral reasons, findings, their localization, and need for further testing.

Description of Cases:
Methods: Retrospective chart review of 55 patients referred to a tertiary care and a private neuro-ophthalmology clinic by vitreoretinal surgeons was conducted. Demographics, referral complaint, visual acuity (VA), findings prompting referral, final diagnosis, and recommended tests and interventions were collected. Results: Among the 55 patients included, referrals originated from 18 different vitreoretinal surgeons. The mean age was 52.2 (SD = 20.0) years, with 60% females and 40% males. Predominant complaints were vision loss (40.0%), visual disturbance (12.7%), optic atrophy (10.9%), and optic nerve edema (9.1%), collectively accounting for more than 70% of referrals. Notably, 31% of patients lacked a pre-existing retinal disease. The mean VA at retina and neuro-ophthalmology visits was 20/80 (logMAR= 0.62) and 20/60 (logMAR= 0.49, p=0.02), respectively. Neuro-ophthalmology referrals stemmed from abnormal examination or test findings in 60% of cases, encompassing suspected optic nerve edema (36.4%), visual field defects (27.2%), pallor (21.2%), afferent pupillary defect (3.0%), decreased color vision (3.0%), macular exudates (3.0%), simultaneous macular and optic nerve edema (3.0%), and thinning on optical coherence tomography (3.0%). Final diagnoses excluding non-organic vision loss (3.6%) and positive visual phenomena (7.3%) were localized to the optic nerve (43.6%), retina (16.4%), cortical pathways (7.3%), extraocular muscles (3.6%), vitreous (1.8%) and multiple components (14.5%) in respective cases and was unknown in 1 case (1.8%). Neuro-ophthalmologic evaluation prompted further testing in 27.3% and resulted in interventions, including medical treatment (9.1%), prisms (1.8%), and referrals to other specialties (14.6%) in 25.5% of cases.

Conclusions, including unique features of the case:
Vitreoretinal surgeons and neuro-ophthalmologist share a variety of patients resulting in diverse complaints. Understanding referral patterns between vitreoretinal surgeons and neuro-ophthalmologists helps identify patients benefitting most from neuro-ophthalmologic assessment.

References: None provided.

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Optic Nerve Glioma Masquerading as Glaucoma in an Adult

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Introduction:
Optic nerve gliomas (ONG) are a relatively rare astrocytic tumor that account for 0.6 – 1.2% of all brain tumors(1). While approximately 90% of ONGs present as slow-growing neoplasms within the first 2 decades of life, ONGs that present in adulthood often hold a poor diagnosis.

Description of Cases:
A 71-year-old female presented to neuro-ophthalmology given the appearance of her optic nerves on CT. The patient had been previously diagnosed with primary open-angle glaucoma with a known superior altitude defect in the left eye and possible nasal defect in the right eye. She had also previously been worked up for possible intracranial hypertension due to headaches and partially empty sella, and the same appearance of fluid in the optic nerve sheaths, however she was never noted to have papilledema and has refused lumbar puncture for years. On exam, her visual acuity measured 20/30 in each eye and a left relative afferent pupillary defect was detected. Visual field testing identified a dense superior defect in the left eye, stable compared to previous glaucoma clinic testing. There was no evidence of optic disc edema in either eye, but there was some pallor, more notably of the left optic nerve. Magnetic resonance imaging (MRI) of the orbits and brain showed left optic nerve enlargement and increased T2 signal of the posterior intraorbital segment without significant enhancement that was most consistent with an ONG. MRI, VA, and HVF findings have remained stable for over a year.

Conclusions, including unique features of the case:
Although ONGs are typically benign tumors in children, existing ophthalmic literature suggests that ONGs presenting in adulthood are often either histologically malignant or clinically aggressive despite low-grade histologic findings. The present case suggests that there may be more ONGs that are undiagnosed, or misdiagnosed as glaucoma, as they may remain small and stable over years.

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Keywords: Tumors, Neuroimaging

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Contact Information: None provided.

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Paradoxical Worsening Of Atypical Third Nerve Palsy After Spontaneous Closure of Indirect Carotid Cavernous Fistula

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Introduction:
Indirect carotid cavernous fistulas (CCFs) are either treated with endovascular intervention or conservative observation. While the "watch-and-see" approach is justified with a high chance of spontaneous closure, we present a case of paradoxical worsening.

Description of Cases:
A 70-year-old female patient, with hypertension and hyperlipidemia, presented with an acute onset of binocular oblique diplopia and drooping of her left upper eyelid. Clinical examination revealed a left isolated pupil-involving third nerve palsy. Urgent computed tomography (CT) angiogram did not reveal intracranial aneurysms. Magnetic resonance imaging (MRI) of the brain and orbits were unremarkable. Blood investigations were normal. She was managed as a left ischemic third nerve palsy. Over the course of 6 months, her left ptosis and ophthalmoplegia completely resolved. However, the left pupil remained persistently dilated. She developed new symptoms of tinnitus and left eye redness. Repeat neuroimaging revealed a left CCF with reflux to the right, associated with bilateral distended superior ophthalmic veins (SOV), left orbital congestion and mild proptosis. A dedicated 4-vessel angiogram (4VA) confirmed it. She opted for clinical observation. Her symptoms spontaneously resolved over the next month. A few months later, her condition recurred with left worsening cockscrew vessels, conjunctival chemosis and central retinal vein occlusion. She acutely deteriorated with recurrence of left third nerve palsy, proptosis, anterior segment ischemia and glaucoma. Urgent neuroimaging showed that the left indirect CCF had spontaneously resolved. 4VA confirmed thrombosis of the CCF and bilateral inferior petrosal sinuses. She received a course of high dose intravenous methylprednisolone to alleviate the severe orbital inflammation. Ptosis and ophthalmoplegia resolved after a week. Unfortunately, her vision did not improve.

Conclusions, including unique features of the case:
CCFs are a rare cause of an isolated pupil-involving third nerve palsy. Clinical deterioration can be due to spontaneous closure of the CCF. Multidisciplinary team care of neurosurgery, oculoplastic surgery and ophthalmology is crucial.

References: None provided.

Keywords: Vascular disorders, Interventional neuroradiology, Orbit, Pupil, Ocular motility

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Contact Information: None provided.

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Prevalence of Myelin-Oligodendrocyte-Glycoprotein Antibodies in Presumed Non-arteritic Anterior Ischemic Optic Neuropathy

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Introduction:
Myelin-oligodendrocyte-glycoprotein associated optic neuritis (MOG-ON) and non-arteritic anterior ischemic optic neuropathy (NAION) both present with acute vision loss, optic disc edema and peripapillary hemorrhages. NAION is a presumptive diagnosis without available biomarker. MOG-ON can be misdiagnosed as NAION as 85% of Caucasian patients have cup-to-disc ratio of 0.3 or less and eye pain might be absent in MOG-ON and present in NAION. Thus, this study sought to determine the prevalence of MOG antibodies in patients diagnosed with presumptive NAION.

Description of Cases:
Methods: This was a prospective study of all patients with the presumptive diagnosis of acute NAION seen in a tertiary neuro-ophthalmology practice from September 2022 until June 2023. NAION was defined by presence of optic disc swelling either unilateral or bilateral. Unilateral cases required a relative afferent pupillary deficit in the involved eye, and a disc-at-risk in the fellow eye to be diagnosed as NAION. All patients must have demonstrated full or partial resolution of disc edema on follow-up visit. Participants without available MOG antibody testing by cell-based assays were excluded. Clinical data from initial and follow-up consultation was obtained. Results: Between September 2022 and June 2023, 33 patients received the presumptive diagnosis of NAION, of whom five did not pursue blood work and four did not attend to follow-up, resulting in 24 patients included for analysis. NAION patients were followed for a median of 7 weeks (6 – 10). Two out of 24 (8.3%) had positive MOG-IgG titres, resulting in a number needed to treat (NNT) of 12.

Conclusions, including unique features of the case:
In contrast to NAION, MOG-ON is a treatable condition with visual outcomes correlating to the time from symptom onset to initiation of treatment. The prevalence of MOG antibodies in 8.3% of patients with NAION in this study justifies routine screening of patients with NAION for presence of MOG-antibodies.

References: None provided.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Vascular disorders, Optic neuropathy, Optic neuritis

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Superficial siderosis causing refractory papilledema following brain tumor resection

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Introduction:
A 60-year-old man presented with months of worsening headaches and vision changes lasting seconds to minutes, occurring multiple times a day with no known triggers. His history was notable for parietal oligoastrocytoma with recurrence as glioblastoma. After three resections, the site was complicated by chronic intracranial hemorrhage. He had received chemotherapy (temozolomide) with radiation. He suffered from coronary artery disease, with a history of stroke and pulmonary emboli.

Description of Cases:
On his initial visit, visual acuity was 20/25 with preserved color vision OU. Dilated fundus exam showed grade III optic disc edema bilaterally. Optical coherence tomography demonstrated elevated average retinal nerve fiber layer (RNFL) thicknesses and decreased average ganglion cell layer (GCL) + inner plexiform layer (IPL) thicknesses bilaterally. Magnetic resonance imaging (MRI) was consistent with elevated intracranial pressure (ICP) and papilledema. Lumbar puncture demonstrated elevated opening pressure and increased protein. Extensive infectious and autoimmune workups were unremarkable. After five months without improvement after treatment with acetazolamide, lumbar puncture redemonstrated elevated opening pressure and protein. Brain MRI showed progression in blood products throughout the brain. He was ultimately diagnosed with superficial siderosis (SS). A ventriculoperitoneal shunt was placed. Upon follow-up 8 weeks later, his headaches and papilledema were improved. Visual acuity was 20/25 OD and 20/60 OS with full confrontation visual fields OU. RNFL thicknesses normalized while GCL + IPL thicknesses remained stable.

Conclusions, including unique features of the case:
SS following brain tumor resection causing papilledema is described in the pediatric neurosurgery literature [1-3] but has been rarely reported among adults. SS causing isolated papilledema and vision loss is rare. Chronic elevated ICP and papilledema due to SS should be considered in all patients with prior brain tumor, intracranial hemorrhage, and papilledema. In some cases, aggressive treatment of elevated ICP and papilledema (which may include interventions such as ventricular shunt placement) may be necessary to prevent visual loss.

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Keywords: High intracranial pressure/headache, Tumors, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease, Chemotherapy and radiation injury, Neuroimaging

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A Case Of Acute Vision Loss Due To Delayed Herpes Zoster Induced Optic Perineuritis

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Introduction:
Herpes zoster ophthalmicus (HZO) results from reactivation of latent varicella zoster virus (VZV) in the ophthalmic division of the trigeminal nerve. While 50% of HZO cases develop ophthalmic complications, optic nerve involvement occurs in less than 1%. Here we describe a case of delayed HZO optic perineuritis which developed despite recent treatment with IV antivirals.

Description of Cases:
A 67-year-old female presented to the emergency room with one week of right sided headaches. She proceeded to develop a vesicular rash in the right V1 distribution, conjunctival injection, corneal pseudodendrites, and anterior uveitis. MRI brain and orbits was negative for any CNS involvement. She was treated with 7 days of IV Acyclovir, topical steroids and antibiotic ointment, with clinical improvement. One week following hospital discharge, her vision OD acutely deteriorated to light perception. Repeat orbital MRI showed right optic sheath enhancement and CSF PCR was positive for VZV. She was treated with repeat course of IV Acyclovir and IV solumedrol with subsequent improvement in vision to 20/50, her baseline.

Conclusions, including unique features of the case:
Optic neuritis is a rare complication of HZO, and there are few reports of HZO related optic perineuritis. Neuroimaging and CSF studies are critical in the evaluation of HZO related optic neuritis which can develop days to weeks after the initial vesicular lesions and generally has a poor visual prognosis. IV antivirals are the mainstay of treatment in these cases, whereas the use of systemic steroids remains controversial. Our case demonstrates remarkable visual recovery from HZO optic perineuritis, when treated with IV steroids in addition to standard antiviral therapy. This suggests that IV steroids may improve visual outcome in patients with HZO related optic perineuritis.

References: None provided.

Keywords: Optic neuropathy, Neuro-ophth & infectious disease (eg, AIDS, prion), Optic neuritis

Financial Disclosures: The authors had no disclosures.

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A case of optic neuropathy secondary to microscopic polyangiitis and giant cell arteritis in the same eye

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Introduction:
We present a unique case of optic neuropathy secondary to microscopic polyangiitis (MPA) and giant cell arteritis (GCA) in the same eye.

Description of Cases:
An 83 year-old female presented with an acute central scotoma in the left eye upon waking, preceded by a periorbital ache. Her medical history included pulmonary fibrosis, hypertension and hyperlipidemia. Initial examination was normal but she returned a month later with the same symptoms. She had no light perception in the left eye, with a left relative afferent pupillary defect and slight pallor of the optic disc. She reported lethargy, poor appetite, weight loss, large limb girdle stiffness and a left peroneal neuropathy. Differential diagnoses of a posterior ischemic optic neuropathy (PION) and atypical optic neuritis were considered. She had markedly elevated erythrocyte sedimentation rate and C-reactive protein, with anaemia and thrombocytosis. Intravenous methylprednisolone was commenced promptly on the presumption of PION from GCA. After 1 day of steroids, her vision improved to 20/40. Magnetic resonance imaging simultaneously showed swelling and enhancement of the left optic nerve with adjacent fat stranding, suggestive of optic neuritis. Left temporal artery biopsy findings were consistent with GCA, showing a thickened intima with active vasculitis, destruction of the internal elastic lamina, scattered epithelioid and giant cells, but no fibrinoid necrosis. Blood work was positive for anti-myeloperoxidase antibodies (MPO), rheumatoid factor and anti-cardiolipin IgM. After initial improvement, she had two further episodes of visual loss within a month but had poor recovery despite treatment.

Conclusions, including unique features of the case:
The constellation of pulmonary fibrosis, peroneal neuropathy, steroid-responsive optic neuritis and positive MPO suggested a diagnosis of MPA. However, the acute onset, poor recovery, constitutional symptoms and histology were in keeping with PION from GCA. Given the clinical picture, our diagnosis is that of a unique overlap of optic neuritis secondary to MPA and PION secondary to GCA.

References: None provided.

Keywords: Optic neuropathy, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Optic neuritis, Vascular disorders

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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A case of Raymond syndrome without facial involvement

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Introduction:
The combination of abducens nerve palsy and contralateral hemiparesis is termed Raymond's syndrome. The French neurologist Fulgence Raymond described the clinical picture that bears his name in 1895. In Classic Raymond's patient, the hemiparesis included central facial palsy. The lesion lies in the medial ventral caudal pons. Here, we report a case of pontomedullary infarction that caused ipsilateral abducens nerve palsy and contralateral hemiparesis sparing the face.

Description of Cases:
A 78-year-old man with past medical history of hypertension and type 2 diabetes visited the emergency room complaining of acute dizziness, horizontal diplopia, worsened by directing gaze to the left and right hemiparesis that had started suddenly from 1 day ago. Neurological examination showed left abducens nerve paresis and right hemiparesis (MRC grade Rt. IV/IV). Both spontaneous and voluntary facial movements were normal. DWI and ADC showed acute small infarction in left anteromedial aspect of pontomedullary junction. Intracranial MRA showed mild focal stenosis of basilar artery.

Conclusions, including unique features of the case:
A patient with abducens nerve paresis and contralateral hemiparesis sparing the face, caused by a lesion in the pontomedullary junction, was recently diagnosed with Raymond's syndrome. Others suggested using the eponym only when central facial palsy is present. This controversy likely reflects uncertainty about the anatomical course of cortico-facial fibers in the brainstem. Regardless of the presence or absence of central facial palsy, the combination of abducens nerve palsy and contralateral hemiparesis should direct the clinician's attention towards the medial ventral caudal pons.

References: None provided.

Keywords: Stroke, Vascular disorders, Ocular motility

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A Case Report Of Posterior Ischemic Optic Neuropathy Following Skin Booster Injection (Juvelook Volume)

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Introduction:
Posterior ischemic optic neuropathy (PION) is an optic neuropathy due to ischemia in the retrobulbar portion of the optic nerve. PION following the use of injectable biomaterials alone is reported to be rare. Herein, we present a case of PION following a skin booster injection (Juvelook volume) (VAIM Co. LTD, Okcheon, Republic of Korea).

Description of Cases:
A 36-year-old male presented to the neuro-ophthalmology clinic for a sudden onset of right monocular visual loss after receiving a Juvelook volume skin booster injection, a hybrid filler composed of low molecular weight hyaluronic acid(HA) and Poly D, L-lactide(PDLLA) in the bilateral inferior orbital margin, lateral canthus, and the nasolabial fold areas. On examination, his best corrected visual acuities (BCVA) were 20/250 in the right eye. Marked right relative afferent papillary defect (RAPD) was present. Orbit MRI showed no abnormalities. A diagnosis of right PION secondary to Juvelook volume injection was made based on clinical ground. One month after, the BCVA improved to 20/50 in the right eye. Pupils were found to be symmetrically reactive to light, and RAPD was equivocal. Fundus showed mild temporal pallor. Central visual field defect was resolved, with inferotemporal visual field defect remaining. OCT showed generalized GCIPL thinning

Conclusions, including unique features of the case:
The suggested mechanism of PION in this case is that the patient was administered filler particles of smaller size, which has a tendency to obstruct the smaller, distant branches. There are several hypotheses to explain the improvement of visual acuity in our patient. The abundant collateral supply may have contributed to the improvement in vision. Moreover, there is possibility of transient embolism due to the exceptionally small molecular size and the biocompatible and biodegradable properties of Juvelook Volume. There is a chance that the filler injection may have temporarily obstructed the blood vessels, or the emboli could have spontaneously dislodged over time.

References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Vascular disorders

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Grant Support: None.

Contact Information: None provided.

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A Dural Mass In Disguise

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Introduction:
Neurosarcoidosis is known as a mimic of various CNS lesions. The authors present a case of neurosarcoidosis involving the optic apparatus mimicking a meningioma on imaging and leading to invasive surgical management.

Description of Cases:
A 64 year-old woman presented with progressive left eye vision loss and blurriness for 1 year. Patient initially underwent left eye cataract surgery without improvement in vision. MRI brain was performed which showed a bilobed dural-based suprasellar mass compressing the optic chiasm and prechiasmatic segments of the bilateral optic nerves, thought to represent meningioma. Patient underwent frontal craniotomy with resection of the presumed meningioma without improvement in her vision. Follow up MRI at 3 months showed residual lesions with increased enhancement. Patient was then referred to Neuro-ophthalmology clinic and examination revealed visual acuity of 20/200 OS with left afferent pupillary defect. Visual field testing revealed dense scotoma in the temporal hemifield and superonasal field in the left eye with supratemporal defect in the right eye. Fundus examination showed bilateral optic disc atrophy, worse on the left. Pathology of the resected mass revealed non-caseating granulomas. Ultimately, the final diagnosis was neurosarcoidosis involving the optic apparatus which was supported by CT chest demonstrating hilar lymphadenopathy. Patient was treated with oral steroids for 3 months and started on Mycophenolate. Patient demonstrated improvement in left eye visual acuity to 20/60 within 6 weeks of starting steroids, though the visual field defects persisted.

Conclusions, including unique features of the case:
1. Neurosarcoidosis can present as asymmetric vision loss by forming granulomatous lesions compressing the optic apparatus. 2. Neurosarcoidosis can mimic meningiomas on imaging, which can lead to unnecessary surgical intervention. Screening for sarcoidosis may be important in preventing invasive surgery in sensitive regions of the brain. 3. Co-morbid ophthalmological conditions should not veer the clinician away from investigating central causes of vision loss when appropriate.

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A Positive Temporal Artery Biopsy Ninety-One Days After Corticosteroid Initiation

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Introduction:
Temporal artery biopsy (TAB) remains the best method to establish a diagnosis of Giant Cell Arteritis (GCA). The American College of Rheumatology [1] recommends obtaining a TAB within two weeks of corticosteroid initiation. Lee and colleagues [2] suggest "histopathologic findings can persist at least 6 to 8 weeks following steroid use". Guevara et al. [3] showed a positive TAB months after corticosteroid initiation. We present a case of TAB-positive GCA ninety-one days after corticosteroid initiation, despite a negative initial biopsy.

Description of Cases:
A 76-year-old female developed acute bilateral vision loss with photosensitivity, neck pain, and occipital tenderness. Other GCA symptoms were negative. ESR and CRP were 11mm and < 1.0mg, respectively. They never elevated above normal. MRI confirmed optic nerve and chiasmal inflammation suggestive of perineuritis. Five-days of 1g/day intravenous methylprednisolone (IVMP) were followed by 60mg/day oral prednisone. Right-sided TAB measuring 3.1x0.3cm showed "no evidence of arteritis on multiple cross sections". Consultation elsewhere was sought by the patient to rule out seronegative Neuromyelitis Optica (NMO) or another diagnosis while continuing corticosteroid treatment. The diagnosis remained elusive and side effects to steroids emerged. The patient returned for further evaluation. A second TAB performed ninety-one days after corticosteroid initiation revealed "focally abnormal artery with changes consistent with healing stage of GCA". Patient was transitioned to weekly Tocilizumab 162mg/0.9mL injections. Vision has remained stable through the clinical course.

Conclusions, including unique features of the case:
This case documents one of the longest intervals for a positive TAB following corticosteroid initiation with a normal initial biopsy. It also shows that despite a negative TAB and normal ESR and CRP, GCA cannot always be ruled out. Despite long delays, a second TAB may be beneficial in making an elusive diagnosis and directing further treatment strategy.

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Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Vascular disorders, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease

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A proposed treatment protocol for leukemic optic neuropathy

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Introduction:
Leukemic optic neuropathy (LON) is devastating complication of hematologic malignancies, wherein cancer cells infiltrate the optic nerve causing compressive or ischemic changes, and ultimately, vision loss. Because of how quickly such lesions can evolve to cause LON, optic nerve infiltration constitutes an oncologic and neuro-ophthalmic emergency. Unfortunately, there is no clearly defined treatment pathway. Steroids, orbital radiation, and/or induction chemotherapy are the mainstay of treatment – but the timing of each intervention has not been formally protocolized to our knowledge. We present a series of cases of leukemic optic nerve infiltration and propose a treatment plan.

Description of Cases:
Five individuals, ranging from 16-27 years of age, with a history of leukemia or lymphoma, presented to our emergency department with acute onset vision changes. Their visual acuity in the affected eye(s) ranged from 20/20 (patient was experiencing episodes of amaurosis) to HM. MRI of the orbits demonstrated enhancement of the optic nerves of the affected eyes in all cases. Dilated fundus exam revealed a range of findings, from disc swelling to optic nerve head infiltration with exudates and macular edema. All individuals received a pulse dose of methylprednisolone for five days, followed by fractionated orbital radiation with or without intrathecal chemotherapy and a steroid taper. Post-treatment visual acuity was significantly improved and remained so for at least two months.

Conclusions, including unique features of the case:
These cases highlight the value of a staged treatment approach to maximize visual recovery in the setting of LON. High dose steroids help decompress the nerve and reduce the likely of compartment syndrome that may result from direct orbital radiation and resultant swelling. As many of these hematologic malignancies are radiosensitive, fractionated radiation further reduces the tumor burden. In our case series, we found that with such an approach, visual acuity improved quickly and was sustained.

References: None provided.

Keywords: Optic neuropathy, Tumors

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A Rare Cause of Diplopia

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Introduction:
Here we present a unique case of diplopia mistaken for temporal arteritis but had an ultimate diagnosis of B cell lymphoma.

Description of Cases:
A 61-year-old woman with no significant past medical history presented with right retro-orbital pain, diplopia and ptosis OD of 3 weeks duration. One month earlier, she reported myalgia, generalized weakness, low and grade fever. Work up revealed elevated CRP 11.4 and ESR 34. She received 1g intravenous methylprednisolone daily for 3 days for suspected Giant cell arteritis. MRI Brain and Orbits with contrast showed right inferior cavernous sinus lesion and right oculomotor nerve enhancement with concern for perineural spread. CTV, CTA head and neck were unremarkable. Neuro-Ophthalmology exam revealed visual acuity of 20/25 OD and 20/20 OS with intact color vision, anisocoria with right pupil dilated and sluggishly reacting to light, limitation of extraocular movements OU with most prominent bilateral abduction deficit and decreased corneal sensitivity OD. Fundus exam, visual fields and OCT were normal in both eyes. She was diagnosed with right cavernous sinus syndrome. Labs for infections and paraneoplastic antibody panel were negative.. Repeat MRI head with contrast revealed unchanged inferior right cavernous sinus lesion with extension into right Meckel's cave and right foramen rotundum with right oculomotor nerve enhancement. Biopsy of cavernous sinus lesion was considered dangerous. Lumbar puncture showed elevated protein and cytometry concerning for atypical mononuclear cells. Repeat lumbar puncture confirmed B-cell lymphoma by flow cytometry. PET scan showed hypermetabolic lymphadenopathy above and below the diaphragm. During hospitalization, she underwent cholecystectomy for acalculous cholecystitis and liver biopsy ,both showed lymphomatous involvement. She received Rituximab and subsequently, intrathecal methotrexate. Hospital course was complicated by acute hypoxic respiratory failure and patient expired.

Conclusions, including unique features of the case:
Cavernous sinus syndrome is a rare presentation of diffuse large B-cell lymphoma. This is an unfortunate case with rapid progression and death.

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Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Skull base

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Abnormal Brain FDG PET in Patients Without Posterior Cortical Atrophy Presenting with Visual Symptoms: A Case Series

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Introduction:
Posterior Cortical Atrophy (PCA) is a rare neurodegenerative syndrome characterized by progressive visuospatial and visuo-perceptual deficits. 18F-fluorodeoxyglucose Positron Emission Tomography (PET) is a valuable diagnostic tool in PCA and often shows marked glucose hypometabolism of the posterior cerebral hemispheres. We present a series of three patients diagnosed as PCA with abnormal PET scans but ultimately found to have alternative diagnoses. This series highlights that other ocular or neurologic pathology can be associated with PET abnormalities similar to those seen in PCA. Specific clinical criteria for PCA exist that take into account the underlying neurodegenerative pathophysiology which should be satisfied when arriving at a diagnosis of PCA.

Description of Cases:
Three patients, two female and one male of ages 50-76, were diagnosed with PCA and presented to neuro-ophthalmology. Two patients developed decreased visual acuity, dyschromatopsia, and central scotomas in both eyes. Findings on ocular coherence tomography were consistent with bilateral optic neuropathies. A third patient developed sudden onset left homonymous hemianopsia with brain magnetic resonance imaging interpreted as normal. Other features of PCA, such as simultagnosia, alexia, or apraxia, were absent in all patients. Brain PET scans showed symmetric hypometabolism of the bilateral occipital lobes in both patients with optic neuropathies, while the imaging of the third patient showed hypometabolism in the right occipital lobe. A re-examination of the third patient's MRI revealed evidence of an ischemic stroke corresponding to the visual field defect and area of occipital lobe hypometabolism.

Conclusions, including unique features of the case:
This series highlights the importance of understanding all clinical features of PCA and how those features inform the clinical diagnostic criteria. Reliance on PET abnormalities alone, in the absence of other diagnostic clinical features, may lead to misdiagnosis as the spectrum of PET abnormalities related to visual deficits or ocular diseases is not fully understood.

References: None provided.

Keywords: Optic neuropathy, Optic neuritis, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease

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An Atypical Presentation of Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease

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Introduction:
A 79-year-old African American man with a past medical history of hypertension presented to the emergency department with pain OD, which started five days prior, progressing to vision loss (initially lower field with eventual complete field involvement).

Description of Cases:
The patient denied any additional symptoms. On exam, acuity was NLP OD, 20/20 OS, with right rAPD, and grade 2-3 disc edema OD. MRI demonstrated longitudinally extensive right optic nerve enhancement. Serum studies showed elevated ESR (107), CRP (2.2), and MOG-IgG seropositivity (1:1000 titer, FACS). CSF studies demonstrated elevated protein. Extensive workup, including paraneoplastic panel, infectious studies, full body PET/CT, spinal cord MRI, and bilateral temporal artery biopsies, was unremarkable. He received a 5-day course of IV methylprednisolone 1g daily, followed by a slow oral prednisone taper. Due to minimal visual improvement, he underwent five PLEX treatments and two IVIG (0.5g/kg/dose). Visual acuity improved to 20/800 OD. He started mycophenolate 1000mg BID and continued prednisone taper. His acuity improved to 20/100 OD by three months after presentation. Four months after his initial presentation, he reported eye pain and vision decrease OD. Acuity was CF @ 3', and a repeat MRI showed optic nerve enhancement, though less than on his initial scan. Due to concern for relapse, he received a 5-day course of oral prednisone 1250mg daily. Two weeks later, his vision had not improved, and there was new development of marked intraretinal fluid OU. Mycophenolate dose was increased to 1.5g BID, and tocilizumab was added. Within one month, his visual function (20/150 OD) and bilateral CME showed significant improvement. The CME resolved without additional specific treatment.

Conclusions, including unique features of the case:
Though his workup was consistent with MOGAD, this is an atypical presentation given his age, poor visual recovery after initial episode, and development/spontaneous resolution of marked CME OU.

References: None provided.

Keywords: Optic neuritis, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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An Unusual Case Of Aberrant Regeneration Of The Oculomotor Nerve Following Coil Embolization Of A Carotid Cavernous Fistula

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Introduction:
The pathogenesis of ocular motor cranial neuropathies presenting after carotid cavernous fistula (CCF) treatment is unclear, with both ischemia and compression previously having been proposed as potential mechanisms.

Description of Cases:
A 62-year-old woman presented to our department with severe left-sided headaches, ptosis of the right eye (OD) and binocular oblique diplopia. Her past medical history was significant for a pituitary macroadenoma without demonstrable visual field defects based on Humphrey visual field testing. On her initial examination, partial ptosis with mild impairment of elevation was seen OD and abduction was slightly impaired for the left eye (OS). On slit lamp and funduscopic examination, no pathological findings were detected. Intraocular pressures were 12 mmHg OD and 16 mmHg OS. A diagnosis of a superior division third nerve palsy OD and a mild abducens palsy OS due to a carotid cavernous fistula (CCF) was made based on CT angiographic findings. Immediately after coil embolization, ptosis OD improved but she developed complete ptosis OS. When seen a month later, the superior division third nerve palsy was resolved OD; however, she had a complete sixth and near complete third nerve palsies OS. One year following presentation, both sixth and third nerve palsies had partially resolved. Upper eyelid retraction was noted OS with attempted downgaze, indicating aberrant regeneration. Since her examination had been stable for over six months, she was referred for strabismus surgery to minimize her diplopia.

Conclusions, including unique features of the case:
Aberrant regeneration in the context of an acquired third nerve palsy is typically either due to trauma or compression, rather than ischemia, as ischemia does not cause axonal discontinuity. The fact that this patient developed signs of aberrant regeneration after coil embolization of a CCF suggests that the oculomotor palsy had been due to compression and not ischemia.

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Keywords: Adult strabismus with a focus on diplopia, Vascular disorders

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An Unusual Presentation of West Nile Virus Infection: Isolated Orbital Inflammation with Radiological Findings

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Introduction:
Infection with West Nile virus (WNV) is usually asymptomatic but in less than 1% of cases it can cause neuro-ophthalmic manifestations including meningo-encephalitis, chorioretinitis, anterior uveitis, occlusive retinal vasculitis, and optic neuritis. The neuro-ophthalmological manifestations of this disease are rarely reported. We present a case of serologically proven, isolated orbital inflammation secondary to WNV infection.

Description of Cases:
A 66-year-old man with no significant past medical history presented with 3-day history of acute onset progressive left retroorbital pain and blurry vision associated with binocular horizontal diplopia, nausea, and vomiting. On further questioning, the patient had a mosquito bite 1 week ago while bird watching in the gulf coast region. The ocular exam was significant for a left relative afferent pupillary defect, left abduction restriction and absence of inflammation or chorioretinal lesions. MRI orbits showed extensive enhancing infiltration throughout the left intraconal orbit, optic nerve sheath, orbital apex, superior orbital fissure and cavernous sinus. Initial CSF studies demonstrated a lack of pleocytosis and normal protein and glucose. He was treated for presumed Tolosa-Hunt syndrome with 3 days of IV solumedrol and had rapid improvement in ophthalmoplegia and his subjective blurry vision. At follow up it was noted his CSF was positive for WNV IgM. Follow-up MRI orbits 3 months later showed complete resolution of abnormal infiltrative enhancement in the left orbit.

Conclusions, including unique features of the case:
This case highlights the unique presentation of an isolated orbital inflammation associated with WNV virus. Although false positive WNV IgM may occur due to cross-reactivity with other arthropod-borne flaviriuses and plaque-reduction neutralization antibody test from CDC is usually needed to confirm the diagnosis. In his case, however, given the temporal relationship with mosquito bite, onset of neurologic symptoms and a positive CSF WNV IgM, he most certainly had WNV infection.

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Keywords: Neuro-ophth & infectious disease (eg, AIDS, prion), Neuroimaging, Optic neuritis

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Association of Race and Obesity in Myelin Oligodendrocyte Protein Antibody Disease (MOGAD) from a Single Institution in the Southwest United States.

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Introduction:
Myelin Oligodendrocyte Protein (MOG) Antibody Disease (MOGAD) is an autoimmune demyelinating disease of the central nervous system. In this qualitative retrospective study at one institution of 18 patients with anti-MOG antibody confirmed disease, we looked at racial incidence, obesity rates, and disease prognosis compared to local demographics and current literature trends.

Description of Cases:
We saw an increased incidence of MOGAD in Hispanic and Black subjects at 28% and 22% respectively, of the cohort compared to the local ethnic composition (11.1% and 7.3% according to State Census Data [1]). Furthermore, we found that 50% of subjects in our cohort were obese (BMI >29.9 kg/m2 in adults and >95 percentile in weight in children) at diagnosis, which is 10% higher than the prevalence of obesity in the surrounding state (~39.4%)[2]. One patient (6% of cohort) had progressive deterioration that presented with bilateral ON that progressed to no light perception bilaterally despite interim recovery of vision after appropriate acute treatment. This patient underwent the greatest number of relapses (6) and stands out as an outlier in clinical disease course and progression given the total average relapses in this cohort was 1.1.

Conclusions, including unique features of the case:
We found a larger percentage of MOGAD in Hispanic/Latinos and Blacks, disproportional even to the local population, which is notable as published demographic data varies widely for MOGAD[3-5]. Additionally, obesity is thought to be more highly associated with MOGAD than other demyelinating disorders[5,6], suggesting along with our data that health professionals in regions with high prevalence of obesity should be aware of the association with MOGAD. We also found progressive deterioration of symptoms to be rare[3] and vision to be the most common residual disability[7] in the one patient that had >3 relapses, suggesting as others have, the higher risk of permanent disability in those with more relapses.

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Keywords: Demeylinating disease, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Optic neuritis

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Ataxia, deafness, optic neuropathy, aphonia associated with ANNA-1/ /"anti-Hu" and LUZP4 antibodies

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Introduction:
Paraneoplastic neurological syndromes (PNS) are a group of immune mediated neurological disorders associated with several types of tumors. We describe a unique case who had two paraneoplastic antibodies: antineuronal nuclear antibody (ANNA-1/"anti-Hu") and Leucine Zipper 4 Autoantibody (LUZP4) with neuro-ophthalmological findings and subsequently detected to have primary mediastinal seminoma.

Description of Cases:
18-year-old man presented to neuro-ophthalmology clinic with subacute onset ataxia, sensorineural deafness, aphonia, binocular diplopia and oscillopsia. On exam, he had end gaze nystagmus, visual acuity was 20/20 OU, fundus exam was unremarkable but retinal nerve fiber layer analysis was concerning for optic neuropathy. Subsequently, he developed focal seizures and myoclonus prompting further testing. Paraneoplastic panel revealed elevated titers of ANNA-1 Antibody (1:3840) and negative gene mutations on genetic panel. On further expanding antibody testing he was also positive for LUZP4. His initial MRI brain and orbits with contrast was unrevealing. CT chest revealed a mediastinal mass and the histopathological examination of the resected mass confirmed seminoma with lymphoid hyperplasia. His testicular ultrasound was negative. Treatment with Intravenous immunoglobulin every 3 weeks showed significant improvement in his symptoms.

Conclusions, including unique features of the case:
Primary mediastinal seminoma is a rare germinal tumor affecting young men and only two other cases associated with ANNA-1 Abs are described. This case is unique for dual antibody positivity and adds to the growing body of literature of PNS. This case highlights the value of testing for paraneoplastic syndromes in cases with atypical neurological and ophthalmological symptoms.

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Keywords: Paraneoplastic syndromes, Optic neuropathy, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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Attenuated phenotype in individuals diagnosed with mitochondrial complex I deficiency caused by homozygous NDUFAF8 c.195+271C>T variant

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Introduction:
NDUFAF8 (encoded by NDUFAF8, MIM *618461) is a mitochondrial respiratory complex I (CI) assembly factor known to form strong protein-protein interaction with the well characterized CI assembly factor NDUFAF5 (encoded by NDUFAF5, MIM *612360), a putative methyltransferase essential for the early stages of CI assembly. Recently, biallelic pathogenic NDUFAF8 variants were reported to cause mitochondrial CI deficiency (OMIM #618776) in 3 affected individuals (3 unrelated families). All affected individuals presented with Leigh Syndrome and revealed an isolated CI deficiency in early infancy. Two of them demonstrated optic nerve involvement and were found to carry a recurrent splicing variant, c.195+271C>T, p.(?), that was initially overlooked due to its deep intronic location. Functional studies demonstrated intron inclusion leading to a non-functional isoform transcript, thus providing evidence for pathogenicity.

Description of Cases:
Patients previously unsolved by clinical testing were identified through Genomics England 100,000 Genomes Project research database. In total 10 affected individuals (8 unrelated families) were identified to carry the same NDUFAF8 c.195+271C>T variant. Six were identified to be homozygous, with the remaining 4 compound heterozygous with another pathogenic/likely pathogenic variant. Clinical data was collected from the available records demonstrated phenotype heterogeneity. Interestingly, a spectrum of disease, from isolated OA to severe syndromic disease was observed in individuals homozygous for NDUFAF8 c.195+271C>T.

Conclusions, including unique features of the case:
Most patients with nuclear determined CI deficiency show severe mitochondrial disorder with/without visual loss. To date, there are limited reports of isolated OA due to pathogenic variants in nuclear genes important for CI function. At NANOS (2022) our group reported a number of patients presenting with OA (poster no.244). Here we present additional families with attenuated phenotype carrying previously reported pathogenic NDUFAF8 variant in homozygous or compound heterozygous state. This emphasizes the variability of CI disease and highlights that previously molecularly unsolved OA may harbor pathogenic variants in nuclear mitochondrial respiratory chain genes.

References: None provided.

Keywords: Genetic disease, Optic neuropathy, Pediatric neuro-ophthalmology, Miscellaneous

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Beyond the Usual Suspects: A Rare Case of Germ Cell Tumor-Associated Optic Neuritis

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Introduction:
Optic neuritis is a rare paraneoplastic phenomenon (1), and the underlying disease is often missed for a long time. It has been described usually in association with small cell cancers or thymoma (2). However, here we report a case of optic neuritis without clear etiology associated with a germ cell tumor in a 35-year-old male.

Description of Cases:
The patient initially presented with sudden onset painful central dimness of vision of the left eye associated with an afferent pupillary defect. Ophthalmoscopy and magnetic resonance revealed swelling of the optic disc and subtle enhancement of the optic nerve, respectively, suggestive of optic neuritis. Despite treatment with steroids and subsequent plasmapheresis, the patient's vision loss rapidly progressed over several days. Further neuroimaging, serum, and CSF workup have remained unrevealing. One month later, the patient presented again with worsening blurred vision and temporal field defect in his right eye and was found to have right optic neuritis. He was treated with a second round of steroids with minimal improvement. Five months later, the patient presented with refractory right lower extremity edema, and the workup revealed a retroperitoneal germ cell tumor. Workup for paraneoplastic optic neuritis (PON), including CRMP5 antibodies, was unrevealing. Still, this presentation with disc edema and subtle nerve enhancement could be consistent with PON (3), though this patient did not have intraocular inflammation.

Conclusions, including unique features of the case:
Although this case's optic neuritis does not present a clear etiology, other paraneoplastic encephalitic processes have been associated with germ cell tumors (4). As such, we propose a possibility of germ cell tumor-associated paraneoplastic optic neuropathy in the s/o seronegative Neuromyelitis Optica. This is probably the first report of this association in the literature.

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Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Demeylinating disease, Paraneoplastic syndromes, Optic neuritis

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Bilateral Infiltrative Optic Neuritis as the Presenting Finding in Metastatic Gastric Leptomeningeal Carcinomatosis and its Dramatic Response to Nivolumab

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Introduction:
Leptomeningeal carcinomatosis (LMC) is a rare consequence of metastatic cancer characterized by dissemination of cancer cells into the pia mater, arachnoid mater, and subarachnoid space, with an overall survival described by a magnitude of weeks to months. Due to the rarity of the disease, few reports describe signs or symptoms of LMC as the first manifestations of gastric cancer, and even fewer describe ocular involvement as the primary presenting symptom. We present a rare case of LMC secondary to previously undiagnosed metastatic gastric adenocarcinoma with infiltrative optic neuritis as a presenting finding, as well as the first case in the literature of a dramatic response to nivolumab.

Description of Cases:
A 58-year-old female with a past medical history of hypertension, hyperlipidemia, and type 2 diabetes presented with three months of blurry vision, headaches, and paresthesias. Ophthalmic exam showed decreased visual acuity, visual field constriction, and bilateral optic disc edema with peripapillary hemorrhages and white infiltrates. Contrast-enhanced MRI showed LMC of the bilateral optic nerves and multifocal areas of dense leptomeningeal enhancement. CSF cytology revealed malignant cells and oncologic workup revealed metastatic gastric adenocarcinoma with Krukenberg disease. After initiation of systemic nivolumab, a PD-1 inhibitor, and chemotherapy, the patient had a significant improvement in her infiltrative optic neuropathy and leptomeningeal disease, both clinically and radiographically. Her visual function improved significantly as well.

Conclusions, including unique features of the case:
Though nivolumab is approved for treatment of metastatic gastric adenocarcinoma, this is the first case that shows a dramatic response with nivolumab as adjuvant to chemotherapy in a case of advanced LMC. Most case reports of gastric cancer-associated LMC describe an extremely high mortality rate with expected survival of only weeks. Our patient is doing very well, with no recurrent optic neuropathy or other systemic manifestations greater than 11 months from her diagnosis.

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Keywords: Optic neuritis, Optic neuropathy, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Tumors, Chemotherapy and radiation injury

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Bilateral Sequential Vision Loss From Multiple Progressive Fusiform Aneurysms With COL1A1 Genetic Variant With Vascular Ehlers-Danlos Syndrome Phenotype

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Introduction:
Vascular Ehlers-Danlos syndrome, characterized by vascular wall dysfunction and intestinal perforation, is established with a heterozygous pathogenic variant in COL3A1 in molecular genetic testing or type III collagen chain synthesis abnormalities on biochemical analysis.1 Rarely, the vascular phenotype can be associated with COL1A1 mutations, typically with substitutions of arginine by cysteine. We present a case of sequential, bilateral compressive optic neuropathy by expanding internal carotid artery (ICA) aneurysms in a patient with a COL1A1 variant.

Description of Cases:
A 50-year-old female with history of recurrent sigmoid diverticulitis with colonic perforation, who presented for neuro-ophthalmic consultation due to progressive visual decline in the right eye. On initial examination, she had hand-motion vision in the right eye, and normal visual acuity (20/20) and normal Humphrey visual field testing (HVF) in the left eye. MRI Orbits showed a large right paraclinoid ICA aneurysm. CTA Head/Neck showed multifocal fusiform aneurysmal dilatation of the bilateral ICAs, with the right ICA aneurysm measuring 10.4 mm, and multiple aneurysms involving left MCA bifurcation, and vertebrobasilar junction. She underwent pipeline stent of the right aneurysm, which had enlarged to 15.2 mm. In subsequent examination, the visual acuity remained poor in the right eye (count-fingers), normal visual acuity in the left eye (20/20) but with new superior arcuate visual field defect. Contrast-enhanced MRI Orbits and MRA Head showed interval dilation of the left ICA aneurysm with mass effect on the left prechiasmatic optic nerve. She underwent pipeline diversion of the aneurysm. Given multiple fusiform and expanding aneurysms, molecular genetic testing was performed, demonstrating COL1A1 (c.2573C>T; p.Ala858Val).

Conclusions, including unique features of the case:
We present an unique case with bilateral sequential compressive optic neuropathy from bilateral enlarging fusiform ICA aneurysms in a patient later found to have COL1A1 genetic variant with vascular Ehlers-Danlos Syndrome phenotype. Progressive fusiform aneurysm, particularly when multiple, should raise concern for genetic connective tissue disorders.

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Keywords: Interventional neuroradiology, Vascular disorders, Optic neuropathy, Genetic disease, Neuroimaging

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Blind Spot in the Battle Against Giant Cell Arteritis

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Introduction:

The accepted treatment for acute giant cell arteritis (GCA) is oral or sometimes IV glucocorticoids. Tocilizumab is the standard of care for long-term management. Almost "immediate" pain relief is a characteristic response to corticosteroid treatment, and absence of response is often attributed to insufficient dosing or an alternative diagnosis. Our case supports medical lore that some patients are relatively resistant to non-methylated corticosteroids.

Description of Cases:

A 69-year-old healthy man awoke with severe left lower jaw and neck pain that spread to the right over a week. He then developed jaw claudication, right occipital tenderness and night sweats. Oral prednisone 60mg daily yielded no improvement. One month after onset, vision OD became "hazy", and he presented for care when "haziness" spread to the left. Visual acuity was 20/40 OU, with a relative afferent pupillary defect and central scotoma OD. CRP was 219.6 and ESR was 85; temporal artery biopsy showed granulomatous arteritis. The pain dissipated "immediately" with IV methylprednisolone, administered for 3 days. When he switched to 80 mg daily oral prednisone, his right occipital tenderness and jaw claudication recurred and vision OS deteriorated to "count fingers". He received another 3 days of high dose IV methylprednisolone, then transitioned to oral methylprednisolone 80mg daily, which provided relief. Intramuscular tocilizumab was started and methylprednisolone slowly tapered.

Conclusions, including unique features of the case:

This patient's GCA symptoms responded only to high dose methylprednisolone, which also halted vision loss OD. Although he received asymmetrical doses of methylated and non-methylated corticosteroids, this case raises the question of whether he has relative glucocorticoid resistance, a phenomenon alluded to in the literature. This putative resistance may be cause by less effective metabolism due to gene polymorphyisms (MDR-1, HLA-DRN1, CYP3A), or perhaps our case simply represents more aggressive inflammation requiring higher than typical doses. These considerations have implications for management of a subset of GCA patients.

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Calciphylaxis in a middle-aged Asian patient: An unusual cause of disc swelling

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Introduction:
Calciphylaxis is a small vessel vasculopathy that typically occurs in patients with renal disease. We present a 56-year-old Malay female who presented with an acute unilateral severe visual loss with pallid disc swelling and systemic signs of calciphylaxis.

Description of Cases:
A 56-year-old Malay female presented with acute painless severe visual loss of the right eye. Her past medical history included diabetic nephropathy with end stage renal failure on haemodialysis complicated by tertiary hyperparathyroidism. She also had hypertension, hyperlipidemia and ischemic cardiomyopathy with triple vessel disease. On examination, the right eye had no perception of light, while the left eye had 6/9 vision. All components of optic nerve function testing including Ishihara, red dot perimetry, and confrontational visual fields were normal for the left eye. There were no signs of any cranial nerves involvement or any long tract signs. Bilateral temporal arteries were non-tender and weakly pulsatile. There was a grade 3 relative afferent pupillary defect in the right eye. The fundus of the right eye showed a pallid chalky white swollen optic disc. The initial impression was that of giant cell arteritis (GCA). Incidentally, she was noted to have lower limb eschar and indurated violaceous dermal plaque. Given that she had acute profound visual loss with pallid disc swelling, she was treated for GCA and given pulsed intravenous methylprednisolone for 3 consecutive days, yet with no improvement. She underwent a right temporal artery biopsy which showed mild intimal fibrosis and intramural calcium deposits with no evidence of GCA, in keeping with calciphylaxis. Skin biopsy of lower limb eschar and indurated dermal plaques found features consistent with calciphylaxis, reinforcing the diagnosis of optic neuropathy secondary to calciphylaxis.

Conclusions, including unique features of the case:
A high index of suspicion is required when managing patients with risk factors for calciphylaxis presenting with acute severe vision loss and pallid disc swelling.

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Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Optic neuropathy

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Case Series: Severe Pediatric Optic Neuritis with Significant Visual Recovery Despite Extensive Ganglion Cell Layer Loss

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Introduction:
Many studies have looked at the correlation between pediatric optic neuritis severity and optical coherence tomography (OCT) retinal nerve fiber layer thickness (RNFL) measurements, but few have specifically analyzed ganglion cell layer (GCL) loss in that same context. Some review articles suggest that visual recovery is inversely proportional to degree of GCL thinning. However, we present three patients who had remarkable visual outcomes despite severe RNFL/GCL loss.

Description of Cases:
A 10-year-old boy presented with visual acuity 20/200 in his right eye (OD) and light perception vision in his left eye (OS), was found to have severe optic disc edema in both eyes (OU) and bilateral long segment optic neuritis on MRI. Workup was negative for MOG and AQP4. His vision improved 6 months after treatment to 20/20 OD and 20/25 OS, despite RNFL temporal thinning (average thickness in microns: 84 OD, 91 OS) and diffuse GCL thinning (61 OD, 57 OS) (Zeiss Cirrus OCT imaging). A 5-year-old girl with recurrent MOG-positive optic neuritis and VA nadir of 20/70 OD and counting fingers vision OS, was treated with IV methylprednisolone and IVIG. Her vision improved 7 months later to 20/20 OU, despite RNFL thinning (66 OD, 72 OS) and diffuse GCL thinning (60 OD, 66 OS). A 5-year-old boy with recurrent MOG-positive optic neuritis and acute disseminated encephalomyelitis had VA nadir of light perception OD, and was treated with IVIG, IV methylprednisolone, and PLEX. His vision improved 11 months later to 20/25 OD, despite diffuse RNFL thinning (63 OD) and diffuse GCL thinning (56 OD).

Conclusions, including unique features of the case:
Our case series highlights three pediatric patients with remarkable visual recovery despite severe loss of the ganglion cell layer. These cases highlight a level of neuroplasticity in the pediatric population that begs further study.

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Keywords: Optic neuritis, Pediatric neuro-ophthalmology, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease, Demeylinating disease, Optic neuropathy

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Cemiplimab Induced Myasthenia Gravis, Painless Myositis, Myocarditis, and Hepatotoxicity with Initially Isolated Neuro-ophthalmological Findings

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Introduction:
Cepilimab is an immune checkpoint inhibitor (ICI) that works by allowing native T cells to attack tumor cells by blocking the tumor inhibitory signal [1]. Herein we present a case of cemiplimab induced diplopia and ptosis, with acetylcholine receptor (AchR) triple antibody positive myasthenia gravis (MG), painless myositis, myocarditis, and hepatoxicity.

Description of Cases:
81-year-old gentleman who presented for 2-weeks of worsening intermittent binocular diplopia, right eye ptosis, fatigable flaccid dysarthria, and dyspnea, 6 weeks after initiating cemiplimab. Notable labs included CPK of ~4800, troponin of ~1800, ALT/AST of ~190/390, AchR binding, blocking, and modulating antibody titers of 65.5, 43, and 68, respectively. A total of IVIG 2g/kg and 5000mg of IVMP were administered over 5 days. Despite this, he required intubation and mechanical ventilation, and the family elected to switch his code status to comfort care 6 days afterwards. He passed away 8 hours after extubation.

Conclusions, including unique features of the case:
To our knowledge, this is the first case in the literature of cemiplimab induced MG, painless myositis, myocarditis, and hepatoxicity. In a recent systematic review, ICI associated myasthenia-myositis' mortality rate approached 60% [2]. One potential pathophysiology of this failure of immune tolerance is the presence of a shared epitope of the PD-1 receptor between tumor cells, skeletal muscle, and cardiac muscle, thereby resulting in CD4+ and CD8+ T cell mediated attack of native cells [3, 4]. It is worth noting that the hesitancy to utilize IVMP in similar cases is unjustified, especially with concurrent use of IVIG [2, 5, 6]. In the context of increasing incidence of ICI related adverse effects (AE), likely secondary to increased usage, management strategies from pre-prescription counseling and testing (HLA subtyping, antibody testing, etc), treatment phase (screening tools for ICI-AE, prophylactic/concurrent immunomodulatory therapy), and standard therapeutic guidelines must be considered.

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Keywords: Chemotherapy and radiation injury, Myasthenia, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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Central Nervous System Recurrence of Diffuse Large B-Cell Lymphoma: Tissue Is The Issue

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Introduction:
Leptomeningeal metastasis occurs when malignancies seed the leptomeninges or cerebrospinal fluid (CSF). They are a rare and devastating manifestation of systemic non-Hodgkin's lymphoma (1).

Description of Cases:
A 37-year-old woman with history of diffuse large B-cell lymphoma (DLBCL) in remission status post EPOCH-R chemotherapy and intrathecal methotrexate chemoprophylaxis presented to clinic with a partial pupil-involving right cranial nerve 3 (CN3) palsy that resolved spontaneously. Neuroimaging and CSF analysis were negative. During this time, she underwent autologous stem cell transplant and was declared in remission. Five months later she developed weakness, numbness, and pain of the extremities and painless right eye vision loss. Dilated fundus exam was normal. MRI brain/orbit and cervical/thoracic spine showed widespread leptomeningeal enhancement, including bilateral CN3 and the right optic nerve. Lumbar puncture was performed three times; CSF cytology showed T cell lymphocytosis, but no monoclonal B cell proliferation. Extensive CSF infectious workup was negative. No lesions could be biopsied due to their location and size. Throughout this time the patient was taking between zero and 8 mg of dexamethasone per day for back pain. Ultimately, still without diagnosis, the patient's vision in the right eye progressed to no light perception. Dexamethasone was held, after which infiltration of the right optic nerve increased in size. Biopsy of the optic nerve sheath and optic nerve revealed DLBCL. She began receiving intrathecal methotrexate with shrinkage of lesions on neuroimaging.

Conclusions, including unique features of the case:
Central nervous system (CNS) relapse is a rare manifestation of DLBCL, occurring in 1.9% of patients who receive chemoprophylaxis (2). The gold standard of diagnosis is identification of malignant cells in CSF. However, high false negative rates can occur, especially with steroid use as in this patient (3). In patients with history of systemic lymphoma, new neurological symptoms raise suspicion for CNS relapse, even if repeat CSF analyses are negative.

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Keywords: Optic neuropathy, Tumors, Ocular motility

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Central Vision Loss After Tick-Bite Induced Alpha-Gal Syndrome Leads to Nutritional Optic Neuropathy

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Introduction:
Alpha-Gal Syndrome (AGS) is a tick-bite associated, life-threatening IgE-mediated hypersensitivity reaction to galactose-alpha-1,3-galactose, an oligosaccharide found in most mammalian meats and derivatives. Patients with AGS must adhere to a diet devoid of these mammalian products. We report here the first case of vision loss due to nutritional optic neuropathy in the setting of AGS.

Description of Cases:
A 55 year-old female presented to the Neuro-Ophthalmology clinic for a history of progressive vision loss in both eyes (OU) accompanied by peripheral neuropathy, facial numbness, and paresthesias. Visual acuity measured 20/300 in the right eye (OD) and 20/350 in the left eye (OS). She identified 3/14 and 2/14 Ishihara plates in OD and OS. Pupils were without afferent pupillary defect OU. Optic nerve exam showed moderate temporal pallor OU with 0.25 cup-to-disc ratio OU. Her retina exam was normal OU. Visual field testing confirmed a central scotoma OU. OCT showed temporal nerve fiber layer atrophy and diffuse ganglion cell atrophy OU. MRI Brain and Orbit were unremarkable. An extensive toxic, rheumatologic and genetic evaluation revealed low vitamin B12 only (230 pg/ml). Further history revealed that, six months prior to her symptoms, she initiated a strictly limited diet after a Lone Star tick bite led to a diagnosis of AGS.

Conclusions, including unique features of the case:
This case illustrates the potentially devastating effects of diet modification associated with AGS, of which up to 18,885 new cases are reported yearly in the United States. There is a dearth of knowledge about this syndrome among providers; only 42% of surveyed physicians were familiar with AGS. We surmise that those who do diagnose this syndrome may not be familiar with the subsequent risk for vision loss that may result from diet restriction, and further education with attention to prevention, is needed.

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Keywords: Optic neuropathy, Visual fields

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Concurrent Wernicke's encephalopathy and posterior reversible encephalopathy syndrome following gastric sleeve surgery

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Introduction:
A 26-year-old female with past medical history of sleeve gastrectomy 4 months prior presents with vision loss, ataxia, nystagmus, ophthalmoplegia, optic disc edema, retinal hemorrhages, and encephalopathy. Visual acuity was 20/200 OU and a high frequency upbeat and downbeat nystagmus were noted. Severe ataxia prevented this patient from being able to stand up.

Description of Cases:
MRI showedT2/FLAIR hyperintensities of the frontal lobes, parietal lobes, and occipital lobes bilaterally, concerning for posterior reversible encephalopathy syndrome (PRES). Extensive workup for infectious and autoimmune causes were negative. Further laboratory testing revealed a low thiamine (vitamin B1) level and she was diagnosed with Wernicke's encephalopathy with PRES. Humphrey visual field testing showed a central scotoma in the right eye worse than left eye. Improvement was seen with thiamine repletion. Subsequent OCT showed GCL and RNFL loss consistent with a metabolic optic neuropathy. Follow up 6 months after complete repletion showed improved VA to 20/30 OU but nystagmus, a central scotoma OD, and ataxia limiting standing without support were still present.

Conclusions, including unique features of the case:
While thiamine deficiency and Wernicke's encephalopathy is a well-documented complication of gastric sleeve surgery, it is very rarely associated with PRES. To our knowledge, this is the first report of superimposed Wernicke's encephalopathy and PRES due to nutritional malabsorption. Clinicians should be aware that while Wernicke's encephalopathy and PRES can present with overlapping signs and symptoms, they may also be present concurrently resulting in severely debilitating symptoms in young patients.

References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Optic neuropathy, Neuroimaging

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Considering an unforeseen diagnosis for patients presenting with Cogan lid twitch sign

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Introduction:
The Cogan lid twitch sign (CLTS) is a twitch (overshoot) of the eyelid that occurs after having the patient look down (resting the lid) and then quickly shifting gaze back to primary position. The CLTS is a classic finding described in myasthenia gravis (MG) with high specificity (99%) and moderate sensitivity (75%) (Singman, Eric L. et al., 2011) . We describe two patients with CLTS due to oculomotor nerve (CNIII) aberrant regeneration.

Description of Cases:
The first patient is a 57-year-old right-handed white man who had chronic ptosis and ophthalmoplegia with variability, fatiguability, and intermittency of his symptoms including CLTS, which suggested MG, but examination and cranial imaging confirmed a compressive cranial nerve (CN) III palsy with aberrant regeneration. The second patient is a 49-year-old Hispanic woman with ptosis and positive CLTS. She also had proptosis, optic atrophy, and a partial right CNIII palsy with aberrant regeneration.

Conclusions, including unique features of the case:
Aberrant regeneration of CNIII can mimic CLTS because of firing of the levator palpebrae superioris during up gaze from the downgaze or primary position. In contrast to CLTS, aberrant regeneration is miswiring of CNIII innervated muscles (e.g., lid and superior rectus) that occurs after damage (often compressive or traumatic) to the nerve. Although CLTS in isolation has a reported specificity of 99%, the additional presence of proptosis, pupil involvement, pain, optic neuropathy, or other findings not compatible with MG should be sought to avoid misdiagnosis.

References: Singman, Eric L., Matta, Noelle S., & Silbert, David I. (2011, September). Use of the Cogan Lid Twitch to Identify Myasthenia Gravis | NOVEL - Journal of Neuro-Ophthalmology. https://collections.lib.utah.edu/details?id=227205

Keywords: Tumors, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Paraneoplastic syndromes

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Corneal Confocal Microscopy Assessment of Pediatric and Young Adult Diabetic Corneal Neuropathy.

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Introduction:
Diabetes, a pervasive metabolic disorder, unfolds into a multitude of comorbidities, with diabetic peripheral neuropathy (DPN) taking a forefront. The corneal nerves, owing to their susceptibility to diabetic degenerative changes, signify a crucial site for early neuropathy detection and monitoring. This descriptive study underscores the clinical relevance of Corneal Confocal Microscopy (CCM) in delineating corneal neuropathy among pediatric and young adult diabetic patients, casting a spotlight on its potential in the neuro-ophthalmology domain, especially in early neuropathy identification and monitoring.

Description of Cases:
The study holistically reviewed studies encompassing pediatric and young adult patients (up to age 30) with Type 1 and Type 2 diabetes. Utilizing data extracted from Corneal Confocal Microscopy (CCM), the prevalence and parameters of corneal neuropathy were evaluated in relation to diabetic status. The parameters scrutinized included corneal nerve fiber density (CNFD), corneal nerve branch density (CNBD), corneal nerve fiber length (CNFL), and corneal nerve fiber tortuosity. The analysis included 914 patients and revealed significant reductions in CNFD for type 1 diabetics compared to controls, accentuating its pivotal role as a diagnostic indicator. Additionally, alterations in CNBD and CNFL were observed, necessitating a further delve into their diagnostic implications. The investigation also brought to light the variability in correlations between systemic health metrics, like glycemic control, and corneal nerve health.

Conclusions, including unique features of the case:
The descriptive analysis heralds the merit of CCM as a robust diagnostic modality for early-stage identification and intervention of corneal neuropathy within this demographic. The insights beckon a nuanced approach towards amplifying the diagnostic acumen of CCM and other neuro-ophthalmologic tools in managing diabetic corneal neuropathy. The study accentuates the need for bridging neuro-ophthalmology and diabetic neuropathy research, targeting enhanced clinical practices and therapeutic interventions for the burgeoning diabetic populace. For more information contact Vinit Majmudar at Majmudv@amc.edu

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Keywords: Neuroimaging, Optic neuropathy, Pediatric neuro-ophthalmology, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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Grant Support: None.

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Evaluation of peripapillary retinal nerve fiber layer thickness in intracranial atherosclerotic stenosis

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Introduction:
Purpose: To evaluate the peripapillary retinal nerve fiber layer thickness (pRNFL) in patients with intracranial atherosclerotic stenosis (ICAS)

Description of Cases:
Methods: A cross-sectional study was performed in a general hospital. The intracranial atherosclerotic stenosis was evaluated by digital subtraction angiography (DSA), computed tomography angiography (CTA) or magnetic resonance angiography (MRA). High-definition optical coherence tomography (HD-OCT) was used to evaluate the peripapillary retinal nerve fiber layer thickness. Results: A total of 102 patients, including 59(57.8%) patients with ICAS and 43(42.2%) patients without ICAS, were finally analysed in the study. The peripapillary retinal nerve fiber layer thickness (pRNFL) was reduced significantly in the average, the superior and the inferior quadrants of the ipsilateral eyes and in the superior quadrant of the contralateral eyes in patients with ICAS compared with patients without ICAS. After multivariate analysis, only the superior pRNFL thickness in the ipsilateral eyes was significantly associated with ICAS (OR,0.968; 95% CI,0.946-0.991; p=0.006). The area under receiver operator curve was 0.679 (95% CI,0.576-0.782) for it to identify the presence of ICAS. The cut-off value of the superior pRNFL was 109.5um, and the sensitivity and specificity were 50.8% and 83.7%, respectively.

Conclusions, including unique features of the case:
The superior pRNFL in the ipsilateral eye was significantly associated with ICAS in this study. Larger studies are needed to explore the relation between pRNFL and ICAS further.

References: None provided.

Keywords: Retina, Stroke, Vascular disorders

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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Facial neuropathy in patients with recurrent painful ophthalmoplegic neuropathy

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Introduction:
The involvement of the cranial nerves not associated with ocular movements such as the trigeminal, facial, or hypoglossal nerves has rarely been reported in recurrent painful ophthalmoplegic neuropathy (RPON). There have been several reports of RPON associated with peripheral facial neuropathy, but the relationship between RPON and facial neuropathy is unclear.

Description of Cases:
Methods A total of six patients [men=3, mean age=50.7(29–68)] from a single tertiary hospital diagnosed with RPON according to the diagnostic criteria of the third version of international classification of headache disorders (ICHD) were enrolled. For differential diagnosis, repeated extensive work-ups including brain MRI, cerebrospinal fluid cytology, serologic testing for autoimmune and tumor markers were performed. Results Four patients (66.7%) showed present or past history of migraine. Among total 20 attacks of ophthalmoplegia from six patients, the abducens nerve was the most commonly involved (65%), followed by the oculomotor nerve (25%). Most of the ophthalmoplegia attacks were accompanied by preceding ipsilateral headache (3.6±2.8 days, 85%). Interestingly, facial nerve involvement was also frequent in our series (5/6, 83.3%). Moreover, one patient experienced repeated attacks of left facial neuropathy for three times and two patients did not have any history of migraine. The type of facial neuropathy was all peripheral in common. All available patients (n=2) showed focal enhancement of the facial nerve on brain MRI. Although postauricular pain was usually preceded by the facial neuropathy, migrainous features were not evident for those attacks. Ophthalmoplegia and facial neuropathy were completely improved in several days to weeks without sequelae (21.3±11.6 days).

Conclusions, including unique features of the case:
From our results, the presence of facial neuropathy was not uncommon in patients with RPON. The clinical characteristics of facial neuropathy in RPON were similar with those of Bell's palsy, but facial neuropathy was typically reversible as in ophthalmoplegia. Our observations may support the cranial neuropathy as a pathomechanism of RPON.

References: None provided.

Keywords: Ocular motility, High intracranial pressure/headache, Miscellaneous

Financial Disclosures: The authors had no disclosures.

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Contact Information: None provided.

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Frontal Muscle flap advancement for Myogenic and Neurogenic ptosis

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Introduction:
Severe blepharoptosis from poor levator function can result from myogenic, neurogenic, traumatic, and congenital causes. Surgical techniques for addressing severe ptosis include levator resection and frontalis suspension, depending on levator function. Frontalis muscle flap advancement (FMFA) involves the direct transfer of force from the frontalis muscle to the eyelid without the insertion of material between the muscle and tarsus. FMFA was first reported in 1901 by Fergus for congenital ptosis, and is widely utilized for this indication in Asia, but less commonly in the West. To our knowledge, there is no literature describing the use of FMFA to address ptosis in CPEO or neurogenic ptosis.

Description of Cases:
We report two cases of FMFA used to address myogenic and neurogenic ptosis with good functional outcomes. Case 1 A 54-year-old man with CPEO presented with severe, visually significant myogenic ptosis. Levator function was 3 mm in both eyes. MRD1 was -1 OU. After addressing his lower lid retraction, he underwent uncomplicated, bilateral, conservative FMFA to minimize the risk of exposure from poor eyelid closure and blink. His MRD1 improved to 1.5 and 2.5 mm with improvement of his peripheral vision. Case 2 A 57-year-old woman presented with a history of thalamic stroke, bilateral large angle exotropia, and severe bilateral paralytic ptosis from nuclear CN III palsies. Her right ptosis improved but the left eye remained closed. After addressing her strabismus, she underwent left FMFA and subsequent revision. Her palpebral fissure improved from 0 mm to 4mm and clearance of her visual axis.

Conclusions, including unique features of the case:
Management of severe blepharoptosis is based on the severity of ptosis, its etiology, and the surgeon's preference. FMFA is an effective technique for addressing congenital ptosis. We present two cases where FMFA was utilized to successfully address myogenic and neurogenic ptosis, obviating the need for autologous graft harvesting or synthetic material implantation.

References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Genetic disease, Stroke

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Fulminant Idiopathic Intracranial Hypertension in Setting of Malignant Arterial Hypertension: Prompt Suspicion Matters

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Introduction:
Fulminant idiopathic intracranial hypertension (IIH) refers to the severe and rapidly progressive form of IIH. We report a series of 5 patients who presented with a combination of malignant arterial hypertension and fulminant IIH. The diagnosis of Fulminant IIH was overlooked in the setting of malignant high systemic blood pressure where bilateral optic nerve disc edema was presumed to be related to hypertensive retinopathy.

Description of Cases:
Retrospective case series of 5 patients (4 men and 1 woman) who presented with malignant arterial hypertension and bilateral optic disc edema were subsequently diagnosed with fulminant IIH. All 5 patients (4 males, 1 female) presented with high blood pressure (BP) of greater than 180/120. All patients were treated initially to control BP and were referred to the neuro-ophthalmology clinic due to progressive loss of vision despite BP being under control. Neuroimaging, lumber puncture, and cerebrospinal analysis confirmed IIH with an average opening pressure of 45.4 cm water (range 40 to 58 cm). 4 patients were managed with high-dose acetazolamide and urgent bilateral optic nerve sheath fenestrations and 2 patients required ventriculoperitoneal shunts. 1 patient was treated with furosemide in addition to a ventriculoperitoneal shunt. Final mean visual acuity levels ranged from 20/300 to hand motions in the better eye and count fingers to hand motions in the worse eye.

Conclusions, including unique features of the case:
In patients with malignant arterial hypertension and optic disc edema, optic nerve appearance may be indistinguishable from papilledema causing delay in treatment of IIH resulting in severe visual loss. Our cases highlight the importance of excluding fulminant IIH in patients with systemic hypertension with bilateral optic disc edema. Prompt work-up with brain MRI with contrast and MR or CT venogram to detect neuroimaging signs of IIH followed by a lumber puncture with opening pressure is essential to initiate rapid treatment of IIH.

References: None provided.

Keywords: High intracranial pressure/headache

Financial Disclosures: Bashaer Aldhahwani; Serena M. Shah; Hong Jiang; Byron Lam: Stoke Therapeutics Consultant

Grant Support: None.

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GFAP Astrocytopathy masquerading as Idiopathic Intracranial Hypertension

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Introduction:
Glial fibrillary acidic protein (GFAP) is an intracellular astrocytic intermediate filament that can be a part of autoimmune/paraneoplastic phenomenon in which patients develop immunoglobulins (IgG) against the GFAP antigen causing various manifestations, called GFAP astrocytopathy. GFAP is found in the retina, within the end foot of Müller cells, and astrocytes. It is targeted by GFAP IgG, leading to breakdown of the retina–blood barrier causing optic disc edema. Few cases show underlying teratoma.

Description of Cases:
1) 23-year-old female presented with bifrontal headaches, horizontal binocular diplopia. Exam revealed papilledema with vessel obscuration at disc margins. Imaging revealed empty sella, bilateral transverse sinus stenosis, tortuous optic nerve sheaths, leptomeningeal enhancement in periventricular region. Later she developed neck stiffness/fever 101 F, spinal tap showed elevated opening pressure >55 mm Hg, pleocytosis (cell count 36/cubic mm) Work-up for infectious etiologies was negative, autoimmune encephalopathy panel from cerebrospinal fluid was sent to Mayo Clinic laboratory revealing positive GFAP on cell binding assay. With steroid treatment, there was significant clinical and radiologic improvement with resolution of papilledema. 2) 38-year-old male presented with bilateral occipital headaches; preceded by flu-like illness. Examination revealed papilledema. Imaging showed partial empty sella and left transverse sinus stenosis. Due to overall clinical picture, idiopathic intracranial hypertension (IIH) was suspected, spinal tap revealed elevated opening pressure of 27 mm Hg, pleocytosis (cell count 44/cubic mm). Autoimmune encephalopathy panel from spinal fluid was sent to Mayo clinic laboratory revealing positive GFAP on cell binding assay. He later improved significantly without immunotherapy with resolution of papilledema. GFAP astrocytopathy cases have favorable outcomes. Immunotherapy is recommended once the work up indicates underlying inflammation. CT chest, abdomen, pelvis did not reveal malignancy in both cases.

Conclusions, including unique features of the case:
GFAP astrocytopathy should be considered as a differential of IIH in the appropriate clinical setting with imaging changes and spinal fluid analysis pointing towards inflammation.

References: None provided.

Keywords: Pseudotumor cerebri, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Paraneoplastic syndromes, Neuroimaging, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Gnarly Carotid Arteries – Another "GCA" Emergency?

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Introduction:
Ocular ischemic syndrome (OIS) is a rare cause of vision loss caused by stenosis of the carotid arteries. While most patients with OIS will experience decreased vision, acute loss of light perception (NLP) is rare. In this abstract, we report an unusual case of NLP vision in a patient with right carotid artery stenosis.

Description of Cases:
An 85-year-old male with a history of coronary artery disease, diabetes, and chronic kidney disease presented with 2 weeks of abrupt and painless complete vision loss in the right eye weeks. He endorsed intermittent headaches but no fever, jaw claudication, or myalgias. CTA head and neck revealed 90% stenosis of his right carotid bulb, prompting admission for presumed blindness from OIS with plans for carotid endarterectomy. On admission, ESR was 51mm/h (< 42.5 mm/h) and CRP 3.1 mg/L respectively (< 11 mg/L) and were attributed to other comorbidities. Neuro-ophthalmology was consulted, and workup was significant for a visual acuity of NLP OD and 20/30 OS, right relative afferent pupillary defect, pallid optic disc edema OD, and patchy choroidal circulation on fluorescein angiography (FA). Given the severity of vision loss, disc edema, FA findings, and inflammatory markers, giant cell arteritis (GCA) was considered as an alternate diagnosis. The patient was empirically started on 1g IV solumedrol, and a temporal artery biopsy confirmed active arteritis. Tocilizumab therapy was initiated and the carotid endarterectomy was canceled.

Conclusions, including unique features of the case:
In this case, GCA was initially misdiagnosed as OIS and involvement of the neuro-ophthalmology team was essential to obtaining the correct diagnosis and treatment, avoiding risky surgery in the process. Severe and acute vision loss in elderly patients, even in the presence of findings suggesting critical carotid artery stenosis, should not prematurely be attributed to carotid disease and still warrant consideration of GCA.

References: Terelak-Borys, Skonieczna, Grabska-Liberek; Ocular ischemic syndrome – a systematic review, Medical Science Monitor : International Medical Journal of Experimental and Clinical Research, Volume 8, Pages RA138-RA144, 2012. Trego, Pagani; Three presentations of monocular vision loss, Optometry (St. Louis, Mo.), Volume 77, Pages 82-87, 2006.

Keywords: Vascular disorders, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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High Grade Optic Pathway Glioma in Child with Neurofibromatosis-Noonan Syndrome

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Introduction:
Noonan Syndrome (NS) is an autosomal dominant disorder that is characterized by facial dysmorphism, congenital heart defects, pulmonary stenosis, abnormal genitalia development, intellectual disability, and low-grade gliomas. Manifestations overlap with neurofibromatosis-1 (NF1) due to similar involvement of RAS/MAPK pathways. Individuals with the overlap syndrome, Neurofibromatosis-Noonan Syndrome (NFNS), have been shown only to have mutations in NF1, despite phenotypic features of NS.

Description of Cases:
We report the case of a 12-year-old boy with a clinical diagnosis of NS who developed a multifocal high-grade optic pathway glioma with disseminated disease within the fourth ventricle. Whole exome sequencing revealed a pathological variant in the PTPN11 gene (p.Asn308Thr) and a likely benign variant in the NF1 gene that did not result in a change in amino acid sequence (p.Ala1057=). Biopsy revealed a diffuse high grade glioma with chromosomal copy number amplification of PDGFRA, KIT, and MYC and relative loss of 17p (including TP53) and proximal 17q (including NF1). Spine MRI and CT chest/abdomen/pelvis revealed extensive retroperitoneal, paravertebral, and intraperitoneal low density infiltrative process suggestive of plexiform neurofibromas, raising the possibility of NFNS. Despite therapeutic interventions including radiation therapy and trametinib, the patient developed liquefactive brain necrosis with uncal herniation and succumbed.

Conclusions, including unique features of the case:
This case illustrates that NFNS may be associated with aggressive high-grade optic pathway gliomas in children, in contrast to the typical benign gliomas observed in patients with NS and NF1. It also suggests that NFNS may be associated with a mutation in PTPN11, in contradiction to prior reports suggesting that NFNS is a variant of NF1 that is only associated with mutations in the NF1 gene.

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Keywords: Genetic disease, Tumors, Pediatric neuro-ophthalmology, Chemotherapy and radiation injury, Nystagmus

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Grant Support: None.

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Homonymous hemianopsia and visual hallucination as a manifestation of Sturge-Weber syndrome without facial nevus

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Introduction:
Sturge-Weber syndrome (SWS) is a rare neurocutaneous syndrome characterized by facial nevus and leptomeningeal angiomatosis with neurological and ophthalmological complications. In its rare variant, SWS type 3, the clinical feature of facial nevus is absent, posing a diagnostic challenge. We present the case of a patient with late-onset SWS without facial nevus who presented with homonymous hemianopsia and visual hallucinations.

Description of Cases:
A 56-year-old man with diabetes presented with a five-day history of headache, visual disturbance and visual hallucinations. He had a headache that worsened when he sneezed or defecated, visual field loss localized to the left side, and visual hallucinations that occurred predominantly when he turned to the left. These hallucinations included images such as a person wrapped in a bandage, a television set, or a rainbow. A visual field analysis showed a bilateral field defect on the left hemifield. Brain MRI showed leptomeningeal enhancement in the right occipital leptomeninges. The cerebrospinal fluid study was normal. The electroencephalogram (EEG) performed on admission and during the first 72 hours of hospitalization showed no epileptic discharge. Cancer work-up and paraneoplastic antibody tests were all negative. He was started on steroid pulse therapy and levetiracetam. After 12 days, the intermittent visual hallucinations resolved, and the visual field defect mostly improved. One and a half years later, he experienced a recurrence of visual hallucinations. He described that everything looked like a square shape or body hair looked like black color. A follow-up brain MRI showed the same findings as the previous one. After increasing the dose of levetiracetam and stopping the immunosuppressant, the symptoms did not occur.

Conclusions, including unique features of the case:
We experienced a patient with leptomeningeal angiomatosis without facial angioma presenting with partial epilepsy and hemianopsia. Clinicians must keep SWS without facial veins in mind as a differential diagnosis of leptomeningeal enhancement with homonymous hemianopia and partial epilepsy.

References: None provided.

Keywords: Visual fields

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Homonymous Hemianopsia as the Presenting Sign of Tumefactive Multiple Sclerosis

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Introduction:
Tumefactive demyelination is a rare form of multiple sclerosis (MS) characterized by demyelinating lesions that present similarly to a brain mass. Misdiagnosis is a common occurrence and often requires further testing. The development of relapsing-remitting multiple sclerosis (RRMS) often coincides with tumefactive MS – commonly affecting young adults and involves exacerbations with intermittent periods of recovery. Internuclear ophthalmoplegia or optic neuritis are common neuro-ophthalmic causes of visual disturbances in MS. Though homonymous hemianopsia has been reported in RRMS as an infrequent disruption of the visual pathway, it remains an unusual presenting sign of tumefactive MS in a previously healthy patient. The authors aim to raise awareness that homonymous hemianopic defects may be a the initial sign of tumefactive MS.

Description of Cases:
A 25-year-old previously healthy female presented with vision changes. Visual field testing revealed a right homonymous hemianopsia with preserved visual acuity. Brain MRI showed a lesion in the left occipital lobe concerning for brain neoplasm versus tumefactive demyelination. Spine imaging and cerebrospinal fluid were unrevealing. Plan for brain biopsy was underway. However, at follow-up, visual field defects had self-resolved and imaging showed near resolution of the occipital lesion. Subsequent surveillance brain MRIs showed a new left temporoparietal lobe lesion and later a new left anterior frontal lobe lesion with associated right-sided paresthesia that also self-resolved. A diagnosis of RRMS per McDonald's criteria was eventually concluded and the patient was started on disease-modifying therapy.

Conclusions, including unique features of the case:
There have been very few cases of visual pathway involvement in MS, specifically tumefactive MS, noted in the literature. This case provides an example of this rare visual finding and emphasizes the importance of recognizing atypical visual patterns in the diagnosis of multiple sclerosis in order to avoid misdiagnosis when uncommon presentations are displayed.

References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Demeylinating disease, Visual fields

Financial Disclosures: The authors had no disclosures.

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Hypertrophic pachymeningitis with serpiginous-like choroiditis: a case report

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Introduction:
We reported a case of multiple episodes of bilateral disc edema.

Description of Cases:
A 43-year-old male complained acute scotoma. The BCVA of his right eye was 20/20 and the left eye was 20/25. Bilateral disc edema was noted .VF demonstrated bilateral enlarge blind spot. Brain MRI discovered narrowing of left transverse sinus and cerebral venous thrombosis inducing IICP was suspected. He then received heparin and diamox treatment. After 3 years, his right vision declined to 20/40. Recurrent bilateral optic disc edema with new light orange retinal lesion contiguously extended from the optic disc was noted.Brain MRI revealed new meningeal thickening. Lab test for autoimmune disease and IgG4 were all negative but QuantiFERON-TB Gold test was positive. No active extrapulmonary or pulmonary infection was found. After 3 months of oral diamox and prednisolone treatment, the thickening of meninges improved. He lost follow-up for another 3 years, and returned to visit for right vision deteriorated. The BCVA of his right eye was no light perception and the left eye was 20/32. Recurrence of bilateral optic disc edema with more extension of the light orange choroidal lesion was noted. The inner retina (OD) showed nearly atrophied in OCT. More meninges thickening found in the repeated MRI. He was admitted for steroid pulse therapy. The optic disc edema subsided within 1 week, a right temporal craniotomy with dural biopsy was then performed. The pathology demonstrated fibrosis. ICP was 300 mm H2O and the cytology was free of malignancy. CSF profile showed elevated WBC with neutrophil predominant. After complete studies, idiopathic hypertrophic pachymeningitis (IHP) and serpiginous-like choroiditis with secondary CRAO was diagnosed. The treatment regimen was targeting an inflammatory disease.

Conclusions, including unique features of the case:
A hypertrophic pachymeningitis wih choroditis can derive from a variety of disease, and differential diagnosis can be made from the lab test, CSF profile, and biopsy.

References: None provided.

Keywords: High intracranial pressure/headache, Neuro-ophth & infectious disease (eg, AIDS, prion), Neuroimaging, Retina

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Idiopathic Granulomatous Optic Neuropathy in the Pediatric Patient: A Case Report

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[1] *San Antonio Uniformed Services Health Education Consortium*

Introduction:
Optic nerve head granulomas are rare findings associated with a number of infectious, inflammatory and neoplastic conditions, most commonly sarcoidosis, tuberculosis, toxocariasis, and lymphoma. Although optic nerve head involvement can be the initial or isolated sign of disease, patients usually present with other systemic signs and symptoms or are found to have systemic involvement in subsequent workup.

Description of Cases:
We present a case of an otherwise healthy 17-year-old female who presented with a two-day history of nearly painless unilateral vision loss OD to 20/200, 3+ rAPD, and zero color plates. Dilated fundus examination demonstrated disc edema OD with extravasation of fluid to the macula and an optic nerve head granuloma. There were no other ocular inflammatory or granulomatous findings. Extensive serum (including ACE and anti-MOG), CSF, and imaging workup was unrevealing other than a mildly elevated ESR, CRP, and ANA (1:80). Further in-depth multi-disciplinary work-up was negative. The patient was started on a short course of rifampin and doxycycline, as well as IV solumedrol with rapid improvement in vision to 20/20 OU. At one-year follow-up, the patient continues to have no visual complaints, pain, or systemic symptoms. She has a 1+ rAPD OD with 20/20 VA and 9/10 color plates (HRR), as well as mild residual gliosis with the granuloma near resolution. She continues on prednisone 5mg PO daily, and no systemic etiology has yet presented itself.

Conclusions, including unique features of the case:
Idiopathic granulomatous optic neuropathy is rare. There are few case reports of optic nerve head granulomas as the first or only sign of sarcoidosis, but this has never been reported in a pediatric patient. This case is a unique example of idiopathic granulomatous optic neuropathy in an otherwise healthy pediatric patient. It highlights the necessity of a broad differential as well as aggressive and appropriate management with steroids even in the face of diagnostic uncertainty.

References: Ganesh, Kaduskar; Optic nerve head granuloma as a primary manifestation of ocular sarcoidosis - A tertiary uveitis clinic experience, Oman J Ophthalmol, 8(3), 157-161, 2015. Jordan, Anderson, Nerad, Patrinely, Scrafford; Optic nerve involvement as the initial manifestation of sarcoidosis, Can J Ophthalmol, 23(5), 232-237, 1988. Lustgarten, Mindel, Yablonski, Friedman; An unusual presentation of isolated optic nerve sarcoidosis, J Clin Neuroophthalmol, 3(1), 13-18, 1983. Oyeniran, Katz, Kodati; Optic Disc Granuloma as a Presenting Sign of Sarcoidosis, Ocul Immunol Inflamm, 12, 1-3, 2022. Padhy, Kumar; Systemic sarcoidosis presenting as optic nerve head granuloma, Indian J Ophthalmol, 67(10), 1714-1715, 2019.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Optic neuropathy, Pediatric neuro-ophthalmology

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Immune Checkpoint Inhibitor Induced Myasthenia Gravis With Neuro-Ophthalmologic Findings

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Introduction:
As of 2022, there are 10 immune checkpoint inhibitors (ICI) that are FDA approved to treat solid tumors. Nivolumab is a program cell death receptor inhibitor (PD-1) used as an immunotherapy treatment for several aggressive cancers. However, it poses significant immune-related adverse effects. One of the most poorly understood and serious conditions that can develop is immunotherapy induced myasthenia gravis (MG). To date there are limited reports of Nivolumab causing isolated MG.

Description of Cases:
An 80-year-old gentleman with acute bilateral ophthalmoplegia, dysphagia, myalgias, and dysphonia after receiving treatment with ICI Nivolumab. The patient previously developed similar symptoms after the use of a non-checkpoint inhibitor immunotherapy that quickly resolved with steroid treatment. The current symptoms developed after two infusions of Nivolumab for metastatic lung cancer and he was urgently admitted to secure his airway. CSF showed albuminocytologic dissociation. Our initial concern was AIDP, but EMG failed to show a demyelinating process. Extensive serum testing was positive for AChR antibodies. The myasthenic antibodies; acetylcholine receptor binding antibody 44.7 (< 0.30), acetylcholine receptor blocking antibody 49 (< 15), and acetylcholine receptor modulating antibody 98 (< 32). Inpatient, he received five days of continuous IVIG 0.4g/kg with little improvement. Post discharge, he noticed weekly improvements with slow prednisone taper, every four-week IVIG infusions, and Mestinon.

Conclusions, including unique features of the case:
As the use of Nivolumab and other ICIs for advanced cancers grow, many providers remain unaware of their associated adverse effects, particularly the onset of de novo myasthenia gravis [1]. The pathophysiology of developing MG after Nivolumab therapy is relatively unknown but thought to be due to the activation of autoreactive T-cells by the blockade of PD-1 [2]. It is important to highlight these cases so physicians can be aware of these life-threatening effects, better understand the causative mechanism, and formulate a standard treatment plan to improve morbidity and mortality.

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Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Ocular motility, Paraneoplastic syndromes, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease

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Large Sub-Hyaloid Hemorrhage Associated With Recurrent Optic Neuritis in Multiple Sclerosis

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Introduction:
Optic neuritis (ON) is a common manifestation of multiple sclerosis (MS), occurring in 15-20% of patients as the initial inflammatory event and in more than half of patients across the disease course. The intraocular manifestations can include swelling of the optic nerve head in more anterior cases, however, retinal manifestations are not expected in MS-associated ON. There is a single case report in the literature describing sub-hyaloid hemorrhage associated with MOG-positive anterior ON, but to our knowledge none in MS. We present a case of sub-hyaloid hemorrhage associated with anterior ON in MS.

Description of Cases:
A 33-year-old female with hypothyroidism presented with monocular vision loss and pain with eye movements OS. Family history was positive for MS in her mother. MRI Brain and Orbits with contrast revealed abnormal left optic nerve enhancement. T2/FLAIR sequences revealed multiple non-enhancing periventricular lesions in the brain and one posterolateral lesion in the cervical spine. MOG and AQP4 antibodies tested by cell-based assay were negative. Given these findings, she was treated for ON secondary to MS with IV methylprednisolone. She returned one month later with sudden vision loss and eye pain OD. Fundoscopy revealed optic disc edema and a large sub-hyaloid hemorrhage OD. MRI imaging revealed new right optic nerve enhancement. MOG and AQP4 antibody testing were again negative. CSF analysis showed >5 unique oligoclonal bands, no pleocytosis or elevated protein, and negative cytology and flow. She was treated with IV methylprednisolone, and, after 2-3 months, the hemorrhage resolved with good visual recovery. No underlying retinal vascular abnormality was identified.

Conclusions, including unique features of the case:
Although retinal hemorrhage has been reported in one case of MOG-associated ON, this is the first report of intraocular hemorrhage associated with ON in MS. Further studies should identify risk factors for developing retinal hemorrhage in these atypical cases.

References: Abel A., McClelland C., Lee MS. Critical review: Typical and atypical optic neuritis. Survey of Ophthalmology. 64(6): 770-779. 2019. doi.org/10.1016/j.survophthal.2019.06.001. Toosy AT., Mason DF., Miller DH. Optic Neuritis. Lancet Neurol. 13(1):83-99. 2014. doi: 10.1016/S1474-4422(13)70259-X.

Keywords: Optic neuritis, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Retina

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Leber Hereditary Optic Neuropathy (LHON) Global Data Collection Program (DCP)

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Introduction:
A non-profit organization created to support patients and promote science for LHON, partnered with a non-profit created to hold patient-owned medical data, to establish a global LHON data collection program (DCP). The purpose of the LHON DCP is to provide researchers worldwide with ready access to a large quantity of de-identified information at no charge.

Description of Cases:
Participants in the LHON DCP must carry an LHON genetic mutation. After registering, each participant is asked to complete a comprehensive general health survey. Secondary questionnaires based on symptoms reported are then presented for the participant to complete. As of October 2023, 152 individuals have registered in the LHON DCP since it launched in October 2022. Of these participants, 70.1% have completed the comprehensive general health survey. The de-identified data includes demographic information, the percentage of each primary symptom experienced, and secondary questionnaire symptoms reported at significant levels.

Conclusions, including unique features of the case:
The preliminary data confirms that the primary symptom experienced by individuals who carry a LHON mutation is central vision loss. It indicates that some patients experience other symptoms commonly experienced in other mitochondrial diseases. The current LHON DCP sample size is a starting point and participation will grow over time. The LHON DCP will allow further LHON-related research and scientific studies to take place more easily. Researchers will be able to do cross-disease research throughout the platform to explore symptoms in common. Queries based on genetics, symptoms or disease on an ever-increasing set of patient-reported data will be possible. As LHON DCP participant numbers increase, that data will allow researchers to better access, understand and ultimately treat LHON patients and their presenting symptoms.

References: None provided.

Keywords: Genetic disease, Optic neuropathy, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Miscellaneous

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Malignant Peripheral Nerve Sheath Tumor (MPNST) Presenting As A Progressive Unilateral Cranial Polyneuropathy

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Introduction:
Malignant peripheral nerve sheath tumor (MPNST) is a rare sarcoma that can be associated with Neurofibromatosis type 1. Commonly arising from benign plexiform neurofibromas, pain, new neurologic signs/symptoms, or a rapidly enlarging mass may signal malignant transformation of a precursor lesion into MPNST. Definitive diagnosis is made by biopsy and may be aided by immunohistochemistry. MPNSTs are locally aggressive and have metastatic potential; therefore, timely treatment with surgical resection and adjuvant therapies is critical.

Description of Cases:
A 67-year-old woman presented with a left sixth nerve palsy and a left Horner syndrome. These signs were preceded by a one-year history of left-sided facial burning, progressive left facial pain, left facial numbness, and decreased left eye tear production. In 1955 at age 12 months, she underwent radiation therapy to the left jaw for treatment of a hemangioma. MRI of the brain with contrast showed abnormal asymmetric enhancement of the cisternal segment of CN V with involvement of CN V2, CN V3, and CN VII, all on the left. The initial trigeminal biopsy was nondiagnostic. Six months later, the patient returned with worsening left-sided facial pain progressive left eyelid ptosis. Examination revealed a new complete left CN III palsy and a partial left CN VII palsy. Repeat MRI brain showed progression of cranial nerve enhancement as well as an indurated nodule at the left upper rear molar. A subsequent biopsy of the submandibular lymph node showed a malignant spindle cell neoplasm leading to a diagnosis of MPNST. Currently, the patient is enrolled in a MPNST clinical trial.

Conclusions, including unique features of the case:
We present a unique case of intracranial MPNST with progressive unilateral cranial polyneuropathy. Clinicians may benefit from increased awareness of MPNST and its potential for aggressive local and metastatic spread, which in this case justified a second biopsy to establish a definitive diagnosis.

References: Bates JE, Peterson CR, Dhakal S, Giampoli EJ, Constine LS. Malignant peripheral nerve sheath tumors (MPNST): a SEER analysis of incidence across the age spectrum and therapeutic interventions in the pediatric population. Pediatr Blood Cancer. 2014 Nov;61(11):1955-60. doi: 10.1002/pbc.25149. Epub 2014 Aug 17. PMID: 25130403.

Keywords: Tumors, Skull base, Neuroimaging, Chemotherapy and radiation injury

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Grant Support: None

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MALT Lymphoma Presenting as Symptomatic Optic Neuritis: A Case Report

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Introduction:
Optic neuritis (ON) is the inflammation of the optic nerve often associated with demyelinating diseases like multiple sclerosis. However, ON with atypical clinical features requires thorough evaluation. Primary ocular adnexal lymphomas are the most common orbital tumors, with mucosa-associated lymphoid tissue (MALT) B-cell lymphomas involving the orbit and the optic nerve. Their diagnosis is challenging as empiric corticosteroids can confound diagnostic workup. We present a case of optic neuritis secondary to MALT lymphoma to illustrate its nuanced workup.

Description of Cases:
51-year-old healthy African American woman presented with one month of progressive blurry vision, color desaturation and left eye pain. Her neurologic exam showed decreased left visual acuity to 20/60, relative afferent pupillary defect, and 0/13 Ishihara plates. The rest of her exam was intact. MRI of the brain was normal, but orbital sequences demonstrated left optic nerve sheath contrast enhancement and enlargement. Another amorphously enhancing lesion was identified in the right inferior orbit, which raised concerns for atypical ON etiologies. Despite visual loss and active inflammation on imaging, corticosteroid therapy was deferred to prioritize diagnostic yield. Broad workup was negative for autoimmunity, systemic neoplasm, and infection. CSF showed a bland profile. IgG4 levels was high at 156, raising concern for IgG4-related ocular disease. Confirmatory biopsy of the right intra-orbital mass demonstrated atypical CD20+ lymphoid infiltrates, but < 10% plasma cells expressed IgG4. Molecular analysis was positive for monoclonal IgH gene rearrangement, confirming the likely diagnosis of MALT lymphoma with bilateral ocular involvement. She initiated bendamustine and rituximab chemotherapy with improvement of her ocular symptoms.

Conclusions, including unique features of the case:
Atypical presentations of ON warrant thorough diagnostic workup. IgG4-related ocular disease and ocular adnexal MALT lymphoma share many similarities that require histologic and molecular analysis to differentiate. Early identification of MALT lymphoma causing ON is crucial to initiate proper therapies, maintain disease control, and preserve visual acuity.

References: None provided.

Keywords: Optic neuritis, Optic neuropathy, Tumors, Orbit/ocular pathology, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Metabolic Optic Neuropathy Secondary To Hyperbaric Oxygen Therapy: A Case Report

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Introduction:
Myopic shifts due to lens changes after hyperbaric oxygen therapy (HBOT) have been previously studied. However, optic neuropathy due to HBOT has not been reported. We describe the case of a patient who developed bilateral optic neuropathy after HBOT.

Description of Cases:
A 68-year-old man underwent HBOT for a diabetic foot ulcer. One month into his course, he developed progressive step-wise bilateral vision loss with each subsequent treatment. HBOT was discontinued after 2 months. On initial ophthalmology evaluation, 1 month after discontinuing HBOT, he reported gradual improvement in vision. His visual acuity was 20/500 in the right eye (OD) and 20/70 in the left eye (OS), and there was no relative afferent pupillary defect (RAPD). Color vision was 0/14 OD and 4/14 OS. Anterior segment exam was notable for moderate nuclear sclerotic cataracts in both eyes (OU), and dilated fundus exam was notable for mild non-proliferative diabetic retinopathy OU. MRI brain/orbits was unremarkable. Serologic testing for infectious, inflammatory, and nutritional etiologies was unremarkable. Two months after discontinuing HBOT, his visual acuity improved to 20/80 OD and 20/30 OS. HVF 24-2 showed decreased foveal thresholds OU and central depression OD. OCT RNFL showed bilateral temporal atrophy. He underwent cataract surgery and was re-evaluated 6 months after discontinuing HBOT. His visual acuity was 20/25 in each eye, there was no RAPD, color vision was 7/10 OD and 9/10 OS. HVF 24-2 showed normal foveal thresholds, but mild persistent central depression OD. OCT RNFL showed stable bilateral temporal atrophy.

Conclusions, including unique features of the case:
The temporal relationship of patient's vision loss and recovery, as well as the pattern of optic atrophy suggest the development of metabolic optic neuropathy secondary to HBOT. We postulate that the mechanism was related to oxidative stress from free radicals. This is the first case of metabolic optic neuropathy following HBOT to be reported in the literature.

References: Riedl, et al. Myopic shift and lens turbidity following hyperbaric oxygen therapy - a prospective, longitudinal, observational cohort study. Acta Ophthalmol. 2019 Sep;97(6):596-602. doi: 10.1111/aos.14010. Epub 2019 Jan 28. PMID: 30690920.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Metastatic Adenocarcinoma Presenting as Orbital Apex Syndrome: Application of Immunohistochemistry in Diagnostic Ophthalmic Pathology

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Introduction:
Orbital Apex Syndrome refers to an array of signs and symptoms that results from the involvement of various structures in the area of the orbital apex by a specific pathology. These may include inflammatory, infectious, traumatic/iatrogenic, neoplastic and vascular conditions. Clinically, the condition can present with visual loss, ophthalmoplegia, paresthesia or anisocoria. Surgery in patients presenting with this condition is primarily indicated for tissue acquisition for pathological diagnosis, identification of responsible microorganisms, debridement of nonviable tissue, decompression of the orbital or optic nerve for pain relief and preservation of visual function, and for prompt implementation of definitive treatment.

Description of Cases:
This is a case of a 52 year old male patient with a subacute history of ophthalmoplegia and vision loss secondary to optic neuropathy. Orbital Apex Syndrome was the primary consideration. Laboratory work up eventually ruled out infectious, inflammatory and ischemic etiologies. During the course of the disease, a new onset supraorbital mass lesion was observed. Surgical pathology of the newly appreciable mass yielded a diagnosis of Metastatic Carcinoma. An essential ancillary examination for identifying carcinomas of unknown primary sites is Immunohistochemistry. CK7 and CK20 expression profile later established a diagnosis of Adenocarcinoma. Further use of complementary organ-specific antibodies, including GATA3, TTF1 and p40 Immunohistochemistry staining would allow for more precise guidance toward the primary source of the carcinoma of unknown primary.

Conclusions, including unique features of the case:
Orbital Apex Syndrome is an uncommon condition that is attributable to a variety of causes. Diagnosis of the disease mainly includes clinical, laboratory and imaging modalities. Our case warranted a biopsy of the lesion and Immunohistochemistry staining that effectively identified the primary origin of the malignancy. Early recognition is critical in these cases, as the condition may pose a threat to the patient's vision and health.

References: None provided.

Keywords: Optic neuropathy, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: The authors had no disclosures.

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Contact Information: None provided.

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More than Meets the Eye: Unmasking a Case of Dermatomyositis with Unilateral Periocular Edema

Thomas Lamson [1], Marielle Mahan [1], Narmien Murdock [1], Andriy Kostyuk [1], Eva Chou [2], Benjamin Osborne [1]

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Introduction:
This is a discussion of a unique case of dermatomyositis presenting with primarily peri-ocular manifestations. The patient unfortunately suffered a prolonged and complicated hospital course in order to properly manage his illness.

Description of Cases:
A previously healthy 20-year-old male presented to the emergency department with two months of waxing and waning right eye swelling and erythematous facial rash. Initially, his edema was confined to the right upper eyelid. He had been treated unsuccessfully for presumed preseptal cellulitis with multiple courses of oral antibiotics and antivirals. During this time, he also developed generalized weakness. His initial examination showed an asymmetric and well-demarcated erythematous facial rash involving the right eyelids, malar region, and temple with associated edema. He was also found to have a rash in a shawl-like distribution on the torso and neck as well as erythematous papules on the extensor surface of his hands. His visual acuity was reduced to 20/60 OD compared to 20/25 OS, with right lower lid entropion and lash abrasions of the ocular surface. Initial serum work-up was significant for elevations of creatine kinase, LDH, AST, and ALT. There was no leukocytosis, and ESR and CRP were normal. CT scan revealed right-sided superficial and preseptal cellulitis. MRI of the head and neck was significant for right-sided periorbital tissue edema and diffuse edema of the neck muscles. Skeletal muscle biopsy demonstrated inflammatory myopathy consistent with dermatomyositis. The patient was started on high dose intravenous steroids and later transitioned to mycophenolate mofetil for long term immunosuppression.

Conclusions, including unique features of the case:
This case is significant for instructing ophthalmologists on the possible ocular manifestations of a serious systemic illness. Recognizing classic features of these processes, especially in atypical presentations, often requires a complete physical examination and careful attention to subjective patient history.

References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Miscellaneous

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Grant Support: None.

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Neuro-ophthalmological Findings of Increased Intracranial Pressure Due to HSV-II Meningitis

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Introduction:

Mollaret's meningitis is a form of recurrent aseptic meningitis usually caused by HSV-II, but can be seen with VZV, HSV-I, and EBV [1]. Patients usually present with typical symptoms of meningitis in addition to seizures, altered mental status, or cranial nerve palsies. The current belief is that episodes are usually self-limited, resolving in 2-5 days. Whole-exome sequencing conducted in such patients revealed abnormalities in autophagy machinery and cell proliferation/apoptosis. Reduced antiviral interferon responses were also discovered [2]. Herein we present a case with signs and symptoms suggestive of increased intracranial pressure only with a positive HSV-II PCR on CSF analysis.

Description of Cases:

36-year-old gentleman who presented to the hospital from an optometry clinic post discovery of bilateral optic disc elevation and disc hemorrhage after he reported a one-month history of headaches, pulse synchronous tinnitus, transient visual obscurations, and new onset "shower of opaque black dots" in his vision. The patient has a history of two self-limited HSV-II meningitis episodes, though he never experienced these visual manifestations before. An MRI showed optic nerve sheath distension and empty sella sign. Lumbar puncture revealed an opening pressure of 34cm H2O, elevated protein of 119mg/dL, hypoglycorrachia of 26mg/dL, and positivity for HSV-II. Valacyclovir 1g TID and acetazolamide 250mg BID were initiated prior to discharge. Computer-assisted visual fields revealed minimal deficits, while Optical Coherence Tomography revealed an RNFL thickness of 167 microns OD and 184 microns OS, along with resolving disc heme and improvement of clinical symptoms upon follow up 3 days later.

Conclusions, including unique features of the case:

The signs and symptoms of isolated increased intracranial pressure without meningism in the context of Mollaret's meningitis secondary to HSV-II are uncommon. This constellation of symptoms should prompt clinicians to consider the possibility of HSV-II meningitis in the absence of meningism while possibly highlighting some emerging, underlying mechanisms of increased intracranial pressure.

References: 1- Shalabi, M., & Whitley, R. J. (2006). Recurrent benign lymphocytic meningitis. Clinical infectious diseases, 43(9), 1194-1197. 2- Hait, A. S., Thomsen, M. M., Larsen, S. M., Helleberg, M., Mardahl, M., Barfod, T. S., ... & Mogensen, T. H. (2021). Whole-exome sequencing of patients with recurrent HSV-2 lymphocytic mollaret meningitis. The Journal of infectious diseases, 223(10), 1776-1786.

Keywords: Neuro-ophth & infectious disease (eg, AIDS, prion), High intracranial pressure/headache, Neuroimaging

Financial Disclosures: Abdulaziz Al Abdulghani; Emma Proctor; Grant Goodfellow; David Kaufman: Research investigator for Viridian Therapeutics; Annie Szmanda; Sunita Yedavally

Grant Support: None.

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Optic neuropathy associated with acute motor axonal neuropathy in the post partum period

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Introduction:
Guillain Barre syndrome (GBS) is an auto-inflammatory disease of the peripheral nervous system characterized by an acute, ascending paralysis. Rarely, it is associated with central nervous system manifestations including optic neuropathy (ON).

Description of Cases:
A 32 year old otherwise healthy woman presented to the emergency department 14 days post-partum with acute onset paralysis of both lower extremities and vision loss of the left eye. Initial MRI shortly after presentation was unremarkable. Within hours she developed quadriplegia and respiratory failure requiring intubation. Lumbar puncture showed elevated protein to 67 mg/dL but normal cell counts and glucose. Nerve condution studies demonstrated diffusely reduced muscle action potentials with normal sensory nerve condition, consistent with acute motor axonal neuropathy (AMAN), a variant of GBS. Intravenous immunoglobulin (IVIG) was initiated. On hospital day 3, ophthalmology was consulted. On exam, the patient did not blink to threat in the left eye and a large relative afferent pupillary defect (rAPD) was present. Extraocular motility was full but induced pain in the left eye. Fundus examination showed a pink, crisp optic nerve head. Repeat MRI orbits demonstrated increased enlargement and enhancement of the left optic nerve. Decision was made to treat with alternating sessions of plasmapheresis and IVIG. On hospital day 10, the patient was transferred out of the ICU after completion of 5 sessions each of plasmapheresis and IVIG. Her visual acuity was 20/20 OD, 20/400 OS, with a left rAPD reduced in size, 6/6 HRR color plates OD, 2/6 OS, and resolution of pain with extraocular movement.

Conclusions, including unique features of the case:
The authors present a case of the AMAN variant of GBS associated with severe optic neuropathy. While corticosteroids are the first line treatment for ON, they can worsen weakness in GBS, complicating management. Albeit rare, in such cases, plasmapheresis, IVIG, and rituximab have been employed successfully.

References: 1. Andersen, Erik W., Monique M. Ryan, and Richard J. Leventer. "Guillain–Barré syndrome with optic neuritis." Journal of Paediatrics and Child Health 58.5 (2022): 887-890. 2. Lüke, C., et al. "High-dose intravenous immunoglobulins for treatment of optic neuritis in Guillain-Barré syndrome." Klinische Monatsblatter fur Augenheilkunde 224.12 (2007): 932-934.

Keywords: Optic neuritis

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Orbital Apex Syndrome With Normal Imaging

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Introduction:
A 75-year-old man presented with a six-day history of acute onset right eye ptosis, right eye pain, and numbness over the right forehead.

Description of Cases:
On initial presentation, clinical examination revealed severe right eye ptosis, binocular diplopia with right eye total ophthalmoplegia, and right forehead numbness. Initial MRI of the brain and orbits with and without contrast was unremarkable. CT angiography revealed an incidental 4mm x 3mm right A2 segment aneurysm. CT venogram of the head demonstrated abnormal asymmetric enhancement of the right carotid cavernous sinus, which was consistent with carotid cavernous fistula, but was later ruled out by a cerebral angiogram. Further patient interview and examination revealed an additional trace right RAPD and decreased right central visual acuity of count fingers at 2 feet. Repeat brain and orbit imaging with and without contrast was ordered. A small, enhancing mass with surrounding edema was revealed, inferolateral to the orbital apex and affecting the superior orbital fissure. Although CT angiography of the head and neck was negative for an acute intracranial process, it incidentally revealed anterior upper lobe pulmonary mass. Further workup revealed a 2.7cm right upper lobe solid pulmonary nodule, with invasion into the left anterior first rib, mediastinum, left superior pubic ramus, and hilar lymph nodes. Lung biopsy was positive for non-small cell lung carcinoma. The patient was then scheduled for treatment of metastatic non-small cell lung cancer, including treatment for skull base metastasis.

Conclusions, including unique features of the case:
Neurological disorders can manifest in subtle ways that may not be immediately evident through imaging alone. A thorough clinical exam acts as an indispensable bridge between the patient's subjective experiences and objective diagnostic data.

References: None provided.

Keywords: Orbit/ocular pathology, Tumors, Skull base, Adult strabismus with a focus on diplopia, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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OSPREY: An Open-label Study to Investigate Safety, Tolerability, and Exposure of the Antisense Oligonucleotide (ASO) STK-002 in Patients with OPA1 Autosomal Dominant Optic Atrophy (ADOA)

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Introduction:
Autosomal dominant optic atrophy (ADOA) is the most common inherited optic neuropathy seen in the general population, presenting in early childhood with slowly progressive visual loss. Over half of all patients are registered legally blind by the fifth decade of life. Most patients carry mutations in the OPA1 gene resulting in loss-of-function with ~50% reduction in cellular OPA1 protein level. OPA1 is a dynamin-related GTPase that localizes to the mitochondrial inner membrane and reduced levels impair mitochondrial function leading to retinal ganglion cell loss. STK-002 is an investigational antisense oligonucleotide (ASO) treatment designed to upregulate OPA1 protein expression by leveraging the wild-type (non-mutant) copy of OPA1 to restore OPA1 levels, thereby potentially stopping or slowing vision loss in patients with ADOA.

Description of Cases:
OSPREY is a multicenter, first-in-human, phase 1 study enrolling patients with a confirmed pathogenic heterozygous OPA1 variant who are ≥6 to ≤55 years old. Part A will enroll 42 patients ≥18 to 55 years old and Part B will enroll 12 patients ≥6 to < 18 years old. STK-002 will be given as an intravitreal (IVT) injection in one eye. The primary objectives are to evaluate safety, tolerability, and pharmacokinetics following single IVT doses of STK-002. The secondary objectives are to evaluate changes in visual function and ocular structure and the impact on quality of life in patients with OPA1-ADOA. Following single eye dosing on day 1, patients will be monitored for 48 weeks. A 3+3 dose escalation design will allow evaluation of up to 4 different doses of STK-002. Enrollment is anticipated to begin in early 2024.

Conclusions, including unique features of the case:
STK-002 has the potential to be the first disease-modifying therapy for patients with OPA1-ADOA, addressing the genetic cause of the disease by restoring OPA1 levels. OSPREY may inform appropriate dosing as well as efficacy measures for future clinical trials.

References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Genetic disease, Pediatric neuro-ophthalmology, Retina, Optic neuropathy

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Outer Retinal Tubulations in Boucher-Neuhäuser Syndrome

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Introduction:
We present the case of a 20-year-old female with complaints of worsening peripheral and night vision. A thorough history reveals hypogonadotropic hypogonadism without ataxia, growth abnormalities, or intellectual impairment. Whole exome sequencing reveals compound heterozygous mutations in PNPLA6, consistent with Boucher-Neuhäuser syndrome (BNS). BNS falls under the PNPLA6 neurodegeneration spectrum and classically presents with a triad of cerebellar ataxia, chorioretinal dystrophy, and hypogonadotropic hypogonadism. 1,2

Description of Cases:
Optical coherence tomography (OCT) reveals outer retinal tubulations. Prior literature describes outer retinal tubulations in other diseases of retinal degeneration with one report of ORTs in BNS. 3,4 OCT angiography (OCTA) reveals diffuse choriocapillaris loss with relative sparing of the retinal vasculature. This is phenotypically similar to choroideremia, yet the findings in BNS are earlier, more severe, and progress with faster choriocapillaris degeneration. 3

Conclusions, including unique features of the case:
Outer retinal tubulations on OCT represent poorly described findings in BNS. These outer retinal tubulations may be mistaken for cystic spaces seen in retinal edema. It is important to differentiate between these to prevent unnecessary intervention. 3,4 Additionally, OCTA may provide a minimally invasive method for accurate, long term evaluation of the choriocapillaris. Accurate visualization of the choriocapillaris may be critical in the diagnosis of rare chorioretinal degenerations, as well as monitoring disease progression and treatment efficacy. While this patient did not present with cerebellar ataxia, it is critical to note that cases of retinal degeneration may be syndromic even if apparently isolated. Patients with BNS typically develop cerebellar ataxia within their first through third decades of life, but some cases report symptom onset in their fifties. 5 This emphasizes the importance of a thorough neuro-ophthalmic exam, imaging, and targeted genetic testing in cases of retinal degeneration to modify treatment and guide patient expectations.

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Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Genetic disease, Retina

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Contact Information: None provided.

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PABPN1 Mutation in an Indigenous New Mexican Family Affected by Oculopharyngeal Muscular Dystrophy

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Introduction:
Oculopharyngeal muscular dystrophy (OPMD) is a rare inherited disorder that primarily affects the eyelids and pharynx. Clinical manifestations of this disease are late-onset with slow progression, occurring around the fifth decade of life with symptoms of ptosis and dysphagia. OPMD occurs due to a trinucleotide repeat expansion in the PABPN1 gene, which results in abnormal protein aggregation in skeletal muscles.

Description of Cases:
A 65-year-old woman presented to oculoplastic clinic for evaluation of bilateral blepharoptosis. Given positive family history of ptosis in sister, father, and paternal grandfather, referral was made to neuro-ophthalmology for further evaluation. On interview, she endorsed 10-15 years of progressive bilateral ptosis. She also reported difficulty swallowing large pills. On examination, this patient had severe bilateral ptosis with moderate motility deficit and right hypertropia. Further extensive family history was obtained, and involvement of other family members was determined based on clinical features of severe ptosis in affected relatives. A pedigree was completed, demonstrating involvement of three generations in a pattern consistent with autosomal dominant inheritance. Fourth generation family members are not yet in the expected age range for disease manifestation and have deferred genetic testing. Genetic testing for this patient identified a pathogenic repeat expansion in the PABPN1 gene (13 repeats), confirming the diagnosis of OPMD. Interestingly, this patient's known ethnic background is indigenous to New Mexico paternally and of Mexico's Sonora region maternally.

Conclusions, including unique features of the case:
Family history and clinical features are key for diagnosis of OPMD, which can be confirmed with genetic testing. Mutations in PABPN1 gene have been identified worldwide, with highest prevalence reported in Bukkharu Jews in Israel and in French-Canadians. We report here a pedigree of OPMD in an indigenous New Mexican family. There is no current cure to arrest the progression of OPMD. This patient elected to undergo bilateral upper lid blepharoplasty due to visually significant ptosis.

References: None provided.

Keywords: Genetic disease

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Papilledema in Setting of Newly Approved Drug for Amyotrophic Lateral Sclerosis

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Introduction:
40-year-old female with history of familial ALS with pathogenic SOD1 variant presented to neuro-ophthalmology clinic for evaluation of vision changes. After receiving her 3rd intrathecal dose of Tofersen (Qalsody), FDA-approved in April 2023 for SOD1-ALS, she presented to the ED with headaches, fever, and neck stiffness. CSF studies showed lymphocytic predominant pleocytosis and elevated protein with negative infectious studies, consistent with aseptic meningitis presumed secondary to Tofersen.

Description of Cases:
At initial visit in November 2022, patient had grade II disc edema OD>OS by the Frisén scale. Humphrey visual fields demonstrated blind spot enlargement with nasal depression OU. Given ongoing Tofersen therapy and visual field changes, patient was empirically started on topiramate but self-discontinued due to side effects. Patient was receiving serial LPs with Tofersen therapy and papilledema remained stable at 4-week follow-up. In January 2023 (dose 5), Tofersen was discontinued due to intolerable side effects. In March, patient had worsened papilledema despite a 12lb weight loss (grade III disc edema with peripapillary hemorrhages OS>OD). She was started on furosemide which was titrated up to 40mg twice daily with gradual improvement in papilledema. In July 2023, patient's disc edema improved to grade I OU.

Conclusions, including unique features of the case:
Limited data exists on the side effects and management of Tofersen – a new drug under the FDA's accelerated approval pathway. 7% of the clinical trial population on Tofersen had a neurologic serious adverse event, including aseptic meningitis, increased ICP, and papilledema. To our knowledge, there is no data on the clinical course and management of papilledema after Tofersen discontinuation. Our patient demonstrated worsening papilledema despite drug discontinuation and required the addition of furosemide for eventual improvement in papilledema 6 months after Tofersen discontinuation. More case reports will be helpful to guide patients with SOD1-ALS (the 2nd most common gene affected in familial ALS) on this new medication.

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Keywords: Genetic disease, High intracranial pressure/headache, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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Persistent Radiological Changes After Cryptococcal Meningoencephalitis In An Immunocompetent Patient With Bilateral Optic Atrophy

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Introduction:
We report an immunocompetent patient with cryptococcal meningitis who had persistent inflammatory brain and optic nerve lesions, years after completing antifungal therapy.

Description of Cases:
In April 2020, a 32-year-old Indian man developed right lower extremity sensorimotor deficits and was treated for presumed tuberculous meningitis. MRI brain showed diffuse focal nodular enhancing granulomatous lesions. After initial improvement he was readmitted with worsening headache, blurred vision and papilledema. Lumbar puncture showed elevated CSF opening pressure (30 cm water) and cryptococcal infection. Despite treatment with antifungal medications, acetazolamide and steroids, he experienced vision loss, altered sensorium and seizures over the next 6 months. Repeat MRI brain showed increased burden of nodular enhancing granulomatous lesions. Repeat CSF studies showed elevated opening pressure, CSF pleocytosis and persistent cryptococcal antigen. A brain biopsy was consistent with “immune reconstitution inflammatory syndrome” prompting aggressive steroid therapy, which stabilized vision. By January 2022, he was off antifungal and steroids and he relocated to Atlanta, USA. Neuro-ophthalmic examination showed bilateral optic atrophy with visual acuity 20/25 RE; 20/800 LE. Repeat MRI brain and orbits (2022/2023) showed persistent contrast enhancement of the optic nerves with diffuse persistent and new areas of parenchymal, leptomeningeal, and pachymeningeal nodular enhancement. Multidisciplinary assessments including repeated CSF examinations were negative for infectious, inflammatory and neoplastic causes. Repeat brain biopsy of the new enhancing areas showed mild inflammation with inactive Cryptococcus. Despite radiological progression, he continues to do clinically well with no clinical progression of neurological or visual deficits.

Conclusions, including unique features of the case:
Persistence of enhancing intraparenchymal lesions without clinical deterioration has been reported years after successful therapy of cryptococcal infection. We report a patient with persistent and new areas of intraparenchymal, leptomeningeal and optic nerve enhancement without clinical deterioration, CSF or pathology evidence for recurrent cryptococcal disease. We recommend careful monitoring of these individuals.

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Keywords: Neuro-ophth & infectious disease (eg, AIDS, prion), Neuroimaging, Optic neuropathy

Financial Disclosures: Elizabeth Akinsoji; Laura Anorue; Neil Lava; Matthew Schniederjan; Sachin Kedar: Consultant for Astra-Zeneca

Grant Support: None.

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Petrous Apicitis Complicated with Ophthalmoplegia and Death - A Case Report

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Introduction:
Petrous apicitis, the infection or inflammation of the apex of the temporal bone, is a rare complication of otitis media after mastoiditis. Clinically, petrous apicitis can manifest as components of the triad of Gradinego's syndrome, such as retro-orbital pain, abducent nerve palsy, and purulent otorrhea. Although the complete triad has become uncommon due to early empirical antibiotic use, it would involve crucial cranial structures that resulted in severe neural compromise and even mortality when it occurred.

Description of Cases:
A 60-year-old male with underlying poor control of diabetes and hypertension had a sudden onset of eye movement limitation in his left eye. Upon examination, the left eye showed complete ophthalmoplegia, ptosis, and absent light reflex. He was admitted two weeks ago for intractable headache and vertigo. He had numbness over his left face. Along with bilateral hearing loss, an otoscopy revealed chronic otitis media in both ears. Upon admission, the head and neck CT showed bilateral mastoiditis extended to the left petrous bone and invaded the left carotid canal. Under the impression of otitis media complicated with mastoiditis and petrous apicitis, he was treated with intravenous ceftriaxone and vancomycin. A subsequent brain MRI study revealed new inflammatory lesions at the left orbital apex and left cavernous sinus. The antibiotics were intensified, and prednisolone 15mg TID was administrated to address the cranial nerve palsies related to the petrous apicitis. The ptosis subsided after seven days under the new regimen. After one month of treatment, his headache was gone, and his ophthalmoplegia partially improved. Unfortunately, he did not attend the outpatient follow-up; he was found dead at home.

Conclusions, including unique features of the case:
Petrous apicitis has a variable presentation with the potential for severe morbidity. Adjacent cranial nerve palsies and any manifestation of Gradinego's triad should raise suspicion to warrant prompt intervention.

References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Graves' disease, Neuro-ophth & infectious disease (eg, AIDS, prion), Orbit, Orbit/ocular pathology

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Contact Information: None provided.

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Practice Patterns for Central Retinal Artery Occlusion at a Canadian Academic Health Sciences Centre

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Introduction:
American and European reports have outlined practice patterns for central retinal artery occlusion (CRAO) in those regions. Canadian data are needed to identify opportunities to improve care for patients with CRAO in Canada. Our objective was to describe CRAO presentation and management at Canada's largest academic health sciences centre.

Description of Cases:
We performed a retrospective analysis of consecutive patients with CRAO presenting to The Ottawa Hospital between 1-June-2019 and 31-May-2023. Study outcomes included demographics, presentation pathways, workup, interventions, and referrals. Seventy-six patients were included. The median (interquartile range [IQR]) age was 68.1 (61.4-81.8) years and 46 (60.5%) were male. The most common site of presentation was an emergency department for 47 (61.8%). The median (IQR) time from vision loss to presentation was 15.0 (3.5-48.0) hours. Twenty-two (28.9%) presented within 4.5 hours. The median (IQR) door-to-ophthalmology time was 12.0 (4.6-22.6) hours. Neurovascular imaging was obtained for 73 (96.1%) patients. Among patients presenting within 48 hours, median (IQR) door-to-imaging time was 6.1 (3.6-9.1) hours. GCA-targeted history/physical was documented for 66 (86.8%) and GCA serology was obtained for 58 (76.3%). Temporal artery biopsy was performed for 19 (25.0%) and GCA was diagnosed in 6 (7.9%). No patient received thrombolysis. Four (5.3%) received putative conservative therapy for CRAO. Empiric glucocorticoid therapy for GCA was initiated for 17 (22.5%). Sixty-four (91.4%) patients with non-arteritic CRAO were referred for secondary stroke prevention. Referral for ocular follow up was made for 60 (78.9%) of the cohort.

Conclusions, including unique features of the case:
We found that patients seek care urgently following CRAO, and generally receive appropriate stroke care. Work is called for to reduce delays to ophthalmologic consultation, to optimize GCA screening, and to promote appropriate secondary prevention. Despite growing evidence for efficacy of thrombolysis in CRAO, our academic hospital system – the largest in Canada – has not yet adopted this within its institutional scope.

References: None provided.

Keywords: Vascular disorders, Retina, Stroke

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Grant Support: n/a

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Rare case of Miller Fisher syndrome initially presented as bilateral Internuclear opthalmoplegia

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Introduction:
Internuclear opthalmoplegia is an ocular movement disorder caused by a lesion of the medial longitudinal fasciculus, usually presenting typical opthalmoplegic features. Common etiologies of INO are stroke, multiple sclerosis. Some cases of myasthenia gravis have been reported as pseudo-INO. Here, we report a rare case of a patient with miller fisher syndrome who initially presented as clinical features of bilateral INO.

Description of Cases:
A 57 year old woman visited Emergency department with symptom of binocular diplopia for 2 days. The patient had history of hypertension, dyslipidemia, non-invasive breast cancer (DCIS). On first day, neurologic exam showed bilateral medial rectus limitation, abducting nystagmus and there was no evidence of other cranial nerve involvement. Deep tendon reflex showed normoreflexia, no other focal neurologic deficit was shown. Imaging studies including contrast enhanced MRI with brainstem thinsection was done but no definite abnormality was found. Further evaluation with CSF study, nerve conduction study, Jolly test, lab test including antibodies were done. After admission, opthalmoplegia was getting worse. The patient showed nearly fixed horizontal gaze with vertical gaze limitation, hyporeflexia on DTR and mild ataxia. Follow up imaging study with MRI also showed no lesion, and the clinical symptom was compatible with miller fisher syndrome. The treatment with intravenous immunoglobulin therapy (IVIG) was started. On third day of treatment slight improvement of lateral rectus limitation was seen. After finishing treatment, DTR recovered to normoreflexia, the patient discharged with improving symptoms.

Conclusions, including unique features of the case:
This patient was a rare case of miller fisher syndrome initially presented as INO clincal features. The case showed that even though the clincal features of INO are seen, we should not exclude rare etiologies like miller fisher syndrome. This patient also showed improvement of symptom after IVIG, which may reflect the effectiveness of IVIG on miller fisher syndrome like other typical Guillan barre syndrome.

References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Demeylinating disease, Nystagmus

Financial Disclosures: The authors had no disclosures.

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Recurrent Diplopia Associated with Maxillary Sinusitis

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Introduction:
This case report discusses the unusual presentation of recurrent diplopia and facial pain in a 59-year-old male patient with a history of maxillary sinusitis surgeries performed 44 and 33 years ago.

Description of Cases:
The patient presented to the neurology department with vertical diplopia and left facial dysesthesia, accompanied by infraorbital pressure. Neurologic examination revealed a limited downward gaze in the left eye and decreased sensation in the left maxillary area, while other cranial nerve functions, eye lid movement, and visual acuity remained normal. Enhanced brain magnetic resonance imaging displayed opacification of the maxillary sinuses on the left, invading the infra-rectus muscle. Based on these clinical findings and imaging, the patient was diagnosed with maxillary sinusitis with orbital invasion and subsequently underwent successful surgical exenteration of the sinusitis.

Conclusions, including unique features of the case:
In conclusion, diplopia associated with maxillary sinusitis is uncommon, and in this case, recurrent sinusitis led to the reappearance of diplopia. While the occurrence of diplopia with maxillary sinusitis is rare, this case underscores the potential for recurrence after surgery. Furthermore, it highlights the success of surgical intervention in treating recurrent cases of maxillary sinusitis. This report contributes to our understanding of the complexities of maxillary sinusitis and its ophthalmic manifestations.

References: None provided.

Keywords: Neuroimaging, Ocular motility

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Relapsing-Remitting Multiple Sclerosis and Intermediate Uveitis: A Consolidated Treatment Approach

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Introduction:
Intermediate uveitis (IU) can be associated with relapsing-remitting multiple sclerosis (RRMS) and often requires prolonged corticosteroids and/or immunomodulatory therapy, resulting in increased medication burden. The efficacy of RRMS disease-modifying therapy (DMT) in managing RRMS-associated IU has not been well-studied.

Description of Cases:
This is a retrospective single-center case series of 10 RRMS patients meeting 2017 McDonald criteria with associated intermediate uveitis per Standardization of Uveitis Nomenclature criteria, treated with either natalizumab (n=6) or the anti-CD20 monoclonal antibodies rituximab, ocrelizumab, and ofatumumab (n=4). In the natalizumab group, 1/6 patients trialed another DMT (glatiramer) before starting natalizumab. In the anti-CD20 group, 1/4 patients trialed other DMTs (glatiramer, dimethyl fumarate) prior to anti-CD20 therapy. Median duration of natalizumab treatment and anti-CD20 treatment was 2.3 years (range 0.9-9.0) and 1.3 years (range 0.9-2.4) respectively. 4/6 patients were receiving oral prednisone for IU treatment prior to natalizumab initiation and 3/4 patients in the anti-CD20 group. Patients were tapered off prednisone over a median duration of 0.3 years (range 0.1-0.5) while receiving natalizumab and 0.7 years (range 0.5-1.9) while receiving anti-CD20 therapy. Since steroid discontinuation, patients receiving natalizumab have not needed additional immunosuppressants for management of IU exacerbations over a median duration of 1.6 years (range 0.5-8.7). In the anti-CD20 group, 2 patients on ocrelizumab and 1 patient on ofatumumab experienced IU exacerbations. All patients in this study remain clinically and radiographically stable without evidence of RRMS flare.

Conclusions, including unique features of the case:
Natalizumab monotherapy may stabilize both IU and RRMS and minimize corticosteroid exposure, as compared to anti-CD20 monoclonal antibodies. Thus, natalizumab may be the DMT of choice in patients with RRMS and concomitant IU. Larger prospective studies are needed to assess the long-term safety and efficacy of these DMT in RRMS associated IU patients.

References: None provided.

Keywords: Demeylinating disease, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Orbit/ocular pathology, Orbit

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Satralizumab Treatment In Adults With AQP4-IgG–Seropositive Neuromyelitis Optica Spectrum Disorder: A Retrospective Case Series

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Introduction:
Neuromyelitis optica spectrum disorder (NMOSD is a rare autoimmune neuroinflammatory disease that primarily affects the optic nerves and spinal cord and can lead to sensory/motor impairment, vision loss and permanent neurological disability. The US Food and Drug Administration approved satralizumab for use in adults with aquaporin 4 autoantibody–positive (AQP4-IgG+) NMOSD in 2020, but real-world data are limited. We describe the experience with satralizumab in adults with AQP4-IgG+ NMOSD in clinical practice.

Description of Cases:
Case information for adults with AQP4-IgG+ NMOSD who received satralizumab for ≥6 months was obtained from US healthcare providers; case collection is ongoing. Patient characteristics, examination findings, diagnostic test results, treatment response and reported adverse events (AEs) were recorded. Adults with NMOSD who were aged 19-81 and of various ethnic backgrounds (Asian, Black/African American, White and Hispanic/Latinx) were included; more than one-third had comorbid or previous autoimmune diseases. NMOSD disease duration ranged from 1 to >25 years; most patients had optic neuritis and/or transverse myelitis symptoms. Approximately 75% received immunosuppressants other than corticosteroids (azathioprine or mycophenolate mofetil) or disease-modifying therapies (rituximab, tocilizumab or eculizumab) as preventative NMOSD treatment before satralizumab. Reasons for switching included treatment intolerance, AEs and inadequate disease control. As of August 2023, individuals had received satralizumab for < 1 to >7 years as monotherapy or in combination with immunosuppressants. To date, almost all individuals have been relapse free with satralizumab and continue to receive satralizumab. Overall, disease control was maintained, with few AEs reported, including neutropenia, leukopenia and elevated lipids and cholesterol.

Conclusions, including unique features of the case:
In this ongoing retrospective case series, satralizumab was effective and well tolerated in people with NMOSD, including those who switched to satralizumab due to ineffectiveness and/or poor tolerability of their previous treatment. These outcomes align with the efficacy and safety outcomes of satralizumab in the Phase 3 SAkura clinical trials.

References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Optic neuritis, Demeylinating disease

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Sequential vision loss in a patient with giant cell arteritis while on intravenous steroid therapy: a case report

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Introduction:
Giant Cell Arteritis (GCA) may present with arteritic anterior ischemic optic neuropathy (AAION) which requires prompt diagnosis and management with IV corticosteroids to minimize the risk of contralateral vision loss. We report a case of vision loss in the unaffected eye two days following treatment with IV corticosteroids following unilateral AAION.

Description of Cases:
An 81-year-old man presented with a temporal headache and jaw claudication followed by unilateral vision loss which occurred about three days prior to his presentation to our service. Neuro-ophthalmic examination revealed a right RAPD and pallid optic disc swelling and he was diagnosed with right ischemic optic neuropathy. Laboratory studies demonstrated normal ESR (12 mm/hr) and elevated CRP (18.4 mg/L). He was admitted for IV steroid therapy and temporal artery biopsy. Three days later, he developed sudden, painless vision loss in the left eye. Visual acuity was “Hand Motions”, and fluorescein angiography revealed a new left choroidal infarction. A positive temporal artery biopsy confirmed the diagnosis of GCA.

Conclusions, including unique features of the case:
Sequential vision loss from GCA is a devastating event which is often preventable with rapid corticosteroid treatment. In their literature review, Kokloni et al identified 21 cases of sequential vision loss in patients with biopsy-proven GCA who received IV steroids1-12. In this group, patients suffered second eye vision loss between 1-12 days following presentation, and treatment was initiated up to eight days later (median 2 days) following first eye involvement. We suspect that our patient’s delayed presentation following the initial AION contributed to ongoing vasculitic inflammation. Our case emphasizes the importance of close follow up, ideally with hospital admission for IV corticosteroid therapy, particularly those with delayed presentation following unilateral AAION.

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Taking One on the Chin: A Precautionary Case of Burkitt's Lymphoma and Radiation Induced Optic Neuropathy

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Introduction:
A case report of 'numb chin syndrome' and a pupil-involving CN3 palsy as heralding signs of lymphoma in a teenager whose treatment led to bilateral blindness.

Description of Cases:
19 year-old Caucasian obese female presented to the emergency department with diplopia for one-week following wisdom tooth extraction for tooth pain and crowding two-weeks prior. The patient reported continued chin numbness after procaine local anesthesia and was found to have a pupil-involving cranial nerve three palsy. MRI brain revealed a hypo-enhancing sellar mass with extension into cavernous sinus. The differential included inflammation, infection, and infiltration. A diagnostic tissue biopsy from the enlarged retro-molar trigone area was performed by otolaryngology. Pathologic evaluation revealed CD10-positive high-grade B-cell lymphoma with 85% of cells positive for MYC gene rearrangement on FISH, most consistent with Burkitt lymphoma. The oncology team performed systemic chemotherapy with fertility preservation and adjuvant whole brain radiation with special attention to cavernous sinus (< 25 Gy total), resulting in full recovery and disease remission. Eleven months after diagnosis, patient presented to clinic with progressive left eye vision loss with left rAPD, left optic nerve pallor, and a left junctional scotoma on automated perimetry. MRI was obtained with concern for disease recurrence versus radiation effect and demonstrated left pre-chiasmal, chiasmal, optic tract and surrounding temporal lobe enhancement on MRI-FLAIR sequencing. Temporal lobe biopsy showed reactive gliosis consistent with post-radiation effects. Patient was started on medium-dose oral steroids and received two doses of systemic bevacizumab for radiation optic neuropathy. Unfortunately, patient progressed to no light perception bilaterally 2 months later, despite treatment.

Conclusions, including unique features of the case:
Mental nerve neuropathy can be a first symptom of malignancy or recurrence[1,2] for which neuro-ophthalmologists should be aware. Radiation neuropathy is rare (0-10% with < 60Gy exposure[3]) but possible especially when radiation is targeted at the visual pathway and should always be used with caution.

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Keywords: Chemotherapy and radiation injury, Orbit/ocular pathology, Tumors, Miscellaneous

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The Unmasking of a Basilar Aneurysm by Masked Facies: Bilateral Eight-and-a-Half Syndrome due to Basilar Aneurysm

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Introduction:
Eight-and-a-half syndrome (EAHS) refers to a rare constellation of symptoms that arises from a lesion of the dorsal tegmentum of the pons, namely the abducens nucleus, paramedian pontine reticular formation (PPRF), medial longitudinal fasciculus (MLF), and facial nerve fascicle. The former three are affected in one-and-a-half syndrome (OAHS), with the addition of the latter cranial nerve seven yielding the moniker EAHS [1]. Here we report a case of EAHS resulting from a basilar aneurysm prompting urgent surgical intervention; interestingly, with post-operative edema, the patient transiently developed EAHS on the contralateral side resulting in bilateral EAHS. Literature review shows this to be the first documented case of bilateral EAHS from an aneurysm.

Description of Cases:
A 57-year-old vasculopathic male with a known, previously stable basilar aneurysm presented with diplopia. Examination revealed right horizontal gaze palsy with an INO concordant with OAHS, and bilateral forehead-involving facial nerve palsies. Digital subtraction angiography (DSA) found a 2 cm mid-basilar dolichoectatic partially-thrombosed aneurysm with mass effect upon the pons; the patient underwent a flow diversion with eventual need for repeat surgery for advancement of the stent after developing worsening symptoms. Post-operatively, presumably due to edema, the patient was found to have significant dysarthria, left sided hemiparesis, and a new left horizontal gaze palsy with persistence of his earlier findings, now with only vertical gaze intact and retention of convergence. With passing time, the left-sided symptoms receded barring the facial droop.

Conclusions, including unique features of the case:
The most common culprit of EAHS is ischemia, with additional etiologies albeit rare including demyelination, intracerebral hemorrhage, infection (tuberculoma), giant cell arteritis, and the most recently documented, a space-occupying cavernoma, listed respectively in order of prevalence [1,2]. In this case we present a new etiology of an already rare phenomenon in hopes of illuminating both the importance of a thorough localizing physical exam and recognition of this syndrome.

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Trapped In My Head

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Introduction:
Camurati- Engelman disease is a rare autosomal dominant disease, produced by mutations in the TGFB1 gene. It is associated with bilateral symmetric diaphyseal hyperostosis of the long bones with progressive involvement of the metaphysis. We describe a gentleman with this disease who presented with bilateral proptosis and bilateral optic neuropathy associated with bilateral sensory neural hearing loss.

Description of Cases:
A 52 year old non-obese gentleman with hypertension and h/o radial keratotomy presented in neuro-ophthalmology for evaluation of bilateral optic disc elevation. He has bilateral hearing loss. Reported pulsatile tinnitus but denied headache or vision loss. On exam visual acuity was 20/20 OD and 20/25 OS , had normal color vision, no afferent pupillary defect, had bilateral proptosis, bilateral lagophthalmos and bilateral lower eyelid retraction. Anterior segment showed radial keratotomy marks OU. Fundus exam showed elevated optic discs OU that seemed longstanding. HVF 24-2 OU was unremarkable but retinal nerve fiber layer thinning was seen OU with intact ganglion cell analysis. Reported longstanding history of muscle weakness of all extremities and bony abnormality since he was a child. He was diagnosed with Camurati–Engelmann disease around age 8. MRI head with contrast 2 years ago was unremarkable. Denied progressive visual loss. Never had a spinal tap. He was recommended another MRI head and orbits to monitor the optic neuropathy.

Conclusions, including unique features of the case:
Ocular manifestations are rare in this rare genetic disease. There is bony overgrowth of the orbit and optic canal stenosis. Orbital bone involvement may result in proptosis, rarely globe subluxation and optic nerve compression. Cranial base involvement leads to foraminal sclerosis and raised intracranial pressure, producing papilledema. Facial palsy, hearing loss and epiphora may occur.

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Carotid-Cavernous Fistula Masquerading As Uveitis

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Introduction:
Unlike the dramatic presentation of a direct carotid-cavernous fistula, an indirect carotid-cavernous fistula typically has a more insidious course and may initially be mistaken for other diseases.

Description of Cases:
A 64-year-old female with no known past medical or ocular history presented with three weeks of right eye redness and pain. She had been previously diagnosed with iritis and scleritis and treated with topical steroids and oral nonsteroidal-anti-inflammatory drugs. The redness and pain had initially waxed and waned, but had worsened over the past three days along with new onset of proptosis. Review of systems was positive for significant travel history over the past two years, but negative for trauma and systemic symptoms. On examination, visual acuity was 20/60 for the right eye and 20/70 for the left eye. Intraocular pressure was 17 mm Hg for the right eye and 8 mm Hg for the left eye. The right eye had mild restriction to both abduction and adduction and there was 4 mm of proptosis of the right eye. Slit lamp examination revealed diffuse injection of the right eye, 2+ cells in the anterior chamber of the right eye, and trace cells in the anterior chamber of the left eye. Computed tomography angiography and venography revealed engorgement of the right superior ophthalmic vein. Magnetic resonance angiography revealed an indirect carotid-cavernous fistula fed by bilateral internal carotid artery and external carotid artery branches. This was confirmed by digital subtraction angiography and patient underwent endovascular coil embolization, followed by complete resolution of her ocular findings, including uveitis, within one week.

Conclusions, including unique features of the case:
This was a unique case of indirect carotid-cavernous fistula that initially manifested as uveitis. It is essential to keep carotid-cavernous fistula on the differential for a red eye, especially when non-responsive to initial therapy.

References: None provided.

Keywords: Neuroimaging, Vascular disorders

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Neurolymphomatosis Manifesting as Oculomotor Palsy in a 65-Year-Old Female with Diffuse Large B Cell Lymphoma

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Introduction:
Neurolymphomatosis is a rare manifestation of lymphoma, typically presenting with infiltrative polyneuropathy or polyradiculopathy. More rarely still, infiltration may involve cranial nerves, and differentiation from compressive or inflammatory neuropathy may be challenging and result in diagnostic delay.

Description of Cases:
A 65-year-old female with stage IV diffuse large B cell lymphoma (DLBCL) without central nervous system involvement presented with right foot drop, initially thought related to chemotherapy or fibular head compression. Six months following diagnosis of DLBLC, and one month after R-CHOP chemotherapy, the patient developed diplopia, ptosis, and dysphagia. Her ophthalmic exam revealed significantly restricted left-sided ductions with associated mydriasis and ptosis. She had palatal hypomobility concerning for left glossopharyngeal/vagus nerve palsy and right ankle dorsiflexion weakness. MRI brain showed enhancement of the left cranial nerve IX/X complex as well as the left orbital apex. PET-CT revealed concordant hypermetabolism at the left superior orbital fissure/oculomotor nerve, left jugular foramen/vagus nerve, and right fibular nerve. Although CSF flow cytology and cytometry were negative, imaging findings raised concern for neurolymphomatosis. She began high-dose methotrexate and rituximab. One month later, PET-CT showed decreased FDG uptake in aforementioned areas, and there was significant improvement of diplopia and ptosis, though mild residual ophthalmoplegia and anisocoria persist.

Conclusions, including unique features of the case:
Diagnosing neurolymphomatosis requires a high index of suspicion. This case highlights the unique role of PET-CT imaging in lymphoma without explicit need for histopathological analysis. While our patient initially presented with right foot drop, cranial nerve involvement is rarely reported as a lymphomatous manifestation. In addition to exemplary neuroimaging, this case may serve to reduce diagnostic delay, accelerate appropriate treatment, and drive improved outcomes for patients in a similar clinical setting.

References: None provided.

Keywords: Neuroimaging, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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Post-Operative Magnetic Resonance Imaging of the Inferior Oblique Muscle

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Introduction:
Inferior oblique myectomy and recession are commonly performed surgeries for superior oblique palsy. While superior oblique palsy is often associated with characteristic magnetic resonance (MR) findings, no previous imaging study has described the appearance of the inferior oblique muscle after surgery. It is unknown if abnormalities signifying prior myectomy or recession are recognizable on MR imaging, and how they might differ for the two procedures. After myectomy via a temporal approach, as described by von Noorden, the cauterized muscle stump retracts into the medial orbit. How far it retracts and whether it reattaches to the globe also remains unclear.

Description of Cases:
We describe post-operative orbital MR findings in 5 patients with a history of superior oblique palsy: 4 patients after inferior oblique myectomy and 1 patient after inferior oblique recession. In each case, the operated muscle exhibited subtle features suggestive of prior myectomy or recession. After both myectomy and recession, the inferior oblique terminated lateral to the inferior rectus and appeared closely apposed to the globe. MR findings after inferior oblique myectomy and recession were indistinguishable in our series.

Conclusions, including unique features of the case:
MR imaging of the orbit is a valuable pre-operative tool for assessing the status of the inferior oblique. However, the post-operative appearance of inferior oblique myectomy and recession is similar, which may explain why the operations produce comparable results. After myectomy the inferior oblique appears to become closely adjacent to the globe, but the resolution of MR imaging is insufficient to determine whether it definitively re-attaches to the sclera. We propose that, after myectomy, the inferior oblique may either re-attach to sclera, form a fibrous adhesion to posterior Tenon's capsule, or remain adjoining but unattached to the globe.

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Keywords: Neuroimaging, Adult strabismus with a focus on diplopia, Ocular motility, Orbit, Orbit/ocular pathology

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Pupil-sparing oculomotor nerve palsy due to neurovascular compression by the posterior cerebral artery

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Introduction:
Localization and differential diagnosis of isolated oculomotor nerve palsy is a common clinical challenge to physicians. Among various etiologies of compressive oculomotor nerve palsy, direct compressions due to cerebral blood vessel itself without aneurysm have rarely been reported. Herein, we report a case of pupil-sparing oculomotor nerve palsy associated with neurovascular compression by the posterior cerebral artery (PCA).

Description of Cases:
A 55-year-old man presented with binocular diplopia and ptosis for 10 days. He reported a preceding right-sided dull headache one day before the neuro-ophthalmologic symptoms. He had no history of trauma or vascular risk factors. Neurologic examination revealed exotropia in the primary position and impaired extraocular movements of the right eye associated with incomplete ptosis. Pupillary light reflex was normal in both eyes. Other neurologic evaluations were unremarkable. CSF cytology, testing for anti-ganglioside antibodies and acetylcholine receptor antibodies, autoimmune, and tumor markers were all negative. Brain magnetic resonance (MR) imaging revealed neurovascular compression with downward displacement of the right oculomotor nerve by the right PCA in the subarachnoid space. Moreover, MR angiography documented significant stenosis of the corresponding area in the right PCA. Despite empirical medical treatments, his symptoms were not much improved.

Conclusions, including unique features of the case:
Complete oculomotor nerve palsy with sudden onset and spared pupil is even rarer in cases due to direct vascular compression as in our case. In the present case, the level of the basilar artery bifurcation was low as anterior to the pons, and the right PCA traveled horizontally in the prepontine cistern. These anatomic conditions may contribute to the direct compression of the oculomotor nerve within the subarachnoid space. Contrary to the usual circumstances, the superomedial parasympathetic fibers in the oculomotor nerve were spared in our case. Oculomotor palsies caused by neurovascular compression may be uncommon, but recognizing the possibility of this as one of the causes is important.

References: None provided.

Keywords: Vascular disorders, Ocular motility

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Retinal Ganglion Cell Organizational Changes Detected With Visible Light Optical Coherence Tomography in a Patient with Visual Field Improvement Despite Stable Ganglion Cell Layer Thinning

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Introduction:
Optical Coherence Tomography (OCT) is a widely used tool for diagnosis in the ophthalmology clinic. OCT utilizes near infrared (NIR) light to produce images. With more recent advances in imaging speed, OCT based on visible light (vis-OCT) has become viable. Based on inherent biological tissue contrast and axial resolution being greater with visible light, neuro-ophthalmic information can be gathered with the technique, such as, in the form of en face visualization of individual retinal ganglion cell (RGC) axon bundle networks, referred to as Vis-OCT-fibergraphy. This technique in combination with analytic methods such as a Retinal Nerve Fiber Layer Optical Texture Analysis (ROTA) can provide further insight into structural changes that may correspond with functional changes in vision.

Description of Cases:
We present the case of a patient with compressive optic neuropathy secondary to a grade I sellar chondrosarcoma. She presented with visual field deficits as well as significant Ganglion Cell Layer/Inner plexiform layer (GCL/IPL) thinning on IR-OCT. Post-operatively and following radiation therapy, the patient gained subjective improvement in vision as well as gains on formal perimetry testing; however, GCL/IPL thinning remained stable and diffuse. Despite these stagnant findings on IR-OCT, there was evidence of RGC structural changes, as demonstrated by a combination of ROTA analysis and Vis-OCT-fibergraphy.

Conclusions, including unique features of the case:
We were able to show an organizational difference in the makeup of RGC fibers – despite unchanged GCL/IPL findings – using a novel imaging technique. Future studies gathering the same data of patients with compressive, sellar lesions may help elucidate what structural changes are occurring to help explain and perhaps predict potential gains in vision after intervention.

References: None provided.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Neuroimaging, Tumors, Optic neuropathy, Visual fields

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Reversibility of transverse venous sinus stenosis after papilledema resolution

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Introduction:
Bilateral transverse venous sinus stenosis (TVSS) or stenosis of a dominant venous sinus are very sensitive radiological findings in patients with intracranial hypertension (IH), yet there is still an ongoing debate whether they constitute reversible or permanent phenomena. Thus, the purpose of this case series was to investigate the reversibility of TVSS in patients with IH, including conservatively treated patients with signs of IH as defined by presence of papilledema. This series included patients diagnosed with IH between 2016-2022, who met criteria for presence of papilledema, as quantified by OCT, and bilateral TVSS, which is considered typical of IH on neuroimaging. During follow-up, included patients must have had confirmation of papilledema resolution as well as subsequent neuroimaging after conservative treatment or CSF flow diversion. Patients with dural sinus vein thrombosis or intrinsic stenosis from sinus trabeculations or significant arachnoid granulations were excluded from the study. The primary outcome was to assess TVSS changes, as measured by combined conduit scores (CCS), after resolution or improvement of papilledema.

Description of Cases:
From 435 patients, we identified 10 who met all inclusion criteria. Our cohort comprised entirely women with a median age of 29.5 years and a median BMI of 32.5 kg/m2. Treatment consisted of acetazolamide in seven patients, of which one had additional topiramate and two underwent CSF flow diversion. Furthermore, six patients demonstrated significant weight loss during follow-up. For the primary outcome, five of 10 patients exhibited no appreciable TVSS change, and five patients demonstrated significant improvement in TVSS, of which four received conservative treatment only. Papilledema resolution or improvement was significantly associated with increasing average CCS, TVSS diameter and grade.

Conclusions, including unique features of the case:
This series demonstrates potential for TVSS reversal in patients with resolved papilledema after solely conservative treatment. Future work should identify factors associated with irreversible TVSS for targeted intervention.

References: None provided.

Keywords: Neuroimaging, High intracranial pressure/headache, Pseudotumor cerebri

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Grant Support: None.

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Significance of MRI Enhancement and Diffusion Restriction Patterns in Leukemic and Lymphomatous Optic Neuropathy

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Introduction:
Optic neuropathy (ON) caused by leukemia or lymphoma is an ocular emergency requiring expedited diagnosis and treatment with significant impact on patients' vision and mortality. MRI of the ON is very helpful in diagnosis, with nerve enhancement and diffusion restriction well described in case series. However, these MRI findings have not been well characterized or linked to outcomes. This case series reviews the enhancement and diffusion restriction findings found with leukemic and lymphomatous ON and correlates them with clinical outcomes.

Description of Cases:
A comprehensive search of two large urban hospital's MRI databases from 2000 to 2023 was performed. We identified seven patients with lymphomatous or leukemic ON who had associated MRI findings. The MRIs were reviewed by neuroradiologists to validate the presence of these findings. There were three types of enhancement findings: (1) isolated ON sheath enhancement, (2) enhancement of both the nerve sheath and ON, and (3) enhancing orbital mass surrounding a non-enhancing ON. Diffusion restriction of the ON was found in all cases except those associated with orbital mass. Those with abnormal DWI signal were likely to have worse vision, although the presence of diffusion restriction in the optic nerve did not necessarily portend a poor visual outcome. Patients with orbital mass seemed to be least visually affected. Many patients survived.

Conclusions, including unique features of the case:
Patients present with one of three patterns of enhancement in leukemic and lymphomatous ON. Most have restricted diffusion of the ON. Although most had very poor vision in spite of treatment, severe or permanent vision loss was not uniform. Enhancement and restriction diffusion patterns in this group of patients may be helpful in determining patients' prognoses, and therefore help guide treatment.

References: None provided.

Keywords: Neuroimaging, Optic neuropathy, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: The authors had no disclosures.

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Superior Oblique Muscle Atrophy Helps Differentiating Small Meningioma in Cavernous Sinus from Isolated Oculomotor Nerve Schwannoma

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Introduction:
The diagnosis of small lesion locating in cavernous sinus is very challenge. Due to oculomotor nerve (CN III) schwannoma sometimes is very difficult to distinguish from small meningioma in cavernous sinus, which only presenting with isolated CN III palsy rather than multiple cranial nerves involvement. We found that superior oblique atrophy observed in coronal MRI scan can help differentiating meningioma which also involving trochlea nerve from isolated CN III Schwannoma.

Description of Cases:
a 34-year-old young man presented with squint eyes for more than 20 years. The symptoms progressed slowly and he wanted to have a strabismus surgery. The neuro-ophthalmologic examination showed BCVA was 20/25 OD and 20/20 OS. Pupils measured 6.0 mm OD and 3.5 mm OS. The right upper eyelid showed retraction in primary gaze. The right eye showed large angle exotropia, and ocular motility showed absent adduction, elevation, and depression. The imaging was remarkable for subtle enlargement and enhancement of right CN III in cavernous sinus portion without aneurysm or other pathogenetic lesions can lead to CN III palsy. The coronal MRI scan of the orbit also revealed obvious atrophy of the right superior oblique muscle which indicating lesions of the trochlea nerve. The finial diagnosis was small meningioma in cavernous sinus rather than an isolated CN III schwannoma.

Conclusions, including unique features of the case:
Superior oblique muscle atrophy observed in coronal MRI scan, as well as the aberrant regeneration phenomenon can help differentiating small size meningioma involved trochlea nerve from isolated CN III Schwannoma.

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Keywords: Ocular motility, Neuroimaging, Tumors

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Erythropoietin for the treatment of methanol toxic optic neuropathy: does it really work? A case series

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Introduction:
Erythropoietin (EPO) has demonstrated neuroprotective properties and has been used in small case series to treat methanol optic neuropathy. This study aims to evaluate the effectiveness of EPO.

Description of Cases:
This retrospective case series included data from patients diagnosed with methanol optic neuropathy between 2022 and 2023 at King Fahad Armed Forces Hospital, Jeddah, Saudi Arabia. Demographic information, time from consumption of methanol to EPO treatment, and other treatments administered were collected. Vision assessment was performed before and after EPO treatment. Follow up periods were included. The case series comprised seven male patients with an average age of 39 years at presentation. Six patients received EPO during the acute phase average time to EPO was 17 days, while one received EPO in the chronic phase 7 months post-vision loss. EPO administration ranged from 1-3 doses. The standard dose of 3 cycles of 20,000 IU of intravenous EPO was administered to six patients. The remaining patient received subcutaneous 500u Darbepoetin alfa weekly doses for 4 weeks. All patients underwent renal dialysis in the acute phase. Intravenous methylprednisolone was given to all patients as an adjunct therapy ranging from 3-10 doses. Two patients underwent electrical therapy, and one received stem cell therapy. Visual acuity at presentation ranged from 20/200 to no light perception (NLP), and at the last follow-up, visual acuity ranged from 20/100 to NLP (2 with VA NLP-LP, 3 VA HM -CF, 1 VA 20/400, 1 VA 20/100). The follow-up period ranged from 13-660 days.

Conclusions, including unique features of the case:
Treating methanol optic neuropathy is challenging and time-sensitive. In this case series, EPO, along with adjuvant steroids, showed variable effects on vision improvement, with some patients experiencing some functional visual gain in the acute phase. Long-term follow-up is needed to determine the overall impact of EPO treatment.

References: None provided.

Keywords: Optic neuropathy

Financial Disclosures: The authors had no disclosures.

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Contact Information: None provided.

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Isolated Lower Motor Neuron Facial Nerve Palsy as a presenting sign in COVID-19 associated Orbital Mucormycosis patients. A Retrospective Observational Study

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Introduction:
The main purpose of this study is to emphasize that isolated facial nerve involvement can be the first presenting symptom in patients suspected of COVID-associated Mucormycosis (CAM).

Description of Cases:
This study is a retrospective observational study conducted at a tertiary care referral center which included patients with a history of CAM, who presented with isolated facial nerve palsy as initial presentation between March 2021 to March 2022 along with their follow-up. All the patients were managed with combined modality treatment with antifungal therapy and debridement of the necrotic tissue and fungal debris. There were 184 eyes of 148 patients diagnosed with CAM. All patients developed rhino-orbital mucormycosis (ROM) following the COVID-19 infection and the duration between diagnosis of COVID-19 and ROM was 36±23 days. 42(28%) patients presented with isolated Facial Nerve Palsy (FNP) as the initial presentation. The mean age was 48.5 years (range 38 to 67years) with a male predominance of 29 (69%). All were unilateral cases and were of Lower motor neuron type presentation. All the patients (100%) were treated with systemic Liposomal amphotericin-B and sinus debridement. At a mean follow-up of 13.1 months, 19 (45%) of the patients had improvement in Facial Nerve function and 23 (55%) had static functioning. None of them had worsened. With medical intervention and tarsorrhaphy, the corneal condition was improved in all patients.

Conclusions, including unique features of the case:
Isolated FNP is an unusual but important sign in the presentation of mucormycosis which can be misdiagnosed with a cerebrovascular accident leading to delay in the management. This is a large case series with isolated FNP in CAM cases. A high index of suspicion for mucormycosis in diabetic patients presenting with isolated facial palsy can save the life and salvage the eye.

References: None provided.

Keywords: Orbit, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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It's Just a Twitch

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Introduction:
We present a rare case of a patient diagnosed with a high-grade glial mass, manifesting with isolated hemifacial spasms (HFS) and eyelid myokymia. While eyelid myokymia is typically considered benign, our case underscores its potential progression into facial myokymia and HFS, indicative of underlying pathological processes.

Description of Cases:
A 58-year-old female sought evaluation at the ophthalmology clinic, reporting several daily episodes of right eyelid, cheek, and mouth twitching lasting a few seconds each. Previously, her primary care physician had diagnosed benign HFS, given the absence of facial paralysis or neurological findings. However, as spasms intensified over subsequent weeks, occurring more frequently, she observed right-sided drooling during sleep, and two episodes of transient dysphagia. Consequently, she was referred to neurology. A subsequent brain MRI revealed a 4x4x3.2cm heterogeneous, peripherally enhancing mass with central necrosis left precentral gyrus and left middle/inferior frontal gyri with 3.5mm right midline shift. There was no EMG or EEG performed. At the time of presentation to our institution, the patient's visual acuity, pupillary responses, and visual fields were normal and he had no papilledema, optic atrophy, retinopathy. Consequently, she was referred to Neurosurgery, started on anti-epileptic medications,underwent an awake craniotomy with frontal lobe mass resection. Postoperatively dysarthria, eyelid myokymia, and HFS resolved.

Conclusions, including unique features of the case:
To our knowledge this is the first case of glioblastoma multiforme, involving the motor cortex, presenting with isolated HFS and eyelid myokymia. Although compressive blood vessels may explain some cases, our findings underscore the rarity of more ominous causes. While isolated facial spasms might be attributed to epilepsia partialis continua, which usually signifies subcortical lesions that compress the motor cortex and cause localized myoclonus, a conclusive determination of etiology remains challenging without preoperative EEG. Recognizing this clinical presentation is crucial, emphasizing the need for further investigation or close monitoring of patients with analogous symptoms in our clinic.

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Keywords: Tumors, Miscellaneous

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Non-neuro-otological positional vertigo-superior vena cava syndrome

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Introduction:
The position-induced dizziness is often considered neuro-otologic origins, such as benign paroxysmal positional vertigo or central positional vertigo. However, the other causes of dizziness were often revealed. In this case report, we introduce the cardiovascular origin of vertigo as positional dizziness.

Description of Cases:
An 81-year-old man visited the Neurology clinic and complaint of positional dizziness. He took medicine for cardiomegaly and hypertension. He also had a pacemaker inserted for his arrhythmia history. He felt dizzy with positional change, especially orthostatic positional change and situp after head bending. He also complained of a swelling feeling when he bent his head. In the neuro-otologic exam, including the Frenzel goggle exam, there was no definite positional induced nystagmus, but he reported the dizzy symptom and dyspnea. His face became red when he bent his head. Because of the history of insertion of a pacemaker, we take a brain and neck CT angiography. We check the chest CT for his dyspnea. The brain CT angiography showed no abnormal vascular lesion. However, there was a focal narrowing of the superior vena cava with collateral circulation. We referred the cardiology department, and the recanalization with balloon angiography was done. After the intervention, his positional vertigo was resolved.

Conclusions, including unique features of the case:
We have to pay attention when the patient with positional vertigo is visited and consider not only the neuro-otologic cause but also the other origins.

References: None provided.

Keywords: Vascular disorders, Tumors

Financial Disclosures: The authors had no disclosures.

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Contact Information: None provided.

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Tacrolimus-Induced Intracranial Hypertension and Papilledema

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Introduction:
Tacrolimus is a calcineurin inhibitor used for immune suppression following solid organ transplantation to reduce the risk of rejection and improving graft survival rates. In rare cases, tacrolimus has been reported to cause optic neuropathy, including optic disc edema. Only a single case report exists documenting papilledema and raised intracranial pressure (ICP) secondary to tacrolimus in a child following renal transplant.

Description of Cases:
We report 3 patients who developed papilledema related to the use of tacrolimus after kidney transplant. In two of the cases, a pronounced elevation in ICP was documented, while in a third case this elevation was presumed. In all cases, papilledema resolved after either discontinuation of tacrolimus and/or initiation of ICP-lowering treatment. One patient was able to successfully continue tacrolimus therapy after undergoing venous sinus stenting. Several medications including cyclosporine, another calcineurin inhibitor, have been implicated in causing intracranial hypertension. The underlying mechanism driving elevation in ICP with this class of medications is unclear, but may be related to disruption of cerebrovascular autoregulation. Patients may develop marked venous congestion, ultimately culminating in a rise in ICP and the subsequent emergence of papilledema.

Conclusions, including unique features of the case:
These cases underscore the importance of recognizing tacrolimus and similar agents as potential contributors to post-renal transplant papilledema. When medical or surgical interventions fail to control intracranial pressure effectively, careful consideration should be given to discontinuing these medications. Visual outcomes in such instances are variable, and are contingent on the severity of vision loss at the time of presentation.

References: None provided.

Keywords: High intracranial pressure/headache, Miscellaneous

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Tooth to brain: a case of multiple intracranial abscesses, retro-chiasmal pathway involvement, infectious optic neuropathy and infectious endocarditis after right lower wisdom tooth extraction

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Introduction:
A case of multiple intracranial abscesses, infectious optic neuropathy, infectious endocarditis secondary to alpha hemolytic streptococcus bacteremia after wisdom tooth extraction.

Description of Cases:
39 Yo Caucasian male had dental procedure done 10/15/2022, followed by high fevers, flu like symptoms, headaches and mental fog that worsened over next 1 month. A blood culture done 12/14/2022 showed alpha hemolytic streptococcus, echo cardiogram showed tricuspid endocarditis, spinal tap done 12/16/2022 showed meningitis but was culture negative. CT brain showed multiple supratentorial abscesses, mass effect and pressure on lateral ventricles. Patient was treated with Ro-cephalin and metronidazole which led to improvement in cognitive symptoms. He presented with visual disturbances on 2/27/2023, was noted to have left inferior quadrantopic defect secondary to retrochiasmal pathway involvement possibly during the acute phase. There was thinning on RNFL/GCC and mild disc pallor was noted in right eye. MRI orbits done 2/28/2023 showed multiple supratentorial intracranial abscesses that were stable and increased T2 hyperintensity of the right optic nerve suggesting he must have had infectious optic neuropathy during the acute phase. He was managed conservatively by neurosurgery and neuro-ophthalmology.

Conclusions, including unique features of the case:
Right optic neuropathy, retro-chiasmal pathway involvement and supratentorial abscesses/ endocarditis after dental extraction procedure. A prophylactic antibiotic after the procedure could have prevented this catastrophe.

References: None provided.

Keywords: Miscellaneous, Neuroimaging

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Grant Support: None.

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Why get a topography when you can get an MRI?

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Introduction:
A 62-year-old male with a history of dry eye and new loss of visual acuity in the left eye over several years. Previously, the patient was correctable to 20/20 in the left eye but was noted by the referring ophthalmologist at their last appointment to have a corrected visual acuity of 20/150. The visual field was full to confrontation and pupils were equally round and reactive. The anterior segment and fundus exam were normal. Given vision loss with unknown etiology, MRI was ordered, which was read as showing proptosis and thickened extraocular muscles, fluid distention of the optic nerves, and small vessel ischemic disease. With the diagnosis unclear, the patient was referred to neuro-ophthalmology.

Description of Cases:
Upon neuro-ophthalmological review of the MRI, it was noted that the orbits and optic nerves had a normal appearance and the left cornea was also noted to have an inferior protrusion consistent with ectasia. On neuro-ophthalmic exam there was no RAPD, Goldmann perimetry was normal, OCT RNFL and macula were normal, and retinoscopy was normal in the right eye but scissored in the left eye. Subsequent Scheimpflug imaging showed an inferior thinning with increased keratometry above the thinning, consistent with pellucid marginal degeneration.

Conclusions, including unique features of the case:
There are no reported cases in the literature of corneal ectasia being noted on MRI or CT. In this case, a careful review of the MRI identified the diagnosis. While MRI is not as sensitive as topography or tomography for the diagnosis of ectasia, in cases of decreased visual acuity without an identified etiology, it may be useful to check the corneal shape in the MRI to expedite diagnosis and potentially avoid extra exams and testing.

References: None provided.

Keywords: Neuroimaging, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Miscellaneous

Financial Disclosures: The authors had no disclosures.

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Changes in Visual Field Mean Deviation in Patients with Presumed Mild Idiopathic Intracranial Hypertension and Lumbar Puncture Noncompliance: A Pilot Study

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Introduction:
Idiopathic intracranial hypertension (IIH) is a sight-threatening condition diagnosed with funduscopic examination, neuroimaging, and lumbar puncture (LP). The use of LP to aid in the diagnosis of IIH is considered the gold standard by the modified Dandy Criteria for IIH; however, some patients are noncompliant with this recommendation. This study assesses changes in visual field mean deviation (MD) in this population. This is a pilot study to a broader analysis of noncompliance in patients with IIH.

Description of Cases:
A total of 296 charts were chosen based on the diagnostic code for IIH. Of these, 33 were determined to have presumed mild IIH with LP noncompliance and were included in the study. A patient was considered to have presumed mild IIH if the following criteria were met: papilledema was grade III or less on the Frisén Scale and the visual field showed mild or no deficits. Measuring the change in visual field MD was done by taking the difference between MDs at the time of presumed IIH presentation and at the time of the most recent follow-up for each eye. This data was then averaged to determine overall change. Our study showed that 69.7% of our sample population had an increase in MD and that the overall average change in MD was +0.74. Of the 33 patients, 5 showed a decrease greater than -1.00.

Conclusions, including unique features of the case:
In this patient cohort, the majority showed an increase in visual field MD over time with treatment for presumed mild IIH despite LP noncompliance. It is important to note that this study does not suggest that patients should forgo an LP in instances of presumed mild IIH. All individuals in our collected sample had negative neuroimaging and had their papilledema closely followed and managed by a neuro-ophthalmologist.

References: None provided.

Keywords: Pseudotumor cerebri, Visual fields, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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Characterization and Visual Outcomes of Fulminant IIH: A Narrative Review

Jacqueline Shaia [1], Jonathan Markle [2], Nikhil Das [2], Rishi Singh [3], Katherine Talcott [4], Devon Cohen [4]

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Introduction:
Fulminant idiopathic intracranial hypertension (IIH) is a rapid vision-degrading presentation of IIH that is poorly studied with only case studies and series reports available. To improve patient care, disease must be better characterized and treatment mechanisms studied. The purpose of this review compile all the available fulminant IIH papers and characterizing patient presentation, comorbidities, treatments, and visual outcomes for patients.

Description of Cases:
SCOPUS and PubMed were searched for papers referencing IIH, benign intracranial hypertension, or pseudotumor cerebri. Abstracts were screened for mention of rapid degradation in vision. All studies were required to meet both the modified Dandy criteria and fulminant IIH criteria defined in Thambisetty et al. 1,237 were included in title and abstract screening and 194 were sought for full-text review. 36 studies met the inclusion criteria and patient demographics, treatment methods, and visual outcomes data was extracted.

Conclusions, including unique features of the case:
Of the 36 studies included, 25 were case studies and 11 were case series. In total, 72 patients with fulminant IIH were reported of which 17 were pediatric patients. Three fulminant cases were reported in male patients leaving 96% of our cohort female. Only 85% of patients were treated with a surgical intervention with optic nerve sheath fenestrations being the most prevalent at 36%. 11% of patients presented with both IIH and anemia and 28% of patients had a CN VI palsy. Of those not treated with surgery, none reported blindness at follow up and had significantly better end visual outcomes ($p < 0.05$). Our work is a call to action of the research needed to improve fulminant IIH understanding and treatment. Currently, there are no evidence-based treatments for this presentation of IIH and the best surgical option is unknown. Multi-institutional and international collaborations will be a critical step for future fulminant IIH research.

References: None provided.

Keywords: Pseudotumor cerebri, High intracranial pressure/headache, Visual fields

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Clinical Characteristics of Idiopathic Intracranial Hypertension in Chinese Patients

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Introduction:
Idiopathic intracranial hypertension (IIH) is a relatively common neuro-ophthalmic disease in Western populations with a potential to cause severe visual loss. However, there are relatively few reports from Asian/ Chinese populations.

Description of Cases:
In this retrospective case notes review, we studied the clinical features of Chinese patients who attended a tertiary referral ophthalmic center in Hong Kong during a 20 year-period (2003-2022), with a diagnosis of IIH, identified from a territory-wide electronic database. Sixteen patients were identified (4 male, 12 female), with a mean age of 31.3 years at the time of diagnosis, with 3 patients under the age of 18. Five patients were of normal weight, 4 overweight (Body Mass Index, BMI >25-30) and 7 obese (BMI >30). Headache, blurring of vision, transient visual obscurations and diplopia which were noted by 7, 6, 5, and 4 patients respectively. Two patients were asymptomatic. Almost all the patients had normal/ near normal visual acuity and colour vision at presentation. The mean lumber puncture opening pressure was 35.8cmH2O (range 25-50). One patient received no treatment, and thirteen patients were treated with acetazolamide/ diuretics alone. One patient had transverse sinus stenting and one treated with lumbar-peritoneal shunt. The mean follow-up period was 8.6 years (0.5-28 years), at the end of which, the papilledema had resolved in all patients. Eleven patients were no longer on treatment for IIH, whilst 5 patients remained on acetazolamide. Only 3 eyes had visual acuity worse than 20/30 and 6 eyes had abnormal visual field due to IIH.

Conclusions, including unique features of the case:
IIH is relatively uncommon in the Hong Kong Chinese population. Similar to Caucasians, there was a female predominance and typical association with raised BMI; however, the visual impairment was relatively mild, and most patients were managed successfully with acetazolamide alone.

References: None provided.

Keywords: Pseudotumor cerebri, High intracranial pressure/headache

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Clinical characteristics of patients with idiopathic intracranial hypertension in central China

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Introduction:
To describe the clinical features of idiopathic intracranial hypertension (IIH) patients in central China.

Description of Cases:
A retrospective chart review of patients diagnosed with IIH at the First Affiliated Hospital of Zhengzhou University was conducted from Jan 2013 to July 2021. The analysis included demographic data, presenting symptoms, comorbidities, imaging features, laboratory data, intracranial pressure (ICP), treatment modalities, and outcomes. The study recruited 199 participants, including 145 females and 54 males, with a mean age at onset of 36 years (range 27 to 45 years). The participants had a mean BMI of 26 kg/m2 (range 23.4 to 29.4 kg/m2). Obesity was found in 67 participants (33.7%). The most common clinical symptom reported was headache, which was experienced by 118 (59.3%) participants, followed by decreased vision, which was reported by 115 (57.8%) participants. The main comorbidity among women was anemia (54, 37.2%), while men were more likely to have severe sleep apnea (7, 13%). The most common imaging features were perioptic nerve sheath distension (159, 79.9%) and transverse sinus stenosis (147, 73.9%). Symptoms were relieved with medication in 117 (58.8%) participants, while 72 (36.2%) underwent surgeries such as venous sinus stenting and ventriculoperitoneal shunt. During follow-up, symptoms resolved in 84 (42.2%) participants, while 115 (57.8%) participants experienced symptom improvement. The ratio of decreased vision was higher in females than in males (P=0.02).

Conclusions, including unique features of the case:
Central China appears to have a lower incidence of obesity compared to Western countries. Among comorbidities related to IIH, anemia and severe sleep apnea were the most common. A significant number of IIH patients underwent surgery. It was found that women had worse visual outcomes compared to men. Further investigation is needed to determine the most effective treatment for IIH in a larger cohort of Chinese patients.

References: None provided.

Keywords: High intracranial pressure/headache

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Combination of severe anemia and renal failure as the cause of atypical idiopathic intracranial hypertension

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Introduction:
More in-depth investigation to identify underlying causes for atypical idiopathic intracranial hypertension (IIH) is recommended. The association between anemia and IIH is still controversial.

Description of Cases:
39 y.o. male with BMI30, PMHx of atypical hemolytic uremic syndrome(HUS) on Eculizumab, ESRD s/p renal transplant complicated by graft failure currently on peritoneal dialysis, central retinal vein occlusion(CRVO) with macula edema left eye was admitted for severe optic disc swelling and recurrent CRVO left eye. Exam found mild decreased visual acuity at 20/25 left eye without RAPD, mild optic disc swelling right eye, grade 4 papilledema, tortuous retinal blood vessels with few dot-belt hemorrhage left eye, otherwise unremarkable ophthalmic and neurological exam. MRI brain and orbit showed tiny remote infarct in left cerebellar hemisphere, mild left optic disc protrusion. Lumbar puncture revealed opening pressure 46CMH2O with normal CSF component. Extensive serum and CSF infectious, inflammatory and hypercoagulable workup negative except positive serum CMV IgG and EBV IgG, severe anemia with RBC 2.32 and hemoglobin 5.9, elevated BUN and creatine with GFR 14. CT chest angiography with potent subclavian veins, and internal jugular veins without thrombosis. Recommended blood transfusion for severe anemia and hemodialysis for renal failure considered as likely cause of intracranial hypertension. Patient left AMA and returned two weeks later with worsening OCT findings of RNFL thickening as well as constricted visual field worse left eye. Repeated LP and opening pressure 29 CMH2O and normal CSF components. He was planned for serial daily LPs also considered lumbar drain. Patient declined intervention and started Lasix 20mg BID; follow with hematology with improved anemia also as a candidate for kidney transplantation.

Conclusions, including unique features of the case:
Combination of severe anemia and renal failure is likely causative for intracranial hypertension in this atypical IIH case. Further follow up needed to establish this association.

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Keywords: Pseudotumor cerebri

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Idiopathic Intracranial Hypertension and Ehlers Danlos Syndrome: Case Series

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Introduction:
Neurologic manifestations associated with Ehlers Danlos Syndrome (EDS) are Idiopathic Intracranial Hypertension (IIH), Chiari Malformations, atlantoaxial instability, cranio-cervical instability, tethered cord syndrome, segmental kyphosis, Tarlov cysts, and various resultant movement disorder. Anecdotal reports from large case series have suggested an association between EDS and IIH, but to date, to the best of our knowledge, no such association has been formally reported in biomedical literature.

Description of Cases:
We present a report case series of three subjects with a clinical diagnosis of EDS with accompanying IIH. All patients were evaluated by Genetics and our institute EDS specialist as well as Neuro-Ophthalmology. All patients were women, had a BMI >38, and initially presented to Neuro-Ophthalmology with headaches. Our patients had other manifestations of EDS like shoulder dislocation, sacroiliac joint dysfunction, and skin hyperelasticity. MRI and LP findings were consistent with IIH. They fulfilled modified Dandy's criteria for IIH and managed either medically or surgically. LP opening pressure ranged between 70-37 cm H2O.

Conclusions, including unique features of the case:
If presented with therapy-refractory headaches, IIH should be considered in patients diagnosed with EDS. Diagnostic screenings by ophthalmoscopic examination for disc edema and testing for possible optic nerve swelling in patients with risk factors might be sensible. We have found that papilledema is not commonly seen in patients with EDS and IIH, therefore caution should be applied in evaluating EDS patients with headaches.

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Keywords: Genetic disease, High intracranial pressure/headache, Pseudotumor cerebri, Neuroimaging, Miscellaneous

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Idiopathic Intracranial Hypertension In A Specialist Eye Emergency Department: A Retrospective Audit Of Patient Presentations And Outcomes

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Introduction:
Bilateral papilledema is a common indication for emergency department (ED) referral. Idiopathic intracranial hypertension (IIH) is a common cause for bilateral papilledema, with the diagnosis often made in ED or soon thereafter. Increasing population obesity, a known IIH risk factor, has led to increasing IIH incidence. This study evaluates patients with suspected IIH at a specialist ophthalmologic ED.

Description of Cases:
Methods: Data from an Australian ophthalmologic ED was systematically collected, including demographics, referral sources, symptoms, workup and management. Adults with bilateral papilledema, and no alternate causes on neuroimaging were included. Patients with known IIH were excluded. Results: 54 likely first-time IIH presentations were identified out of 42,891 ED cases from September 1st 2022- September 1st 2023, IIH incidence was ~125 cases per 100,000 ED presentations. Of these patients, 98% were female. Average age was 28.6 years (standard deviation 6.7 years). Visual acuity worse than 6/9 was present in 17%, and headache in 80%. Optometrists made 85% of referrals. 14% of patients had neuroimaging prior to presenting to ED. 72% of patients underwent neuroimaging in / prior to ED. 74% of patients were overweight/obese, and 35% had weight loss discussions in ED. Medications were initiated in 39% of cases.

Conclusions, including unique features of the case:
This study analyses demographics, investigations, and management of suspected IIH at a specialized ophthalmologic ED. Despite the strong association between IIH and weight, there was a low proportion of weight loss discussions identified, likely reflecting the challenges of weight loss discussions. The literature overall has indicated patient receptiveness to weight loss education, and the limited discussion on weight loss strategies presents an avenue for targeted interventions in our patients. We hope to use this data to formulate a standardised multidisciplinary approach to IIH workup and management in our centre for best patient care.

References: None provided.

Keywords: High intracranial pressure/headache, Pseudotumor cerebri

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Idiopathic intracranial Hypertension presenting with isolated facial nerve palsy

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Introduction:
Idiopathic intracranial hypertension is complex syndrome that typically affects obese woman of childbearing age. There is some evidence of hormonal causes and high association with polycystic ovarian syndrome. Frequently, patients with IIH present with headaches, pulse synchronous tinnitus, and transient visual obscurations. Horizontal diplopia due to abducens palsy is the most common cranial nerve deficit. Cranial nerves III, IV, VII and IX and XII are rarely affected. Isolated unilateral cranial nerve 7 palsy has rarely been reported in the literature.

Description of Cases:
We present a case of a 30-year-old woman with a BMI of 36 and a past medical history of hypertension, hypothyroidism, and polycystic ovarian syndrome, who presented in our emergency department with acute-onset right facial droop. On the initial exam, the patient had right peripheral facial palsy and an otherwise non-focal neurological exam. Ophthalmologic exam: visual acuity 20/20 bilaterally, full extraocular movements. Auto threshold visual field was normal bilaterally. Funduscopic exam revealed papilledema. Optic coherence tomography showed bilateral ganglion cell layer thinning. MRI/MRV indicated stenosis of the distal transverse sinuses bilaterally, with no evidence of dural venous sinus thrombosis. Venous manometry showed 12 mm pressure differential across the right transverse sigmoid sinus. The opening pressure was 32 mmHg with normal cerebrospinal fluid composition. The patient was started on acetazolamide 500 mg BID, resulting in a rapid resolution of her symptoms, including her facial palsy. She returned to the clinic eight months later with headaches and horizontal diplopia secondary to an IIH flare.

Conclusions, including unique features of the case:
This is a rare presentation of IIH. Our patient had no history of diplopia, transient visual obscurations or positional headaches. Acute facial palsy with associated blurred vision and right eye pain. nPeripheral facial palsy is often overlooked in the setting of increased intracranial hypertension. Clinical ophthalmologists and neurologists should be aware of atypical presentations.

References: None provided.

Keywords: Pseudotumor cerebri, High intracranial pressure/headache, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease, Interventional neuroradiology

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Intracranial Hypertension And Acute Vision Loss Following Initiation of Chemotherapy Conditioning in a Patient with Myelodysplastic Syndrome in Transformation

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Introduction:
In myelodysplastic syndrome, hematopoietic stem cell transplantation offers the potential for cure with a variety of cytotoxic therapy regimens utilized prior to transplantation. The use of chemotherapy in transplant conditioning, however, can be associated with a variety of side effects ranging in rarity and severity. We present a case of intracranial hypertension following initiation of chemotherapy in a patient prior to planned bone marrow transplantation.

Description of Cases:
A 10-year-old male presented for neuro-ophthalmic consultation following initiation of chemotherapy due to progressively worsening headaches and bilateral blurry vision. Chemotherapy cycle included venetoclax, decitabine, gemtuzumab, fludarabine, and high dose cytarabine. On initial examination, the patient had 20/20 visual acuity in the right eye, decreased vision in the left eye (20/50), dyschromatopsia bilaterally (4/12 plates right eye, 2/12 plates left eye), and Frisen-equivalent grade 5 optic nerve edema bilaterally with diffuse, peripapillary hemorrhage. MRI orbits, brain, and vessel imaging were unremarkable and lumbar puncture had an opening pressure of 55 mmHg. Humphrey visual fields demonstrated diffuse suppression with central island of vision in the right eye and inferior greater than superior depression in the left eye. The patient was started on intravenous acetazolamide, an optic nerve sheath fenestration was performed on the left eye with definitive CSF diversion deferred due to thrombocytopenia. Following treatment, visual fields showed significant improvement in both eyes, improvement in disc edema to Frisen grade 4 and 3 in the right and left eyes, respectively, and visual acuity 20/20 OD and 20/30 OS. The patient underwent interventricular catheter and reservoir placement following improvement in thrombocytopenia for more definitive CSF diversion.

Conclusions, including unique features of the case:
We present a rare case of intracranial hypertension following chemotherapy initiation. Two prior cases of intracranial hypertension following administration of cytarabine are described in the literature. Prompt recognition and treatment of this rare side effect can help prevent permanent visual morbidity.

References: None provided.

Keywords: High intracranial pressure/headache, Pediatric neuro-ophthalmology

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Grant Support: None.

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Macular Retinal Lesions in Patients with Idiopathic Intracranial Hypertension: a case series.

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Introduction:
Idiopathic intracranial hypertension (IIH) is a syndrome most often encountered in overweight women of childbearing age. In correlation with the rise in obesity, there is a concomitant increase in the incidence of IIH. This syndrome poses significant risks of visual complications linked to the severity of papilledema and secondary optic atrophy. In IIH patients, macular alterations also occur but are under-researched and poorly understood. The aim of our study was to identify and describe retinal anomalies associated with IIH in an effort to understand the underlying pathophysiological mechanisms and their impact on visual prognosis.

Description of Cases:
We conducted a retrospective study by reviewing medical records of IIH patients. Ninety-five patients with IIH and macular lesions were included. Clinical and paraclinical data were analyzed to describe the population's characteristics, and OCT imaging was used to characterize macular lesions and assess their prevalence. Lesions could be categorized into the following subgroups: subretinal fluid, macular stars, vascular occlusions, choroidal neovascularization, chorioretinal folds, and inner nuclear layer microcysts. Among the notable findings, 13 cases of Acute Macular Neuroretinopathy were identified. Additionally, we described a new retinal lesion, previously unreported in literature, observed in 17 patients from the case series, which involves interpapillomacular thinning of all retinal layers.

Conclusions, including unique features of the case:
The findings suggest a complex interaction between retinal and choroidal vascularization, influenced by papilledema and retrobulbar pressure in IIH. The identification of a previously unreported retinal lesion and the high prevalence of Acute Macular Neuroretinopathy cases broaden our knowledge concerning retinal anomalies associated with IIH and highlight the need for additional research in this area.

References: None provided.

Keywords: Pseudotumor cerebri, Retina

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Persistent Intracranial Hypertension Secondary to IgG4 Related Disease

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Introduction:
IgG4 related disease is a chronic, immune mediated fibroinflammatory disorder with a wide range of manifestations. We report a case of IgG4 related disease with isolated meningeal involvement resulting in intracranial hypertension.

Description of Cases:
A 32-year-old female presented to an outside hospital with progressive headaches, blurred vision, pulsatile tinnitus, and new onset seizures. Initial examination revealed visual acuity of 20/40 with grade 4 disc edema in both eyes. MRI brain/orbit demonstrated dural enhancement, hydrocephalus, and chiari 1 malformation. A ventriculoperitoneal shunt was placed and meningeal biopsy demonstrated nonspecific signs of acute and chronic inflammation with adjacent cerebritis. The patient improved following shunt placement but required shunt removal a few months later due to intracranial infection. Following shunt removal, the patient noted worsening vision prompting presentation to the emergency department at our hospital. She was found to have 20/400 vision with pale edematous discs in both eyes. MRI brain showed dural and leptomeningeal enhancement. Lumbar puncture was performed with opening pressure of 29 with evidence of CSF inflammation (positive oligoclonal bands and IgG index of 1.3), without infection. Disc edema improved with oral acetazolamide, however, the patient had persistent seizures and later developed altered mental status. Broad infectious and autoimmune lab workup, including serum IgG4 levels, were within normal limits. Repeat meningeal biopsy met criteria for probable IgG4 related disease. The patient had stabilization of symptoms and improvement of dural and leptomeningeal enhancement on oral steroids.

Conclusions, including unique features of the case:
1. IgG4 related disease has a wide range of manifestations that can include intracranial hypertension due to meningeal inflammation. 2. Serum IgG4 levels in IgG4 related disease may not be elevated if the disease process is isolated to a single organ system. 3. Occasionally, repeat biopsy may be warranted in cases of persistent inflammation to achieve a specific diagnosis.

References: None provided.

Keywords: High intracranial pressure/headache, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Orbit/ocular pathology

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Contact Information: None provided.

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Pseudotumor Cerebri Due to A Rare Cause of Primary Hypoparathyroidism: Barakat Syndrome

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Introduction:
Pseudotumor cerebri (PTC) is a clinical entity defined by papilledema and increased intracranial pressure (ICP) with normal neuroimaging besides the increased ICP signs. Hypoparathyroidism and associated hypocalcemia are on the list of underlying etiologies of PTC. Hypocalcemia may increase ICP by interfering with the arachnoid villi's calcium-dependent ability to absorb cerebrospinal fluid (CSF). Barakat (HDR) syndrome is characterized by the triad of primary hypoparathyroidism (H), sensorineural hearing loss-deafness (D), and renal anomalies (R). Here we present a PTC case due to primary hypoparathyroidism related to Barakat syndrome.

Description of Cases:
A fourteen-year-old male was admitted after the incidental finding of bilateral optic disc edema in a routine eye exam without any symptoms. He was diagnosed with primary hypoparathyroidism and sensorineural hearing loss in infancy. Over the years he developed nephrocalcinosis and hypocalcemic seizures. Whole exome sequencing has recently identified a pathogenic GATA3 variant (c.1099C>T; p.R367*) which causes Barakat syndrome. The neuro-ophthalmological exam was unremarkable besides bilateral optic disc edema. Brain MRI revealed posterior globe flattening and optic nerve sheath distension. Lumbar puncture opening pressure was 32 cm/H2O with normal CSF formula. Optical coherence tomography showed an increase in pRNFL thickness (OD/OS:141µm/145µm). Computer-assisted visual fields were normal. Laboratory studies showed significant hypocalcemia (Ca:6.64 mg/dl) without spasms or any other signs of it. Calcium was replaced and acetazolamide (500mg-750mg/day) was started. His vision remained normal during the one-year follow-up.

Conclusions, including unique features of the case:
In the literature, hypoparathyroidism and hypocalcemia-associated papilledema were reported anecdotally. To our knowledge, this is the first case of PTC with genetically diagnosed Barakat syndrome among the ~200 reported. This syndrome should be considered if hypoparathyroidism is detected with either hearing loss or renal disease. Current treatment is symptomatic management of hypocalcemia. It is crucial to emphasize that hypoparathyroidism and hypocalcemia may cause PTC without any signs or symptoms of hypocalcemia.

References: None provided.

Keywords: Pseudotumor cerebri, High intracranial pressure/headache, Genetic disease

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Safety and efficacy of medial eyelid crease incision approach to optic nerve sheath fenestration in patients with vision-threatening papilledema

Alexandra Pietraszkiewicz [1], Bryce Baugh [1], Azraa Ayesha [1], Kathleen Digre [1], Judith Warner [1], Meagan Seay [1], Alison Crum [1], Sravanthi Vegunta [1], Douglas Marx [1], Bhupendra Patel [1], Bradley Katz [1]

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Introduction:
We recently published a multidisciplinary protocol to guide treatment of vision-threatening papilledema (VTP). Many patients treated using that protocol underwent optic nerve sheath fenestration (ONSF). Ten years ago, we transitioned to a medial eyelid crease incision approach to ONSF. The purpose of this investigation was to review the safety and efficacy of this surgical approach in patients with VTP.

Description of Cases:
Methods: We performed a 10-year retrospective review of patients undergoing ONSF. We reviewed demographics, pre- and post-op acuity and visual fields. We documented complications and the number of patients who required an additional procedure. Results: To date, we identified 39 eyes in 25 patients (80% female) who underwent ONSF. Indications included IIH (60%), venous sinus thrombosis (20%), pseudotumor cerebri syndrome (12%), hemorrhagic leukoencephalopathy (n=1), and an obstructive tumor in the jugular foramen (n=1). No serious complications were encountered. Bilateral ONSF was performed in 48% (n=12). Follow-up ranged from 1 day to 3 years. We divided acuity into category 1 (20/40 or better), category 2 (20/50 to 20/200), and category 3 (worse than 20/200). Pre-operatively, 62% (n=23), 13% (n=5), and 24% (n=9) were in categories 1, 2, and 3, respectively. At the latest visit, 59% (n=20), 20.5% (n=7), and 20.5% (n=7) were in categories 1, 2, and 3, respectively. Average mean deviation (MD) was -20 db pre-operatively (n=26) and -11 db at the last visit (n=19). Non-operative contralateral eyes were analyzed separately (n=11). MD improved in 7 eyes and average MD improved from -15db to -8db. One patient had a VP shunt prior to ONSF; 5 patients had a VP shunt, and 3 patients had venous sinus stenting following ONSF. Additional analysis is underway.

Conclusions, including unique features of the case:
Medial eyelid incision ONSF is a safe and effective surgery in patients with VTP. Following ONSF, visual acuity remains stable and visual fields improve substantially.

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Successful Treatment of Chiari Idiopathic Intracranial Hypertension Syndrome with Dural Venous Sinus Stent after Ventriculoperitoneal shunt: A Case Report

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Introduction:
IIH is a condition characterized by elevated intracranial pressure and various associated symptoms. Chiari malformation 1 is characterized by cerebellar tonsil protrusion below the foramen magnum. Cases with overlapping diagnosis are called chiari idiopathic intracranial hypertension syndrome. Currently, treatment includes acetazolamide and cerebrospinal fluid shunt placement with both treatments being associated with many side effects and risks. Dural venous sinus stent is being explored as an alternative treatment. This case report describes the use of a venous sinus stent after ventriculoperitoneal shunt in the treatment of chiari idiopathic intracranial hypertension syndrome.

Description of Cases:
A 32-year-old female presented to the neuro-ophthalmology clinic with a 1.5-year history of headaches, transient visual obscurations, pulsatile tinnitus, and blurred vision. Upon examination, severe papilledema was found, and the patient was sent to the emergency department (ED) for imaging and was started on 500 mg of acetazolamide BID. Imaging revealed a diagnosis of idiopathic intracranial hypertension and Chiari malformation 1. The patient underwent ventriculoperitoneal (VP) shunt placement due to intolerance to acetazolamide. At 7-month follow-up with neuro-ophthalmology, papilledema and blurry vision resolved, and the acetazolamide was discontinued. However, at 10-month follow up, papilledema had recurred, so the patient resumed acetazolamide. At 11-months post-shunt, the headaches had returned and were worsening. She underwent dural venous sinus stent (DVSS) placement due to the presence of a pressure gradient of 13 mmHg in the right transverse sinus, subsequently reducing the pressure gradient. Two months after the stent placement, the patient reported resolution of headaches, papilledema was resolved, and visual fields were stable. The stent was confirmed to be patent 6 months post-operatively. At 19.5 months post-stent placement, the patient was completely off acetazolamide and symptoms remain resolved.

Conclusions, including unique features of the case:
DVSS demonstrated greater improvement than VP shunt placement in this case of chiari idiopathic intracranial hypertension syndrome.

References: None provided.

Keywords: Pseudotumor cerebri, High intracranial pressure/headache, Interventional neuroradiology

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Grant Support: None.

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The Peripapillary Retina – A Common Juncture in Stargardt Disease and Idiopathic Intracranial Hypertension

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Introduction:
Stargardt disease represents one of the most common inherited retinal degenerations affecting young adults and is caused by the accumulation of visual cycle byproducts such as lipofuscin within the photoreceptors. Separately, IIH is its own rare, acquired condition that leads to headaches, pulsatile tinnitus, and vision loss. In this case we describe a rare case of concurrent Stargardt disease and IIH, drawing attention to the common anatomical juncture between the two in the peripapillary retina.

Description of Cases:
A 35-year-old woman was referred for evaluation of disc edema following a 2-month history of positional bilateral transient visual obscurations that were becoming more frequent. On initial presentation, her best-corrected visual acuity was 20/20 in both eyes. Dilated fundus examination showed Frisen grade 1 papilledema as well as a bulls eye maculopathy with numerous pisciform flecks surrounding both the macula and optic disc. SD-OCT demonstrated parafoveal outer retinal atrophy in a bulls eye pattern with intermittent drusenoid deposits. SW-AF revealed hyperautofluorescent flecks along the posterior pole with central hypoautofluorescence. Notably hyperautofluorescent flecks were also observed around the optic disc bilaterally. Lumbar puncture was performed with an elevated opening pressure of 33 cm H2O with a normal cell count and normal protein, suggesting a diagnosis of IIH. Panel-based genetic testing revealed two pathogenic mutations in ABCA4. The patient had no other relevant systemic medications and no history of vitamin A supplementation or vitamin A derivative use.

Conclusions, including unique features of the case:
Peripapillary sparing of the retina in Stargardt disease is a notable disease feature and separates the condition from other macular dystrophies. In the case of this patient, the peripapillary retina was notably affected, with hyperautofluorescent flecks seen within the peripapillary retina. We hypothesize that elevated intracranial pressure may expose the peripapillary disc to free retinol, which has been reported to be elevated in the CSF of patients with IIH.

References: None provided.

Keywords: High intracranial pressure/headache, Genetic disease, Retina

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Two Sides of the Same Coin

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Introduction:
Idiopathic intracranial hypertension (IIH) classically presents with vision symptoms, headaches, pulsatile tinnitus, and an ophthalmic examination showing optic nerve edema. The diagnosis of IIH must exclude structural lesions and therefore neuroimaging is largely normal; although sometimes an astute appreciation of flattening of posterior globes, dilatation of optic nerve sheaths, empty sella, and/or enlarged Meckel's cave may support the diagnosis. This study reports two cases of IIH with atypical manifestations: nystagmus and chorioretinal folds and presents features for early recognition, thus allowing timely management to prevent vision loss.

Description of Cases:
The first case is a 25-year-old woman who presented with worsening visual acuity and oscillopsia. She had pendular nystagmus bilaterally; after an extensive workup, MRI showed signs of increased ICP and LP resulted in an improvement in symptoms. The patient improved on acetazolamide. The second case was a 32-year-old man who presented with decreased vision in the left eye. His vision began to decline a year prior and he was initially thought to have an epiretinal membrane. He was subsequently found to have chorioretinal folds; and after extensive workup MRI showed signs of increased ICP and LP with elevated opening pressure. Initiation of acetazolamide stabilized his visual fields.

Conclusions, including unique features of the case:
Overall, both cases represent different atypical manifestations of IIH affecting the visual pathway. Pendular nystagmus can be acquired efferent visual pathway dysfunction, the pathophysiological mechanism is not fully known, but the patient has responded well to acetazolamide. In the second case, the retina was affected, impairing the afferent visual pathway. Importantly, there are effective treatments to prevent the accumulation of damage from the increased intracranial pressure including medications, CSF diversion, cerebrovenous stenting, or optic nerve sheath fenestration. Taken together, these findings suggest a full neuro-ophthalmic examination should be performed to evaluate for manifestations of IIH and allow early detection and treatment to prevent vision loss.

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Keywords: High intracranial pressure/headache, Nystagmus, Retina, Visual fields, Ocular motility

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Venous Sinus Stenting for Treatment of Refractory Pseudotumor Cerebri Syndrome: Neuro-ophthalmologic Evaluation and Outcomes in a Chinese Cohort

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Introduction:
Together with optic nerve sheath fenestration and cerebrospinal fluid diversion, venous sinus stenting (VSS) is one of three main surgical treatments for medical refractory pseudotumor cerebri syndrome (PTCS). VSS in Chinese patients with PTCS has not been comprehensively evaluated using neuro-ophthalmic examination.

Description of Cases:
We conducted a retrospective cohort study of patients with medically refractory PTCS who underwent VSS from March 2019 to June 2022 at our neuro-ophthalmology division. Visual outcomes, demographic and clinical characteristics, papilledema, and OCT were evaluated. Eleven patients (22 eyes) were assessed (men: 4, women: 7, mean age: 50.00±11.88 [range: 28 –73] years, mean BMI: 24.67±2.36 [range: 21.8–28.0] kg/m2). Ten patients presented with transient visual obscuration and tinnitus, whereas three experienced headaches. After surgery, papilledema and visual functions improved dramatically in eight patients, and stabilized in three patients with advanced optic atrophy before surgery. The peripapillary retinal nerve fiber layer decreased after surgery, whereas the macular ganglion cell inner plexiform layer (GCIPL) stabilized. There were no severe complications after VSS.

Conclusions, including unique features of the case:
VSS was effective and safe for medically refractory PTCS, especially during early stages of disease. Optical coherence tomography measurement of the GCIPL was useful for predicting the prognosis after surgery.

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Keywords: High intracranial pressure/headache, Pseudotumor cerebri, Vascular disorders

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What Is The Best Approach To Pediatric Idiopathic Intracranial Hypertension? - A Case Series

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Introduction:
Idiopathic Intracranial Hypertension (IIH) is a challenging cause of preventable blindness, which can occur in children with atypical features. Although OCT has been found to be useful in the diagnosis of IIH in adults, there is a lack of data supporting its use in the pediatric population. In addition, the current rise in pediatric obesity has shown elevated rates of IIH presentation, requiring a multi-disciplinary approach to management. The purpose of this case series is to report a series of pediatric patients diagnosed and treated for IIH via a multidisciplinary team.

Description of Cases:
A 7-year-old female presented with headaches, blurry vision, grade IV papilledema, and OCT retinal nerve fiber layer (RNFL) average thickness: 510 µm OD / 496 µm OS. A 14-year-old male presented with headaches, vision loss, and grade III papilledema. OCT RNFL: 220 µm OD / 206 µm OS. An 8-year-old female presented with grade II papilledema, OCT RNFL: 141 µm OD / 214 µm OS, but no symptoms. A 13-year-old female presented with headaches, transient visual loss, and pulsatile tinnitus with grade II papilledema, OCT RNFL: 211 µm OD / 179 µm OS. All patients were thoroughly evaluated by neuro-ophthalmology, prescribed Acetazolamide, and referred to a pediatric weight loss management team. Upon close follow-up, all patients had significant improvement in symptoms, OCT RNFL/GCC average thickness, and no recurrence in papilledema with subsequent weight loss.

Conclusions, including unique features of the case:
Careful and objective follow-up in IIH pediatric patients via neuro-ophthalmology and weight loss management team provides best long-term reduction in symptoms with improvement in OCT RNFL/GCC thickness.

References: None provided.

Keywords: Pediatric neuro-ophthalmology, Pseudotumor cerebri

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A Rare Case of SMARCA4-Deficient Undifferentiated Thoracic Tumor Presenting with Headache and Hallucinations

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Introduction:
SMARCA4-deficient undifferentiated thoracic tumors are novel tumors first described in 2015, with limited reported cases to date. They typically occur in male middle-aged smokers and are highly aggressive. They can be metastatic on presentation, most commonly to the lymph nodes, bones, or adrenal glands. We present a unique case of metastatic SMARCA4-deficient thoracic tumor, in which the initial symptoms were headaches and visual hallucinations.

Description of Cases:
A 62-year-old male presented with 3 weeks of headaches and well-defined hallucinations ("a cowboy" or "small furry things") more so in his left inferior visual field, which lasted from 15 minutes to 1 hour, with and without headaches. The headaches were biparietal, non-positional, and pressure-like. Static perimetry showed a left inferior quadrantanopia, and MRI brain revealed a right occipital lobe mass. Further workup showed a left upper lobe cavitary lesion and renal, adrenal, and retroperitoneal nodules. He underwent a craniotomy 7 days after presentation, and the biopsy showed metastasis from a poorly differentiated thoracic tumor that was SMARCA4-deficient. A mediastinal lymph node biopsy also showed the same pathology. The patient received radiation and chemotherapy, but ultimately expired two months after presentation due to intraparenchymal and subdural hemorrhages.

Conclusions, including unique features of the case:
SMARCA4-deficient thoracic tumors usually present with respiratory symptoms, and the most common metastases are mediastinal. Brain metastases are relatively uncommon in these tumors; there have been 3 reports of brain metastasis with seizures in the literature to date, only one of which also reports definitive pathology by brain biopsy. Notably, our patient did not present with seizures but rather with headaches and likely release hallucinations, highlighting the range of potential neurologic manifestations of SMARCA4-deficient thoracic tumors at initial presentation.

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Keywords: Tumors, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Visual fields, Neuroimaging

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Hyperglycemic hemianopia: A reversible complication of nonketotic hyperglycemia

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Introduction:
To report a case of reversible visual field defect from non ketotic hyperglyacemia

Description of Cases:
A 56 year old female complained of painless blurring of vision in her left visual field associated with seeing non-existent images of trees ; grass and people. She has diabetes mellitus and hyperlipidaemia. On examination, her best corrected visual acuity was 6/7.5 in both eyes. Her intra-ocular pressures and colour vision were normal. Neuro-ophthalmic examination was essentially normal except for a left sided hemianopia on confrontation. Fundoscopy was normal without any diabetic retinopathy detected. An automated perimetry confirmed the presence of a left incomplete homonymous hemianopia. MRI of the brain did not reveal any cerebral infarcts nor haemorrhage. There were numerous punctate foci of T2 and FLAIR hyperintensities, in the centrum semiovale bilaterally, deep and periventricular white matter of both cerebral hemispheres with no discernible enhancement Her presenting fasting blood glucose level was 17.7 mmol/L and her HBA1c was 11%. The blood glucose level was brought under control with s/c injection insulin ; gliclazide 60 mg bd ; metformin 850 mg tds and sitagliptin 100 mg om. Her visual field defect began to resolve 1 week after her blood glucose was brought under control. 4 months later no field defects were detected on automated perimetry.

Conclusions, including unique features of the case:
Severe non ketotic hyperglycaemia can cause reversible field defects as well as palinopsia. It is important to check the fasting blood glucose level of diabetic patients who present with visual field defects.

References: None provided.

Keywords: Higher visual functions

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Right-sided representational neglect due to bilateral parietal lesions

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Introduction:
Neglect can manifest in two forms: perceptual neglect and representational neglect (RN). Perceptual neglect occurs when a patient is unable to attend to or process information from one side of their body or environment. RN, on the other hand, occurs when a patient is unable to imagine or represent one side of their body or environment. Right-sided RN is much less common than left-sided RN, and it is often accompanied by perceptual neglect. However, here we present a case of a patient who exhibited pure right-sided RN following bilateral parietal lesions.

Description of Cases:
A 61-year-old healthy male volunteer with a history of sudden dizziness five years ago was referred for abnormal brain MRI results. Neurological examination was normal, and his score on the Korean Mini-Mental State Examination was 27. Neuropsychological testing revealed mild frontal/executive dysfunction. On a clock drawing test, he correctly drew the clock face and numbers, but placed both clock hands on the left side of the clock. He showed no signs of perceptual neglect on the conventional neglect battery. To assess representational neglect, the Familiar Square Description Test and the O'Clock Test were used. The result of the Familiar Square Description Test and O'Clock test were consistent with RN. DTI revealed reduced fractional anisotropy in the right inferior longitudinal fasciculus, parahippocampal cingulum, and corpus callosum when compared to control subjects matched for age and sex.

Conclusions, including unique features of the case:
This case supports previous research that RN neglect is more common in patients with bilateral brain damage. Additionally, it suggests that the neural basis of RN may be located in the parietal lobe and the white matter tracts connecting it.

References: None provided.

Keywords: Higher visual functions, Stroke

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"Dark Cherry-Red Spot" from Ophthalmic Artery Occlusion, a Possible Initial Manifestation of Active Tuberculosis

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Introduction:
In patients with tuberculosis (TB), involvement of the optic nerve has been associated with either arachnoiditis exudation in chronic meningitis or with tuberculoma1-2, however a central retinal or ophthalmic artery occlusion is rarely seen3. We describe a patient with unilateral vision loss and a "dark cherry-red spot," which led to the diagnosis of an ophthalmic artery occlusion (OAO). Soon after he was diagnosed with active pulmonary TB, raising the possibility that OAO was the initial presentation of his TB.

Description of Cases:
A 27-year-old male with G6PD developed painless fluctuating vision loss of the left eye which then became constant. His exam showed visual acuity of 2/80 OS with fundoscopy revealing an unusually "dark cherry-red spot" without swelling of the optic nerve head. Fluorescein angiogram showed very delayed filling of the "watershed" zone between the nasal and temporal choroidal beds, and very delayed retinal arterial filling. He was diagnosed with an ophthalmic artery occlusion. His workup pointed towards an embolic etiology but, other than a PFO, no source of emboli or hypercoagulability was found and he was started on clopidogrel for secondary stroke prevention. During his hospitalization, MRI brain and orbits showed left perineuritis, workup of which included a screening T spot test which resulted positive for TB. CTA chest showed multiple pulmonary nodules and bronchoalveolar lavage PCR was positive for TB. Due to the perineuritis and concern for active pulmonary TB, he was started on oral prednisone and 4 drug regimen for TB, though with no reported vision improvement to date.

Conclusions, including unique features of the case:
A "dark cherry-red spot" has not been previously described but led to the discovery of an OAO in a patient who would soon be diagnosed with active pulmonary TB. His workup for embolic risk factors was unrevealing, introducing the potential that the OAO was the initial manifestation of active TB.

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Keywords: Vascular disorders, Neuro-ophth & infectious disease (eg, AIDS, prion), Orbit/ocular pathology

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Contact Information: None provided.

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Abrupt Vision Loss in DIDMOAD

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Introduction:
Wolfram syndrome, otherwise known as DIDMOAD (diabetes insipidus, diabetes mellitus, optic atrophy, deafness), is a result of mutations to the WFS1 or WFS2 genes and is typically inherited in an autosomal-recessive manner. Its natural history typically entails progressive, symmetric, gradual vision loss beginning between 8-13 years of age, frequently with an acuity of 20/200 or worse within 10 years of disease onset.

Description of Cases:
A 27-year-old woman presented for acute vision loss in each eye 8 years prior, aged 19. She recalled waking with acute, painless, severe vision loss OU without any antecedent illness, toxic habits, or acute changes in nutrition (she had been a vegetarian for 7 years). In retrospect, mild dyschromatopsia had been noted at age 13 without any other vision loss. Her vision had been static since. She was seen by multiple neuro-ophthalmologists with normal MRIs of the brain and orbits without a diagnosis before seeking a 3rd opinion. The past history included diabetes mellitus (diagnosed age 9). Medications included B-complex vitamins. There was no family history of ophthalmic disease. She did not drink, and did not smoke. The examination revealed acuities of 20/80 OD, 20/70 OS, pupils which reacted sluggishly from 5.5-4.5 OU without rAPD, and sharp, pale nerves (most temporally) and cecocentral loss in each eye on HVF 24-2 fast. Prior work-up included a B12 of 1,002 and unrevealing MRIs of the brain and orbits. Genetic testing revealed a heterozygous for c.505G>A, p.(Glu169Lys) in 1 allele of the WFS1 gene and a heterozygous c.2020G>A, p.(Gly674Arg) mutation in the other.

Conclusions, including unique features of the case:
This case illustrates the potential phenotypic variability of DIDMOAD with two atypical features: LHON-like stepwise vision loss and relatively good visual function after decades of visual symptoms.

References: None provided.

Keywords: Genetic disease, Optic neuropathy

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Amiodarone-Associated Simultaneous Bilateral Ischemic Optic Neuropathies

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Introduction:
Amiodarone, commonly prescribed as an antiarrhythmic drug, has been documented to cause ocular toxicity, the most common being verticillate keratopathy. The most serious side effect is optic nerve injury, with often permanent unilateral or bilateral visual loss. Amiodarone-associated optic neuropathy (AAON) had a wide range of clinical presentations and poorly understood pathophysiologic mechanisms.

Description of Cases:
A 56-year-old man presented with painless sequential visual loss over 3 days. At presentation, visual acuity was 6/15 OD and hand motion OS. Pupils were sluggish, but there was no relative afferent pupillary defect. Anterior segment examination was unremarkable; intraocular pressure was 15 mmHg OU; eye movements were normal. Fundoscopy exam showed swollen optic discs and peripapillary splinter hemorrhages. Visual fields testing showed inferior altitudinal defects OU. Contrast-enhanced MRI showed normal optic nerves and brain Inflammatory markers were normal. The patient was treated with beta-blockers for arterial hypertension for five years (blood pressure 125x80 mmHg). Three months earlier he had started using amiodarone for arrythmia control. Amiodarone was discontinued after he developed visual loss in coordination with the cardiologist. Optic swelling persisted for 3 months, after which the optics became pale. Visual acuit and visual fields remained unchanged after 6 months, with no improvement or worsening.

Conclusions, including unique features of the case:
This case highlights the complexity of diagnosing AAON, and its distinction from non-arteritic anterior ischemic optic neuropathies (NAION). Although AAON may trigger NAION-like optic neuropathies, the clinical presentation and lack of improvement after discontinuation of amiodarone in our patient was very suggestive of bilateral sequential NAION. However, given the potential progressive worsening of vision with AAON, discontinuation of amiodarone should be done whenever possible based on cardiac status.

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Keywords: Optic neuropathy, Visual fields, Vascular disorders, Miscellaneous

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Autosomal Recessive Leber's Hereditary Optic Neuropathy Triggered by Superior Mesenteric Artery Syndrome

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Introduction:
Autosomal recessive Leber hereditary optic neuropathy (LHON) may differ in presentation from mitochondrially inherited LHON. This case reports a teenaged female with autosomal recessive LHON (arLHON) due to homozygous pathogenic variants in DNAJC30 who developed vision loss apparently triggered by superior mesenteric artery (SMA) syndrome, a previously unreported trigger for LHON.

Description of Cases:
A 17-year-old female with no past medical history presented with two weeks of intractable vomiting and was found to have superior mesenteric artery (SMA) syndrome with nutcracker syndrome. During admission, she developed bilateral simultaneous painless vision loss and was referred to ophthalmology. Ophthalmology exam showed best-corrected visual acuity of 20/400 in each eye. On Ishihara testing, she identified 0/11 test cards in the right eye and 2/11 in the left. Posterior segment exam was normal. On optical coherence tomography (OCT), the retinal nerve fiber layer (RNFL) was mildly thickened in both eyes (146 µm OD, 149 OS). Contrast-enhanced magnetic resonance imaging of the brain and orbits revealed T2 hyperintense lesions with faint enhancement involving the midbrain and dorsal pons and extending into the area postrema in the medulla. The patient was treated empirically for possible neuromyelitis optica spectrum disorder (NMOSD) with three days of intravenous methylprednisolone with no improvement. However, cerebrospinal fluid was unremarkable, and AQP-4 and myelin oligodendrocyte glycoprotein antibodies were negative. On further questioning, the patient revealed that her brother had a history of vision loss due to arLHON. The patient then underwent targeted genetic testing confirming homozygous pathogenic variants in DNAJC30, establishing the diagnosis of arLHON.

Conclusions, including unique features of the case:
The present case reveals SMA syndrome as a risk factor for conversion to symptomatic arLHON. We hypothesize that malnutrition may increase productive of reactive oxygen species, and the subsequent oxidative stress may trigger vision loss.

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Keywords: Optic neuropathy, Pediatric neuro-ophthalmology

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Bilateral Sequential Non-arteritic Anterior Ischemic Optic Neuropathy Induced by Methamphetamine Abuse

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Introduction:
Non-arteritic anterior ischemic optic neuropathy (NAION) is a relatively common optic neuropathy in older aged adults above the age of 50. This disease can also present in patients of younger age, although much less common. The vast majority of these younger patients have associated risk factors for NAION, including hypertension and diabetes. Here, we present a case in which a previously healthy 41-year-old woman developed bilateral sequential NAION induced by methamphetamine abuse.

Description of Cases:
A 41-year-old woman without significant past medical history presented to neuro-ophthalmology clinic with acute vision loss in her left eye (OS) following a similar episode in her right eye (OD) two months prior. Vision was 20/40 OD and 20/15 OS. An afferent pupillary defect was present OS. Visual field testing showed incomplete altitudinal defect OD and inferior altitudinal defect with high reliability OS. Dilated fundus exam revealed cupless discs in both eyes, partial optic nerve atrophy superiorly OD, and Grade 2 optic nerve edema OS, with supporting results on optical coherence tomography. A full workup for potential etiologies of her presentation was performed. The only abnormality was substantial levels of methamphetamines and amphetamines in her urine drug screen. The patient was diagnosed with bilateral sequential NAION from methamphetamine abuse. She has not shown to her follow-up appointments.

Conclusions, including unique features of the case:
We report a case of bilateral sequential NAION in a patient younger than the typical age group for this disease, but with significant methamphetamine abuse precipitating each episode. Although methamphetamine abuse is not a known risk factor for NAION, this drug is known to cause vasoconstriction and vasospasms. Her small, crowded nerves are risk factors for ischemia in the setting of methamphetamine abuse, and with a negative medical history of other systemic diseases, this case presents compelling evidence that methamphetamine abuse may precipitate NAION.

References: None provided.

Keywords: Optic neuropathy, Visual fields

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Bitemporal hemianopsia in a case of tilted optic nerves

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Introduction:
Tilted optic nerves are known to cause visual field defects, most commonly a superotemporal defect, however bitemporal hemianopia in the absence of a compressive chiasmal lesion is uncommon (1-3). We report a case of tilted optic nerves as the cause of bitemporal hemianopia in a patient with neuro-ophthalmologic symptoms of blurred vision and headache.

Description of Cases:
A 43-year-old female with essential hypertension presented to the neuro-ophthalmology clinic with new onset blurred vision. Ophthalmic history included high myopia corrected with bilateral laser-assisted-in-situ-keratomileusis (LASIK) 13 years prior to presentation. She endorsed increasingly frequent headaches for six months but otherwise denied diplopia, transient visual obscurations, photopsia, photophobia, and retrobulbar pain. Ophthalmic examination revealed normal best corrected visual acuity and normal visual fields to confrontation, however perimetry testing using Humphrey Visual Field 24-2 demonstrated bitemporal defects with densely enlarged blind spots of both eyes. Optical coherence tomography (OCT) demonstrated normal retinal nerve fiber layer and ganglion cell complex thickness. Funduscopic examination demonstrated tilted optic nerves bilaterally with normal disc margins. Neurologic examination was normal. Magnetic resonance imaging with gadolinium using pituitary protocol showed no mass or mass effect onto the optic chiasm and no signs of increased intracranial pressure. The patient's vision remained normal and repeat perimetry nine months later demonstrated the same pattern.

Conclusions, including unique features of the case:
Bitemporal hemianopia is commonly seen in pathologies affecting the optic chiasm, however tilted optic nerves are an alternative cause for this visual field defect. When coupled with clinical symptoms such as headache, exclusion of a compressive chiasmal lesion is necessary for a final diagnosis.

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Keywords: Visual fields, Perimetry, Neuroimaging, Orbit/ocular pathology

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Caffeine and Vodka Induced Paracentral Acute Middle Maculopathy

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Introduction:
A 49-year-old Caucasian male presented to the eye clinic complaining of acute onset blurred and distorted vision in the right eye that started 2 weeks prior to presentation. He stated that the blurriness is a specific spot in the right eye 20 degrees to the right of central vision. The disturbance is worse when he is looking at certain objects but appears to be constantly present without changes in size and area. Denies flashes or floaters. He denies issues in the left eye. He denies any noticeable inciting events or trauma. No other vision complaints. The patient has no past ocular or medical history, is not on any medications currently, and a thorough review of systems was negative. Patient is a full-time attorney. Patient denies tobacco use or elicit drug use.

Description of Cases:
Visual acuity was 20/15 in both eyes, IOP normal, there was no rAPD, EOMs full in both eyes. The anterior exam and DFE were within normal. Fundus photo showed no retinopathy in either eye. Fundus autofluorescence and intravenous fluorescein angiogram were within normal limits. Humphrey visual field (HVF) 30-2 showed a paracentral inferior depression that respected the horizontal meridian. HVF was normal in the left eye. Optical coherence tomography (OCT) showed distortion and thickening in the inner nuclear layer paracentral to the fovea more prominent superiorly with preservation of the outer retinal layers. This distortion remained constant in all follow ups. Last follow up was 3 months after presentation.

Conclusions, including unique features of the case:
Given the distortion present on OCT and focal visual field loss, it was suspected that the patient had Paracentral Acute Middle Maculopathy. Although the patient denied any noticeable inciting events or trauma on initial visits, he admitted to having drank several drinks of a mixture of Vodka and Red Bull estimated around 7 drinks on his final follow up visit.

References: None provided.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Retina, Perimetry, Vascular disorders, Visual fields

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Can Visual Electrophysiology be used to screen patients with normotension glaucoma

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Introduction:
Normotension glaucoma (NTG) is a common form of primary open angle glaucoma where the intraocular pressure is not elevated (< 22mmHg) but there is chronic, progressive optic neuropathy with characteristic nerve head cupping, RNFL thinning and visual field loss. There are a number of conditions that can appear similar to NTG, particularly early on in the presentation when progression has not been established. Visual electrophysiology (Pattern visual evoked potentials (PVEP), flash VEP, Pattern electroretinogram (PERG), full-field ERG) can elucidate the source of visual loss. Abnormalities of the electroretinogram call into question the diagnosis of NTG. PVEP delay with or without accompanying N95 loss, seen in optic nerve disease, is not thought to be characteristic of glaucoma.

Description of Cases:
Between 1 January 2016 and 31 December 2021, 65 patients (115 eyes) with presumed NTG underwent visual electrophysiology using ISCEV standard protocols. All patients had either a CT scan or MRI that did not demonstrate a compressive lesion of the anterior visual pathway. 65 (56.5%) eyes showed PVEP delay; of which 27 had both N95 and P50 reduction on PERG, 12 had reduced N95 without P50 reduction and 8 had only P50 reduction in addition to the PVEP delay. 12 eyes had normal PVEP latency by reduced N95 amplitude. There were 17 eyes with some full-field ERG abnormality of which 4 eyes (of 2 patients) had more definite rod system dysfunction.

Conclusions, including unique features of the case:
Assuming that patients with glaucoma alone ought not to have other significant electrophysiological abnormalities, this group of patients suggests that the diagnosis of NTG should only be made after at least a more thorough assessment of visual electrophysiology with consideration of neuroimaging. Although visual electrophysiology is time-consuming, it is safe and non-invasive and could have a role as a first-line screening investigation to indicate which patients with supposed NTG might bear further investigation.

References: None provided.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Optic neuropathy, Retina

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Case Report Of Early Visual Symptoms Heralding Fludarabine Ocular Toxicity

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Introduction:
Fludarabine, a purine analog used to treat hematological malignancies and suppress immune function prior to bone marrow transplantation (BMT), may cause toxic effects including myelosuppression, lymphocytopenia, opportunistic infection, encephalopathy, coma, death, and blindness with high dose treatment (>96 mg/m2/day x5-7 days), but these are rarely reported with low doses1,2.

Description of Cases:
55-year-old male with aplastic anemia received fludarabine 30mg/m2 plus cyclophosphamide for four days preparing for BMT. Following the first infusion he noted reduced contrast and photophobia. The second day, flickering lights. The third day, micropsia, image tilt, and palinopsia. These symptoms initially improved, but 4 weeks after infusion he experienced profound, painless vision loss in both eyes. He presented 2 weeks later with 20/800 visual acuity in each eye. Pupils were round, equal, and minimally reactive to light without relative afferent pupillary defect. Slit lamp exam, dilated fundus exam, OCT RNFL and INL(Fig.1), and fluorescein angiography were normal. HVF revealed global depression. ERG showed preserved a-wave and absent b-wave, characterizing bipolar cell loss(Fig.2). MRI T2/FLAIR demonstrated bilateral optic nerve and periventricular hyperintensity(Fig.3). 4 months later acuity was 20/150 in each eye, pupil reactivity improved, and disc pallor was noted. OCT showed pronounced thinning of INL and RNFL(Fig.4). Repeat HVF demonstrated bilateral inferior quadrantanopias with dense central components. MRI was stable(Fig.5).

Conclusions, including unique features of the case:
Following low dose fludarabine this patient developed profound bilateral vision loss with evidence of bipolar cell injury. Ocular toxicity with low dose fludarabine has been reported3,4, but to our knowledge this is the first report of symptoms with first infusion. Contrast sensitivity loss and palinopsia strongly suggest visual pathway impairment and clinicians should be aware of these symptoms. Although ocular toxicity is typically irreversible, recovery has been reported5, raising the question of whether timely intervention may improve outcomes. Further study regarding early visual symptoms during low dose fludarabine infusions is warranted.

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Keywords: Chemotherapy and radiation injury, Optic neuropathy, Miscellaneous

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Case Series: Two Patients With Optic Neuropathy Associated With Guselkumab Initiation

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Introduction:
Immunotherapeutic agents have been implicated as a cause of paradoxical immune-mediated optic neuropathy and other ocular manifestations. We present two patients suffering from Psoriatic Arthritis (PsA), with recent induction of Guselkumab, an IL-23 inhibitor, who within weeks developed unilateral vision loss, and were found to have optic papillitis in the affected eye. There are no reports of optic papillitis associated with PsA on its own. The most common reported side effects of Guselkumab in the clinical trial data were nasopharyngitis, upper respiratory tract infection, hypertension and arthralgia. To date, there is a single case report of mild anterior uveitis associated with Guselkumab use.

Description of Cases:
66 yo F with history of PsA, and recent flare ups, presented to the clinic 1 week after initial Guselkumab dose complaining of sudden, painless superior visual field deficit OS. On exam she had an RAPD and a superior arcuate visual field defect OS associated with optic disc edema and a trace anterior cellular reaction. Her central vision was preserved. 55 yo F with history of PsA and recent induction of Guselkumab presented 4 days after her second dose with painless vision loss OD. On exam she had VA of 20/400 OD, an RAPD, dyschromatopsia and constricted visual field. Fundoscopy revealed 360 degrees of optic disc edema and no evidence of vitritis or uveitis. Contrast-enhanced MRI imaging in both did not show retrobulbar enhancement and both patients had extensive unrevealing infectious/inflammatory workup. After treatment with high dose steroids, the optic papillitis resolved, however visual field deficits persisted. Guselkumab was stopped in the 55 yo patient.

Conclusions, including unique features of the case:
We present the first series of two patients who developed optic papillitis within a few weeks of Guselkumab initiation. It is important to recognize potential side effects of new biological medications that are being increasingly used to treat autoimmune and inflammatory disorders.

References: None provided.

Keywords: Optic neuropathy, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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Grant Support: None.

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Chronique Optic Neuropathy due to Nd YAG capsulotomy induced by Acutes spikes of Intra Ocular Pressure

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[1] *Selarl Du Dr MOKHTARI*

Introduction:
YAG capsulotomies are considered effective and safe. The four mains complications are ocular hypertonia, retinal detachment, refractive changes and macular edema. They are rare, when the procedure respects the rules of the art, namely a limited number of impacts, and energy delivered. We describe 9 patients with optic neuropathies secondary to uncontrollable ocular hypertonia.

Description of Cases:
9 patients presented acute, fluctuating and uncontrollable ocular hypertonia, despite maximum medical treatment in the form of local quadritherapy and Diamox. In the majority of cases, the pallor of the optic nerves predominated over the excavation. The appearance of the visual fields was sometimes typical of glaucoma and sometimes distorted by the coexistence of macular edema, or the decrease of the visual acuity. The majority of patients presented profound and irreversible declines in visual acuity. The significant fluctuation of IOP values makes one-off measurements unreliable. Patients with a better prognosis where those who quickly benefited from filtering surgery such as trabeculectomy, which revealed to be the best way to decrease the mean Intra ocular pressure and here fluctuation.

Conclusions, including unique features of the case:
Optic neuropathies secondary to ocular hypertonia complicating YAG capsulotomies are potentially blinding. They require aggressive treatment from the outset. Filtering surgery is the best way to control not only the average value of ocular hypertonia but also its fluctuation. In the presence of chronic optic neuropathy in a patient who previously undrewent ND YAG procedure, consider increased intra ocular pressure as a possible cause, even if the intra ocular pressure is in the normal range.

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Keywords: Optic neuropathy, Optic nerve trauma and treatment, Visual fields

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Clinical Characteristics and Treatment of Optic Neuritis in Asians

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Introduction:
The Optic Neuritis Treatment Trial was a landmark study which had implications globally. However, the trial was performed in a predominantly White population and it remains unclear if these observations are applicable to Asians. The purpose of our retrospective descriptive study is to report the clinical characteristics of Asian patients diagnosed with optic neuritis from 2018-2023 at our institution.

Description of Cases:
53 eyes of 53 patients were evaluated. Mean(SD) age was 46.1(18.2) years, and 73.6% were female. There were 30(56.6%) Chinese, 11(20.8%) Indian, 6(11.3%) Malay and 6(11.3%) Others. 3 patients had bilateral optic neuritis, and their worse eye was chosen for analysis. It was the first, second and third or more attack for 39(73.6%), 8(15.1%) and 6(11.3%) patients, respectively. Median(IQR) duration of symptoms was 5(7) days. Only 23(47.2%) had ocular pain and 19(35.8%) had disc swelling. Causes of optic neuritis included 6(11.3%) multiple sclerosis, 9(17.0%) NMOSD, 11(20.8%) MOGAD and 27(50.9%) idiopathic. Presenting logMAR(SD) visual acuity was 0.97(0.79) and worsened to 1.24(0.87) at the nadir. Presenting HVF MD(SD) was -15.66(10.66), PSD was 6.85(4.04), OCT RNFL average thickness(SD) was 122.9(72.1)microns, average GCIPL thickness was 71.9(15.2)microns. MRI showed retrobulbar optic neuritis in 31(58.5%), chiasmal involvement in 8(15.1%), and both retrobulbar and chiasmal involvement in 14(26.4%) patients. White matter lesions and spinal cord involvement were present in 16(30.2%) and 7(13.2%) patients, respectively. 41(81.1%) of patients underwent IV methylprednisolone for a mean(SD) duration of 4.4(0.9)days. 13(24.5%) patients underwent plasmapheresis for a mean(SD) of 5.3(1.0)cycles. Of these 13 patients, 8(61.5%) had NMOSD, 2(15.4%) had MOGAD, 2(15.4%) had multiple sclerosis and 1(7.7%) was idiopathic. Mean(SD) duration of hospital stay was 8.9(6.9)days. 6(11.3%) required long-term immunosuppressants, with mycophenolate mofetil(3), rituximab(2) and azathioprine(1).

Conclusions, including unique features of the case:
This is the first study to describe the clinical characteristics of Asian patients with optic neuritis in such detail, and our results differ from the White population.

References: None provided.

Keywords: Demeylinating disease, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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CRAO + Pupil-Involved CN III Palsy after Nasal Embolization: Where's the lesion?

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Introduction:
The cavernous sinus is a vital intracranial nexus that carries arterial and venous vasculature, autonomic fibers, and several cranial nerves. Cavernous sinus syndromes affect some or all of these features and may be caused by an aneurysm of the cavernous ICA (1). Generally, cavernous ICA aneurysms produce no symptoms and are seen incidentally, but can cause indolent ophthalmoplegia (2). Oculomotor (CN III) palsy may present with or without pupil involvement depending on the cause. Central Retinal Artery Occlusion (CRAO) presents with painless vision loss most commonly caused by embolic ischemia. Here, we present a case of simultaneous CRAO with ipsilateral pupil-involved CN III palsy following nasal embolization.

Description of Cases:
An 80-year-old vasculopathic female with atrial fibrillation on anticoagulation presented for intractable epistaxis. She underwent bilateral internal maxillary and right facial artery embolization for which anticoagulation was held. Shortly after the procedure, she developed ptosis OD, vision loss OD, and facial pains. Examination revealed a right pupil-involving CN III palsy. Visual acuity OD was no light perception. Fundoscopic examination revealed retinal ischemia with a cherry red spot suggestive of CRAO. Follow-up imaging revealed partially thrombosed aneurysms of the cavernous ICA, right larger than left.

Conclusions, including unique features of the case:
This case demonstrates an uncommon presentation of a CRAO with ipsilateral pupil-involved CN III palsy. The authors hypothesize that a pressure gradient from the ECA to the ICA may have caused the aneurysm to partially thrombose. Mass effect may have resulted in the CN III palsy while emboli from the aneurysm itself may have resulted in the CRAO (3). Other culprits such as atrial fibrillation off anticoagulation and iatrogenic embolic etiologies are also plausible. To the authors best knowledge, this is the first case of concurrent CN III palsy and CRAO occurring after nasal embolization for epistaxis in the setting of undiagnosed cavernous ICA aneurysms.

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Keywords: Non-organic visual disorders, Ocular motility, Optic nerve trauma and treatment

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Diagnosis and Management of Radiation-Induced Optic Neuropathy following Proton Beam Therapy for Sphenoid Wing Meningioma

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Introduction:
Proton beam radiation therapy in selected cases allows for delivery of higher radiation doses whilst sparing surrounding tissues[1]. Proton radiation has been used with increasing frequency over the last few decades, yet risk to the optic nerve and appropriate management of radiation-induced optic neuropathy remains uncertain[1-5].

Description of Cases:
An 82-year-old female with a history of age-related macular degeneration presented to her retina physician for one day of sudden onset painless vision loss with development of an inferior altitudinal visual field defect OD. Her history was notable for proton beam radiation therapy of a right sphenoid wing meningioma with 50.4 GyE approximately 10 months prior. Evaluation revealed no retinal cause of vision loss. She received a bevacizumab injection OD and was referred for MRI brain/orbits. Over the following 24 hours, her vision worsened to complete “gray” vision loss OD. MRI revealed abnormal thickening and enhancement of the intracanalicular and intracranial right optic nerve. She was admitted to the hospital where she received IV solumedrol (1 gram x 3 days) followed by an oral prednisone taper. Follow up with neuro-ophthalmology two weeks later revealed light perception vision, afferent pupillary defect, optic nerve pallor, severe ganglion cell thinning, superior and inferior retinal nerve fiber layer (RNFL) thinning OD as well as inferior RNFL thinning and a superotemporal visual field defect OS. A diagnosis of radiation-induced optic neuropathy was made, and systemic bevacizumab was recommended to stabilize vision loss.

Conclusions, including unique features of the case:
This case illustrates that although proton beam therapy may reduce side effects on surrounding structures compared to traditional photon radiation, radiation-induced necrosis of the optic nerve may still occur. Radiation optic neuropathy often does not respond to steroid treatment, and hyperbaric oxygen may preserve vision if initiated within 72 hours[4-6]. Strongest evidence exists for systemic bevacizumab which may prevent further vision impairment[7-12].

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Keywords: Chemotherapy and radiation injury, Optic neuropathy, Tumors

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Exploring Nimodipine's Potential in NA-AION: A Preliminary Investigation

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Introduction:
Non-arteritic anterior ischemic optic neuropathy (NA-AION) is one of the most common optic neuropathies in adults, often resulting in irreversible vision loss. Unfortunately, current treatment options for NA-AION are limited. We propose a study to explore the potential of nimodipine, a calcium channel blocker with centrally-acting vasodilatory and neuroprotective properties, to fill this treatment gap. Nimodipine, primarily indicated for the treatment of cerebral vasospasm following an aneurysmatic subarachnoid hemorrhage, has also demonstrated promise in various neurological disorders, offering the potential to enhance ocular perfusion and alleviate the ischemic damage and possible auto-regulatory vasospasm to the optic nerve in NA-AION

Description of Cases:
Our Case-Study assessed two healthy eyes from the same individual (the author) before and after nimodipine administration. Optical Coherence Tomography Angiography (OCT-A) was used to measure vascular perfusion density in the optic nerve head and the peripapillary area. Flow velocity in the ophthalmic artery was evaluated using Transorbital Doppler with a linear array transducer (7-15MHz frequency range, intonation angle < 20 degrees, and a 2mm sample volume). Measurements were taken before and after a 2-hour Nimodipine infusion administered intravenously at 10ml/h, well-tolerated by the participant.

Conclusions, including unique features of the case:
Our study revealed an increase in 3D volumetric vascular perfusion density within the optic nerve after Nimodipine as determined by OCT-A. Additionally, color-coded Doppler analysis indicated a decreased Pulsatility Index, suggesting relaxation in central retinal artery and ophthalmic artery of both eyes after Nimodipine. These findings suggest potential role of Nimodipine to enhance optic nerve perfusion and possibly a favorable role in NA-AION treatment. Doses can be titrated to prevent systemic hypotension, and the drug can be administered either alone or as a combination therapy with prednisolone. These findings hold implications for the future management of NA-AION, highlighting Nimodipine's potential role in improving optic nerve head perfusion and a possible therapeutic significance in NA-AION.

References: None provided.

Keywords: Optic neuropathy, Vascular disorders, Stroke, Optic nerve trauma and treatment

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Feel nothing, see nothing.

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Introduction:
Giant cell arteritis (GCA) is an ophthalmic emergency with the well-recognized clinical presentation of vision loss with headaches, scalp tenderness, or jaw claudication, along with elevated inflammatory biomarkers. However, the diagnosis is often challenging given a subset of patients with occult GCA do not present with classic symptoms and serum biomarkers changes could be non-specific. Prompt biopsy is needed to confirm the diagnosis. We present a case of occult GCA with initial normal fundus examination and normal biomarkers but subsequent development of bilateral central retinal artery occlusion.

Description of Cases:
A 76-year-old Caucasian man with a history of diabetes, hyperlipidemia, and recurrent DVTs presented to the emergency room with one day of painless vision loss in the right eye. The patient denied headaches, scalp tenderness, jaw claudication, or other systemic symptoms. Initial examination revealed count-fingers vision and an APD in the right eye and 20/40 vision in the left eye. Dilated eye exam was unremarkable including normal appearance of the optic nerve and retina in both eyes. CBC and ESR were normal while CRP was only mildly elevated (1.3mg/dL). MRI of brain and orbits were unremarkable. Two days after presentation, the patient developed acute vision loss in the left eye. A second eye exam showed count-fingers vision in both eyes and a macular cherry red spot in both eyes. He was started on high dose intravenous corticosteroids immediately. Other stroke work up including CT angiogram of head and neck and echocardiogram were unremarkable. A bilateral temporal artery biopsy was performed which confirmed the diagnosis of GCA.

Conclusions, including unique features of the case:
Occult GCA should be considered in patients older than 50 years with painless acute vision loss, especially with elevated serum biomarkers. Even with normal biomarkers and an initially normal exam, patients need to be closely monitored for changing symptoms to be offered prompt treatment.

References: None provided.

Keywords: Vascular disorders, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Retina, Miscellaneous

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Glioblastoma (CNS WHO grade 4) masquerading as bilateral atypical optic neuritis

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[1] University of Michigan, [2] Michigan Medicine

Introduction:
Malignant optic nerve gliomas are extremely rare, and can present as optic neuritis 1, ischemic optic neuropathy, or retinal vessel occlusion 2. Patients have rapidly progressive, painful or painless vision loss, and tumors arise from optic nerves, chiasm, or tracts. Our patient presented with rapidly progressive, bilateral, painless vision loss, and was found to have a glioblastoma with chiasmal involvement. Our case details unique clinical/imaging features to aid in early diagnosis of this rare entity.

Description of Cases:
A 63-year-old male presented emergently with 2 weeks of progressive, painless, bilateral blurred vision. Ophthalmic examination revealed visual acuity of count fingers OD, and 20/25 (eccentric) OS, with right afferent pupillary defect, and unremarkable fundus examination. Initial concern was atypical bilateral optic neuritis. MRI demonstrated chiasmal enlargement, with enhancement extending into the pre-chiasmatic optic nerves and tracts, without other intracranial lesions. There was notable diffusion restriction of the right optic nerve, which raised concern for an infiltrative process, such as lymphoma, less likely optic neuritis. CSF studies, including cytology, were negative. He was empirically treated with 1 gram methylprednisolone for three days without improvement. His vision continued to decline and 3 days later, visual acuity OD progressed to no light perception. He ultimately underwent biopsy of right optic nerve, with pathology showing glioblastoma, CNS WHO grade 4.

Conclusions, including unique features of the case:
High grade optic nerve gliomas are rare, with less than 70 cases reported 2. Unfortunately, prognosis is poor, with similar survival rates to supratentorial glioblastomas 3. Our case details specific imaging features of extensive diffusion restriction of the optic nerve, which initially alluded to an aggressive, infiltrative process, ultimately confirmed by pathology. It is important to keep high grade gliomas on the differential for atypical optic neuritis, with rapid progression of vision loss, without response to steroids. Biopsy should be pursued early to confirm diagnosis and initiate treatment.

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Keywords: Optic neuritis, Tumors, Neuroimaging

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Linezolid Induced Toxic Optic Neuropathy - A Case Series

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Introduction:
Linezolid is recommended by the World Health Organization to treat multidrug-resistant tuberculosis (MDRTB) as well as complicated infections. However, the associated toxicities, particularly neuropathies, pose a significant barrier to its long-term use. We recently witnessed cases of optic and peripheral neuropathy in patients being treated for skin infection and MDRTB, which we describe in this case series.

Description of Cases:
We encountered four cases of linezolid-induced toxic optic neuropathy over a period of one year between January 2022 and February 2023. For all, demographic data and detailed history were recorded, followed by a comprehensive ocular and neuro-ophthalmic examination supplemented by neuroimaging. The patients were followed up for a period of six months. The indications for the use of linezolid were MDRTB in three patients and complicated skin infection in the remaining one. The mean duration of linezolid use was 12.5 months at a dosage of 600 mg once daily. The mean cumulative dosage was 265.6 grams. All were men with a mean age of 45.25 years, presenting with defection vision ranging from 6/9 to 2/60. A normal pupillary light reflex was noticed in all patients. Fundus examination revealed a hyperaemic disc in three patients and disc oedema in the remaining one. Dyschromatopsia was observed in all patients. Automated perimetry revealed a central scotoma in one patient and peripheral field constriction in another, while being normal in the remaining two. Magnetic resonance imaging revealed prominent optic nerves with bright signals in two patients. For all patients, linezolid was discontinued and substituted with another drug resulting in complete visual recovery.

Conclusions, including unique features of the case:
Linezolid has a duration-dependent toxic effect. Ophthalmologists and physicians must be aware that monitoring of visual function is important in patients on long-term linezolid therapy and that early recognition of toxicity and discontinuation of the drug results in complete visual recovery.

References: None provided.

Keywords: Chemotherapy and radiation injury, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Neuro-ophth & infectious disease (eg, AIDS, prion)

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Myelin Oligodendrocyte Glycoprotein Antibody Disease Optic Neuritis Masquerading As Fulminant Idiopathic Intracranial Hypertension

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Introduction:
Myelin oligodendrocyte glycoprotein antibody disease (MOGAD) is an autoimmune disorder, characterized by demyelination and inflammation affecting the optic nerves, spinal cord, and brain. In this report, we present a unique case of MOGAD-optic neuritis (MOGAD-ON) mimicking fulminant idiopathic intracranial hypertension (IIH).

Description of Cases:
A 32-year-old male presented with 5 days of worsening bilateral vision loss, headaches, and pain with eye movement. Visual acuity measured CF OD and 20/25 OS, right RAPD, and bilateral optic disc edema on fundus exam. CT revealed evidence of bilateral optic neuritis, and subsequent MRI w/wo contrast showed evidence of T1 enhancement of bilateral optic nerves and optic nerve sheath, suggesting acute bilateral optic neuritis with perineuritis. MRV showed narrowing of the right transverse sinus without occlusion, but was otherwise unremarkable. The patient underwent lumbar puncture which demonstrated an opening pressure of 30 with normal CSF. Given the elevated ICP and neuritis, dorzolamide and 5-days of IV methylprednisolone 500 mg were prescribed. The patient demonstrated significant improvement following steroids with visual acuity improving to 20/25 OD and 20/20 OS by day three. The rapid steroid response and the eventual anti-MOG titer 1:100 confirmed the diagnosis of MOGAD-ON with elevated ICP. The patient completed his IV steroids and was discharged with an oral steroid taper with outpatient follow up with neuro-ophthalmology.

Conclusions, including unique features of the case:
This case report demonstrates the uncommon presentation of MOGAD-ON masquerading as fulminant IIH. While both MOGAD-ON and IIH can present with papilledema and elevated ICP, the etiology and management are different. Furthermore, this case underscores the importance of interdisciplinary collaboration between ophthalmologists and neurologists in complex presentations. A timely and accurate diagnosis enables the initiation of specific antiinflammatory or immunomodulatory treatments that can halt the progression of disease, prevent further relapses, and preserve visual function.

References: None provided.

Keywords: Optic neuritis, High intracranial pressure/headache, Demeylinating disease, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Neuroimaging

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Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease Presenting with Posterior Scleritis

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Introduction:
Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is a central nervous system inflammatory disease that is pathophysiologically distinct from multiple sclerosis and aquaporin-4-positive neuromyelitis optica. The clinical spectrum of MOGAD is variable and includes acute disseminated encephalomyelitis (ADEM), recurrent optic neuritis, autoimmune encephalitis and orbital inflammation. We describe a unique presentation of MOGAD with posterior scleritis and right optic neuritis.

Description of Cases:
A 50-year-old woman presented to the ED with acute vision loss accompanied by severe pain in the right eye which woke her up from sleep. On examination, visual acuity was no light perception in the right eye, with RAPD and swollen right optic disc. She had right upper lid hyperemia and medial conjunctival injection. B-scan ultrasonography showed scleral thickening and fluid band consistent with right posterior scleritis (classic T sign). MRI brain and orbits showed long-segment optic nerve enhancement, extending from intraorbital to the prechiasmatic segments, associated with fat stranding and enhancement of right intraconal fat and right posterior sclera. She underwent extensive infectious and inflammatory work-up, which were negative with exception of positive MOG (1:40 titer). Following 5 days of pulsed IV steroid and 5 sessions of plasma exchange therapy, she had significant recovery of vision and improvement of pain. She is doing well on long term immunotherapy with rituximab.

Conclusions, including unique features of the case:
While there is no evidence to suggest the presence of MOG within scleral tissue, cell-mediated immune responses may be triggered by its presence on the outer surface of myelin sheath, with robust inflammation resulting in extension via the optic nerve sheath to adjacent orbital tissues. We hypothesize that the inflammation may have spilled over into the scleral tissue in our patient resulting in posterior scleritis.

References: None provided.

Keywords: Demeylinating disease, Optic neuritis

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Navigating the Vascular Terrain of the Human Optic Nerve in 3D

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Introduction:
Non-arteritic anterior ischemic optic neuropathy (NAION) is the second most common optic neuropathy in adults. Despite extensive research, the etiology of NAION remains uncertain, although there is a general consensus that reduced perfusion through the paraoptic short posterior ciliary arteries (sPCAs) and their branches causes ischemia. However, a 3D visualization of these vessels has never been performed.

Description of Cases:
Multiple methods of analysis are being performed. First, both orbits were harvested from a patient with clinically-presumed NAION. The orbits were fixed and 10-micron serial sections stained (mostly) with Hematoxylin and Eosin (H&E) were made throughout both orbits (2500 slides on the involved side). These slides are being scanned and digitized using a Zeiss Axio Z1 Scanner at a 20x magnification level. We are employing Zeiss (Zen) software to create a 3D reconstruction of the blood vessel, and Zeiss's advanced image segmentation tool [Intellesis: an artificial intelligence ("Al") system] to distinguish veins and arteries. Second, we are sectioning six additional fresh human orbits stained with the Verhoeff-Van Gieson stain to visualize the vasculature and connective tissue structure. Third, we are performing a quantitative 3D and 4D (time-lapse) imaging of other human orbits with “tissue clearing” using light-sheet fluorescence microscopy to hopefully demonstrate the vascular tree of the paraoptic vessels in 4D in a single block of tissue.

Conclusions, including unique features of the case:
Intellesis (Al" software), with manual modification by a researcher, facilitated the analysis of vascular structures within and around the optic nerve, which potentially will save countless man-hours for our future studies. Correction of a few slides was sufficient to teach the model how to distinguish between large veins and arteries, however, further training is required for identification of smaller vessels. The 3D/ 4D imaging of the vascular structures of the human optic nerves will enable our future studies of biomechanical stresses upon those blood vessels.

References: None provided.

Keywords: Miscellaneous

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Contact Information: None provided.

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No light perception following uneventful cataract surgery

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Introduction:
As retro and peribulbar anesthesia carry the risk of injection of the anesthetic agent into the optic nerve, a subtenon's block with a blunt tipped cannula is preferred during ocular surgeries.

Description of Cases:
An 81 year old male with presenting vision in right eye of 6/18, N18 underwent small incision cataract surgery under subtenon anaesthesia. His vision on post operation day 1 was perception of light. On examination he had a grade 3 RAPD and disc edema. MRI Brain and Orbit was unremarkable. Blood investigations was significant for anemia. Blood sugar levels, ESR, CRP were within normal levels. Autoimmune and vasculitis workup was negative. Vision had worsened to no light perception when patient reviewed with reports. Trial of steroids was given with no improvement. The left eye showed no evidence of optic neuropathy. As the above findings make the diagnosis of ischemic optic neuropathy unlikely, direct trauma to the optic nerve during subtenons block was considered as the most likely diagnosis. The cannula for subtenons injection was measured on a cadaveric specimen and found to be long enough to reach the optic nerve insertion.

Conclusions, including unique features of the case:
Although subtenons block is considered a safer option to peribulbar block, it still carries the risk for direct trauma to the optic nerve hence due precaution should be taken. On review of literature, only one case report of trauma to the optic nerve following subtenon's block was found.

References: Kim SK, Andreoli CM, Rizzo JF, III, Golden MA, Bradbury MJ. Optic neuropathy secondary to sub-tenon anesthetic injection in cataract surgery. Arch Ophthalmol. 2003;121:907–909.

Keywords: Trauma, Optic nerve trauma and treatment, Optic neuropathy

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Non-arteritic Anterior Ischaemic Optic Neuropathy In The Pachychoroid Disease Spectrum

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Introduction:
Increased peripapillary choroidal thickness has been reported as a pre-disposing factor for non-arteritic anterior ischaemic optic neuropathy (NAAION). We describe two patients with features of Pachychoroid Disease Spectrum (PDS) presenting with NAAION.

Description of Cases:
Case 1: A 58 year-old Chinese male with hyperlipidaemia presented with sub-acute blurring of the left inferior visual field. There was left optic disc swelling and sub-retinal fluid at the macula, distinct from the disc. Intraocular inflammation was absent. Fundus autoflourescence showed features in keeping with old CSR bilaterally. Fundus fluorescein angiography (FFA) demonstrated a smoke-stack pattern of leakage at the macula but only mild leakage at the disc. Spectral domain ocular coherence tomography (SpOCT) revealed pachyvessels. Neuroimaging, serological and cerebrospinal fluid (CSF) investigations were unremarkable. Disc swelling resolved without treatment. The patient subsequently required intravitreal Aflibercept and photodynamic therapy for CSR recurrence. In the following year, the patient presented with NAAION of the fellow eye. Case 2: A 64 year-old Chinese male with well-controlled hypertension presented with a 1-month history of central right blurring of vision, with sudden blurring of the right inferior field on waking 2-weeks prior to presentation. There was right optic disc swelling with CSR, which was distinct from the disc oedema. Pachyvessels were identified in both eyes. Neuroimaging, serological and CSF investigations were unremarkable.

Conclusions, including unique features of the case:
To our knowledge, these are the first observations of NAAION occurring in PDS. In terms of occlusive vasculopathy risk, neither patient was diabetic. Both patients were hyperopic, which is in keeping with other reports of patients with PDS. Whilst peripapillary pachychoroid syndrome (PPS) has been described as a PDS variant, our patients did not have macular oedema extending from the disc nor a peripapillary fluid pocket, which was typically described. The presence of pachyvessels likely leads to a crowded disc phenomenon, contributing to the development of NAAION.

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Keywords: Optic neuropathy, Retina

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Non-Small Cell Lung Cancer Metastases to the Optic Nerve leading to Vision Loss

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Introduction:
Ocular tumors are relatively rare, with metastasis accounting for most cases. Most cases of intraocular metastasis involve the choroid, but optic nerve involvement is especially infrequent. Previously reported cases of optic nerve metastasis suggest a constellation of fundoscopic findings that could point to the involvement of the optic nerve; however, our patient interestingly did not exhibit these signs.

Description of Cases:
A 67-year-old male with a history of non-small cell lung cancer was diagnosed about two years prior to presentation with known metastases to the choroid which had been treated with external beam radiation therapy around the same timeframe. He presented with new eye pain for one week and worsening vision loss for one year. The patient was NLP at presentation. Initial work-up was remarkable for neovascular glaucoma. There was no evidence of intraocular masses at presentation. Enucleation was performed at the patient's request for pain. Significantly, after the enucleation of the affected eye was performed, pathology confirmed extensive metastatic disease in the optic nerve which included the optic nerve sheath as well as the choroid, retina, and sclera.

Conclusions, including unique features of the case:
This presentation describes a rare case of intra-orbital nerve involvement with simultaneous involvement of choroid from primary non-small cell lung cancer. Interestingly, in this case, our patient presented with gradual vision loss without an obvious mass on fundal physical exam or B-scan imaging. This contrasts the few reported cases of similar patients who demonstrated either choroidal or optic disc lesions, retinal hemorrhage, or papilledema at presentation. Though metastases are the most common adult intraocular tumors, involvement of optic nerve is relatively rare. Optic nerve metastatic disease also may portend a worse prognosis given its association with involvement of the central nervous system.

References: None provided.

Keywords: Orbit/ocular pathology, Chemotherapy and radiation injury, High intracranial pressure/headache, Orbit, Tumors

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Grant Support: None.

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Optic Chiasmal Prolapse in Primary Empty Sella Syndrome : A Rare Presentation

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Introduction:
Empty sella syndrome is characterized by the flattening or shrinkage of the pituitary gland, resulting in the sella tursica being filled with cerebrospinal fluid. Primary empty sella syndrome(PES) arises without any prior pituitary pathologies, in contrast to secondary empty sella syndrome which occurs post medical, surgical, or radiation treatment of pituitary pathologies. PES involves an anatomical defect in the diaphragma sellae which when coupled with increased intracranial pressure can cause the chiasma to herniate into the sella. This can result in various forms of vision loss, such as bitemporal or binasal hemianopsia, unilateral temporal defects and arcuate scotomas.

Description of Cases:
A 26-year-old female presented with a persistent headache for 6 months not associated with nausea, vomiting, tinnitus, postural changes, or visual disturbances. She was on treatment for infertility. She had no other endocrinal abnormalities or any previous interventions. Her Body Mass Index(BMI) was 27 kg/m2. On examination, best corrected visual acuity was 20/20. Colour vision and pupil reaction was normal. Slit lamp biomicroscopy revealed unremarkable anterior and posterior segment examinations. Humphrey Field Analysis 30-2 showed an enlarged blind spot with constriction of the superior visual fields in both the eyes. She was advised Magnetic Resonance Imaging(MRI) scan of the brain which revealed a T2 hyperintense kinked optic chiasma with intrasellar herniation. She was diagnosed with optic chiasmal prolapse due to primary empty sella syndrome. She was then referred to a neurosurgeon who advised conservative management and weight loss.

Conclusions, including unique features of the case:
Existing literature reports many cases of chiasmal prolapse in secondary empty sella syndrome. However, there is only one other case reported by Byrne et al. attributing chiasmal prolapse to primary empty sella syndrome. This case is presented due to its uncommon manifestation, emphasizing the significance of considering chiasmal prolapse as a potential cause of vision loss in cases of empty sella syndromes.

References: None provided.

Keywords: Neuroimaging, High intracranial pressure/headache, Visual fields

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Optic nerve sheath meningioma in Chinese patients - A case series

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Introduction:

Though being rare and benign in nature, primary optic nerve sheath meningioma (ONSM) can result in progressive irreversible painless visual loss. With the advancement in precision radiation therapy (RT) and recent literature supporting its role in the treatment of ONSMs, our study target to report patient characteristics and disease pattern of ONSMs in the Chinese population of which reported data was limited as compared to Caucasians literature.

Description of Cases:

A retrospective chart review was conducted on 24 patients who were diagnosed with radiological primary ONSM between 1991 & 2021 from 2 tertiary eye centers in Hong Kong. The mean age of patients was 51 (range: 24-80) with a female predominance (83%). Majority of cases presented with visual acuity of 20/40 or better (75%), optic disc swelling (64%), painless progressive visual loss (54%) while inferior visual field defects being the most observed pattern (38%). Tubular enlargement (66%) was the most frequent radiological appearance followed by nodular (21%) and globular (12%) appearances. Initial misdiagnosis was not uncommon (42%) with MRI misinterpretation by non-neuroradiologists (70%) being the predominant reason for delay in diagnosis. A change in treatment trend can be observed along time with 46% of patients underwent various types of RT of which 75% of these patients attaining stable or improved vision with the mean follow-up duration of 52 months.

Conclusions, including unique features of the case:

As compared to Caucasians, Chinese patients present at an older age, with more frequent disc swelling and inferior VF defect. Atypical presentation with acute vision loss is rare but possible which can impose diagnostic challenge. Misdiagnosis is not uncommon, thus ophthalmologists' awareness of ONSM and high clinical suspicion are crucial in early timely diagnosis of this disorder. Fractionated stereotactic RT is an effective and safe treatment option which should be offered to patients with ONSM when visual decline is evident.

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Keywords: Tumors, Optic neuropathy, Orbit, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: Nil

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Optic Neuritis In COVID-19 Infected Patients

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Introduction:
To investigate the clinical manifestations, treatment and prognosis of COVID-19 associated optic neuritis.

Description of Cases:
Single-center observation study. Patients with COVID-19 associated optic neuritis were identified from December 1,2022 to January 31,2023. The main outcome measures were neuro-ophthalmic manifestations, coexisting neural autoantibody, radiologic characteristics and clinical outcomes. All patients were followed-up at least 8 months after discharge until September 2023. Twelve patients (nine females and three males, eighteen involved eyes) were identified with a median age of 40(26.75) years (ranged 26-69 years). The mean interval between COVID-19 infection and optic neuritis was 10.42±7.1 days (ranged 2-25 days). Optic disc edema occurred in ten patients (83.3%); eye pain occurred in nine patients (75%). The median score of VFSS at nadir was 5.5 (2), and eight patients (66.7%) had severe vision loss. Seven patients (58.3%) were the first episode of optic neuritis, four patients (33.3%) were recurrent. Three patients (25%) fulfilled the diagnose of ADEM. All patients were seronegative for AQP4-IgG whereas four patients (33.3%) were seropositive for MOG-IgG, and one patient was seropositive for CRMP5-IgG. Four patients (80%) had optic nerve MRI enhancement, five patients (41.7%) with long-segment optic nerve lesions, and six patients (50%) had brain MRI lesions. Cerebrospinal fluid cytokines were elevated in seven patients (7/9,77.8%). All patients received glucocorticoid therapy; two patients received IVIG synchronously. The median VFSS score at 1-month and at the last follow-up were 2 (3.5) and 1（2） respectively. Ten patients (83.3%) recovered well, and only one patient (8.3%) relapsed during the follow-up.

Conclusions, including unique features of the case:
In this cohort, we found that COVID-19 related optic neuritis mainly occur about 10 days after COVID-19 infection. MOG-ON and ADEM-ON can be noted. Many patients had severe vision loss at first, but most of them recovered well.

References: None provided.

Keywords: Optic neuritis, Demeylinating disease

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Optic Neuritis Masquerade Syndrome

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Introduction:
Optic Neuropathy Masquerade Syndrome (ONMS) is a group of diseases that occurs with ocular inflammation of the optic nerve, which can simulate optic neuritis or neuropathy and neuroretinitis. The clinical case represents an atypical form of optic neuritis caused by testicular seminoma

Description of Cases:
A 29-year-old male developed painless acute progressive visual loss in the left eye. The past medical history was remarkable for testicular inflammation. The neurophthalmological examination showed the following positives findings: VA: PPL in the left eye, central scotoma, and RAPD. Fundus of the eye revealed edema of both optic discs with retinal folds. Left eye showed hemorrhages and cotton wool spots. The optic disc edema was also observed in OCT with left macular edema. Brain MRI showed enhancement of the optic nerves. Blood test demonstrated high levels of ALT, LDH: , Beta HCG 1. The immunological and panel infection were normal. Left testicular biopsy was positive for seminoma. (PET-CT) was positive for retroperitoneal and inguinal lymphadenopathy. Patient was treated with steroids and chemotherapy with improvement in clinical manifestations.

Conclusions, including unique features of the case:
Paraneoplastic optic neuropathy (PON) is an optic nerve inflammation associated with systemic malignancy. The prevalence rate is estimated to be around 10 % of patients, between 50–75 years. The most common sites for primary malignant disease are breast, lung, and prostate. In young adults, PON is less common. Reports of testicular cancer until the time of this review there are only 4 . One case was for seminoma who presented with orbital metastasis. In our patient, the metastatic lesion was not evident since immunological response or endocrinological factors probably played an importante role. ONMS should be considered as a differential diagnosis of atypical optic neuropathy in young patients; especially when it is bilateral, with an asymmetric course and rapid progression. PON could be presented without an obvious metastatic lesion.

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Keywords: Optic neuropathy, Miscellaneous, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Optic neuritis, Tumors

Financial Disclosures: The authors had no disclosures.

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Contact Information: None provided.

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Optic Neuropathy Associated with POLG Mutations: A Case Series

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Introduction:
Many published cases of POLG-associated optic neuropathy lack robust documentation regarding severity of vision loss, visual field defects, and optical coherence tomography analysis1-5. In addition, all published cases of POLG-associated optic neuropathy are associated with systemic symptoms, most commonly muscle weakness, ptosis, and ophthalmoplegia1-5.

Description of Cases:
We describe the clinical characteristics of three patients with POLG-associated optic neuropathy without associated systemic symptoms. Case 1 is a 61-year-old female with visual acuity of 20/100 in the right eye (RE), 20/80 in the left eye (LE). Visual field testing showed bitemporal depression with extension across the vertical meridian inferonasally. Case 2 is a 40-year-old female with visual acuity of 20/40 RE, 20/30 LE, and a central scotoma on visual field testing. Case 3 is a 40-year-old male with visual acuity of 20/300 in the RE, 20/350 in the LE. Visual field testing showed a cecocentral scotoma in both eyes. All three patients had bilateral temporal optic disc pallor, temporal retinal nerve fiber layer thinning, and ganglion cell layer thinning. All patients presented at an adult age without associated systemic symptoms and had separate POLG mutations that had not been previously documented with vision loss. Two of our cases had evidence of additional stressors on mitochondrial function: Case 2 had a history of smoking and alcohol use and was found to have a vitamin B12 deficiency; and Case 3 was found to have a copper deficiency.

Conclusions, including unique features of the case:
Clinicians should be aware that POLG mutations can present as isolated optic neuropathy primarily affecting the papillomacular bundle. With mitochondrial failure being the likely underlying pathogenic mechanism in POLG-associated optic neuropathy, helping affected patients eliminate mitochondrial stressors may be important in reducing the risk for progressive vision loss in this otherwise currently untreatable disorder.

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Optic Neuropathy with Novel Triple Targeted Therapy for Anaplastic Thyroid Cancer: Case Series

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Introduction:
Anaplastic thyroid cancer (ATC), one of the most lethal human malignancies. Even with radical surgery, radiotherapy, and chemotherapy it accounts for 50% of thyroid cancer mortality. The combination of PD-1 inhibitor (pembrolizumab), BRAF inhibitor (dabrafenib), and MEK inhibitor (trametinib) significantly improves survival outcomes in these malignancies. Overall, survival rates in the study exceeded 5 years. Optic neuropathy is a rare but established neuro-ophthalmic immune-related adverse event (irAE). We herein present the largest case series in English literature of optic neuropathy with novel triple targeted therapy for ATC.

Description of Cases:
Case 1: A 70 year old male with diagnosis of ATC presented with vision loss left eye (OS) after one month post-treatment. Examination showed left RAPD grade I right eye (OD) and grade II OS. Humphrey visual field (HVF) showed inferior arcuate visual field defect (VFD) OD and inferior altitudinal VFD OS. Case 2: A 60 year old male with diagnosis of ATC presented two months post treatment with new onset of blurred vision. Examination showed bilateral anterior uveitis 3+ cells, 360-degree posterior synechiae, grade V optic disc edema OU, and central serous retinopathy OU. Case : A 57 year old male with diagnosis of ATC presented with vision loss OS for 12 days. Examination showed left RAPD, grade III-IV optic disc edema OS. Work up for alternative etiologies for all patients were negative.

Conclusions, including unique features of the case:
This is the largest case series in English literature, highlighting the variable nature of optic neuropathy associated with novel triple target therapy for ATC and its significant diagnostic challenges. Although targeted cancer therapy has transformed the field of immunotherapy, their ocular irAEs are significant. Providers must be aware of the potential ocular side effects of such treatments.

References: None provided.

Keywords: Chemotherapy and radiation injury, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Miscellaneous, Optic neuropathy, Optic neuritis

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Pallid Disc Edema in Non-arteritic Anterior Ischemic Optic Neuropathy: Not Always Giant Cell Arteritis

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Introduction:
A "chalky white" or "pallid" swollen optic disc is highly suggestive of arteritic anterior ischemic optic neuropathy (AAION) in the appropriate age group. In contrast, non-arteritic anterior ischemic optic neuropathy (NAION) is generally characterized by hyperemic disc edema, though pallid edema has been rarely reported. We present a patient with acute vision loss and pallid optic disc edema who was ultimately found to have NAION.

Description of Cases:
An 86-year-old man presented with sudden vision loss OS starting 3 days prior. He had intermittent headaches without other symptoms of giant cell arteritis. Medical history was notable for diabetes, hypertension, obstructive sleep apnea, hypothyroidism, atrial fibrillation status-post Watchman, subarachnoid hemorrhage, and papillary urothelial carcinoma status-post nephrectomy. Initial vision was 20/30 OD and counting fingers OS. There was a left RAPD and ocular motility was intact. The right visual field was full while the left was globally constricted. Fundoscopy revealed retinal drusen OU and a pallid swollen disc with associated splinter hemorrhages OS. Workup revealed normal age-adjusted inflammatory markers. MRI of the brain was negative for acute process. Given concerns for AAION, the patient was prescribed oral prednisone. Left-sided temporal artery biopsy (TAB) showed no vasculitis; corticosteroids were stopped. Two weeks later, the patient was found to have a new nasal visual field defect OD. Repeat brain MRI showed a large right posterior cerebral artery stroke, accounting for the nasal defect OD. Corticosteroids were re-prescribed and a right-sided TAB was again negative for vasculitis. Six weeks later, the patient's vision improved to 20/30 OD and 20/50 OS with resolution of the pallid disc edema in the left eye.

Conclusions, including unique features of the case:
Pallid disc edema, often considered pathognomonic for AAION, can occur in NAION. In a visual field defect which respects the vertical meridian in one eye, consider a disorder affecting the chiasm or posterior visual pathways.

References: Agostino A, Farmer J, Blanco P, Veinot JP, Nair V; Efficacy of bilateral temporal artery biopsies and sectioning of the entire block of tissue for the diagnosis of temporal arteritis, Cardiovasc Pathol, Jul-Aug;59,107425, 2022. Characteristics of patients with nonarteritic anterior ischemic optic neuropathy eligible for the Ischemic Optic Neuropathy Decompression Trial, Arch Ophthalmol, Nov;114(11),1366-74, 1996. Hayreh SS, Podhajsky PA, Zimmerman B; Ocular manifestations of giant cell arteritis, Am J Ophthalmol, 125:509-20, 1998. Pollock SC, Arnold AC, Miller NR; Vessels in full view: preserved vascular clarity in acute arteritic anterior ischaemic optic neuropathy, Acta Ophthalmol, 2019 Nov;97(7):727-28. Tomsak RL; Ischemic Optic Neuropathy Associated With Retinal Embolism, Am K Ophthalmol, 99, 590-592,1985.

Keywords: Optic neuropathy, Vascular disorders, Visual fields, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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Paracentral Acute Middle Maculopathy: A Complication of Papillophlebitis

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Introduction:
Papillophlebitis is a rare, poorly understood condition that can present as an incomplete CRVO with acute painless vision loss in typically young, healthy females. The authors present the first reported case of papillophlebitis with secondary paracentral acute middle maculopathy (PAMM) lesions in a young with anatomic recovery after oral steroids.

Description of Cases:
A 43-year-old female with no significant past medical history presented with a 3-day history of bitemporal headache and an inferonasal visual field defect in left eye following a motor vehicle accident. Ophthalmological examination revealed BCVA of 20/20, normal color vision and no afferent pupillary defect in either eye. There was an absolute scotoma in the inferonasal visual field in the left eye. Anterior segment examination was unremarkable in either eye. In the left eye, fundus examination revealed 360 degrees of optic disc edema with disc hemorrhages and superior macular whitening. Humphrey visual field revealed an absolute inferonasal field deficit which correlated with the superior macular whitening. FA revealed normal perfusion and no ischemic areas. OCT macula revealed middle retinal whitening suggestive for PAMM lesions in the superior macula. MRI brain/orbit and lab workup was largely unremarkable for any hypercoagulable etiologies. The final diagnosis was papillophlebitis with secondary PAMM lesions due to venous congestion. She was started on oral steroid taper with complete resolution of disc edema and improvement of inferonasal field deficit. VA remained stable at 20/20 OU with full color vision in both eyes.

Conclusions, including unique features of the case:
1. We report the first case of papillophlebitis complicated by PAMM lesions secondary to venous congestion. 2. A broad differential and workup is important in these patients as papillophlebitis is a diagnosis of exclusion. 3. Although no standardized treatment exists, oral steroids can be administered and in severe cases, intravitreal anti-VEGF can be considered.

References: None provided.

Keywords: Retina, Vascular disorders, Visual fields, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease

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Prevalence of Familial Optic Disc Drusen Using Optical Coherence Tomography

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Introduction:
Optic disc drusen (ODD) may present in multiple individuals and generations within a family, indicating a hereditary predisposition for the development of ODD. As the condition is mainly asymptomatic, individuals are often unaware of their ODD, and consequently, the prevalence of ODD within families remains unknown. The aim of this study is to screen family members to ODD patients for the presence of ODD, to find the prevalence of familial ODD.

Description of Cases:
Method: In this descriptive case series study, family members, aged 18 years or older, of patients with ODD (index patients) were included. Biological familial relations to the index patients included: children, grandchildren, siblings, half siblings, parents, and grandparents. Recruitment began in August 2023 and is expected to stop in November 2023. The presence of ODD was ascertained using a dense optic nerve head EDI-OCT scan, in accordance with the Optic Disc Drusen Studies (ODDS) Consortium guidelines for ODD detection. Preliminary results: At present, we have included six families (Family A to F) in the study, with 5, 3, 1, 2, 2 and 1 family members, respectively, to the index patients. In four out of the six families screened, at least one family member presented with ODD. In family A, 3 out of the 5 screened family members presented with ODD. In family B, 0 out of 3 screened family members presented with ODD. In family C, the one included family member presented with ODD. In family D, 1 out of 2 screened family members presented with ODD. In family E, 0 out of 3 screened family members presented with ODD. In family F, the one included family member presented with ODD.

Conclusions, including unique features of the case:
We found familial ODD in four of the six screened families. This indicates that familial ODD is more prevalent than expected.

References: None provided.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)

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Contact Information: None provided.

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Recurrent Popper Induced Non-Arteritic Anterior Ischemic Optic Neuropathy: A Novel Entity

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Introduction:
Poppers are volatile alkyl nitrite compounds that are inhaled as recreational drugs, known to the ophthalmic community for maculopathy causing subfoveal damage to the ellipsoid zone. Alkyl nitrates are a source of nitric oxide, a potent vasodilator, inducing reduced blood flow and therefore may alter perfusion to the optic nerve head (ONH).

Description of Cases:
A 46-year-old male with no past medical history presented to the emergency department with painless, superior visual field loss upon awaking in his left eye. Examination revealed preserved visual acuity of 20/20, Ishihara 11/13, left RAPD. A left superior altitudinal defect was confirmed on visual field testing and on fundoscopy left optic disc edema with flame shaped haemorrhage was observed. Ten days later, OCT imaging demonstrated subsided disc swelling. He presented to the emergency department 2 weeks thereafter reporting new inferior visual field defect in the same eye. OCT imaging revealed increased RNFL thickness in the superior part of the optic nerve. Extensive work up including brain and orbit MRI with contrast and blood tests for inflammatory, infectious and genetic causes came back negative. At the four-month follow-up, visual field testing showed persistent concentric visual field defect with global reduction of RNFL and RGCL on OCT imaging. Only at this time the patient acknowledged using Poppers both evenings prior to visual loss.

Conclusions, including unique features of the case:
We report the first described case of recurrent Popper induced Non-Arteritic Anterior Ischemic Optic Neuropathy (NAION). The temporal relationship between symptom onset and Popper use and a negative systemic work up, suggest the drug to be implicated. We hypothesize an ischemic event to the ONH due to typical NAION presentation. The proposed mechanism is similar to that hypothesized for sildenafil related NAION, which also works through a similar pharmacological pathway. Both clinicians and patients should be aware of this newly described association.

References: None provided.

Keywords: Optic neuropathy

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Contact Information: None provided.

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The Natural History Of Optic Nerve Sheath Meningiomas In A Tertiary Referral Centre

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Introduction:

Optic nerve sheath meningiomas (ONSM) are rare, benign meningothelial cell tumours that can cause progressive visual loss. There are limited data on the natural history, diagnosis and treatment outcomes and progression of optical coherence tomography (OCT) changes. We therefore aimed to describe: (1) the natural history; (2), the effects of treatment and; (3), the diagnostic process of optic nerve sheath meningioma,

Description of Cases:

We conducted a retrospective interventional cohort study of all patients with ONSM treated in our centre between 1st January 1990 and 1st August 2022. Data collected included: demographics, OCT retinal nerve fibre layer (RNFL) thickness, visual acuity, and visual field, investigations, and treatment. Thirty-eight patients were included, including six bilateral ONSM, of which two had a diagnosis of neurofibromatosis. Thirty-seven diagnoses were made by contrast-enhanced magnetic resonance imaging (MRI), with 10 requiring two or more MRIs, and six patients three or more MRIs and one requiring non contrast computed tomography (CT). Of 25 patients treated with radiotherapy, 9 showed marked reversal of field loss or improvement in visual acuity, 8 stabilised and 8 continued to deteriorate. Two patients developed mild radiation retinopathy. Mean VA in the radiotherapy group was 0.61 and 0.66 LogMAR at baseline and last recorded follow-up respectively, consistent with stabilisation or improvement in most, while mean global RNFL thickness was 84 µm at baseline and 56 µm at the last recorded visit. In the non-radiotherapy group mean initial VA was 1.30 logMAR declining to 2.00 LogMAR at last recorded follow-up, compared to a mean global RNFL thickness of 70 µm at baseline declining to 55 µm.

Conclusions, including unique features of the case:

Diagnosis was made by MRI with contrast, with 11/38 cases requiring repeat imaging. Radiotherapy was well tolerated and effective, stabilising or improving visual function in most cases, although RNFL thickness continued to progressively decline.

References: None provided.

Keywords: Neuroimaging, Optic neuropathy, Tumors, Visual fields

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The Presence of Macular Edema In Optic Neuritis

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Introduction:

The diagnostic classification criteria for optic neuritis (ON) have recently been codified to reduce misdiagnosis, and includes the anatomic location of optic nerve inflammation, which differs between ON subtypes. There is a less described inflammatory component, however, involving the non-myelinated prelaminar and inner nuclear retinal nerve fibers, contributing to the development of microcystic macular edema (MME), postulated to be from Mullerian cell dysfunction during acute inflammation. While this has been studied in multiple sclerosis (MS), there has been less research comparing MS, myelin oligodendrocyte associated disease (MOGAD), and neuromyelitis optica spectrum disease (NMOSD).

Description of Cases:

A literature review was performed using the term “optic neuritis”, “macular edema,” “macular star,” “multiple sclerosis,” “neuromyelitis optica,” or “myelin oligodendrocyte.” Fourteen articles were found between 2012 and 2023, investigating the OCT characteristics of MS, NMOSD and MOGAD using OCT and OCT Angiography including RNFL thinning and MME. We reviewed the relationship between MME, RNFL, and visual acuity. MME and RNFL thinning were seen in MS, NMOSD and MOGAD. MS was the most studied, with worsened long-term visual acuity in patients with MME. Compared to MS, NMOSD showed more severe RNFL thinning with worse visual outcomes. Comparison of MOGAD to MS and NMOSD showed conflicting data, but MOG antibodies resulted in RNFL thinning even without ON, and there was no analysis of the relationship of MME to RNFL thinning in MOGAD.

Conclusions, including unique features of the case:

Optic neuritis with MME is associated with development of RNFL thinning, was present in all three disease processes, and was related to worsened visual outcomes. Further studies are needed to investigate MME as a marker of active inflammation, and if additional treatment targets should be focused on this process in order to preserve the RNFL and improve visual outcomes.

References: None provided.

Keywords: Optic neuritis, Demeylinating disease, Retina

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The Relationship Between Visual Field Defects in the Setting of Chorioretinal Coloboma and Optic Disc Drusen

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Introduction:
Ocular colobomas are a rare genetic phenomenon resulting from improper closure of the embryonic fissures that arise in the inferior iris, optic disc, choroid, and retina. They occur in 0.14% of the population and are associated with retinal detachment and visual field (VF) defects. Optic nerve head drusen (ONHD) are collections of proteinaceous materials that have calcified and thought to be due to dysplasia of the optic disc and associated with anterior ischemic optic neuropathy (AION). Rarely, the presentation of both colobomas and ONHD have been reported in the literature and their relationship remains undefined. This case report highlights the unusual presentation of combined colobomas and ONHD and their effect on vision.

Description of Cases:
The patient is a 67-year-old female presenting with a VF defect of the superior-temporal region of the right eye in the setting of an inferior chorioretinal and iris coloboma. She was followed by her eye doctor for decades without evidence of vision changes until 2022. Examination revealed unchanged visual acuity and a superior arcuate defect involving the blind spot. The chorioretinal coloboma is located inferior to the posterior pole approaching the optic nerve (ON). The ON appeared anomalous. Autofluorescence showed hyperfluorescence at the inferior sector of the ON, OCT showed a hyperreflective irregular ovoid mass with hyporeflective core within the optic disc, and B-scan with evidence of calcific deposits all consistent with ONHD.

Conclusions, including unique features of the case:
Overall, chorioretinal colobomas are extremely rare and can affect the anatomy. Colobomas have been noted to be associated with abnormal blood vessels within their surroundings. ONHD is associated with VF defects and AION. The combination of ONHD and colobomas is not well described. We report a case of a healthy patient with a newly developed VF defect, reminding us that continued vigilance in monitoring patients with chorioretinal colobomas for ONHD and VF defect is warranted.

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Keywords: Genetic disease, Retina, Orbit, Miscellaneous, Optic neuropathy

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Grant Support: None.

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The Spectrum of Isolated Retinal Artery Occlusion Secondary to Giant Cell Arteritis: A Systematic Review

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Introduction:
The spectrum of isolated arteritic retinal artery occlusions (RAO) secondary to giant cell arteritis (GCA) is not well described. We systematically reviewed the literature to investigate the clinical features of isolated RAOs associated with GCA.

Description of Cases:
This review follows the Preferred Reporting Items for Systematic Reviews (PRISMA) guidelines. Two independent reviewers used Covidence (Melbourne, Victoria, Australia) for screening and data extraction; a third reviewer resolved conflicts. The inclusion criteria were articles describing isolated arteritic RAO linked to GCA; the exclusion criteria were cases of non-isolated RAO, AION, or cranial nerve palsy from GCA. Of 1656 studies identified, 41 full-text articles were included. The most common study designs were case reports (51.2%; 21/41), followed by cohort studies (12/41; 29.3%), and cross-sectional studies (4/41; 9.8%). The articles described 168 patients, all aged 60 years or older; of the 72 patients with reported gender, 58.3% (42/72) were female. The three primary types of RAO described were central retinal artery occlusion (CRAO), branch retinal artery occlusion (BRAO), and cilioretinal artery occlusion (CLRAO); the most commonly reported presentation was unilateral CRAO, followed by bilateral involvement of any RAO, unilateral CLRAO, and unilateral BRAO. Most RAOs types were accompanied by typical GCA signs and symptoms (e.g., headache, jaw claudication, anorexia/weight loss). Using the Joanna Briggs Institute (JBI) critical appraisal tool guidelines, most articles were rated as good quality (27/41; 65.9%); the rest were fair (6/41; 14.6%) and poor (8/41; 19.5%).

Conclusions, including unique features of the case:
Clinicians should be aware that GCA patients can present with a broad spectrum of isolated unilateral and bilateral RAOs.

References: None provided.

Keywords: Vascular disorders

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Vision loss from Tuberculous Optochiasmatic Arachnoiditis following Tuberculous Meningitis

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Introduction:
Tuberculous meningitis is a disease process with diverse and possibly severe neuro-ophthalmologic sequelae. Vision loss occurring after tuberculous meningitis treatment may result from persistent infection, therapy-related toxicity, or associated inflammatory processes.1-3 We presents a case of vision loss due to tuberculous optochiasmatic arachnoiditis following treatment for tuberculous meningitis.

Description of Cases:
A 37-year-old male presented to Neuro-Ophthalmology clinic for vision loss beginning 4 months after an ICU stay for tuberculous meningitis. His ICU course was marked by placement of an external ventricular drain for hydrocephalus. Medical therapy included isoniazid, rifampin, pyrazinamide, levofloxacin, and a course of high-dose dexamethasone. In Neuro-Ophthalmology clinic, he reported bilateral decreased vision beginning 10 days prior. His best correct visual acuity was 20/20 on the right and 20/50 on the left with dyschromatopsia on the left but no afferent pupillary defect. Humphrey visual field testing showed dense temporal and superior deficits bilaterally. Anterior segment and funduscopic exams were normal. MRI of the brain showed a new, enhancing, 1.4 cm mass lesion of the sella with mass effect on the optic chiasm as well as enhancement in the left anterior temporal lobe most consistent with either tuberculous optochiasmatic arachnoiditis (TOA) or immune reconstitution inflammatory syndrome (IRIS). The patient was restarted on triple therapy for TB (Isoniazid, Rifampin, Levofloxacin for a full year) as well as a 3-month dexamethasone taper with visual acuity improvement to 20/20 in both eyes but only partial recovery of his visual field deficits. Serial brain MRIs showed gradual decrease in the size of the sellar mass, with complete resolution by the 11 months mark.

Conclusions, including unique features of the case:
This case presents a rare complication of tuberculosis infection most consistent with tuberculous optochiasmatic arachnoiditis (TOA), and outlines the associated diagnostic dilemma presented by vision loss after infection with (and treatment of) CNS tuberculosis.

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Keywords: Neuro-ophth & infectious disease (eg, AIDS, prion), Visual fields, Neuroimaging

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Weight loss to sight loss: A case of bilateral NAION in a young female after aggressive weight reduction and treatment of diabetes

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Introduction:
Bilateral visual field defects secondary to NAION in a young female using antidiabetic/ weight loss medication

Description of Cases:
A 36 year old caucasian female noted shadows in her field of vision both eyes 5/4/2023, she was admitted to ER 5/8/2023-5/9/2023 and noted to have elevated optic nerves both eyes with hemes. her vision was 20/20 OU, color vision was full. MRI/ MRV showed no intracranial abnormality. Spinal tap pressures 6/1/2023 noted to be 15 cm of h20 with normal csf labs. Visual fields showed inferior defects in both eyes. Optic nerve OCT showed no drusen. She described an intentional 37 lbs weight loss over 3 months with her antidiabetic medication. Her work up for infectious/ autoimmune / optic neuropathy was negative. Her monoclonal gammopathy profile was positive but not thought to be significant per hematology.

Conclusions, including unique features of the case:
While weight loss and diabetic control are goals of treatment, aggressive weight loss and aggressive diabetic control possibly caused bilateral NAION in this young female. General physicians need educated about this possibility of vision loss with rigorous management. Additional need for studying adverse outcomes in subsequent patients on similar medication.

References: None provided.

Keywords: Miscellaneous

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Blindness, pain and swelling, Oh my!

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Introduction:
Patient is a 57-year-old WF referred after a 10-week course of progressive right eye visual loss, and pain with eye movement.

Description of Cases:
Initial exam showed VA of 20/200 OD, 20/30+ OS. No RAPD. Ultrasound showed “papilledema” of the right optic nerve (ON). MRI revealed patchy enhancement of the intra-orbital, canalicular and pre-chiasmatic segments of the right ON. Brain MRI showed multiple non-enhancing foci of abnormal T2 signal intensity within the supra-tentorial and subcortical white matter. She was diagnosed with optic neuritis and received 5-days high-dose methylprednisolone. Over the next 8-weeks, her VA OD declined to NLP (20/25 OS). Three weeks following PLEX x5, the patient complained of band-like pain, tingling, and numbness at T6-T10. MRI showed persistent right ON enhancement. Upon referral: VA: NLP OD, 20/20 OS. 3+RAPD OD. Color vision normal OS. Funduscopic exam OD showed 2-3+ edema. The left ON showed early swelling, with C/D of 0.1. Visual fields in OS showed early inferior and superior nasal steps. The spinal discomfort and changes in the bilateral ON changes prompted a diagnosis of sero-negative neuromyelitis optica. She received 2 cycles of IV cyclophosphamide. However, persistent enhancement of the right ON, and evidence of swelling and worsening visual fields OS prompted a RIGHT optic nerve biopsy.

Conclusions, including unique features of the case:
Biopsy demonstrated a pilocytic astrocytoma of the optic nerve longitudinally extensive. Unusual features: 1) "new onset of optic neuritis" in a 57 yo patient; 2) Negative anti-MOG Ab and anti-Aquaporin 4 Ab (NMO)despite bilateral "optic neuritis"; 3) marked 3+ swelling and evidence of peripapillary hemorrhages are rare in optic neuritis; 4) longitudinal extensive enhancement of the optic nerve is most common in NMO or MOGAD and not ON. 5) there was PERSISTENT swelling of the optic nerve and lack of any visual improvement despite repeated courses of high dose steroids and PLEX.

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Keywords: Tumors, Optic neuritis, Visual fields, Demeylinating disease, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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It's Always The Cancer

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Introduction:
The effect of tyrosine kinase inhibition (TKI) in the pathophysiology Giant cell arteritis (GCA) is poorly understood. Dasatinib is a second generation tyrosine kinase inhibitor, used in the treatment of imatinib intolerant chronic myeloid leukaemia (CML), due to its potent inhibition of BCR-ABL. The authors propose that dasatinib may have exerted a therapeutic effect of limiting the underlying inflammatory process of GCA, and that its withdrawal contributed to acceleration of a forme-fruste disease process manifesting in AAION.

Description of Cases:
A 77 years female with known CML and prior ophthalmic history of leukaemic retinopathy and optic nerve swelling at presentation, was successfully treated with Dasatinib. Years later, the patient suffered 3 months of increasing focal headaches. Attributing this to a side effect of the medication, she stopped the medication abruptly. Two weeks later, the patient awoke with sudden and complete loss of vision in the left eye to NLP. Examination revealed a left RAPD, pallid swelling of the left optic nerve and associated cilioretinal artery occlusion, thrombocytosis, elevated CRP and ESR and delayed choroidal filling defect. Findings were consistent with AAION and this was confirmed with biopsy. MRI did not show evidence of CNS relapse.

Conclusions, including unique features of the case:
In diagnosing neuro-ophthalmic conditions in the context of cancer, the cancer itself, the treatment of the cancer or paraneoplastic pathology should be strongly considered. The recurrence of disc swelling may have prompted multiple investigations to exclude CNS relapse. Careful history and examination however resulted in a confident alternative diagnosis and prompt steroid treatment. We do not expect unrelated neuro-ophthalmic diagnoses to be made in the context of active cancer. However, this is arguably related in that cessation of the CML treatment, dasatinib, led to GCA coming to the fore, and manifesting AAION. This patient was unfortunate enough to suffer two different causes of optic nerve head swelling.

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Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Neuroimaging, Optic neuropathy, Paraneoplastic syndromes

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Occam's Razor or Hickam's Dictum?

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Introduction:
Sweet's syndrome is an autoimmune disease that presents with fever, elevated inflammatory markers, neutrophilia, and rashes (1,2). It is characterized by neutrophilic infiltration of tissues in the absence of infection. It is classified in three forms: classical, malignancy-associated, and drug-induced. Hematologic malignancies such as AML are most associated with Sweet's (1,2). Rarely, Sweet's can involve the CNS and eye: it has been reported as causing scleritis (3), uveitis (4,5), optic neuropathy (6), and one previous case of orbital inflammation and pachymeningitis (7).

Description of Cases:
One year prior to presentation, an 81-year-old man was diagnosed with cutaneous Sweet's after developing fevers and a bullous rash. Skin biopsy showed neutrophilic dermatosis without infection. He then presented with painless, subacute vision loss of the right eye. On MRI brain/orbits, he had bilateral orbital inflammation involving the extraocular muscles (sparing their tendons) and EOM compression of the right optic nerve. Infectious testing was negative. Thyroid function testing was normal. CT of the chest, abdomen, and pelvis was unremarkable. Hematological cell counts were preserved; hematopathology was negative for lymphoproliferative malignancy. However, genetic testing of peripheral blood showed TET2 mutation, which confers high risk for myelodysplastic syndrome. His vision returned to baseline after a 5-day course of high-dose methylprednisolone. Five months later, as his prednisone was tapered, he developed new left abducens palsy. Repeat MRI brain/orbits showed recurrent orbital inflammation, left abducens enhancement, and pachymeningitis. He underwent occipital dural biopsy, which showed lymphohistiocytic and neutrophilic infiltration. Dural histiocytic and IGG4 staining were negative. He underwent lumbar puncture with normal CSF profile. MOG, ANA, and ANCA antibodies were negative; ACE and IgG subclass testing were normal. His abducens palsy resolved with a second course of methylprednisolone.

Conclusions, including unique features of the case:
The patient had a very rare case of Sweet's-related orbital inflammation and pachymeningitis, which may be idiopathic or secondary to early myelodysplastic syndrome.

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Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Orbit, Paraneoplastic syndromes, Neuroimaging, Optic neuropathy

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Postoperative Papilledema: Not sure if I'm a fan!

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Introduction:
17-year-old male with history of Fanconi anemia (FA) s/p bone marrow transplantation (BMT), inflammatory bowel disease (IBD, and autism spectrum disorder (ASD) is found to have optic nerve swelling after undergoing unremarkable cataract surgery in the right eye. Neuroimaging demonstrated Brain MRI demonstrated a large ring-enhancing lesion centered on the corpus callosum with smaller lesions in the occipital lobe and pons. Clinical history and neuroimaging were determined to be characteristic of FANS, a novel and rare syndrome that has been observed at tertiary centers in recent years (1).

Description of Cases:
17-year-old male with FA s/p BMT, IBD, and ASD presented to clinic with squinting of both eyes. After routine cataract surgery of the right eye, postoperative EUA demonstrated severe optic edema. Brain MRI demonstrated a large ring-enhancing lesion centered on the corpus callosum with extension to the bilateral frontal lobes. Smaller lesions also noted in the occipital lobe and pons. Differential considerations for a large ring-enhancing lesion in an immunosuppressed child with Fanconi Anemia include primary neoplasm and infection. Clinical history and neuroimaging were determined to be characteristic of FANS, a novel syndrome observed at tertiary centers in recent years (1). Biopsy was deferred due to risk of hemorrhage. Antibody serologies for JC virus were positive, but plasma and urine PCR were were negative. The patient was admitted for high-dose steroids. Serial EUA and MRI showed reductions in papilledema severity and the size of the inflammatory mass.

Conclusions, including unique features of the case:
This is the first case of FANS, a possibly novel syndrome that may be associated with JC virus re-activation (2). This case illustrates the difficulty of differentiating FANS from malignancies, such as glioblastoma and lymphoma. While a clinical diagnosis of FANS was made to initiate treatment, there are no similar cases in the literature or guidelines for navigating this diagnostic challenge.

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Keywords: Progressive multifocal leukoencephalopathy, Increased intracranial pressure, JC virus, Papilledema, Magnetic resonance imaging (MRI)

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Stop the treatment - methotrexate-associated diffuse large B-cell lymphoma

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Introduction:

Methotrexate-associated lymphoproliferative disease (MTX-LPD) is rare and has been reported primarily in patients with rheumatoid arthritis treated with MTX. Cessation of MTX results in spontaneous regression in 59% of patients.

Description of Cases:

A 78-year-old woman presented with initially intermittent binocular horizontal diplopia and decreased appetite. Past medical history was notable for polymyalgia rheumatica on prednisone 5 mg daily and MTX 10-20 mg weekly for six years. She denied transient vision loss, new headaches, or jaw claudication. A non-tender mass of the right nasal dorsum was noted. On exam her vision, color vision and visual fields were normal. Pupils were isocoric without RAPD. She had a subtle abduction deficit with slowing of abducting saccades. On dilated examination there was no optic disc swelling or retinal ischemia. Blood tests on admission: CRP 74 mg/L, ESR 45 mm/Hr, normal leucocytes (6.2x10*9/L) and platelets (274x10*9/L). Temporal artery ultrasound showed no perivascular edema or thickening. CT sinuses without contrast and MRI sinuses with contrast showed three lesions of the nasal cavity and a clival lesion. All lesions displayed low MRI T2 and T1 signal with contrast enhancement and restricted diffusion. Right nasal cavity biopsy showed Epstein-Barr virus-negative diffuse large B cell lymphoma. MTX was discontinued. Three weeks later FDG-PET CT imaging showed marked interval improvement with near complete disease regression.

Conclusions, including unique features of the case:

Consider MTX-LPD in patients on long-term methotrexate presenting with neurological symptoms. MTX cessation is the initial first line treatment for MTX-LPD. The mechanism is not fully understood, it is thought that excessive inhibition of TH1 cells, effector memory CD8+T cells, and EBV-specific CD8+ T cells by MTX at the time of LPD development, and their restoration after MTX cessation are specific features of the development and regression of LPD.

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Keywords: Skull base, Tumors, Neuroimaging, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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To Do or Not To Do

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Introduction:
Prompt diagnosis and management are crucial to prevent irreversible visual damage in invasive fungal sinusitis (IFS). To our knowledge, this is the first report of compressive inflammatory optic neuropathy without direct intraorbital or apex IFS.

Description of Cases:
A 29-year-old female with acute myeloid leukemia (AML) status post chemotherapy presented with right-sided headaches and periorbital swelling. Ocular exam was unremarkable, including best corrected visual acuity (BCVA) of 20/20 OU, normal color vision, and no relative afferent pupillary defect (RAPD). Neurologic exam was non-focal. Labs showed neutropenia and thrombocytopenia. MRI with gadolinium demonstrated opacification within the bilateral ethmoid and sphenoid sinuses. High T2/FLAIR signal was noted with bilateral medial inferior frontal lobes, corresponding to restricted diffusion and leptomeningeal enhancement. Concerning for IFS with intracranial extension, urgent right orbital, optic nerve, and multi-sinus decompression were performed. Biopsy was consistent with invasive Aspergillus species. Despite antifungal treatment and surgical intervention, right eye vision deteriorated to counting fingers only, with interval development of a right RAPD. After a multidisciplinary discussion, large-dose IV steroid treatment was initiated, and vision OD recovered to 20/25. She continued on oral steroids with a gradual taper while maintaining systemic antifungal therapy. Following five sinus washouts, no fungal elements were identified in the final pathology. Repeat MRIs revealed gradual improvement of frontal lobe celebrities and never demonstrated optic nerve enhancement. At follow-up, 12 months after the initial diagnosis, the patient's examination showed BCVA 20/20 OU, persistent 2+ RAPD OD, and stable RNFL/GCC loss OD>OS.

Conclusions, including unique features of the case:
Managing compressive inflammatory optic neuropathy in the setting of immunosuppression and IFS with intracranial extension poses unique challenges. The balance between further immunosuppressing treatment for optic neuropathy must be weighed against the risk of infection progression. Remarkably, our patient survived after steroid therapy while obtaining remission of her AML and preservation of 20/20 visual acuity.

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Keywords: Chemotherapy and radiation injury, Neuro-ophth & infectious disease (eg, AIDS, prion), Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Optic neuropathy, Optic nerve trauma and treatment

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Mind Games

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Introduction:
The Heidenhain Variant of Creutzfeldt-Jakob disease represents a difficult diagnostic dilemma that ties together neurology and ophthalmology through its typical presentation with early visual symptoms, that can delay or mislead diagnosis. Herein we describe the initial presentation, diagnosis and eventual progression of a case of the Heidenhain variant, that of a 79-year-old erudite man who initially presented with metamorphopsia.

Description of Cases:
He denied loss of visual field or acuity but later developed visual impairment. Given the speed of deterioration he was admitted. His family stated that he had episodic confusion and word finding difficulty especially in the mornings. He denied fluctuating consciousness, abnormal movements, convulsions, tongue bite or incontinence. Examination revealed the inability to count fingers in any quadrant OU. He could detect movement and describe colors. There was reduced short-term recall. He had difficulty with clock drawing ascribed to his visual impairment. The rest of his neuro-ophthalmologic examination was normal. MRI showed cortical diffusion restriction in the occipital and parietal cortex. EEG demonstrated left sided frontotemporal arrhythmic delta activity. Antiseizure medication trial with no improvement. Serum and urine labs unremarkable save for mild vitamin B12 deficiency. Initial CSF was unremarkable except for a protein of 73.3 mg/dL. He soon developed profound blindness with confabulation, and subsequently, fluctuating and worsening cognition. He died 2 months from symptom onset and 9 days after neuro-ophthalmologic examination.

Conclusions, including unique features of the case:
Positive RT-QuIC and protein 14-3-3 suggested probable prion disease. Autopsy and histopathology confirmed spongiform encephalopathy. The initial presentation with visual symptoms offered a unique diagnostic challenge. Without neuro-ophthalmological examination and workup, a diagnosis may not have been rendered. This variant is a clinical diagnosis, and benefits from awareness and suspicion in cases where visual phenomena precede cognitive decline. The rapid progression of his condition also sets his case apart from other cases of sporadic CJD.

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Keywords: Neuro-ophth & infectious disease (eg, AIDS, prion), Neuroimaging, Higher visual functions

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A Case of Bilateral Vision Loss and Encephalopathy

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Introduction:
We describe a case of myelin oligodendrocyte glycoprotein antibody-associated bilateral optic neuropathy and meningoencephalitis, which responded well to multiple immunomodulatory treatments.

Description of Cases:
A 45-year-old man presented with acute bilateral vision loss. Three days prior he had developed bilateral blurred vision, which progressed quickly to near complete blindness. He reported no headaches, nor any neurologic or systemic symptoms. Visual acuity was hand motion level bilaterally. Pupils were 4 mm, fixed and non-reactive. Dilated funduscopic exam was consistent with bilateral proliferative diabetic retinopathy that was stable compared to a recent eye exam. There were no other neurologic deficits. MRI brain and orbits showed bilateral optic perineuritis with prominence of the orbital fat and mild proptosis as well as leptomeningeal T2/FLAIR hyperintensities and ventriculitis. Lumbar puncture yielded a lymphocytic pleocytosis, moderately elevated protein, and a low glucose. On hospital day 3, the patient became gradually less arousable with new meningismus. He was intubated and treated with broad-spectrum antibiotics. Repeat neuroimaging showed diffuse meningeal T2/FLAIR hyperintensities. Repeat lumbar puncture showed worsening pleocytosis with neutrophilic predominance. A brain biopsy was performed which showed evidence of meningoencephalitis, with T cells in the brain parenchyma and a lymphohistiocytic infiltrate of T cells and histiocytes. Serologic workup revealed a MOG titer of 1:1000 by cell-based assay. Given the very high MOG antibody titer and lack of alternative etiology, the patient was diagnosed with an extreme case of MOG antibody disease. The patient was started on immunomodulatory treatment, and steadily improved with high-dose steroids and plasma exchange. He was ultimately discharged to a skilled nursing facility with plans for maintenance rituximab.

Conclusions, including unique features of the case:
Aseptic meningitis is an uncommon manifestation of myelin oligodendrocyte glycoprotein antibody related autoimmune dysfunction but should be considered in culture-negative meningoencephalitis. MOGAD with severe neurologic impairment can respond plasma exchange in cases refractory to steroids.

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Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Optic neuropathy, Neuroimaging, Optic neuritis, Demeylinating disease

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A Case of Misunderstood Signal

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[1] *Sankara Nethralaya*

Introduction:
Compressive optic neuropathy of the intracanalicular portion of the optic nerve secondary to benign peripheral nerve sheath tumor (Schwannoma) is a very rare description. This is the second case report being described till now.

Description of Cases:
A 60-year-old man presented with a history of painless decrease in vision OD noticed 19 months back. Records revealed a diagnosis of optic neuritis in OD. Magnetic resonance imaging (MRI) of the brain and orbit revealed a T2 FLAIR hyperintense lesion in the canalicular portion of the optic nerve with contrast enhancement. He was treated with high-dose intravenous methylprednisolone (IVMP) , thereafter, he noticed a progressive decrease in vision in OD over the next 9 months for which he received an injection of Rituximab. Cerebrospinal fluid(CSF) and serum myelin oligodendrocyte glycoprotein (MOG) and aquaporin-4 (AQP4) antibodies were negative. Oligoclonal bands (OCB) was positive in CSF and negative in serum. Thereafter he noticed a complete loss of vision in OD. He was again treated with IVMP and azathioprine. He came to us for a second opinion. On examination, his visual acuity in OD was perception of light and OS was 6/6. Fundus examination revealed a pale optic disc in OD. A repeat MRI was suggestive of an oval lesion in the right optic canal, isointense on T1, and hyperintense on T2, with homogenous moderate contrast enhancement. He underwent an excision biopsy of the lesion. Histopathological examination (HPE) revealed a non-capsulated tumor, composed of spindle cells arranged in a cellular and slightly myxoid pattern. HPE was suggestive of a schwannoma. The vision did not improve after surgery.

Conclusions, including unique features of the case:
Poor recovery of vision in cases of optic neuritis with an involvement of the intracanalicular portion of the optic nerve , despite the treatment should prompt us to rule out small tumors in the optic canal.

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A diagnosis difficult to ingurgitate

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Introduction:
The most common pituitary masses are generally benign pituitary adenomas, meningiomas, craniopharyngiomas, and Rathke's cell cleft tumors. The incidence of pituitary metastases among all intracranial metastases is 0.87% and account for less than 1% of operative sellar tumors with breast, lung, renal, and prostate as the primary malignancy.

Description of Cases:
A 58-year-old male with COPD, GERD, hypertension presented with bilateral transient vision loss and progressively worsening peripheral > central vision OU. ROS was positive for hypotension, headaches, and increased urination. Initial eye exam revealed VA 20/50 OD, 20/100 OS, without APD, and could only perceive the control Ishihara plate OU. His anterior and posterior segment exams were unremarkable. OCT showed borderline RFNL thinning superionasally OD and no RFNL thinning OS, although GCC was diffusely thin bilaterally. HVF 30-2 was unreliable with an inferior dense altitudinal defect involving fixation OS and a dense temporal field defect OD. Neuroimaging revealed a 2 cm homogenous sellar mass and he underwent EEA resection with pituitary stalk sacrifice. Pathology revealed poorly differentiated metastatic adenocarcinoma. Primary cancer workup showed gastroesophageal junctional mass. His initial hospital course was complicated by CSF leak, panhypopituitarism, diabetes insipidus, and encephalopathy; notably, his vision subjectively improved to "near perfect." One-week post-discharge, he reported 4 days of new progressive blurry vision and headache. Repeat MRI pituitary revealed a recurrent mass centered on the optic chiasm involving the lower hypothalamus and bilateral optic tract. He was deemed non-operative given aggressive recurrence; Radiation Oncology was consulted urgently and he completed 5 cycles of external beam radiation therapy to the pituitary gland (4.0 Gy 6FFF) and started on urgent chemotherapy.

Conclusions, including unique features of the case:
This is the first cited case of primary esophageal adenocarcinoma with metastasis to the pituitary gland. Despite initial resection and improvement in his vision, this patient had aggressive tumor recurrence into the optic chiasm within 2 weeks.

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Keywords: Skull base, Tumors, Visual fields, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Neuroimaging

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Behind Every Great Man is a Woman Rolling Her Eyes

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Introduction:
Reports of atypical cases have increased awareness that Leber's Hereditary Optic Neuropathy (LHON) is not solely a disease of young men. Here, we present a case of an older woman who presented with bilateral sequential loss of vision, and, after several diagnostic dilemmas, was ultimately found to have LHON.

Description of Cases:
Our patient presented with a one-month history of progressive central vision loss in the right eye. Her visual acuities were 20/200-1 and 20/25-2; she had no afferent pupillary defect. Fundus examination revealed cup-to-disc ratios of 0.9 and 0.7 with an inferior notch on the right. Visual fields showed superior arcuate and ceco-central depressions on the right and an inferior nasal step on the left. OCT showed bilateral, superior and inferior RNFL thinning. She was diagnosed with normal-tension glaucoma with new central involvement. Laboratory studies and neuro-imaging were unremarkable. One month later she presented with new central vision loss on the left. OCT showed increased average RNFL, indicating mild swelling. Due to concern for an acute-on-chronic process, she was treated with steroids and later plasmapheresis with modest improvement. Extensive laboratory evaluation, lumbar puncture, temporal artery biopsy, and PET CT were normal. Mitochondrial genetic testing was ordered, and 6 weeks later resulted positive for a pathogenic variant at position 11778, confirming a diagnosis of LHON. She began treatment with Idebenone and her vision improved to 20/40- and 20/30 over 10 months.

Conclusions, including unique features of the case:
This case describes a 72-year-old woman who presented with glaucomatous visual field defects and optic nerve cupping, then developed features concerning for an inflammatory optic neuropathy, and was finally diagnosed with LHON. She had no classic risk factors or family history for the disease. It is thought that her history of multiple bouts of COVID-19 infection in the preceding year, undiagnosed dysautonomia, GI problems and pre-existing glaucoma may have all contributed.

References: None provided.

Keywords: Optic neuropathy, Genetic disease, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease

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Not Another Non-Arteritic Ischemic Optic Neuropathy: A Wolf In Sheath's Clothing

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Introduction:
The differential for vision loss with optic disc edema is broad. Here we present a case initially diagnosed as NAION, whose exam and imaging findings were concerning for alternative diagnoses.

Description of Cases:
A 72-year-old man presented to his local hospital with 1 month of transient vision loss in the right eye that subsequently progressed to NLP vision, found to have right optic disc edema. His MRI Brain and CTA head and neck were interpreted as normal, ESR/CRP normal, and the patient was diagnosed with NAION. He was referred to our institution given persistent photopsias and progressive vision loss. On exam, vision was NLP OD, 20/40 OS with an APD OD, reduced color perception OS by Ishihara, and oculomotor and neurologic exam were otherwise intact. Dilated ophthalmoscopy revealed right Frisen Grade 4 disc edema. On our review of his MRI, there were concerning findings suggestive of neoplastic (compressive tumor, optic nerve meningioma, paraneoplastic) or inflammatory causes (NMO/MOG, MS/demyelinating optic neuritis, sarcoidosis). Intensive multidisciplinary discussion led to initial steroid and PLEX treatment, while infectious/inflammatory workup was pending. Initial conservative biopsy of the right optic nerve sheath and surrounding tissue was non-diagnostic. A second biopsy of the optic sheath and nerve was non-diagnostic. Three weeks later, worsening vision in the remaining eye led to a third optic nerve biopsy revealing Grade IV glioblastoma.

Conclusions, including unique features of the case:
The decision to pursue an optic nerve sheath vs optic nerve biopsy, thereby sacrificing potential visual recovery was challenging. Malignant optic gliomas are extremely rare (1) and may be misdiagnosed without thorough neuroradiological review. Characteristics include unilateral onset progressing to bilateral optic tract involvement within months, and are uniformly fatal (2). An initial misreading of the MRI led to a misdiagnosis of NAION for an NLP optic neuropathy. NLP vision is unusual in NAION (3), and should raise suspicion for alternative diagnoses.

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All that Glitters is not Gold

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Introduction:
Giant cell arteritis (GCA) remains an elusive diagnosis that varies on a case-by-case basis. Although temporal artery biopsy remains the gold standard for diagnosis of GCA, MRI protocols developed to highlight the status of the head and neck vessel walls as well as a data-driven nomogram for calculation of risk for GCA have proven especially useful. Our case displays the clinical value of these advances first-hand.

Description of Cases:
A 76-year-old Caucasian woman awoke with binocular oblique diplopia, severe headache, nausea and vomiting. On arrival in the emergency department, a brain attack was called. CT scan was normal and tissue plasminogen activator was administered. Blood count, platelet count, and erythrocyte-sedimentation rate were normal and C-reactive protein was 7.4 mg/dL (0.0-0.8 mg/dL). Her symptoms persisted. An MRI/MRA with contrast were unrevealing after 24 hours. On ophthalmic examination, she had a comitant right hypertropia and esotropia but no other pertinent findings.Two days later, with her diplopia only minimally improved, an MRI orbits with contrast showed enhancement of the orbital fat and optic nerve sheaths in both orbits.

Conclusions, including unique features of the case:
Initially, we were suspicious of a brainstem stroke, as this could conceivably produce a skew deviation, headache, nausea and vomiting. Although her c-reactive protein was elevated and GCA was discussed at presentation, the lack of other complaints steered us away. However, in the correct clinical context, if one observes enhancement of the orbital fat on brain MRI, GCA should be more strongly considered. Notably, MRI protocols that isolate scalp vessel walls may be helpful. Vessel wall imaging (VWI) has proven to be both sensitive and specific. Some authors have suggested, if clinical suspicion for GCA is low, normal VWI may obviate the need for superficial temporal artery biopsy, as the negative predictive value of normal VWI has been reported to be over 98%.

References: None provided.

Keywords: Neuroimaging, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Neuro-ophth & infectious disease (eg, AIDS, prion), Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease, Stroke

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Get Out of the Sun, or Drop In for Something Wild and Gnarly?

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Introduction:
Primary extra-axial glioblastoma multiforme (GBM) is rare with scarce reporting in literature. This results in diagnostic dilemma when appearance of the lesion mimics the findings of dural or extra-dural malignancy such as meningioma or metastasis. In patients with known cancer, the latter diagnosis is the highest on differential.

Description of Cases:
64 year old man presented with one month of dysequilibrium and paresthesia around the right eye, one week onset of double vision, blurry vision, paresthesia to entire right face, facial asymmetry, constant hiccupping and dysphagia. He had a relevant history of melanoma of the right brow s/p Mohs surgery. He presented to outside ED where noncontrast MRI brain was negative. On presentation, his exam was concerning for right 3rd (pupil sparing), 5th, and 7th cranial nerve palsies with additional concern for area postrema syndrome. MRI skull base revealed soft tissue enhancement anterior to the midbrain and pons in the prepontine cistern. He presented for admission and further diagnostic workup. With concern for metastatic melanoma, CSF cytopathology was negative on 3 lumbar punctures. Infectious workup was negative and PET did not reveal additional sites of cancer. Neurosurgery recommended biopsy which was deferred due to high risk access. He was discharged home on steroids and presumed metastatic melanoma. The patient worsened clinically and repeat imaging revealed expansion with leptomeningeal spread. Biopsy was performed "compatible with glioblastoma, IDH-wildtype, WHO grade IV." He was negative for metastatic melanoma. He completed whole-brain radiation (30Gy in 10 fractions). He ultimately elected for home hospice care.

Conclusions, including unique features of the case:
This case was uniquely challenging due to the presumed diagnosis of metastatic melanoma, where this served as a red herring. Negative CSF cytology, PET scan, and deferred biopsy, added to diagnostic delay. Ultimately, the extra-axial appearance of the lesion was highly atypical for the final diagnosis of primary GBM, requiring biopsy for confirmation.

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Keywords: Neuroimaging, Skull base, Tumors

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Let Yourself Go with the Flow!

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Introduction:
Lymphomatoid granulomatosis (LYG) is a rare EBV-associated lymphoproliferative disease that most commonly affects the lungs, skin and, rarely, the central nervous system (CNS). Isolated CNS LYG is rare, with only 40 cases of primary CNS disease found in a 2020 review article.

Description of Cases:
An 88-year-old woman with a history of diabetes mellitus, hypertension, hyperlipidemia, and coronary artery disease presented with right ptosis and binocular horizontal diplopia that had begun earlier that day. Examination was significant for anisocoria and a complete right third cranial nerve palsy. MRI brain revealed enhancement of the right oculomotor nerve as well as mass effect and edema in bilateral medial frontal lobes. Cerebrospinal fluid studies were remarkable for protein of 183 mg/dL, lymphocytic pleocytosis of 72 cells/cubic mm (84% lymphocytes), and flow cytometry showing a small population of variable-sized B lymphocytes with no definitive light chain expression, suggesting a B-cell lymphoproliferative disorder. Ultimately, leptomeningeal, pial, and parenchymal core biopsies were obtained from an enhancing lesion in left frontal lobe showing angiodestructive granulomatous mixed inflammatory infiltrate and exuberant reactive astrocytes, mostly T-cells and histiocytes, and a scant population of EBV-positive cells, consistent with the diagnosis of lymphomatoid granulomatosis (LYG).

Conclusions, including unique features of the case:
This case highlights a rare etiology of a pupil-involving third nerve palsy. Despite MRI brain demonstrating enhancement of the third nerve initially and CSF suggesting lymphocytic pleocytosis, these were nonspecific findings and markers that are more specific were negative. Ultimately, a brain biopsy was necessary to confirm this EBV-driven lymphoproliferative disorder.

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Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Neuroimaging

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Are you Loki, by any chance?

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Introduction:
This case study explores the clinical pictureof a 45-year-old female of central Asian descent, who, with a history of triple-negative invasive ductal breast carcinoma (cT2 pN1) in remission for two years, presented with double vision and persistent asthenia. Triple-negative breast carcinoma, known for its aggressive behavior and lack of estrogen, progesterone, and HER2/neu recepto rs, poses unique challenges in its clinical course and management. The interplay of this specific breast cancer subtype with subsequent manifestations forms a distinctive backdrop for understanding the complexities encountered in this case.

Description of Cases:
While ophthalmological examination revealed no abnormalities, a neurological examination exposed decreased sensation on the right side of the face and upper limb, coupled with right upper limb ataxia. MRI detected a central pontine lesion with heterogenous enhancement, challenging initial diagnostic impressions. Further complicating the scenario were bilateral mediastinal and hilar lymphadenopathies on CT imaging, leading to a preliminary diagnosis of sarcoidosis. Despite an initial response to high-dose corticosteroids, the patient's condition relapsed, necessitating additional immunosup pressants. Five months later, clinical improvement coincided with a reduction in pontine lesion size and mediastinal adenopathy disappearance. However, a subsequent downturn occurred, revealing new-onset symptoms and a considerable progression of the pontine lesion.

Conclusions, including unique features of the case:
Despite an initial diagnosis of neurosarcoidosis, further investigation uncovered a coincidental brain metastasis of invasive ductal breast carcinoma. The patient's response to corticosteroids and subsequent identification of a perivascular pattern of metastatic tumor invasion highlight the complexity of these overlapping pathologies. This case emphasizes the importance of vigilant reevaluation and consideration of diagnoses in atypical presentations.

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Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Tumors, Ocular motility

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Before I got my eye put out

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Introduction:
A 64-year-old man was referred to the neuro-ophthalmology clinic for evaluation of papilledema.

Description of Cases:
His medical history included type 2 diabetes with peripheral neuropathy, hyperlipidemia, hypertension, non-rheumatic aortic valve stenosis and benign neoplasm of skin. He reports intermittent blurry spot and photopsia that began in the left eye with progression to both eyes, worse with straining. Optometric examination showed bilateral optic disc edema with excellent visual function. An initial MRI of the brain showed bilateral dural thickening, enhancement, and extraconal orbital edema. Lumbar puncture with CSF studies was largely unremarkable except for elevated protein. Serum and urine protein electrophoresis and EMG/NCS were also normal. CT of the chest and abdomen revealed marked progressive nonspecific perinephric retroperitoneal stranding, new splenomegaly, scattered pulmonary micronodules, calcified granulomas, and marked aortic valve calcification. PET did not show any fludeoxyglucose uptake. When the patient was seen by neuro-ophthalmology, there was persistent optic nerve swelling. Additional imaging and cardiac studies were unrevealing. He continued to experience progressive neuropathy and repeat EMG/NCS was performed, which showed severe demyelinating polyneuropathy that led to obtaining nodal/paranodal antibodies and serum vascular endothelial growth factor (VEGF). VEGF was highly elevated. Repeat testing showed increased kappa and lambda-free light chains. The patient was diagnosed with polyneuropathy, organomegaly, endocrinopathy, monoclonal component, skin changes (POEMS) based on clinical criteria and was started on immunotherapy with daratumumab, lenalidomide, and dexamethasone. During his recent follow-up, he had near-resolution of his visual symptoms and slight improvement of his neuropathy. Optic disc swelling also improved on OCT.

Conclusions, including unique features of the case:
POEMS is a rare multisystemic disorder that can present with ocular findings. Approximately a third of patients present with papilledema; common ocular symptoms include blurry vision, diplopia, and ocular pain. This patient's initially normal protein electrophoresis and electrophysiology made it challenging to make the diagnosis.

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Keywords: Demeylinating disease, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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Mass Effect? An Etiologic Search for Progressive Hindbrain Decline

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Introduction:
Anti-Kelch-like protein 11 rhombencephalitis is a cytotoxic T cell-mediated paraneoplastic syndrome associated with testicular seminomas that commonly presents with ataxic gait, dysmetria, dysarthria, tremor, nystagmus, gaze palsies, and hearing loss [1-4]. Diagnostic uncertainty often exists for this disease, as symptoms may manifest prior to the identification of a malignancy and additional anti-neuronal antibodies (e.g., anti-NMDR) are often present[5,6]. Manifestations of this syndrome are often treatment refractory[7]. We present a case of anti-Kelch-like protein 11 rhombencephalitis that exemplifies its core clinical features, a typical workup, the difficulty of diagnosis, and its resistance to treatment.

Description of Cases:
A 54-year-old man with a history childhood left inguinal hernia repair complicated by left orchiectomy presented for 2 years of progressive nystagmus. Initial evaluation suggested a progressive hindbrain syndrome featuring downbeat nystagmus, vertigo, and cerebellar gait abnormalities. MRI, broad lab work, and lumbar puncture led to detection of Kelch-like protein 11 IgG antibodies in the CSF. Evaluation for malignancy included a negative PET/CT and, given a history of hematospermia, a testicular ultrasound, which demonstrated a 1.4 cm hypoechoic mass of his solitary testis. Orchiectomy was performed with pathology showing calcified fibrotic changes, which could suggest a regressed testicular germ-cell tumor. Treatment with high-dose intravenous methylprednisolone, plasmapheresis, and escalating doses of cyclophosphamide have stabilized, but not improved, his symptoms.

Conclusions, including unique features of the case:
This case is unique due to the rarity of anti-Kelch-like protein 11 rhombencephalitis, the challenging surgical decision-making surrounding orchiectomy in a patient with only one testis, the lack of a definitive causative malignancy for this paraneoplastic syndrome, and the long course of misdiagnosis. Sharing an example of this disease provides a rare opportunity to learn about it as part of the differential for progressive, treatment-refractory rhombencephalitis. Furthermore, this case emphasizes the importance of evaluating for autoimmune and age- and gender-specific neoplastic diseases in working up progressive cerebellar signs.

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Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Nystagmus, Paraneoplastic syndromes

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Monocular Vision Loss in a Patient with Altered Mental Status

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Introduction:
A 64-year-old male with a history of CRVO and Dry AMD presented to an ophthalmologic ED with severe, acute monocular vision loss OS for 7 days, preceded by two months of bilateral blurry vision, severe headaches, and bilateral peri-orbital pain worse with EOMs that interrupted sleep. The patient's past medical history also includes steroid-induced diabetes mellitus, systemic hypertension, ankylosing spondylitis, ulcerative colitis, and CKD, for which he underwent a kidney transplant 7 months prior and takes tacrolimus and oral prednisone. The history was also relevant for fatigue and weight loss, confusion, which had progressed over the previous week, incoherent speech, and right foot drop.

Description of Cases:
VA = 20/30 OD and NLP OS. CVF suggested a temporal defect. DFE revealed cotton wool spots OS. The patient underwent macular and RNFL OCT, as well as a FA, which were unrevealing. He was admitted to the hospital for a diagnostic evaluation. Shortly thereafter he developed a stroke in the distribution of the left ACA. CT head revealed left ACA territory infarct extending to the periventricular cortex. MRI/MRA revealed evidence of a left maxillary and sphenoid sinusitis, as well as large areas of diffusion restriction corresponding to hypo-attenuation visualized on CT. CRP and ESR were elevated at 104.4 and 64, respectively. Sphenoid sinus biopsy revealed fungus with septate hyphae with 45-degree branching, and a large thick-walled vessel with intraluminal fungi, extensive with fibrin, suggestive of true angioinvasive, systemic fungal disease. He unfortunately passed away shortly after.

Conclusions, including unique features of the case:
This presentation is unique due to the patient's initial presentation without any clear systemic diagnosis. The need for acute and detailed diagnostic investigation can be overlooked in ophthalmic venues because of a lack of seemingly significant findings. Despite our aggressive work-up, our patient died from an infectious disease that may have been effectively treated if he had presented earlier.

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Primary CNS Lymphoma of T-cell Origin Presenting with Multiple Cranial Neuropathies

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Introduction:
Primary central nervous system lymphoma (PCNSL) is an uncommon form of non-Hodgkin lymphoma restricted to the nervous system, representing only 2-4% of newly diagnosed intracranial tumors. While the vast majority are of B-cell origin, PCNSL of T-cell origin (TPCNSL) are rarely reported, accounting for 2-8.5% of cases. We report a case of TPCNSL presenting initially with multiple cranial neuropathies.

Description of Cases:
A 64-year-old man with chronic eosinophilic dermatitis on dupilumab presented with four days of painful vision loss OS. Initial exam revealed acuities of 20/30 OD and hand motion OS, an rAPD OS, and disc edema OS. Subsequently, a partial, pupil-involving left CNIII palsy, left V1-3 hypesthesia, and a peripheral right CNVII palsy developed. MRI brain/orbits demonstrated enhancement of multiple cranial nerves including the left optic nerve and sheath. Symptoms were initially steroid-responsive, and rituximab was started given concern for seronegative ANCA-associated vasculitis. He returned one month later with worsening vision with acuities of 20/100 OD and hand motion OS, bilateral disc edema, and boxcarring within arterioles of superior > inferior temporal arcade OS, suggestive of hyperacute non-embolic CRAO. CSF studies revealed mild pleocytosis, elevated protein, and non-specific atypical inflammatory cells on cytology. Repeat MRI brain revealed interval cervicomedullary and cerebellar lesions with prominent leptomeningeal enhancement and new cortical and subcortical punctate areas of diffusion restriction. PET-CT showed markedly intense cerebellar uptake but no evidence of systemic disease. Skin biopsy was negative. Brain biopsy was ultimately diagnostic of TPCNSL with pathology consistent with peripheral T-cell lymphoma, notably with evidence of vascular invasion.

Conclusions, including unique features of the case:
We report a rare case of TPCNSL presenting initially with multiple cranial neuropathies, subsequent CRAO, and progressive leptomeningeal disease with histologic evidence of vascular invasion. A combination of ocular hypoperfusion and CNS findings (e.g. CSF pleocytosis) should raise suspicion for lymphoma with vascular involvement.

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Rewriting The Story: A Tale Of Ataxia And Atrophy

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Introduction:
Clinical variability, both within and among families with the same disease, often makes recognition and classification difficult in certain diseases.

Description of Cases:
A 42-year-old female presented with bilateral optic atrophy, progressive ophthalmoplegia, and cerebellar syndrome. Her only brother died at age 44 due to kidney failure from vasculitis. Her symptoms began at age 10 with ptosis and diplopia, treated with IV methylprednisolone and cyclophosphamide, without improvement. At 11, she noted painless, sequential, acutebilateral visual loss a year apart. At 21 , she suffered a left sensitive and hemiparesis episode with partial recovery after 6 months. A diagnosis of primary CNS vasculitis was made by rheumatology, and was started on mycophenolic acid 500mg/bid On neuro-ophthalmic examination she had 20/800 vision in both eyes (OU), isochoric pupils, + RAPD OD. On primary gaze, she showed exotropia and left hypotropia, with horizontal jerk, gaze-evoked nystagmus, and limited adduction OU. Fundus examination revealed diffuse pallor OU. She had unsteady, widened-base gait, dysmetria and dysdiadochokinesia in lower limbs,, hyperreflexia and paresthesia in left lower limb and cognitive decline. Goldmann perimetry showed a 40º concentric loss OU. MRI did not show signs of demyelinating, ischemic lesions or vasculitis. But a enlargement of the ventricular system and subarachnoid cisterns, as well as a lacunar infarct adjacent to the left putamen.

Conclusions, including unique features of the case:
We considered hereditary/mitochondrial optic neuropathies as a possible diagnosis. LHON as it is the most common and LHON-plus can present with other neurologic signs as in the patient. MELAS was an additional differential as they present with stroke-like episodes before 40 years old. However, the lack of a classical mitochondrial or degenerative phenotype led us to order whole exome sequencing. Deficiency of Adenosine deaminase 2 (DADA2) was diagnosed, which is a monogenic autoinflammatory disorder presenting with a broad spectrum of manifestations, including immunodeficiency, vasculopathy and hematologic disease.

References: None provided.

Keywords: Genetic disease, Vascular disorders

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Third Cranial Nerve Schwannoma presenting as acquired exotropia: a diagnostic dilemma

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Introduction:

A 25-year-old female presented to our neuro-ophthalmology clinic with gradually progressive exodeviation of the left eyeball from last 3 years. She had mild ptosis and proptosis in her left eye with 3mm of anisocoria. On examination she was found to have large exotropia with minimal motility limitation in the left eye. She underwent MRI brain and orbit, which showed a features suggestive of a schwannoma.

Description of Cases:

A 25-year-old female presented with complaints of gradually progressive exodeviation of the left eyeball from last 3 years. Her eyes were well aligned in childhood photographs. She reported associated frontal headache and eye straiHer best corrected visual acuity was 20/20 in both eyes (BE). There was mild ptosis and proptosis in her left eye with 3mm of anisocoria, but no relative afferent pupillary defect (RAPD). She had 60 prism dioptres exotropia for distance and near. There was -1 deficit of adduction; elevation and depression each in the left eye (LE) while her abduction was normal. Ocular motility was normal in the right eye (RE).Dilated fundus examination was unremarkable in BE. Composite image of MRI Brain and orbit showed a mulberry shaped enhancing nodular lesion measuring 6.1×7×7.6 mm along the course of the left oculomotor nerve in the interpeduncular fossa, which was hypointense on T2 and isointense on T1weighted images, suggestive of a schwannoma (figure 1a,1b). CT angiography revealed no aneurysm compressing the 3rd cranial nerve (Figure 1c).

Conclusions, including unique features of the case:

Our case represent the localising sings of isolated 3rd nerve palsy depicting the importance of points favouring the diagnosis of oculomotor schwannoma were a combination of features of isolated acquired oculomotor palsy along with the tumour location along the course of oculomotor nerve in the interpeduncular cistern on neuroimaging.

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Through Thick and Thin: A Case of Idiopathic Hypertrophic Pachymeningitis

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Introduction:

Hypertrophic pachymeningitis is a rare, potentially vision threatening, disorder characterized by local or diffuse thickening of the dura mater 1-2. Symptoms often include headache and cranial nerve involvement with cranial nerves II and VII affected predominantly due to nerve compression or orbital idiopathic orbital inflammation 3. While often associated with conditions such as ANCA-related diseases, IgG4-related diseases, intracranial hypotension, infections, or neoplasm, idiopathic cases have been described.

Description of Cases:

We present the case of a 73-year-old male with distant history of acute myeloid leukemia status-post allogeneic bone marrow transplant who presented with several weeks of rapidly worsening vision to CF OD, 20/60 OS, an afferent pupillary defect, and dyschromatopsia. He was started on oral steroids and IVIg for presumed cancer associated retinopathy vs. autoimmune retinopathy. MRI subsequently revealed diffuse thickening and enhancement of the pachymeninges and focal perineural enhancement of the optic nerves OD>OS. OCT imaging showed progressive, bilateral retinal nerve fiber and ganglion cell layer thinning. After extensive multidisciplinary workup including brain biopsy, no underlying etiology was identified. A diagnosis of idiopathic hypertrophic pachymeningitis was made based on neuroradiological findings of thickened dura, histopathological findings of non-specific inflammation, and exclusion of known secondary etiologies. High dose pulsed IV steroids were initiated which resulted in rapid neuroradiological and symptomatic improvement, and no systemic etiology has presented itself over the two-year course of management.

Conclusions, including unique features of the case:

Hypertrophic pachymeningitis is a rare entity often associated with conditions such as intracranial hypotension, infection, autoimmune disease, or neoplasm. This case is a unique example of idiopathic hypertrophic pachymeningitis in a patient with known history of acute myeloid leukemia, and it highlights the necessity of a broad differential and expedited workup, including potentially invasive testing such as brain biopsy, as well as early treatment when hypertrophic pachymeningitis is identified given the potential for rapid and profound vision loss.

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Keywords: Optic neuropathy, Neuroimaging, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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Ischemic Optic Neuropathy: Thinking Outside The Box And Brain

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Introduction:
This is one of the first reported cases of ischemic optic neuropathy with intracranial hypertension in the setting of jugular venous sinus thrombosis.

Description of Cases:
A 25-year-old male with a history of Alport syndrome status-post bilateral failed kidney transplants, end-stage renal disease on hemodialysis, seizure disorder, hypertension, and recurrent deep venous thromboses on apixaban presented with acute painless vision loss in the left eye (OS) upon awakening. Visual acuity was 20/20 in the right eye (OD) and light perception OS with a relative afferent pupillary defect OS. He had superior segmental swelling of the optic disc OD and diffuse pallor with 360-degree swelling of the disc margin OS. MRI brain and orbits with and without contrast, MR angiography and venography of the brain were normal. Ocular coherence tomography showed an average retinal nerve fiber layer thickness of 276 um OD and 124 um OS. Humphrey visual field 30-2 revealed an inferior altitudinal defect OD. His lumbar puncture had an elevated opening pressure of 41.5 cm H2O. Chest CT with contrast showed severe blockage of the left proximal internal jugular vein (IJV) with Doppler ultrasonography confirming a left IJV thrombosis. Hypercoagulable work-up revealed positive lupus anticoagulant and the patient was transitioned to warfarin. He was treated with erythropoietin, high-dose steroids and started on 125 mg acetazolamide.

Conclusions, including unique features of the case:
This is a unique case of bilateral ischemic optic neuropathy with elevated ICP from unilateral IJV thrombosis. When patients with vascular risk factors present with elevated ICP and a lack of IIH symptoms, extracranial causes should be considered including jugular venous thrombosis.

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Keywords: Optic neuropathy, Vascular disorders, High intracranial pressure/headache

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An incomplete dorsal midbrain syndrome and neurocysticercosis reactivation: A case report

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Introduction:
Neurocysticercosis is the most common helminthic infection affecting the human central nervous system (CNS). The most common site of infection is the cerebral parenchyma. However, extraparenchymal CNS infection can also occur and may have diverse presentations.

Description of Cases:
A 72-year-old man presented to our clinic referring an ongoing vertical diplopia which began 2 months prior to his visit. He had a history of neurocysticercosis (NCC) which required a ventriculoperitoneal shunt (VPS) in 1997. On examination he had a best corrected visual acuity of 20/25 in both eyes based on the Snellen chart. Color vision, tested with the Ishihara charts was 8/8 in both eyes. No evident RAPD was noted. In primary gaze an esotropia of 15º Hirschberg was found with a right head tilt. Smooth pursuit examination showed limited elevation in both eyes. Horizontal abducting saccades were slightly slowed and vertical saccades triggered convergence-retraction nystagmus.The optic disc had a cup of 30% in both eyes, but the neuroretinal rim of the left optic disc had a white-yellow coloration. An optic nerve optical coherence tomography (OCT) was requested which revealed a superior-temporal defect in the retinal nerve fiber layer of the left eye. Based on the history and examination, an incomplete dorsal midbrain syndrome (DMS) was identified. Brain magnetic resonance imaging (MRI) showed intraventricular cystic lesions occupying the fourth ventricle, one of which was ring-enhancing after gadolinium administration suggesting active cysticercus infection. Medical treatment with prednisone and albendazole improved the symptoms.

Conclusions, including unique features of the case:
Extraparenchymal CNS NCC is rare. Initially, it was uncertain why this patient had an incomplete DMS. Once MRI-ruled out the most probable causes (compressive and ischemic), a VPS failure versus a second reactivation of NCC arose as the next working diagnosis as both may initially present with this clinical scenario. Medical treatment improved the symptoms, leaving NCC as the etiology.

References: 1. J Fan, R Tang , L Zhang, PT Hoang, F Ayoade, et al.; Atypical Presentations of Extraparenchymal Neurocysticercosis, J Neuroophthalmol, 43(3), 370-375, 2023.

Keywords: Neuro-ophth & infectious disease (eg, AIDS, prion), Ocular motility

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Recurrent ophthalmoparesis/partial Tolosa Hunt Syndrome secondary to presumed extra-pulmonary tuberculosis: a Diagnostic Dilemma

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Introduction:
Recurrent ophthalmoparesis raises concern for a variety of conditions such as granulomatous, autoimmune, local infiltrative pathologies. Detailed work-up is often mandatory and biopsy may not be amenable.

Description of Cases:
A 21-year-old male came with swelling and pain of the right upper eyelid for a month. Examination showed BCVA of 20/20 in both eyes (BE), upper eyelid edema and mild erythema in the right eye (RE). Fundus was normal in BE The patient was treated as allergic lid edema with partial relief. 2 weeks later the patient developed periorbital edema and diplopia. Motility examination showed -2 elevation deficit. B-scan ultrasonography revealed thickening of the right lateral rectus (RLR) with increased echogenicity in supero-temporal orbit. Differential diagnosis were cysticercosis, myositis, dacryoadenitis, non-specific-orbital-inflammatory disease (NSOID) or IgG4 disease dacryoadenitis. Computed tomography (CT scan) of orbit revealed area of focal hyperdensity involving the right lacrimal gland. He was started on non-steroidal-anti-inflammatory drugs. However, the patient's symptoms worsened to complete mechanical ptosis, right hypotropia and -4 elevation deficit in RE. Complete blood count, ESR, Serum ACE, Serum IgG4 assay was normal/negative. With suspicion of ruptured cysticercosis, the patient was started on Tablet Albendazole 400mg and oral steroids in tapering doses. The patient showed remarkable improvement. 3 months later, the patient had recurrence of diplopia and pain in RE. There was -4 abduction limitation. There was hyperesthesia in V1 area. MRI scan orbit revealed a well-defined hyperintense lesion in the orbital apex extending into the right cavernous sinus. On retrospective history, patient revealed tuberculosis in childhood. Recent HRCT chest scan revealed an old Koch's lesion in the right lung. Patient was diagnosed as orbital-apex syndrome due to extra-pulmonary tuberculosis. Patient had good resolution with anti-tubercular-therapy and oral steroids.

Conclusions, including unique features of the case:
The case highlights recurrent ophthalmoparesis with negative workup. Initial work up was negative. Detailed history and systemic findings estabished diagnosis.

References: None provided.

Keywords: Ocular motility, Neuroimaging, Orbit, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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Cease the Seizure

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Introduction:
Cavernous hemangiomas are the most common benign orbital lesions in adults. They are often asymptomatic, but may present with proptosis, diplopia, vision deficits, and eye movement restrictions. CT scan shows round, well-defined margins if lesion is intraconal and pear-shaped lesions at orbital apex. MRI shows isointense lesions to muscle on T1-weighted images and hyperintense lesions to muscle on T2-weighted images. Surgical treatment is indicated for worsening proptosis, vision decline, or significant visual field defects.

Description of Cases:
48-year-old female presented with recurrent episodes of seizure-like activity, headaches, left eye pain, episodic blurry vision, and a new persistent vision decline. She was seen by Neurology for seizures. Neurology workup did not show any etiology for her seizures and on return visit, they appreciated a new RAPD, and delayed P100 with concern for optic neuritis, which was ruled out with laboratory and CSF studies, and attention to orbital apex on the MRI imaging showed a well-circumscribed lesion. She was given methylprednisolone 1000 mg IV x 3 days in hospital and discharged on a three-day course of 1250mg prednisone. At her initial neuro-ophthalmology clinic visit, she noted improvement of vision with no RAPD. OCT average RNFL was normal OU. Two weeks later, she presented with vision of 20/150, 4+ RAPD OS, and diffuse inferior defect on HVF 30-2. She was trialed on methylprednisolone 500 mg x 3 days and as she was tapered off the steroids, she developed recurrent visual field defect which resolved following decompression of the orbital apex. She opted for orbital lesion excision via craniotomy for headaches which resolved following surgery.

Conclusions, including unique features of the case:
To our knowledge, seizure-like activity has not been published from a sole orbital cavernous hemangioma. Our case demonstrates the responsiveness of cavernous hemangiomas to high dose steroids. We demonstrate the resolution of visual field defect following surgical decompression from compressive optic neuropathy.

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Doubled Vision, Inflamed Suspicion

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Introduction:
We report a case of orbital metastasis to an extraocular muscle, initially mistaken for orbital myositis, marking the first sign of metastatic lung adenocarcinoma. Such cases are scarcely reported, highlighting the diagnostic challenges that can precede primary cancer identification.

Description of Cases:
A 71-year-old man with hypertension and pseudophakia presented with a three-month history of progressive binocular horizontal diplopia and mild ocular pain. Review of systems was negative. Examination demonstrated visual acuity of 20/20 OU and no relative afferent pupillary defect. Extraocular motility revealed limited, painful left eye abduction and a 25-prism diopter esotropia worse on left gaze. Exophthalmometry and cranial nerve exams were unremarkable. Initial MRI and MRA with gadolinium indicated possible idiopathic orbital inflammation or focal myositis, showing enlargement and enhancement of the left medial rectus muscle. After five weeks, despite oral steroid treatment, the patient's diplopia worsened, and follow-up motility examination revealed additional supraduction and excyclotorsion deficits. Mycophenolate mofetil was initiated with no improvement. Repeat neuroimaging at eight weeks after initial presentation revealed progression of the medial rectus abnormalities, demonstrating a more discrete lesion. Transconjunctival biopsy identified atypical basophilic cells, CK7 and TTF-1 positive, suggesting adenocarcinoma. PET/CT scans confirmed multifocal lung masses and other metastatic sites. The patient underwent left orbital radiation therapy and is awaiting systemic chemotherapy.

Conclusions, including unique features of the case:
Isolated extraocular muscle involvement in systemic malignancy is rare, posing diagnostic challenges when mimicking benign conditions. This case exemplifies the risks of misdiagnosis and the necessity for thorough reevaluation when clinical progression deviates from expectations. Key lessons include avoiding diagnostic fixation, exploring alternative etiologies for atypical findings or neuroimaging, and recognizing the rarity of orbital metastases.

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Keywords: Adult strabismus with a focus on diplopia, Tumors, Orbit/ocular pathology, Neuroimaging

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What's the bloody diagnosis?

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Introduction:
A 73-year-old male was referred for incidental optic nerve head edema after evaluation for diabetic eye exam. On history, he endorsed 3-4 months of right-sided pressure, transient visual deficits lasting 1 second occurring 5-6 times per day, and subtle binocular diplopia in peripheral gaze only. Medical history was remarkable for hypertension, diabetes, dyslipidemia, gout and a previous coronary artery and kidney stent.

Description of Cases:
He had normal visual acuity and colour function. He had limited abduction in the right eye (-1) and elevated intraocular pressure OD compared to OS. Fundus examination revealed clear media, but showed 360-degree disc margin elevation with hyperemia and small flame hemorrhages at the right optic nerve. Formal visual fields were full. Work-up included infectious and inflammatory blood markers. CT scan showed a well-circumscribed intraconal mass measuring 1.8 x 2.6 x 1.6 cm, arising from or involving the medial rectus muscle with progressive enhancement over time, with deviation of the lamina papyracea medially indicating bony remodeling and slow growth. MRI showed a right orbital, medial intraconal, ovoid, well-circumscribed mass that was T2 heterogeneous, T1 isointense to muscle with heterogenous enhancement, separate from the optic nerve, but difficult to separate from the medial rectus muscle. The mass was felt to be most in keeping with a cavernous hemangioma. A formal angiogram was performed for embolization, but showed no visible vascular malformation. Biopsy was performed which revealed embryonal rhabdomyosarcoma. Metastatic work-up was negative. Oncology initiated curative management with chemotherapy and local radiation.

Conclusions, including unique features of the case:
Adult-onset primary orbital rhabdomyosarcoma is rare. This patient was referred for incidental optic nerve head edema, but had subtle orbital findings that were unrecognized by other providers. Radiographically, the pathology was thought to be benign cavernous hemangioma until unsuccessful angiogram. This case highlights the subtleties of early orbital pathology and an atypical presentation of a very malignant entity.

References: [1] Bompas E, Campion L, Italiano A, Le Cesne A, Chevreau C, Isambert N, et al. Outcome of 449 adult patients with rhabdomyosarcoma: an observational ambispective nationwide study. Cancer Med 2018;7:4023–35. https://doi.org/10.1002/cam4.1374. [2] Sanz-Marco E, España E, Alamar A, Pérez-Rojas J, López-Prats MJ, Díaz-Llopis M. [Orbital alveolar rhabdomyosarcoma masked by ethmoid sinusitis in a 25-year-old]. Arch Soc Esp Oftalmol 2014;89:182–5. https://doi.org/10.1016/j.oftal.2012.10.012. [3] Kelly A, Moran M, Primrose W. Alveolar ethmoidal rhabdomyosarcoma in a young adult male. BMJ Case Rep 2013;2013:bcr2013008737. https://doi.org/10.1136/bcr-2013-008737. [4] Bagdonaite L, Jeeva I, Chang BYP, Kalantzis G, El-Hindy N. Multidisciplinary management of adult orbital rhabdomyosarcoma*. Orbit 2013;32:208–10. https://doi.org/10.3109/01676830.2013.764442. [5] Othmane IS, Shields CL, Shields JA, Eagle Jr Ralph C, Gunduz K, Fitch S. Primary orbital rhabdomyosarcoma in an adult. Orbit 1999;18:183–9. https://doi.org/10.1076/orbi.18.3.183.2704.

Keywords: Orbit/ocular pathology, Tumors, Orbit, Optic neuropathy, Vascular disorders

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A Watertight Nerve

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Introduction:
A seven-year-old mildly overweight boy with a history of headaches presented for a routine eye exam. He was exposed to cocaine in utero and was born with an undescended testis, macrocephaly, and plagiocephaly. Visual acuity was 20/20 in both eyes. Color vision was normal. Fundus exam revealed atypical bilateral optic nerve head edema; while disc margins were sharp with healthy rims, arterioles, and venules, there was prominent circumferential peripapillary fluid. Humphrey visual fields demonstrated enlargement of the physiologic blind spots. There was diffuse head and neck lymphadenopathy. Lumbar puncture (LP) demonstrated an elevated opening pressure (42 cm H2O). Oral acetazolamide was initiated for pseudotumor cerebri syndrome. LPs continued to reveal elevated opening pressures (low 30s cm H2O). Headaches improved with riboflavin. As visual function and optic nerve appearance remained stable, Diamox was discontinued after 18 months. Biannual eye examinations, including perimetry, have remained unchanged as a teenager. At age 15, he was referred to Allergy and Immunology for diffuse lymphadenopathy. Genetic testing identified a pathogenic variant (p.P715L) in Signal Transducer and Activator of Transcription 3 (STAT3), which has been linked to STAT3-gain-of-function (GOF) syndrome.

Description of Cases:
STAT3-GOF syndrome was described in 2014 as a cause of early onset autoimmune and lymphoproliferative disease. Ocular findings have been reported in three patients, including bilateral posterior uveitis and cystoid macular edema in a 17-year-old female (c.1974G>C); papilledema with gliotic sheathing of the proximal arterioles and venules in a 20-month-old girl who later developed severe vision impairment (c.2144C>T); and more typical papilledema in a 12-year-old boy which responded to acetazolamide and immunotherapy (c.2147C>T).

Conclusions, including unique features of the case:
Atypical papilledema, when present with systemic autoimmunity, raises the possibility of STAT3-GOF syndrome. Surgical shunting or prolonged ICP-lowering medication proved unnecessary in this case due to largely intact visual function and lack of any progressive symptoms.

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Keywords: High intracranial pressure/headache, Genetic disease, Pediatric neuro-ophthalmology, Visual fields, Pseudotumor cerebri

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Don’t judge a book by its cover. Also, don’t diagnose a patient by a radiological report.

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Introduction:
Myelin Oligodendrocyte Glycoprotein (MOG) is an important cause of optic neuritis in the pediatric population. Intraorbital radiological findings in MOG optic neuritis may resemble infiltrative processes. Precise clinical history and examination is mandatory to rule out differentials and treating our patients adequately.

Description of Cases:
A 6-year-old boy presented with a 3-day onset visual decline in his left eye (OS), accompanied by pain with eye movements. Her mother perceived the affected eye “larger” than the fellow eye from the beginning of symptoms. Right eye examination was unremarkable with 20/20 visual acuity. Left eye examination revealed RAPd, optic nerve edema associated with retinal vessel tortuosity. Exophthalmometry showed a 1mm asymmetry (OD 18mm, OS 19mm). Urgent MRI was requested for which neuro-radiology reported an infiltrative process, suggestive of optic nerve glioma. Despite reported findings, clinical suspicion suggested an inflammatory process and we decided to start treatment with IV methylprednisolone. His vision improved to 20/25 after 6 weeks. 4 months later, he presented to the ER due to partial seizures. New MRI which revealed lesion localized to the right parietal lobe suggestive of ADEM and received treatment with IV methylprednisolone. Due to unavailability of anti-MOG antibodies, diagnosis was delayed. After 3 months, mild optic neuritis developed in his right eye. After this third event, anti-MOG antibodies resulted positive. Our patient fully recovered from each event and has been event-free after immunotherapy was initiated.

Conclusions, including unique features of the case:
This case shows how inflammatory optic neuritis may be confused through radiologic features with an infiltrative optic neuropathy in the pediatric population. Also, the relapsing and remitting course of the disease despite initial treatment with IV steroids within the first 8 months since its debut, shows the importance of early immunosuppressive therapy and/or long term use of steroids in pediatric patients with MOGAD.

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Keywords: Demeylinating disease, Optic neuropathy, Pediatric neuro-ophthalmology, Neuroimaging

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A Messy Tie Situation; A Descriptive Study Of A Case of Down-Gaze Palsy

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Introduction:

A 61-year-old male with no known medical history presented to his primary doctor with excessive daytime sleepiness leading to a diagnosis of narcolepsy with cataplexy. Six months later, he developed low libido, and diffuse weakness. He was diagnosed with low testosterone. That same month, he presented to neuro-ophthalmology with difficulty moving his eyes. Examination was normal aside from significant slowing of downgaze; subtle, slowing of up gaze, best noted on diagonal saccades. Voluntary saccades were slower than pursuit, vestibular ocular reflex was intact. There was no fatigable ptosis.

Description of Cases:

This patient with progressive palsy of vertical gaze, arousal and endocrine symptoms further workup was warranted. MRI with contrast showed T2 hyperintensity with enhancement in the hypothalamus extending to the pituitary stalk, pituitary gland enlargement and scattered T2 white matter lesions in both frontal lobes. Cerebrospinal fluid analysis showed elevated protein, elevated nucleated cell count with a lymphocytic predominance. CSF ACE was borderline elevated. Chest CT showed evidence of prior granulomatous disease. Skin biopsy of the left hand was negative for sarcoid and lymphoma. He was treated with intravenous methylprednisolone 1 gram per day for 5 days with no alleviation of symptoms. PET demonstrated a mass in the nasopharynx. Biopsy showed squamous cell carcinoma. Serum paraneoplastic panel was negative including anti-Ma antibodies. He was treated with carboplatin, paclitaxel and radiation. The cancer was in remission and his symptoms regressed over 1 month.

Conclusions, including unique features of the case:

We believe this to be a case of seronegative paraneoplastic encephalitis presenting as a sarcoid-like reaction with a yet-to-be-discovered antibody. In this case the presence of mild elevation in ACE level in CSF and granulomatous lung findings in combination with imaging findings point toward a sarcoid-like reaction. There is a possibility that this type of presentation could be misdiagnosed and treated as sarcoidosis, allowing the progression of an underlying malignancy.

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Keywords: Ocular motility, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Paraneoplastic syndromes, Tumors

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Conundrum at the Crossroads : Sarcoidosis Masking Coexisting Metastatic Invasive Ductal Breast Carcinoma

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Introduction:
This case study delves into the nuanced clinical journey of a 45-year-old female of central Asian descent, who, with a history of triple-negative invasive ductal breast carcinoma (cT2 pN1) in remission for two years, presented with double vision and persistent asthenia. Triple-negative breast carcinoma, known for its aggressive behavior and lack of estrogen, progesterone, and HER2/neu receptors, poses unique challenges in its clinical course and management. The interplay of this specific breast cancer subtype with subsequent manifestations forms a distinctive backdrop for understanding the complexities encountered in the presented case.

Description of Cases:
While ophthalmological examination revealed no abnormalities, a neurological examination exposed decreased sensation on the right side of the face and upper limb, coupled with right upper limb ataxia. MRI detected a central pontine lesion with heterogenous enhancement, challenging initial diagnostic impressions. Further complicating the scenario were bilateral mediastinal and hilar lymphadenopathies on CT imaging, leading to a preliminary diagnosis of sarcoidosis. Despite an initial response to high-dose corticosteroids, the patient's condition relapsed, necessitating additional immunosuppressants. Five months later, clinical improvement coincided with a reduction in pontine lesion size and mediastinal adenopathy disappearance. However, a subsequent downturn occurred, revealing new-onset symptoms and a considerable progression of the pontine lesion.

Conclusions, including unique features of the case:
Despite an initial diagnosis of neurosarcoidosis, further investigation uncovered a coincidental brain metastasis of invasive ductal breast carcinoma. The patient's response to corticosteroids and subsequent identification of a perivascular pattern of metastatic tumor invasion highlight the complexity of these overlapping pathologies. This case emphasizes the importance of vigilant reevaluation and consideration of diagnoses in atypical presentations.

References: 1. Carbonell, W. Shawn, et al. "The vascular basement membrane as “soil” in brain metastasis." PloS one 4.6 (2009): e5857. 2. Deen, Jacqueline, Nick Mellick, and Laura Wheller. "Concurrent Diagnoses of Cutaneous Sarcoidosis and Recurrent Metastatic Breast Cancer: More than a Coincidental Occurrence?." Case Reports in Dermatological Medicine 2018 (2018).

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Ocular motility, Tumors

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For this movie, you need popcorn: First Case of Optic Nerve Cavernoma in the United States Hispanic Population

Adriana Rodriguez Leon [1], Joan Maley [1], Aygun Asgarli [1], Matthew Thurtell [1]

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Introduction:
Cerebral cavernous malformations (CCMs) incidence ranges between 0.3 to 0.5%. Of those, less than 1% affect the optic pathway (OP). Most CCMs are sporadic, solitary lesions. In its autosomal dominant (AD) familial form, cavernomas can be caused by heterozygous germline loss of-function mutations in genes CCM1/KRIT1, CCM2/Malcavernin, or CCM3/PDCD10. The founder mutation involving KRIT1 accounts for disease in Hispanic Americans, and this is the first OP cavernoma described in the literature in this population.

Description of Cases:
A 40-year-old man with uncontrolled hypertension, originally from Cuba, presented with acute onset vision loss OS. He reported a history of mild vision loss OS in 2008 with spontaneous recovery and residual vision deficit. Over years, he had episodes of mild vision loss OS where he did not seek medical attention. In December of 2022, he presented to our institution with acute onset profound vision loss OS associated with severe retroorbital pain increasing with eye movements. Due to initial concern for optic neuritis, IV methylprednisolone was started, without response. Examination showed severe vision loss, a dense RAPD, and optic atrophy OS, indicating a severe optic neuropathy OS which was confirmed by OCT (Optical Coherence Tomography). Imaging showed a heterogenous, multilobulated, hyperintense left optic nerve sheath lesion in the context of intraparenchymal lesions with similar characteristics ("popcorn"), suggesting an optic nerve cavernoma. Common etiologies were ruled out. In lieu of biopsy or resection, our patient underwent genetic testing with DNA sequence analysis showing a pathogenic variant (c.1261A>T) in the KRIT1 gene that is associated with AD CCM, also known as familial CCM.

Conclusions, including unique features of the case:
While most CCMs are sporadic, its AD familial form can be caused by mutations in several genes including CCM1/KRIT1. In Hispanic Americans KRIT1 mutation is responsible for the disease process and this is the first case of OP cavernoma in this population.

References: 1) Anglaret S, Lecler A. Optic Nerve Cavernous Venous Malformation. Neurology. 2021 Jan 5;96(1):31-32. doi: 10.1212/WNL.0000000000011092. Epub 2020 Oct 22. PMID: 33093225. 2) Stellon MA, Elliott RJ, Taheri MR, Jean WC. Cavernous malformation of the intracranial optic nerve with operative video and review of the literature. BMJ Case Rep. 2020 Dec 17;13(12):e236550. doi: 10.1136/bcr-2020-236550. PMID: 33334745; PMCID: PMC7747611. 3) Perrelli A, Ferraris C, Berni E, Glading AJ, Retta SF. KRIT1: A Traffic Warden at the Busy Crossroads Between Redox Signaling and the Pathogenesis of Cerebral Cavernous Malformation Disease. Antioxid Redox Signal. 2023 Mar;38(7-9):496-528. doi: 10.1089/ars.2021.0263. Epub 2022 Nov 1. PMID: 36047808; PMCID: PMC10039281. 4) Liu JK, Lu Y, Raslan AM, Gultekin SH, Delashaw JB Jr. Cavernous malformations of the optic pathway and hypothalamus: analysis of 65 cases in the literature. Neurosurg Focus. 2010 Sep;29(3):E17. doi: 10.3171/2010.5.FOCUS10129. PMID: 20809758.

Keywords: Neuroimaging, Tumors, Optic neuropathy

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Hunting Syndromes: A Challenging Consideration of Tolosa-Hunt Syndrome

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Introduction:
Tolosa-Hunt Syndrome (THS) is a painful ophthalmoplegia with cavernous sinus enhancement that responds to steroid treatment. It is a diagnosis of exclusion and requires a broad differential and close follow-up.

Description of Cases:
A 58-year-old woman with hyperlipidemia presented with severe right eye and face pain, nausea, and vomiting. Initial exam showed occludable angles OU with IOP 14 mmHg OU. LPI on the right eye did not improve her pain. 3 weeks later, she developed worsening vision and ophthalmoparesis. Outside visual acuity was 20/150 OD ph20/70; 20/20 OS, with 12/12 Ishihara color plates with each eye. There were limitations in right eye elevation, depression, and adduction. MRI with and without contrast found an enhancing mass along the wing of the right sphenoid extending to the orbital apex and partially encasing the cavernous right internal carotid artery. She was diagnosed with THS, and symptoms improved after initiating oral prednisone. Two weeks after completing the taper, she experienced pain, diplopia, and new right-sided ptosis. Prednisone was restarted. Repeat MRI demonstrated improved R cavernous sinus enhancement. She was referred to our center and described improvement without resolution of her symptoms. Exam showed 2mm relative ptosis OD, R V1/V2 hypoesthesia, and small comitant exophoria. Her symptoms worsened again and were not controlled by escalating doses of prednisone. Repeat MRI re-demonstrated the enhancing lesion. Resection was performed, and pathology suggested a benign vascular malformation. Post-operatively she had resolution of pain, though she had worsening ptosis and exotropia in the pattern of a third nerve palsy.

Conclusions, including unique features of the case:
This case highlights the challenge of a steroid-responsive diagnosis of exclusion. While her diagnosis was initially consistent with THS, her relapse and worsening despite corticosteroids raise the question of an incorrect diagnosis versus incomplete treatment. Her final diagnosis raises the question of why symptoms presumably from her vascular malformation responded to corticosteroids.

References: None provided.

Keywords: Ocular motility, Orbit/ocular pathology

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Metastatic Malignant Melanoma Masquerading as Tolosa-Hunt Syndrome

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Introduction:

Tolosa-Hunt syndrome (THS) is an idiopathic granulomatous inflammatory disease that affects the cavernous sinus, superior orbital fissure, or orbit, and typically causes ocular pain and ophthalmoplegia. It is a diagnosis of exclusion. Here, we present a rare case of metastatic melanoma involving the left cavernous sinus which masqueraded initially as THS.

Description of Cases:

A 76-year-old man had one week of left-sided headaches, periorbital pain, binocular diplopia, and complete left upper eyelid ptosis. He had a history of left eye choroidal melanoma treated seven years ago with Iodine-125 episcleral plaque radiotherapy and crizotinib for 1 year, achieving complete remission. Later, he developed radiation-induced cataract and glaucoma in the left eye. The neuro-ophthalmic evaluation revealed complete ophthalmoplegia and V1 hypoesthesia in the left eye. Neuro-imaging displayed left cavernous sinus enhancement from the orbital apex to the inferior orbital fissure. Blood work and CSF analysis were negative, suggesting Tolosa-Hunt syndrome. Treatment with intravenous methylprednisolone initially helped, but a follow-up MRI showed an increased affected area. Subsequent biopsy confirmed metastatic melanoma in the left cavernous sinus. He underwent stereotactic radiotherapy, and later scans revealed metastatic disease in the liver.

Conclusions, including unique features of the case:

Painful ophthalmoplegia and cavernous sinus enhancement may be from THS, however, this is a diagnosis of exclusion. In the right clinical context, surgical biopsy may be critical for accurate diagnosis. Specifically, in patients with a history of uveal melanoma, one must have a high index of suspicion for metastasis or alternative diagnosis, particularly in cases with an unusual response to treatment.

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Keywords: Miscellaneous

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Not So Straight Fourward

Lauren Colwell [1], Delaney Curran [1], Christopher Ito [1], Julia Jennings [1], Priya Janardhana [1], Philip Skidd [2], Chantal Boisvert [2]

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Introduction:
This case highlights the diversity in presentation for IgG4 related disease affecting bilateral optic nerves and encourages investigation of IgG4 associated disease for optic perineuritis, especially if there is pachymeningeal enhancement, uveitis and cerebral thrombi.

Description of Cases:
56-year-old Ghanaian woman presented with recent photophobia and a vague history of progressive vision loss in both eyes. She denied fevers, fatigue, weight loss or pain with eye movements. She had 20/40 vision in the right eye and no light perception (NLP) in the left. She had an afferent pupillary defect in the left eye and color plates of 0/14. Exam was remarkable for bilateral 1+ anterior chamber cells, mild vitritis and pale optic nerves. She had diffuse constriction on humphrey visual field 30-2. Angiography showed superior sagittal and cavernous sinus thrombi. Work-up was negative for malignancy, infection and auto-immune process including negative tuberculosis, sarcoidosis, NMO and MOG. Patient was started on apixaban and followed outpatient. She re-presented nine months later with hand motion vision in the right eye. Repeat imaging revealed persistent cerebral thrombi, chronic left sphenoid sinus disease with bony changes, diffuse pachymeningeal enhancements extending into the cavernous sinuses and orbital apex along the optic nerves. Sphenoidectomy had chronic inflammation and plasma cells with IgG4+ cells up to 140 cells per high power field suggestive of IgG4 related disease.

Conclusions, including unique features of the case:
The association between IgG4 related pachymeningitis with associated optic neuropathy has been documented in case reports [1], but far rarer to be accompanied with uveitis and cerebral sinus thrombi [2]. Initially an anchoring diagnosis of thrombi causing vision loss was made, but with her progressing disease a biopsy revealed the final diagnosis. Patient was managed with three days of high dose steroids with slow oral taper and her vision returned to baseline of 20/40 in the right eye.

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Keywords: Optic neuritis, Skull base, Orbit/ocular pathology, Visual fields, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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Optic Chiasm Glioblastoma: Genetic Analysis Trumps Histopathology

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Introduction:
Biopsy of lesions in the optic nerve or chiasm is usually avoided because of the risk of vision loss. When performed, specimens are small, sometimes leading to inconclusive or misleading findings.

Description of Cases:
A 46-year-old male presented with blurred vision OS. MRI revealed two foci of gadolinium enhancement, in the left optic chiasm and right optic tract. Blood work, including MOG and NMO antibodies, and CSF analysis were negative. The patient's visual symptoms worsened. Humphrey 24° threshold testing showed an incongruous right hemianopia, with sparing of the lower temporal quadrant OD. A whole-body PET/CT scan found no malignancy. The patient underwent biopsy of the optic chiasm. Histopathology revealed a moderately cellular neoplasm composed of atypical discohesive cells with enlarged nuclei, prominent eosinophilic nucleoli, and abundant vacuolated cytoplasm. Immunohistochemical stains for CD68 and S100 were positive, whereas GFAP, OLIG2, SOX10, and multiple others were negative, supporting a histiocytic neoplasm[1]. Five weeks later, results became available from capture-based, next-generation sequencing targeting the coding regions of 529 cancer genes and select introns of 47 genes. Alterations associated with histiocytic neoplasms (i.e. BRAF, MAP2K1) were absent. However, there was a nonsense mutation in the PTEN gene, a hotspot mutation in the TERT promotor, and focal amplifications of the CDK4 and MDM2 genes. Additionally, there was chromosome 6q loss, 7 gain, and 10q loss. Based on these findings, the diagnosis was revised to IDH-wildtype glioblastoma[2]. The patient began treatment with temozolomide while continuing radiation therapy. Four months later, his acuity remained 20/20 OD and 20/400 OS with a right homonymous hemianopia.

Conclusions, including unique features of the case:
Glioblastoma of the visual pathway is rare, with only 6 cases reported in the optic chiasm[3]. Tumor morphology can be variable (“multiforme”), confounding histopathological interpretation, especially of minute specimens. In this setting, next generation sequencing of pathology specimens for genetic analysis may provide vital diagnostic information[4].

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Keywords: Tumors, Optic neuropathy, Neuroimaging, Visual fields

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Pterygopalatine fossa: A hidden chamber that could cause visual manifestations.

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[1] *Stanford University*

Introduction:
Pterygopalatine fossa (PPF) is an important structure anatomically that has contact to Central nervous system (CNS) through inferior orbital fissure and it could be hub for spread of various inflammatory/infectious and neoplastic process to CNS. Here we report a case of rare malignancy from the PPF causing visual defects.

Description of Cases:
24-Year-old male from Vietnam presented with one year of progressive numbness on the right side of face, vision decline to light perception in the right eye over the course of two weeks. Exam revealed mydriatic pupil in the right eye with ptosis, restricted extraocular movements in all directions, reduced sensation in V1 & V2 dermatomes with only hand motion in right eye. Fundus exam was normal bilaterally. Imaging revealed contrast enhancing lesion in PPF extending to orbital apex through inferior orbital fissure compressing right optic nerve, also to anterior region of cavernous sinus causing compression of cranial nerves 3,4,6. Wide range of differentials considered including extra-pulmonary CNS Tuberculoma as patient is from endemic region (Vietnam and exposure to Tuberculosis in the past from family member), IGG-4 disease, sarcoidosis, lymphoproliferative disorder as they cause infiltrative mass lesions. Serum work up included infectious/inflammatory panels with QuantiFERON gold turning out positive twice, IGG-4 was negative. CT Chest was normal. Spinal fluid analysis was bland, biopsy with Histologic sections revealed basaloid neoplasm forming cribriform patterns in a myxoid and hyalinized background. Fusion stamp Next generation sequencing showed MYB: NFIB fusion protein confirming Adenoid Cystic Carcinoma (ACC).

Conclusions, including unique features of the case:
PPF mass lesions have wide range of differentials and biopsy should be considered in the right clinical setting. ACC is a rare diagnosis that requires high clinical suspicion and emphasizes the importance of anatomical location of the lesion to be considered in the differential along with clinical course that could point clinician in the right direction.

References: None provided.

Keywords: Neuroimaging, Optic neuropathy, Skull base, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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Grant Support: none

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There Must Be Something in The Water

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Introduction:
Pythium insidiosum, also known as "swamp cancer," is a zoonotic fungus-like aquatic oomycete found in tropical and subtropical environments. While infection in animals has been well described, human infection is rare and often treatment resistant. Pythium keratitis is the most common ocular manifestation in humans, but orbital soft tissue invasion has also been reported. This report highlights a case of orbital Pythium insidiosum masquerading as Langerhans cell histiocytosis in a 4-year-old female that was successfully treated using a novel immunotherapy.

Description of Cases:
A four-year-old female presented to the emergency department with a two-week history of right lower eyelid edema and erythema despite 48-hours of amoxicillin-clavulanate. The patient was admitted to the hospital for presumed orbital cellulitis and started on broad-spectrum intravenous antibiotics. Despite treatment, the patient failed to improve. An MRI revealed significant inflammation of the right periorbital soft tissues and inferior orbit. The decision was made to proceed with an exploratory orbitotomy with tissue biopsy. Preliminary pathology demonstrated mixed inflammatory infiltrate with eosinophilic micro-abscesses on a background of scattered large histiocytes, suggestive of Langerhans cell histiocytosis (LCH). IV steroids were initiated with plans for chemotherapy. Despite high clinical suspicion, final pathology found the specimen to be negative for S100 protein and CD1a and positive for fungal elements. The patient was started on high-potency antifungals without improvement. After 5 days of antifungal therapy, the patient underwent a second orbitotomy. A tissue specimen was sent for fungal polymerase chain reaction testing which identified the causative microbe as Pythium insidiosum. The patient was started on a novel Pythium insidiosum Antigen (PIA) immunotherapy with excellent results.

Conclusions, including unique features of the case:
This case highlights the successful diagnosis of a rare zoonotic pathogen known as Pythium insidiosum. Despite early diagnostic missteps, the patient ultimately received the appropriate treatment, a novel immunotherapy, and demonstrated improvement in symptoms.

References: None provided.

Keywords: Orbit/ocular pathology, Pediatric neuro-ophthalmology, Orbit

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Unveiling The Shadows: When Vision Fades In Myasthenia Gravis

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Introduction:
A 27-year-old woman with a history of type 2 diabetes presented to the emergency department with a 3-day history of decreased vision in her left eye and pain with eye movements. She had presented to the emergency department 5 years earlier for right upper eyelid ptosis and binocular diplopia but lost to follow up.

Description of Cases:
Initial examination revealed left eye visual acuity of 20/200, relative afferent pupillary defect, disc edema with superior disc hemorrhage, left upper lid ptosis, near complete bilateral ophthalmoplegia. MRI with contrast revealed longitudinal left optic nerve and nerve sheath enhancement from disc to chiasm and no other brain or spinal cord lesions. Serum and CSF laboratory workup revealed high titers of aquaporin-4 antibodies, acetylcholine receptor antibodies, and anti-Smith, -chromatin, and -dsDNA antibodies. The patient was diagnosed with optic neuritis secondary to neuromyelitis optica spectrum disorder (NMOSD), ocular MG, and systemic lupus erythematosus (SLE). She was treated with intravenous methylprednisolone followed by plasmapheresis. Visual acuity in the left eye improved to light perception. She was discharged on oral prednisone, hydroxychloroquine, and pyridostigmine. Rituximab infusions were planned after discharge.

Conclusions, including unique features of the case:
The co-occurrence of MG and NMOSD is rare and therefore poses a diagnostic challenge. Limited observational studies have been published which suggest that despite being relatively rare conditions with distinct pathophysiology, MG, NMOSD, and other systemic autoimmune diseases co-occur rarely, but at rates far higher than would be expected by chance. This suggests a possible shared underlying immunopathologic process. Given the rarity of co-presentation and uncertainty of underlying pathophysiology, the ideal approach to disease modifying treatment of comorbid MG, NMOSD, and SLE is unknown. Treatment considerations included initiation of hydroxychloroquine with risk vs benefit discussion given retinal toxicity, maculopathy and possible exacerbation of MG. Rituximab was ultimately selected for ongoing immunotherapy given hypothesized B-cell mediated pathogenesis of each condition.

References: None provided.

Keywords: Optic neuritis, Myasthenia, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: The authors had no disclosures.

Grant Support: None

Contact Information: None provided.

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Ocular Post-Mortem Analyses with Histopathological and Molecular Assessments in Leber Hereditary Optic Neuropathy Following AAV2 Gene Therapy

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Introduction:
Leber hereditary optic neuropathy (LHON) is a rare disease that causes severe vision loss. Lenadogene nolparvovec is a novel AAV2 gene therapy for LHON patients carrying the m.11778G>A MT-ND4 mutation.

Description of Cases:
Two patients with MT-ND4 LHON, participating in the RESCUE clinical study, received an intravitreal injection of AAV2-ND4 in one eye and a sham injection in the other. During the study, both patients developed intraocular inflammation in the treated eye within 2 months of gene therapy: one patient had moderate inflammation in the anterior chamber and vitreous, while the other had mild vitritis; both events resolved within months. Patient 1 died of acute alcohol toxicity and the other (patient 2) of cardiac arrest. Post-mortem molecular (ddPCR) analyses of the eyes were conducted. For patient 1, there was noted an angiocentric lymphocytic chronic inflammation at the optic nerve head and in the temporal retina. This was not seen in patient 2. In patient 1, AAV2-ND4 distribution was asymmetric in the treated eye, most prevalent in temporal retinal ganglion cells, sparse in photoreceptors, and absent in optic nerve, vessels, retinal pigmented epithelium, and choroid. A much lower level of AAV2-ND4 was detected in the retina of the untreated eye.

Conclusions, including unique features of the case:
This is the first postmortem study of human eyes unilaterally injected with AAV2-based gene therapy. In one patient, there was persistent inflammation and AAV2-ND4 retinal transfection was evident in the injected eye and detected at a much lower level in the contralateral eye. The analysis of eyes, nerves, optic chiasm and optic tracts, available from patient 2, may confirm and better characterize this transfer.

References: None provided.

Keywords: Optic neuropathy, Retina, Neuro-ophth & systemic disease (e.g. MS, MG, thyroid)

Financial Disclosures: Alfredo A. Sadun: Consultant for Stealth BioTherapeutics.; Nancy J Newman; Leonardo Caporali; Fred Ross-Cisneros; Elisa Boschetti; Valérie Biousse; Lindreth DuBois; Henry Liu; Philippe Ancian; Magali Taiel: Employee of GenSight Biologics (Paris, France).; Valerio Carelli: Received research support and/or personal compensation from Santhera Pharmaceuticals, Chiesi, and GenSight Biologics

Grant Support: None.

Contact Information: None provided.

Hot Topics [2.0 CME] - Monday, March 4th

Moderators: Collin McClelland, MD & Yaping Joyce Liao, MD, PhD

Upon completion of this session, participants should be able to: (1) Review point-of-care utilization of updated international MOGAD criteria, (2) Define the role of neuro-ophthalmologists in the treatment of obesity in IIH, (3) List the pros and cons of using ChatGPT in Neuro-Ophthalmology, (4) Discuss the use of physician extenders in Neuro-Ophthalmology, including optometrists, physician assistants, and orthoptists.

- **Best Practice Patterns: Updated international MOGAD Criteria, Can They Be Implemented in the Real World?** *Jeffrey Bennett, MD, PhD*
- **Medicine: Are We Doing Enough to Address Obesity in the Context of IIH?** *Michael Garcia, MD*
- **Technology and Ethics: ChatGPT in Neuro-Ophthalmology**, *Heather E. Moss, MD, PhD*
- **Introducing Optometry into Your Practice**, *Amanda D. Henderson, MD & Colin Kane, OD*
- **Introducing PAs into Your Practice**, *Judith Warner, MD & Irina Krikova, PA*
- **Introducing Orthoptists into Your Practice**, *Crandall Peeler, MD & Rachael Jenkins, CO*
- **The Limits of Extenders**, *Melanie Truong-Le, DO, OD*

BEST PRACTICE PATTERNS: UPDATED INTERNATIONAL MOGAD CRITERIA CAN THEY BE IMPLEMENTED IN THE REAL WORLD?

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LEARNING OBJECTIVES

1. The attendee will be able to explain list the clinical presentations of demyelinating injury in Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease (MOGAD).
2. The attendee will be able to enumerate supportive MRI and clinical findings observed in MOGAD.
3. The attendee will be able to describe optimal methods and fluid for MOG-IgG testing.
4. The attendee with be capable of applying the new international diagnostic criteria for MOGAD in clinical practice.

CME QUESTIONS

1. The most common clinical presentation of MOGAD in adults is
    A. Optic neuritis
    B. Acute disseminated encephalomyelitis
    C. Longitudinally extensive transverse myelitis
    D. Cortical encephalitis with seizures
    E. Ataxia

2. According to the new 2023 International Criteria, MOG-IgG testing is best performed

    A. using an enzyme-linked adsorbent assay
    B. on CSF using a fixed cell binding assay
    C. using a live cell binding assay on serum and/or CSF
    D. before treatment with high dose corticosteroids or plasma exchange
    E. C and D

3. Supportive criteria for MOGAD acute optic neuritis include all the following except

    A. Longitudinally extensive optic nerve lesion on MRI (>50% of length of optic nerve)
    B. Bilateral clinical optic neuritis
    C. Optic disc edema
    D. Bilateral MRI lesions of the optic nerves
    E. Perineuritic optic sheath enhancement

KEYWORDS

1. Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease (MOGAD)
2. MOG-IgG
3. optic neuritis

4. cerebrospinal fluid

Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is a rare inflammatory disorder of the central nervous system (CNS) characterized by the presence of serum or cerebrospinal fluid (CSF) autoantibodies against myelin oligodendrocyte glycoprotein (MOG-IgG). The frequency of clinical presentations varies by age: optic neuritis (ON) is the most common adult presentation, whereas acute disseminated encephalomyelitis (ADEM) is the most frequent in children. Longitudinally-extensive transverse myelitis (LETM) is observed regularly across ages; infratentorial and supratentorial syndromes such as brainstem disorders, myeloradiculitis, cerebellar syndromes, cortical encephalitis, and cerebral deficits are less common.[1] MOGAD is estimated to have an incidence of 3.4-4.8 per million persons per year and a prevalence of 1.3-2.5 per 100,000 persons.[2] Men and woman are affected equally, and the condition may be monophasic or relapsing.

Inflammatory CNS disorders associated with serum MOG-IgG regained clinical attention with the advent of the 2015 diagnostic criteria for neuromyelitis optic spectrum disorders (NMOSD).[3] Approximately 30-40% of patients meeting the 2015 criteria for aquaporin-4-IgG (AQP4-IgG) seronegative NMOSD were noted to be seropositive for MOG-IgG by conformationally sensitive, cell-binding assays.[4,5] MOGAD meeting 2015 NMOSD criteria frequently presented with simultaneous ON and LETM, LETM more frequently involved the lower spinal cord and conus, and optic neuritis was more frequently bilateral with improved visual recovery.[6,7] While initially considered a secondary cause of NMOSD, subsequent clinical, demographic, radiologic, and histopathologic features summarily distinguished MOGAD as a distinct entity from NMOSD and multiple sclerosis (MS).[1,8]

Multiple clinical reports and case series have greatly expanded the clinical spectrum of MOGAD. The most frequent MOGAD presentation is unilateral or bilateral ON in adults and acute disseminated encephalomyelitis (ADEM) in children.[9-11] ON occurs most often in isolation; however, it may be accompanied by additional syndromes such transverse myelitis in adults or acute disseminated encephalomyelitis in children. MOGAD ON is typically painful and severe (<20/200 vision).[12] Approximately 40% of cases are clinically bilateral, and 80% show significant disc edema. MRI typically shows intra-orbital, longitudinally-extensive inflammation involving >50% of the optic nerve; some lesions may extend to involve the optic chiasm. Perineuritic gadolinium enhancement, which may extend into or involve the orbital fat, may distinguish MOGAD ON from ON arising from NMOSD or MS. MOGAD spinal cord lesions are often longitudinally-extensive and involve the central cord (H-sign).[13,14] Supratentorial and infratentorial brain white matter lesions tend to be ill-defined; deep grey matter lesions and cortical involvement with or without overlying meningeal enhancement may be observed.[15,16]

Recently, new diagnostic criteria for MOGAD were proposed by the International MOGAD Panel (Table).[17] The criteria are based on the presence of one or more core demyelinating events, positive MOG-IgG testing in the serum or CSF, negative AQP4-IgG serologic testing, supportive clinical and MRI features, and the exclusion of a better diagnosis. An attack must be localizable to the CNS, last at least 24 hours, and have MRI or clinical findings to support a demyelinating event. MOG-IgG must be detected in the serum or CSF using a cell-based assay. A live cell-based assay expressing full-length MOG and employing an IgG-specific secondary is preferred; however, all commercial cell-based MOG-IgG assays can be utilized to distinguish clear positive, low positive, positive without titer, and negative results. Serologic MOG-IgG testing that is low positive, positive without titer, or negative with positive CSF MOG-IgG require negative AQP4-IgG serologic testing and additional supportive clinical and/or MRI criteria. Clinical and imaging criteria were selected to maximize the positive predictive value of MOG-IgG testing. MS or a better diagnosis should be excluded.

The new 2023 International MOGAD Panel criteria will impact future diagnosis, management, and clinical investigation. Challenges will include access to serologic testing, cell binding assay sensitivity and specificity, false-positive MOG-IgG serology, and the availability of ancillary clinical and radiologic data. For MOGAD ON, accurate diagnosis will necessitate the clinical diagnosis of optic neuropathy, careful funduscopic exam, and dedicated orbital MRI imaging. Therefore, the new MOGAD diagnostic criteria needs to be applied to real-life cohorts of patients with neuro-inflammatory disease to evaluate its performance. Three recent intra-institutional, retrospective studies have shown that the sensitivity, negative predictive value, and positive predictive value of the International MOGAD Panel criteria are high (sensitivity: 93-100%; negative predictive value: 100%; and positive predictive value: 81.5-100%).[18-20] Delayed MOG-IgG testing and insufficient clinical or MRI studies limited the application of the diagnostic criteria in multiple cases. Notably, in a small study of 27 subjects presenting with a core demyelinating phenotype, the specificity of the International MOGAD Panel criteria was only 55%.[19] Each of the three false positive cases had low-titer serum MOG-IgG; the final diagnoses were idiopathic intracranial hypertension, bevacizumab optic neuropathy, and progressive MS. Moving forward, prospective trials will be needed to assess the sensitivity and specificity of the criteria within each core phenotype.

Table. International MOGAD Panel diagnostic criteria

A. Core clinical demyelinating event	1) Optic Neuritis; 2) Myelitis; 3) Monofocal or polyfocal cerebral deficits; 4) Brainstem or cerebellar deficits; 5) Acute disseminated encephalomyelitis; 6) Cerebral cortical encephalitis
B. Positive MOG-IgG cell-based assay	*Serum* Clear positive* - no supporting features required Low positive* - ≥ 1 supporting feature required# Positive with no titer - ≥ 1 supporting feature required# *CSF* Positive but seronegative - ≥ 1 supporting feature required#
Supporting clinical or MRI features	*Optic Neuritis* Bilateral simultaneous clinical involvement Longitudinal MRI lesion (>50% of nerve length) Perineural optic sheath enhancement Optic disc edema *Myelitis* Longitudinally MRI Lesion (≥ 3 vertebral segments) Central cord lesion or H-sign Conus lesion *Cerebral, brainstem, or cerebellar syndrome* Multiple ill-defined T2 hyperintense lesions in supratentorial and/or infratentorial white matter Deep gray matter involvement Ill-defined T2-hyperintensity involving the pons, middle cerebellar peduncle, or medulla

	Cortical lesion +/- lesional or overlying meningeal enhancement
C. Exclusion of better diagnoses including MS	

* See appendix for assay-specific titer cutoffs;[17] #AQP4-IgG seronegative

CME ANSWERS

1. A
2. E
3. D

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MEDICINE: ARE WE DOING ENOUGH TO ADDRESS OBESITY IN THE CONTEXT OF IDIOPATHIC INTRACRANIAL HYPERTENSION?

Michael Garcia, MD; Assistant Professor of Medicine
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LEARNING OBJECTIVES

1. Describe obesity, epidemiology, and what defines clinically meaningful weight loss
2. Explain effective multidisciplinary approach to obesity management
3. Describe current and near future pharmacologic treatment options for obesity in the context of IIH

CME QUESTIONS

1. What percentage weight loss defines clinically meaningful weight loss?

    A. 3%
    B. 5%
    C. 10%
    D. 15%

2. In IIH, 10% weight loss from baseline is necessary for disease remission

    A. True
    B. False

3. Who qualifies for use of pharmacotherapy for obesity management (in addition to expected lifestyle/behavioral modifications)? **Select all that are correct.**

    A. Patient with BMI 29 kg/m^2 and type 2 diabetes
    B. Patient with BMI 31 kg/m^2
    C. Patient with BMI 25 kg/m^2, type 2 diabetes, hyperlipidemia, obstructive sleep apnea

4. Within the hypothalamic region of the central nervous system, which nuclei are the targets of most anti-obesity medications?

    A. Arcuate nucleus and paraventricular nucleus
    B. Supraoptic nucleus
    C. Posterior nucleus and dorsomedial hypothalamic nucleus

KEYWORDS

1. Obesity
2. Weight management
3. Anti-obesity medications

HIGHLIGHTS

- The obesity epidemic continues to worsen each year. As of 2020, nearly 42% of adults in the United States meet criteria for obesity with BMI ≥ 30 kg/m^2. The prevalence of IIH mirrors the increase in obesity rates due to its strong association, with higher prevalence in women and more specifically ages 20 to 44.
- A more accurate definition of obesity is excess adiposity that increases risk of adverse metabolic conditions. Better methods of measurement include bioelectric impedance, air/water displacement plethysmography, and DEXA.
- Individuals have different fat distribution at different body weights; thus, BMI alone may not accurately capture degree of adiposity.
- When evaluating clinically important weight loss, a marker of 5% decrease from baseline is used due to improvements in metabolic condition and risk reduction. In regards to IIH, it is suggested that the greater the weight loss, the better, to result in reduced symptoms and ICP; however, the amount of weight loss indicated for disease remission is unclear.
- Obesity management is multifactorial and begins with appropriate screening and implementation of measures for patients at risk or with already elevated BMI. All individuals should initiate nutrition, exercise, and behavioral modifications. Anti-obesity medications should be considered in individuals with BMI ≥ 27 kg/m^2 and ≥1 comorbidity or BMI ≥ 30 kg/m^2.
- Anti-obesity medication options are few, but multiple drugs are under investigation. Current FDA approved medications have a central pathway as the primary mechanism of action. Most act in the hypothalamus, within the arcuate nucleus (on Agouti-related protein (AgRP) and proopiomelanocortin (POMC) neurons) and subsequently melanocortin-4 receptor (MC4R) neurons in the paraventricular nucleus to affect food intake and energy homeostasis.
- Dopamine and serotonin pathways are also involved in the mechanism of action of some anti-obesity medications
- When tailoring lifestyle and pharmacotherapy to an individual, consider obesity phenotypes to further guide care: hungry brain, hungry gut, slow burn, emotional hunger.
- In the context of IIH, early anti-obesity medications may be contraindicated due to effect on blood pressure. More recent options include those in the GLP-1 receptor agonist class
    - Mechanism of action: act centrally to reduce appetite/increase satiety, increase insulin release, decrease intestinal motility (delay gastric emptying), increase lipolysis
    - Contraindications: personal or family history of medullary thyroid cancer, multiple endocrine neoplasia type 2
    - Adverse effects: nausea, vomiting, diarrhea, pancreatitis, gallbladder and biliary diseases
- Liraglutide is a daily injection with dose titrated to 3 mg/day. In the study that led to approval, just over 60% of participants achieved 5% weight loss from baseline..
- Semaglutide is a weekly injection with dose titrated to 2.4 mg weekly. In the study that led to its approval, 87% of participants reached 5% weight loss from baseline..
- Drugs pending approval include tirzepatide, a dual GLP-1/GIP receptor agonist. In its study, ~91% of participants attained 5% weight loss from baseline
- Drugs under investigation have novel mechanisms of action, the majority of which are incretin-based therapies.
- Dual and multi-agonists are being investigated, combining GLP-1 receptor agonists with glucose dependent insulinotropic polypeptide (GIP) and or glucagon.
- It is important to note that there are non-responders with all anti-obesity medications.
- Current use of GLP-1RA is limited by cost/insurance coverage and availability.

- Combination therapy for obesity is most effective: nutrition, exercise, behavioral modifications with consideration of anti-obesity medications and potentially bariatric surgery in appropriate individuals.

SUMMARY

EPIDEMIOLOGY

The prevalence of obesity in the U.S. continues to rise, with prevalence nearly 42% as of 2020. Prevalence differs by state and different ethnicities, which important when individualizing treatment (CDC 2023). Idiopathic intracranial hypertension (IIH) is strongly associated with obesity and prevalence has increased along with obesity. Prevalence estimates in the general population range from 0.03-7.8 per 100,00 people per year, with significantly higher prevalence of 19.3 per 100,000 in women age 20 to 44 years with obesity, and overall higher incidence in women over men (Wang 2021; Wall 2014).

DEFINING OBESITY

Obesity has classically been defined using body mass index (BMI) with BMI $\geq$30 kg/m^2 qualifying obesity. There is a notable gap in this definition, as it does not define level of adiposity, which in excess is a better characterization of obesity due to associated metabolic conditions. While waist circumference can be used in the clinical setting to further assess for abdominal obesity, more accurate measures of excess adiposity include bioelectric impedance, air/water displacement plethysmography, and DEXA, though these are not always practical to perform for all patients (Garvey 2016). BMI also fails to account for differences in fat distribution in different patient populations, and thus may over or underestimate adiposity level. For example, Asian American individuals have higher rates of central adiposity and increase in risk for metabolic conditions at lower BMI levels (Li 2023). Further, we must recognize that obesity and metabolic conditions disproportionately affect LatinX and African American populations due to a variety of factors including environmental, traditional dietary patterns, family dynamics, socioeconomic status, and health disparities. Culturally tailored interventions are key for managing obesity in these and all individuals (Alemán 2023; Lofton 2023).

Clinically meaningful weight loss is defined as at least 5% weight loss from baseline weight due to known improvements in weight associated comorbid conditions. Further metabolic improvements and risk reduction occurs with each percentage point above 5% (Garvey 2016; Kompaniyets 2023; Ryan 2017; Garvey 2022). Specific to IIH, the degree of weight loss necessary for symptom improvement and disease remission is unknown. (Mollen 2018; Sinclair 2010; Mollen 2021). A small study using caloric restriction demonstrated that mean weight loss over 3 months of 15% from baseline led to reduced ICP, papilledema, and improved symptoms (Sinclair 2010). Studies evaluating bariatric surgery demonstrated that weight loss of 24% from baseline is needed to normalize ICP to ≤25 cmCSF, while long-term maintenance of symptom and disease control may be best attained by maintaining and BMI ≤ 30 kg/m^2 (Hermes 2023; Mollen 2022). However, it is unclear the definitive relationship between amount of weight loss and change in intracranial pressure.

APPROACH TO OBESITY MANAGEMENT

Appropriate screening for excess adiposity must occur in primary care and specialty settings. For individuals with BMI in overweight or obesity categories, implementation of dietary, exercise, and behavioral/lifestyle modifications should occur. The next step in treatment is consideration of adjunct

pharmacotherapy, for individuals with BMI ≥ 27 kg/m^2 and ≥1 comorbidity or BMI ≥ 30 kg/m^2 alone. Consideration of pharmacotherapy assumes that nutrition, exercise, and behavioral modifications are implemented and being actively monitored (Draznin 2022). For some individuals, metabolic and bariatric surgery may be an important piece of management and indicated based on the following: BMI ≥ 35 kg/m^2 and certain individuals with BMI 30-34.9 kg/m^2 with severe diabetes or metabolic syndrome (Garvey 2016; Eisenberg 2023). Ultimately, combination therapy is frequently required to attain successful long-term weight management (LeBlanc 2018).

USE OF ANTI-OBESITY MEDICATIONS

The timeline for FDA approved anti-obesity medications has been bleak. Phentermine has been available for many years; however, since the year 2000, three of eight initially approved medications have been taken off the market due to post-marketing adverse event patterns. In part due to this, anti-obesity medications are underutilized, with only 2% of eligible patients being treated with pharmacotherapy (Thomas 2016).

Anti-obesity medications act by decreasing energy intake through different mechanisms. Orlistat is the only currently approved medications that works solely through a peripheral pathway (lipase inhibitor), while all other approved medications have a central pathway as the primary mechanism of action. The medications in the CNS at least partly by targeting the homeostatic and reward regions of the brain. Within the hypothalamus, normal physiology includes hormone signals that act on the Agouti-related protein (AgRP) and Proopiomelanocortin (POMC) neurons within the arcuate nucleus, which affects downstream output to melanocortin-4 receptor (MC4R) neurons in the paraventricular nucleus to affect food intake and energy homeostasis (Higgs 2017; Jais 2017). Anti-obesity medications act on different parts of this pathway. The reward pathways in the brain are also important, as medications may also affect dopamine and serotonin pathways, along with opioid and GABA receptors (Chakhtoura 2023). Just as we tailor initial lifestyle management based on individual patient factors, when evaluating anti-obesity medication options, we may consider obesity phenotype categorization. More specifically, individuals may fit the following phenotypes: hungry brain, hungry gut, slow burn, and emotional hunger. These may not be mutually exclusive, but current research shows there may be improved efficacy with medications when using a phenotype-guided approach (Acosta 2021; Zandvakili 2023).

In the context of IIH, early medications were contraindicated due to known side effects of increased blood pressure. More recently since 2014, GLP-1 receptor agonists (GLP-1RA) are now available for use as adjunct medication for obesity management. GLP-1RAs act centrally to reduce appetite/increase satiety and have other noted effects: to increase insulin release, decrease intestinal motility (delay gastric emptying), and increase lipolysis (Wang 2023). In the study of liraglutide that led to its approval, 60-63% of study participants achieved clinically relevant 5% weight loss. Most recently, once-weekly semaglutide was approved for obesity treatment. With the most promising study results to date for approved medications, about 87% of study participants reached 5% total body weight loss (Wilding 2021). While impressive, we must be aware that there are non-responders to pharmacotherapy (in this case ~13% did not achieve clinically important weight loss) (Jensterle 2022).

In addition to weight loss benefits, GLP-1RAs have also shown benefit in atherosclerotic cardiovascular risk and are being studied as a potential treatment for MAFLD and MASH. Contraindications include personal or family history of medullary thyroid cancer and multiple endocrine neoplasia type 2. Side effects are mostly GI related such as nausea, vomiting, diarrhea, and also include the potential to cause pancreatitis and gallbladder and biliary diseases. Recent research evaluated GI specific adverse events

when these medications were used at weight loss specific doses. There were higher incidences of pancreatitis, bowel obstruction, and gastroparesis compared to use of bupropion-naltrexone (another FDA approved medication for weight loss) (Sodhi 2023). An important observation has been the risk of weight regain with cessation of GLP-1RAs.

FUTURE DIRECTION AND DRUGS UNDER INVESTIGATION:

There are a number of drugs under investigation with novel mechanisms of action, the majority of which are incretin-based therapies. Incretins are gut peptide hormones released in response to food ingestion. Additional targets for these dual and multi-agonists in combination with GLP-1RAs include glucose dependent insulinoptropic polypeptide (GIP) and glucagon. These molecules affect insulin release, increase satiety, and may alter lipid metabolism. Other agents include leptin sensitizers, amylin/calcitonin dual agonists, and drugs targeting the ghrelin pathway (Chakhtoura 2023; Muller 2022; Nauck 2021).

Tirzepatide, a dual GLP-1/GIP receptor agonist, is next in line. In the 72-week study, once weekly administration led to ~91% of study participants attaining 5% weight loss from baseline at the highest dose used in the study (Jastreboff 2022). This is pending FDA approval. The use of GLP-1RAs is currently limited by cost/insurance coverage and availability from the manufacturer.

We must remember that combination therapy is ultimately most effective: nutrition, exercise, and other behavioral modifications and for the right patients, consideration of anti-obesity medications and potentially bariatric surgery. Obesity is a chronic condition that requires long-term management rather than the assumption that a definitive cure is attained when weight loss occurs.

CME ANSWERS

1. **B**
2. **B**
3. **A and B**
4. **A**

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ETHICS: CHAT GPT IN NEURO-OPHTHALMOLOGY

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LEARNING OBJECTIVES

1. To understand how large language models are generated and (could be) used by physicians
2. To critically assess output of chatbots powered by large language models given neuro-ophthalmology prompts
3. To utilize chatbots powered by large language models in accordance with medical ethics principles now and in the future

CME QUESTIONS

1. A chatbot powered by a large language model trained on publicly available (> 12mo old) Journal of Neuro-ophthalmology archives is made available for NANOS members. Which of the following prompts is likely to generate the best response:

    A. Tell me the history of the field of dermatology.
    B. Summarize the risk factors for NAION.
    C. What was of most interest to neuro-ophthalmologists in the past year?
    D. What dog breed is best suited for a single person living in an apartment?

2. When given a prompt to "answer a question with references" a chatbot powered by a large language models (e.g. chatGPT) will refer to Pubmed or another data base to verify the accuracy of the generated response.

    A. True
    B. False
    C. It depends

3. A neuro-ophthalmology fellow proposes three ways to become more efficient using chatbots powered by LLMs: 1. Generating responses to synthetic patient portal message and storing them as smart phrases to use in responding patient portal messages. 2. Improving the language in their NANOS annual meeting abstract submission by entering the draft as a prompt, asking for clarification of the language and pasting the output into the abstract portal. 3. Improving their assessment and plans in patient notes by entering the draft as a prompt, asking for clarification of language, proofreading it for accuracy and then pasting it in the patient note. Select the best correct response.

    A. all are great ideas without ethical concerns
    B. none are an ethically appropriate use of LLM in neuro-ophthalmology with no options for fixing them
    C. improving clinical documentation (3) is the most ethically problematic
    D. improving an abstract (2) is the most ethically problematic
    E. generating template patient portal responses (1) is the most ethically problematic

KEYWORDS

1. Large language models (LLMS)
2. Medical ethics
3. Answer questions
4. Summarize or edit text

HIGHLIGHTS

Large language models are trained on massive, but finite, amounts of data and "learn" by context. When used to power chatbots they provide textual output in response to user entered written prompts. This can be ethically problematic with regards to

- What the LLM does with the prompt text, which can be a violation of patient privacy if PHI is contained in the text
- The accuracy and completeness of the output text, due to limitations in what information the model was trained on and the lack of referencing to ground truth during output generation.
- Access to LLM powered tools by patients and providers

SUMMARY

Our personal and professional lives are replete with models that classify (e.g. lab test norms, OCT segmentation) and predict (auto-text complete). In recent NANOS meetings we have heard presentations on supervised (i.e. programmer defines the categories) and unsupervised (i.e. model figures out the categories) machine learning models which have a promise of supporting complex clinical classification tasks. Generative artificial intelligence (AI), for example the large language model GPT3.5 and the chatbot it powers (ChatGPT), take a leap forward beyond classification and prediction to generate new content.

Current generative AI models leverage recent breakthroughs in computer science (i.e. transformer architecture) to train in an unsupervised way on massive amounts of ordered data. Simply put, but not so simply accomplished, the models process training data to identify patterns. Based on these patterns, the models can evaluate input prompts and generate output. Large language models (LLMs) like GPT3.5, the transformer model underlying ChatGPT, are trained using text data consisting of ordered characters and spaces.

A chatbot (e.g. ChatGPT) is the interface that collects user input in the form of text and displays text output generated(predicted) by the LLM. An LLM powered chatbot can generate text to answer questions, summarize text and edit text. The reason ChatGPT can perform these mind-boggling, seemingly magical, tasks so well is its size and complexity. Training on massive amount of data generates models with large number of parameters (e.g. >100 million in Chat GPT3, compared to 1 parameter in a blood test interpretation task and 2 parameters in a linear regression model).

When proposing application of LLMs to medical practice one must consider medical ethics, with its core principles of beneficence (benefit), non-maleficence (lack of harm), autonomy and justice. Non-maleficence is a particular concern for several reasons. First, LLM output is based on patterns in the data it was trained on. Like a medical student who has not yet taken certain classes, an LLM has not yet determined patterns in content it hasn't been exposed to. This can impact accuracy of output and

generalizability. Second, unlike a human student who (hopefully) is processing information and referencing ground truth, an LLM is interpreting and generating text based on pattern identification. There are no references provided in the output that the user can use to assess the veracity of the content. In fact, because LLM's generate text based on patterns output can include plausible nonsense or hallucinations, for example plausible appearing references for scientific papers that do not exist. Third, ingestion of a user input prompts is effectively dissemination of information, which can be a breach of privacy depending on the content of the prompt. Strategies to overcome these issues including model tuning, feedback, human editing of output and closed models.

Ultimately results of chatbot/LLM enabled medical tasks will need to be compared end to end to current medical practice to determine benefit and/or acceptability to patients, providers and other stakeholders in the healthcare system. As LLMs become more widely used in medicine, justice must be considered as implementation may exacerbate existing and/or introduce new inequities in health care.

CME ANSWERS

1. A.
2. B.
3. C.

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INTRODUCING OPTOMETRY INTO YOUR PRACTICE

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LEARNING OBJECTIVES

By the end of this talk, the attendee will be able to:
1. Describe neuro-ophthalmology practice challenges related to the national/international shortage of neuro-ophthalmologists
2. Explain ways in which integration of an optometrist into a neuro-ophthalmology practice may help address these practice challenges
3. List potential neuro-ophthalmic clinical scenarios that may be ideal for optometrist involvement

CME QUESTIONS

1. Based on the recent article by DeBusk, et al, in the *Journal of Neuro-Ophthalmology*, what is the median wait time for a new patient to see a neuro-ophthalmologist in the United States?

    A. 6 days
    B. 3 weeks
    C. 6 weeks
    D. 3 months

2. Which would *not* be an ideal clinical scenario for management with an optometrist within a neuro-ophthalmology practice?

    A. Consultation for “rule out” papilledema
    B. Long-term immunosuppressive management of a patient with ocular myasthenia gravis
    C. Examination and triage of a patient presenting with acute onset of diplopia
    D. Annual examination and ancillary testing for a patient with a history of pituitary adenoma status post complete resection

3. What is the most important aspect of integration of an optometrist into a neuro-ophthalmology practice?

    A. Establishment of an open line of communication between the optometrist and a neuro-ophthalmologist at all times
    B. Involvement of only optometrists who have completed a neuro-optometric residency
    C. Involvement of only optometrists who have completed an ocular disease residency
    D. Establishment that the optometrist is capable of independently handling neuro-ophthalmology cases at the level of a neuro-ophthalmologist

KEYWORDS

1. neuro-ophthalmology

2. optometry
3. practice management
4. patient access

HIGHLIGHTS

1. Introductory data

    A. Shortage of neuro-ophthalmologists
    B. Geographical inequities of access to neuro-ophthalmic care
    C. Wait times to establish care with a neuro-ophthalmologist
    D. Potential solutions for the problem(s)

2. The Wilmer Experience

    A. History of optometrists within the Wilmer Neuro-Ophthalmology Division
    B. Recruiting optometrists for a neuro-ophthalmology practice
    C. Practice model
    D. Relevant patient access data

3. Challenges to Implementation

4. Clinical scenarios
    A. Urgent/same day triage
    B. "Rule out" consults (eg, papilledema, etc)
    C. Stable diplopia/prismatic correction
    D. Clinical monitoring (eg, patients with pituitary tumors, homonymous visual field defects after stroke, etc)

5. Conclusion

SUMMARY

Neuro-ophthalmologists typically care for patients with complex systemic disease with visual manifestations. Because of the nature of our work, our clinical evaluations are typically more time intensive than those performed by many of our colleagues in other ophthalmic subspecialties. Prior studies have evaluated the benefits of access to neuro-ophthalmologic care for patients with neuro-ophthalmic conditions, with the overwhelming conclusions that diagnostic errors are reduced, unnecessary testing is avoided, and patient outcomes are improved, when subspeciality neuro-ophthalmologists are involved.[1-6] Despite the demonstrated value of access to neuro-ophthalmic care, there is a shortage of neuro-ophthalmologists in the United States and around the world, a shortage which may worsen in the future if current trends continue.[7,8] Recently, survey data from our own North American Neuro-Ophthalmology Society was published, which demonstrated evidence of this shortage. Specifically, the median wait time for a new patient to see a neuro-ophthalmologist was six weeks, only eight states had enough neuro-ophthalmologist coverage to meet the suggested threshold of one full-time equivalent neuro-ophthalmologist per 1.2 million population, and six states had no neuro-

ophthalmologist at all.[7] These data demonstrate not only overall limited access to neuro-ophthalmic care, but also significant geographic inequities. There are many potential long-term solutions to this issue, including various approaches to expand the pipeline for neuro-ophthalmology. However, in the short term, the shortage persists. One way to address the shortage, which can be (and is being) implemented now, is for qualified and interested optometrists to act as "neuro-ophthalmologist extenders", much in the way that nurse practitioners and physician assistants fill this role for other specialities. Additionally, the higher-level training of optometrists when compared with other, more typical, physician extenders, allows more flexibility in the implementation of such a model.

The Wilmer Neuro-Ophthalmology Division first added an optometrist nearly ten years ago. Since then, we have consistently included optometry in our neuro-ophthalmology coverage. While we have placed advertisements for recruitment of interested and qualified optometrists, most of our recruitment success has occurred from optometrists with whom we have interacted during their training (ie, ocular disease optometry residencies). However, nationally, most ocular disease optometry residencies do not directly rotate with neuro-ophthalmologists. Potential practice models may vary significantly, depending on the practice setting and institution. At Wilmer, we currently operate based on a profit and loss (P&L) compensation structure by division. Therefore, we have had success in implementing a model in which our optometrists have their own independent clinic schedules. The optometrist currently employed by our division devotes most half-day sessions (seven of nine) to neuro-ophthalmology, and the remainder to comprehensive optometry practice. Additionally, another qualified optometrist in a rural satellite location devotes a smaller portion of her time to seeing neuro-ophthalmic patients, thus improving access to neuro-ophthalmic care for patients in this area. The breakdown can be adjusted to fit the needs of an individual neuro-ophthalmic practice or of an individual optometrist. If a practice operates under a different compensation model, another approach would be more direct co-management of patients, thus increasing the feasible patient volume within a given neuro-ophthalmology clinic session.

Challenges to implementation of optometry within a neuro-ophthalmic practice may stem from both the optometry and neuro-ophthalmology perspectives. Optometrists sacrifice potential patient volume when choosing to evaluate more complicated neuro-ophthalmic cases rather than other potential optometric patients (ie, contact lens fittings, routine eye examinations, diabetic eye checks, etc), and, in many cases, this may affect their overall income. Additionally, only a minority of optometrists complete residency training after optometry school, and only a subset of these complete training relevant to neuro-ophthalmic practice. Conversely, some neuro-ophthalmologists may have reservations regarding the adequacy of optometric training to prepare optometrists for the clinical nuances of neuro-ophthalmic patients and, thus, may be hesitant to pursue this partnership.

We have maintained that the key to implementation of a successful optometrist – neuro-ophthalmologist partnership is open communication between the doctors. As with any qualified practitioner, the optometrists in our practice know their limits and when is it appropriate to reach out to their partnering neuro-ophthalmologist for guidance. On the other hand, at least one of our neuro-ophthalmologists is always available to discuss cases with the optometrist. Most commonly, this occurs in the clinic, as we frequently practice in a room directly adjacent to our optometrists. Additionally, guidelines to define appropriate cases for optometric evaluation and follow up are also helpful, specifically with regards to scheduling protocols and decision trees. We have had success with our optometrists performing urgent/same-day triage, which improves patient access to care, eliminates unnecessary Emergency Department visits, and allows discussion of the case (and in-person evaluation, if indicated) with the neuro-ophthalmologist in clinic. Other clinical scenarios in which we have found optometrist evaluation ideal is in initial "rule out" papilledema consults, for follow up appointments and

prescribing of prismatic correction for patients with diplopia that has already been worked up by a neuro-ophthalmologist, and for clinical monitoring of patients with neuro-ophthalmic issues that have stabilized (ie, homonymous hemianopia after stroke, pituitary tumors that have been resected or have not required treatment due to lack of impact on the visual pathways, prior non-arteritic anterior ischemic optic neuropathy, etc.). While some of these patients also could be released from a neuro-ophthalmic practice and followed by a comprehensive optometrist or ophthalmologist, we have found that many of our patients prefer to maintain a relationship with our neuro-ophthalmology group after having a significant neurologic event affecting their vision. The multidisciplinary teams at Johns Hopkins also prefer this approach. Additionally, from a financial standpoint, following these stable neuro-ophthalmic patients, prescribing glasses and prism glasses, and offering routine ophthalmic care to our established neuro-ophthalmic patient base, provides an additional revenue stream for neuro-ophthalmic practices, and optometrists can help us achieve this.

In summary, we have found the integration of optometrists into our Neuro-Ophthalmology Division to be a win-win-win-win scenario. We as neuro-ophthalmologists are able to increase access to care while reducing the strain on our own clinical time. Our optometrists have fulfilling practices in which they are challenged yet feel supported. Our patients have shorter wait times to access care. Finally, our department leadership is satisfied with our division's clinical availability.

CME ANSWERS

1. C
2. B
3. A

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INTRODUCING PAs INTO YOUR PRACTICE

Irina Krikova PA-C
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LEARNING OBJECTIVES

1. The attendee will be able to describe the potential role of a PA in a neuro-ophthalmology practice.
2. The attendee will understand the history of the PA profession.
3. The attendee will be able to describe why are we happy to have a PA in our practice and why you need one

CME QUESTIONS

1. What year was the PA profession established?

    A. 1867
    B. 1907
    C. 1967
    D. 1987

2. Can a PA provide independent care for patients?

    A. Yes
    B. No

3. Can a PA bill for seeing patient if the supervising physician does not see the patient?

    A. Yes
    B. No

CME ANSWERS:

1. C
2. A
3. A

KEYWORDS

1. Physician Assistant
2. Practice management
3. Supervising-physician
4. Collaborating -physician

In the mid-1960s, it became apparent there would be a shortage of primary care physicians. In 1965 Eugene A. Stead Jr MD at Duke University Medical Center (1), created a curriculum to train Physician Assistants. His first class comprised four Navy Hospital Corpsmen who had received medical training during their military service. Dr. Stead based the curriculum of the PA program on his knowledge of the fast-track training of doctors during World War II, in which accelerated 3-year medical school programs were used. PA training is considered Masters level training, and typically takes 2 or 3 years. A PA is qualified to be licensed and start clinical work upon graduation, receiving on-the-job training from their supervising physician. Some take optional PA residency training programs, but many become specialized in certain areas through work experience. The PA profession currently has more than 168,300 practitioners in the U.S., engaging in more than 500 million patient interactions each year.

PAs are licensed providers who practice in every specialty and setting. Most state laws require PAs to have an agreement for collaboration with a physician in order to practice. In 2017, the American Academy of PAs passed a new policy, Optimal Team Practice (2) to reduce practice constraints. This policy suggested that states eliminate the requirement for a specific relationship for a PA to practice, and allow PAs to be eligible for direct payment by insurers. In Utah, as of 2021 (3), PAs are required to "consult, collaborate with, and refer to appropriate members of the health care team" (Utah State Legislature SB 27) (4). The degree of collaboration required depends on PA hours of experience in the area in question. PAs with greater than 10,000 hours (about 5 years) of post-graduate clinical practice experience have collaboration agreements determined by the employer, group, hospital or health care facility credentialing system. PAs with less than 10,000 hours of experience must practice in collaboration with a physician, or with a PA with more than 10,000 hours of experience. When a physician or physician practice agrees to collaborate with a PA, the practice has to provide information describing how the collaboration will occur, and methods for evaluating PA competency, knowledge and skill.

In our academic practices, we have had the pleasure of working with two Physician Assistants over the last 30 years. The first, Jon Lindgren, was with us from the mid-1990s through his retirement in 2013, and the second, Irina Krikova for the last 11 years. Jon had had years of experience running the employee clinic at a large mining operation, followed by decades in dialysis centers in the area. Irina came to us after a short stint as a hospital-based provider supporting Neuro-Surgeons. She had had training in ophthalmology in her home country of Russia, so already had interest and education in our field.

On discussing the role of a PA in our clinic, our faculty commented:

In clinical care: Irina is critical in making clinic more efficient. She primarily sees follow up patients, taking interval histories, performing examinations, including 90 D fundus, strabismus, slit lamp, and comprehensive neurologic exams ordering and resulting clinic tests, and collaboratively creating assessments and plans of care. In most instances, the attending "pops in" to verify the exam and plan of care. In some instances, Irina can send the patient on their way, and discuss with the supervising attending. In this case, we will have the patient moved to her schedule. We have an "attestation for that".

She has particular expertise and interest in Headache management. Irina provides Botox treatment for migraine. Depending on insurance, in some cases, Irina can do Botox injections for patients and bill on her own. In some cases, insurance dictates that the supervising physician be present. In rare instances, insurance does not allow Irina to bill for Botox at all.

Irina spends a lot of time in patient education, in particular headache education, and medication and non-medication headache management. She also provides detailed discussion of patient treatment plans for idiopathic intracranial hypertension (IIH) and headache, including medication risks, benefits and alternatives. She works on prism adjustments, and Peli lenses assessment and placement. Irina sometimes works on insurance approval for medications and is involved in peer-to-peer discussion when needed for prior authorization. Irina is critically important in answering most, if not all patient questions through our Electronic Medical record (EMR). She works on Family Medical Leave Act (FMLA) and disability forms.

She billed almost $50,000 in 2023, about ½ of which was independent Botox for headache, with the remainder being independent clinic visit. It is difficult to calculate the financial balance sheet for clinic productivity, as her involvement allows a higher level of patient care and efficiency for the primary providers when she is in clinic, approving refills, returning telephone calls, but these activities do not translate directly into billing on her part.

In education: Irina is involved in teaching at all levels. PA students, NP students, Ophthalmology, Neurosurgery and Neurology residents, and medical students. The PA and NP students are at the University of Utah, and the Utah Valley University respectively. The medical students and residents receive teaching in clinic, honing their skills in funduscopy, and strabismus measurements. Irina is a Maestro with the Maddox rod!

In research: Irina participates in many of our research projects, assisting in patient recruitment and enrollment. She has been helpful in performing general medical examinations for a variety of research efforts in other divisions of the department. She has recently begun to promote new techniques, and last year had a poster at NANOS on direct-indirect ophthalmoscopy.

Working with a Physician Assistant can add value and efficiency to clinic flow, improve patient care with patient education, add depth to the skills of trainees, and bringing her own vitality to us all by providing interesting perspectives on the world, music, dance and philosophy.

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USE OF ORTHOPTISTS IN YOUR CLINIC

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Asheville , NC

Crandall Peeler, MD
Assistant Professor of Ophthalmology and Neurology
Boston Medical Center
Boston, MA

LEARNING OBJECTIVES

The attendee will be able to:
1. Identify skills and training of an Orthoptist.
2. Describe how Orthoptists can improve clinic efficiency.
3. Describe how Orthoptists can improve patient care.
4. Understand how Orthoptists can bill and generate clinical revenue.

CME QUESTIONS

1. Which organization certifies Orthoptic students in the Board exams?

    A. American Association of Certified Orthoptists (AACO)
    B. American Orthoptic Council (AOC)
    C. Joint Commission on Allied Health Personnel in Ophthalmology (JCAHPO)
    D. American Academy of Ophthalmic Professionals (AAOP)

2. How long is the Orthoptic postgraduate training?

    A. 6 months
    B. 1 year
    C. 18 months
    D. 2 years

3. Orthoptists' skills include:

    A. Assessing the angle of deviation and binocular potential using the Synoptophore
    B. Assess for incommitant strabismus using the Hess screen.
    C. Treating diplopia with prism glasses
    D. All of the above

KEYWORDS

1. Orthoptist
2. Sensorimotor examination

3. Diplopia/Strabismus
4. Prism glasses

HIGHLIGHTS

The utilization of Orthoptists in a Neuro-Ophthalmology clinical setting will be discussed in detail.

SUMMARY

This presentation will describe how Orthoptists are trained and how they can work in your Neuro-Ophthalmology clinic can improve efficiency, patient care, and clinical/surgical volume and revenue.

1. Skills/training

Orthoptists are trained in American Orthoptic Council accredited fellowship programs. This is a postgraduate, 2 year (24 month) clinical and academic education program offered at 17 major academic medical centers around the United States. The full-time, clinically-based training includes at least 2000 hours of supervised clinical practice and 1250 patient encounters, with a focusing on identifying, measuring, and treating ocular misalignment and amblyopia . The American Orthoptic Council Board written and practical exams are offered once a year and recertification is every 3 years with 45 Continuing education credits. Approximately 15 to 25 new Orthoptists become certified each year. Some Orthoptists specialize in Neuro-Orthoptics and work only with Neuro-Ophthalmologists. Others may focus on Pediatric strabismus or specialize in stroke, traumatic brain injury, and rehabilitation.

2. Clinic efficiency

Orthoptists are mid-level providers uniquely skilled in assessing strabismus and diplopia in Pediatric Ophthalmology and Neuro-Ophthalmology clinics. Orthoptists can perform a full extraocular muscle exam including motor and sensory fusion evaluation. They can assist in diagnosing complicated infranuclear, nuclear, and supranuclear palsies, perform strabismus measurements, and determine the prism strength needed to achieve fusion. They are also often trained in advanced tests of fusion and ocular motility such as the Synoptophore and Hess screen. By focusing of these crucial, yet time-intensive, portions of the clinical strabismus evaluation, Orthoptists can allow Neuro-Ophthalmologists to evaluate more patients per clinical session and spend more time on history taking and testing review. The use of virtual Orthoptics visits has also been studied in the UK and were associated with large decreases in patient wait times for appointments[1].

3. Improving patient care

Orthoptists are well-versed in Neuro-Ophthalmic diagnoses, patient education, and communication to help improve patient outcomes and satisfaction. A recent UK study showed a very high level of concordance in diagnoses assigned by Orthoptists performing initial evaluations of patients who were later assessed by a Neuro-Ophthalmologist. In the same study, patients also reported high levels of satisfaction with virtual Orthoptics follow-up visits[2].

4. Revenue generation

After an initial evaluation and diagnosis is made by an Ophthalmologist, Orthoptists can follow patients independently in their own Orthoptics clinic, freeing up additional Ophthalmology appointment slots. In follow-up, Orthoptists can adjust prism strength as needed, follow patient alignment for signs of deterioration or progression, and prescribe eye exercises when indicated. When working alongside an Ophthalmologist, the examinations components performed by an Orthoptist allow Ophthalmologists to bill for the sensorimotor examination in addition to clinic visit charges. Orthoptists functioning independently in follow-up clinics can also bill for the sensorimotor exam, increasing overall collections in the practice. One study published in 2015 showed that adding an Orthoptist to an Ophthalmology clinic generated an additional $70,000 in clinical revenue[3].

CME ANSWERS

1. B
2. D
3. D

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THE LIMITATIONS OF EXTENDERS

Melanie Truong-Le, DO OD
Dallas, Texas

LEARNING OBJECTIVES

1. Role of optometrists as extenders
2. The difference between an optometrist and a neuro-optometrist
3. Limitations of optometrists

CME QUESTIONS

1. A neuro-optometrist is someone who can diagnose neuro-ophthalmic problems?

   A. False
   B. Trues

2. Optometrists who are extenders of neuro-ophthalmology:

   A. Practice a special branch of neuro-optometry.
   B. Can prescribe oral steroids for temporal arteritis, optic neuritis.
   C. Can diagnose neuro-ophthalmic diseases independently due to specialized training as a neuro-optometrist.
   D. Work closely with neuro-ophthalmologists and serve as gatekeepers to evaluate routine vision, refractive, surface ophthalmic problems.

3. There are no limitations to extenders as they have the support and diagnostic ability by way of association with a neuro-ophthalmologist.

   A. False
   B. True

KEYWORDS

1. Neuro-optometry
2. Neuro-optometrist
3. Extenders in neuro-ophthalmology
4. Optometrist extenders

HIGHLIGHTS

Optometrists are skilled at refractions and vision related needs.
Based on their education and training, optometrists can identify problems related to refractive needs.
Optometrists are not trained to make neuro-ophthalmologic diagnoses.
Optometrist can be a valuable team member in assessing patients referred to the neuro-ophthalmic practice.
Optometric extenders do not practice neuro-optometry

SUMMARY

I. Introduction - Optometrists as extenders to a neuro-ophthalmology practice

To properly provide sufficient coverage, a ratio of 1 clinical full time equivalent (FTE) for every 1.2 million individual is needed in the United States (1). There are fewer neuro-ophthalmologists than there are patients in wait which is demonstrative of inadequate current supply of neuro-ophthalmologist to the US population. The reasons are multifold from change in payment models, inability to recruit and retain, and the transition of practice of current neuro-ophthalmologists (2-5). In a more recent study by DeBusk et al, it was determined that the median wait time to see a neuro-ophthalmologist was 6 weeks while in almost ¼ of he US, the wait time was 12 or more weeks (2). Due to the complex nature of neuro-ophthalmologic patients and the lack of availability in appointments, the limitations become evident, and we are inundated in many institutions. For instance in Texas with a population of 28,701,845 and FTE coverage was 1 to 2,759,792 while in Iowa with its population of 3,156,145 the FTE cover was 1 to 2,104,096; there was ample coverage in Massachusetts with a population of 6,902,149; Massachusetts enjoyed a 1 to 841,725 FTE coverage but this is far and few (2).

II. Definition of an extender and how an optometrist becomes an extender in a neuro-ophthalmology practice:

An extender is a provider that is not a neuro-ophthalmologist but takes on the role of screening and helping to manage neuro-ophthalmic patients. Generally, this term may encompass nurse practitioners, physician assistants, and optometrists. Specifically, the role of optometrists who work closely with neuro-ophthalmologists by extension to help manage and care for patients with neuro-ophthalmic problems.

III. What does an optometrist who practice as extenders of neuro-ophthalmology do?

1) Initial evaluator and gatekeeper to screen new patients who have not had comprehensive eye exam.
    a) Such as patients that are referred by a primary care physician, nurse practitioners, internal medicine, geriatricians, ENT, neurologists, or neurosurgeons.
2) Initial evaluations of new referrals for double vision patients, dizziness, and transient blurry vision patients that have not been fully vetted and investigated. These patients will see our optometrist extenders initially and will treat conditions and answer questions.
3) Special consideration:
    a) Traumatic Brain Injury: Remote and with chronic problems
    b) Rule out optic nerve edema or papilledema vs pseudopapilledema
    c) Managing and following stable neuro-ophthalmic patients:

This working relationship can help to alleviate burden and wait time; but data has not been established to support this model of care. More time is needed to establish the benefits and improvements that is hoped for by working closely with our optometric extenders. There are limitations to this model, and the limitations has to do with the scope of practice and the complex nature that neuro-ophthalmic conditions, thus causing concern for delay in care or inappropriate testing as depicted by Stunkel et. Al (6,7).

IV. Limitations of optometrists by education, by training, by scope of practice

A. Is this classified as the practice of neuro-optometry?
B. What is neuro-optometry? Neuro-optometry represents a broad area within optometry that deals with vision related problems such as accommodative spasms, small eye misalignments often described as "binocular vision problems", often poorly defined visual processing problems. It is recognized and described by two organizations:
    1. College of Optometrists in Vision Development, which focuses on vision therapy; COVT therapists are certified by a number of criteria through COVD (college of optometrists in vision development)
    2. Neuro-Optometric Rehabilitation Association, International Brain injury related visual problems

V. What is the difference between an optometrist who are extenders of neuro-ophthalmology and an optometrist who practice neuro-optometry?

There is significant difference scope of practice due the difference in education and training. How does one become an optometrist? They are accepted into a 4 year degree program typically after receiving a bachelor's at a university or undergraduate college, and the comparison between an ophthalmologist and optometrist

VI. Case scenarios

A. GCA needing immediate IV or oral steroids
B. Optic neuritis previously diagnosis with a flare
C. Idiopathic intracranial hypertension on acetazolamide with increase swelling of optic nerves.

V. Conclusion

Optometrists are excellent at the work that they do. They are gatekeepers to vision related problems and are well versed in routine vision and ophthalmic problems. With proper training they can be great extenders in care of neuro-ophthalmic patients. However, it is important to maintain a clear understanding of what they are. They are not practicing neuro-optometry. They are not diagnosticians and do not make neuro-ophthalmic diagnoses independently, and they have limitation of practice due to their education, training, and experiences.

CME ANSWERS

1. **A**
2. **D**
3. **A**

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Global Perspectives: Lost in Translation? What a Major Neuro-Ophthalmic Trials Are Applied Locally (US/Canada) Versus internationally [2.00 CME] Monday, March 4th

Moderators: Clare Fraser, MBBS & Jonathan D. Trobe, MD

Speakers will describe how major neuro-ophthalmic trials are applied locally versus internationally. Upon completion of this session, participants should be able to: (1) Learn the major findings of clinical trials in neuro-ophthalmology, (2) Learn how these findings are being incorporated into clinical practice, (3) Learn how incorporation of these findings differs across the world.

- **Idiopathic Intracranial Hypertension (IIHTT):** *Mark J. Kupersmith, MD & Susan P. Mollan, MBCHB, FRCOPHTH*
- **Temporal Artery Biopsy and Ultrasound in Diagnosis of Giant Cell Arteritis (TABUL):** *Steffen Hamann, MD, PhD & Joseph F. Rizzo III, MD*
- **Corticosteroid Randomization After Significant Head Injury (CRASH):** *Richard J. Blanch, MD & Kimberly P. Cockerham, MD, FACS*
- **Study to Assess the Efficacy and Safety of Raxone in LHON Patients (LEROS):** *Patrick Yu-Wai-Man, BMedSci, MBBS, PhD, FRCPath, FRCOphth & Nancy J. Newman, MD*
- **Optic Neuritis Treatment Trial (ONTT):** *Neil R. Miller, MD & Gordon Plant, MBBS*

IIHTT AND OTHER STUDIES– WHAT HAVE LEARNED ABOUT DEVELOPING AND CONDUCTING CLINICAL TRIALS

Mark J Kupersmith, MD
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THE IDIOPATHIC INTRACRANIAL HYPERTENSION TREATMENT TRIAL (IIHTT)

Susan P Mollan, MBcHB FRCOphth
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Birmingham, United Kingdom

LEARNING OBJECTIVES

1. Summarize the objectives of the Idiopathic Intracranial Hypertension Treatment Trial (IIHTT).
2. Describe the findings of the IIHTT.
3. Gain knowledge of the different responses world-wide to the results of the IIHTT.
4. Discuss the controversy in the role of weight loss in the IIHTT.
5. Consider the challenges of using perimetric mean deviation as the primary outcome measure in IIH clinical trials.

CME QUESTIONS

1. What was the primary outcome of the IIHTT?

    A. Colour vision
    B. Intracranial pressure
    C. Visual acuity
    D. Visual field mean deviation

2. What was the MOST common serious side effect of acetazolamide listed here?

    A. Depression
    B. Dysgeusia
    C. Metabolic acidosis
    D. Paraesthesia

3. A low sodium diet alone should be recommended for weight loss in a person living with obesity and IIH.

    A. True
    B. False

KEYWORDS

1. Pseudotumor Cerebri Syndrome (PTSC)
2. Idiopathic Intracranial Hypertension
3. Visual field mean deviation
4. Acetazolamide

5. Weight loss

HIGHTLIGHTS FROM A UNITED KINGDOM CLINIC

Idiopathic Intracranial Hypertension (IIH) is a condition which can lead to chronic headaches and visual loss secondary to raised intracranial pressure (ICP) in the absence of a structural cause in the brain.[1] The world-wide incidence and prevalence of IIH has grown, with young obese women most commonly affected.[2,3] There is a disease spectrum ranging from mild to severe, and for the majority of patients the visual prognosis is good.[4] However, around 7% require escalation of treatment to save sight, with surgical choice being largely dictated by local expertise.[5,6] The emerging pathophysiology is that of systemic metabolic dysregulation.[7]

Acetazolamide, a carbonic anhydrase inhibitor, has long been used in the treatment of IIH as its potential action at the choroid plexus to reduce cerebrospinal fluid (CSF) production. In 2014, the IIH Treatment Trial (IIHTT) evaluated the use of acetazolamide along with a multicomponent dietary intervention and compared it to placebo combined with the multicomponent dietary intervention in those with active and acutely diagnosed IIH with mild visual loss defined as a mean deviation between -2 to -7dB in either eye.[8] The primary outcome at 6 months was the change from baseline in perimetric mean deviation in the more affected eye.

The IIHTT used high doses of acetazolamide, with more than 40% of patients treated with 4000mg of acetazolamide daily.[8] This dose may not be tolerable in a real-world setting, as was evidenced by a NANOS clinician poll summarizing the preference for a dose of between 1– and 2 g daily which was conducted in the preparation of the IHTT.[9] Moreover, a previous UK study demonstrated that 48% of patients discontinued acetazolamide when daily doses of 1500mg were used.[10] Side effects of acetazolamide are well known and include paresthesia, dysgeusia, vomiting and diarrhea as well as malaise, fatigue, and depression. The most common serious adverse effect is metabolic acidosis.[11]

The dietary plan and lifestyle modification program offered in the IIHTT study is termed a “multi-component dietary intervention”. It covered all three disciplines of weight loss and lifestyle modification: nutrition, physical activity, and behavior. All participants were assigned to a weight loss coach with weekly telephone communication. Participants were given pedometers for measuring steps and rubberized exercise tubing for resistance exercise. Nutritional instruction included meal planning, calorie counting, portion control, fat counting, and energy density. Participants were given a 500- to 1000-calorie deficit goal and instructed to follow a partial meal replacement diet. Weight loss coaches guided participants who declined to use these products in preference to pre-prepared food in the marketplace that was portion-controlled and calorie-controlled. A goal of 10% weight decrease from baseline on average was projected during the study. The low sodium component was included in the event that normal-weight persons entered the trial to ensure that all enrolees would have dietary management.[11] In the UK, most patients cannot access weight management services readily. The multicomponent approach is only offered in hospital weight management services, which have specific referral criteria, such as body mass index, ethnicity and co-morbid conditions. Therefore, for the majority, acetazolamide is used without the professional weight management intervention used in the IIHTT. Although some clinicians may be tempted to suggest one component of a multi-component therapy to their patients, we advise caution.[12] For example, a low salt diet can lead to temporary body weight reduction due to extracellular and total body water reductions but no recorded changes in body fat mass or visceral fat area. In addition, physical activity may improve cardiovascular health, but activity alone is not recommended as a weight loss intervention.[12]

As with all clinical trials there is limitation on the hypothesis, inclusion criteria and choice of primary outcome such that there will always be a number of questions that remain regarding management.[13,14] Following the IIHTT, UK practitioners have wondered if a patient recently diagnosed with IHH and a visual field mean deviation better than -2dB should be treated with acetazolamide. The IIHTT inclusion criteria were extended beyond -5db to facilitate recruitment and included those with a mean deviation of between -5db and -7db. Should one wait until the mean deviation is worse than -7dB considering escalation of therapy and surgical intervention? Clinical trials are often limited by their timing of their primary outcome point, as in the IIHTT which was 6 months. This timing is balanced by retention of participants and funding. Following the IIHTT clinicians in the UK often ask how long they should continue acetazolamide for, and this is query that currently we have no answer for.

The use of Humphrey visual fields in the IIHTT meant that many clinics in the UK switched from using Goldman perimetry to Humphrey visual fields to assess their IIH patients. While the IIHTT investigators reported the known challenges with automated perimetry in this condition, of accurate reliable visual fields;[15] this change has reduced the burden on delivering Goldman perimetry clinically. It also provides the potential for visual outcomes to be pooled across studies for metanalysis. A key strength of the IIHTT has been the analysis of the optical coherence tomography (OCT) imaging findings.[16] That analysis has paved the way for the directed use of OCT, alongside Humphrey visual field testing, for monitoring of papilledema. This was particularly convenient during the COVID-19 pandemic when there was uncertainty over the amount of face to face time that was safe and hence visual fields were only reserved for those in whom has increased visual symptoms or the papilloedema on OCT was progressing. This has left a legacy for some cases of only performing OCT imaging at a follow-up due to capacity within the National Health Service. This may include people in the hospital headache service that are on monoclonal antibody therapies for their headaches and require ocular surveillance; those whom become pregnant and where the obstetric team require reassurance of ocular remission; and those who have completely asymptomatic IIH and require very long-term monitoring.

SUMMARY

In this session we have explored some of the differences in approach to treating IIH following the results of the IIHTT. We have also recognized the importance of this trial for advancing the monitoring and management of IIH. The undertaking of clinical trials should not be underestimated, and while choices in trial design may limit the applicability of the trial results world-wide, there are always benefits that become apparent overtime. Acetazolamide remains the main pharmacological therapy for IIH worldwide. The IIHTT has provided rigorous support for its use.[8] Working together to interpret the literature we hope to apply the best quality of evidence to managing IIH, where three main principles apply:

1. Treat the underlying disease;
2. Protect the vision;
3. Reduce disease related morbidity.

CME ANSWERS

1. **D,** the primary outcome of the IIHTT was perimetric mean deviation as measured with a 24-2 Humphrey visual field.
2. **C,** metabolic acidosis is the most serious side effects of acetazolamide listed here. Metabolic acidosis is not a benign condition and signifies an underlying disorder that needs to be corrected to minimize morbidity and mortality.

3. **False,** weight management experts recommend weight loss interventions to be multicomponent and there should include advice about nutrition, caloric intake, physical activity alongside behavioural interventions.

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ULTRASOUND OR BIOPSY FOR GIANT CELL ARTERITIS DIAGNOSIS CONFIRMATION: TABUL AND BEYOND

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LEARNING OBJECTIVES

The attendee will be able to:

1. Know the approach to the clinical diagnosis of giant cell arteritis (GCA)
2. Know the approach to confirmation of the diagnosis of GCA, including ultrasound and temporal artery biopsy
3. Know the primary findings of the TABUL study
4. Know the relative advantages and disadvantages of employing ultrasound or temporal artery biopsy in the diagnosis of GCA
5. Appreciate differences among academic institutions in approaching the diagnosis of GCA

CME QUESTIONS

1. Which of the following is true?

    A. Given improved diagnostic criteria, the diagnosis of GCA no longer requires routine use of ancillary diagnostic testing, like biopsies or ultrasound
    B. Ultrasound (of either the temporal artery or axillary arteries) is equally sensitive but less specific than temporal artery biopsy in the diagnosis of GCA
    C. Temporal artery biopsy is more sensitive and more specific than ultrasound in the diagnosis of GCA
    D. Ultrasound is less sensitive but more specific than temporal artery biopsy

2. Which of the following is true?

    A. The interpretation of a temporal artery biopsy is fairly similar across pathologists
    B. The interpretation of an ultrasound of the temporal artery is fairly similar across specialists who are trained to perform this technique
    C. It is more cost effective to routinely obtain an ultrasound rather than a biopsy of the temporal artery, without any significant decline in diagnostic accuracy
    D. The TABUL study (published in 2016) found that the ultrasound technique was still emerging technically and not yet capable of replacing a biopsy of the temporal artery

3. Which of the following is true?

    The TABUL study:
    A. Concluded that ultrasound cannot replace a biopsy of the temporal artery

B. Reported that both sensitivity and specificity in the diagnosis of GCA can be increased by using a combination strategy in which a biopsy of the temporal artery is obtained in cases in which the ultrasound was negative
C. Reported that incorporation of risk stratification (based upon initial clinical features and inflammatory serology) increases sensitivity and specificity in the diagnosis of GCA over and above the results of a biopsy *and* ultrasound of the temporal artery
D. Reported that, even when considering cost of medical consequences of acute GCA, the use of clinical judgement and ultrasound is more cost-effective than clinical judgement and biopsy
E. All of the above

KEYWORDS

1. Giant cell arteritis
2. Temporal artery biopsy
3. Temporal artery ultrasound
4. Cost effectiveness

HIGHLIGHTS

Giant cell arteritis (GCA) is a type of autoimmune inflammation primarily affecting medium and large vessels with a predisposition for cranial arteries derived from the carotid artery. It is considered a clinical emergency as it can lead to rapid, severe and irreversible visual loss most commonly caused by anterior ischemic optic neuropathy (AION) [1-3]. Beyond that, GCA-related stroke, which may be fatal, has been reported in 2.7-7.4% of cases [4, 5]. Extra-cranial involvement in GCA affecting the aorta and its major branches, known as large-vessel GCA, has been described in 20-80% of cases [6-8].

Historically GCA was thought to be confined to the cranial arteries. Therefore, a biopsy of the temporal artery (TAB) has been considered the gold standard for diagnosis, although false negative outcomes may be >40 %, depending upon the source. This high false negative rate is due to several factors, including insufficient length of tissue, presence of "skip lesions," and more > 10 days duration of treatment with corticosteroids prior to the biopsy [2, 9]. Although the specificity of TAB for diagnosing GCA is close to 100%, a sensitivity as low as 39%, but varying up to 90%, has thus been reported [10].

The importance of temporal artery ultrasound as a means to diagnose GCA was first introduced in 1997, where it was described that GCA could be diagnosed based on the presence of the so-called ‘halo sign’ – a homogenous, hypoechoic wall thickening [11]. The use of ultrasound to diagnose GCA has since been supported by five meta-analyses, in which ultrasound yielded an overall sensitivity of 68-88% and specificity of 77-91%, in comparison with TAB, for the diagnosis of GCA [12-16]. In a recent ‘head-to-head’ comparison of temporal artery ultrasound versus TAB, where 78 patients underwent both procedures, TAB had a sensitivity of 69% and a specificity of 100%, whereas ultrasound had a sensitivity of 63% and a specificity of 79% [17].

THE TABUL STUDY

The study entitled "The Role of Ultrasound Compared to Biopsy of Temporal Arteries in the Diagnosis and Treatment of Giant Cell Arteritis (TABUL) is a diagnostic accuracy and cost-effectiveness study, that prospectively examined 381 patients with new or suspected GCA [10]. The main study aim was to assess the relative merits of TAB and ultrasound in the diagnosis of GCA.

METHODS

Each proposed study site required training and demonstration of satisfactory performance on the performance and interpretation of the ultrasound test. Minimal technical specifications for the ultrasound device were required for all proposed study sites. Twenty sites successfully completed the required training and then participated in the study. Ultrasound and later biopsy were performed within seven days of initiation of corticosteroid therapy. The chief ultrasound abnormality that supported an interpretation of vasculitis was the "halo" sign, which is created by a dark hypoechoic area around the lumen of an artery. No training or validation of accuracy was conducted with respect to the interpretation of biopsies.

The *first primary objective* of the TABUL study was to evaluate the sensitivity and specificity of ultrasound as an alternative to biopsy in patients who were referred with suspected GCA and in whom a TAB was going to be performed. The *second primary objective* was to perform a cost-effectiveness analysis to compare ultrasound as an alternative to biopsy for diagnosing GCA. The *primary outcome measure* was the ("reference") diagnosis made by a clinician two weeks into the study; the treating physician was masked as to the ultrasound result for the first two weeks, although thereafter the result could be provided upon request if consideration was being given to stopping corticosteroids.

Patients were not entered into the study if they had received a prior diagnosis of GCA, or had had a prior TAB, or had received "higher doses" of corticosteroids (defined as >20mg of daily oral prednisolone or equivalent) for more than 7 days before ultrasound could be performed. Of the original 381 patients, 257 patients received a "reference" diagnosis of GCA, and 124 patients were diagnosed as *not* having GCA. For patients with a baseline diagnosis of GCA, the incidence of polymyalgia rheumatica (PMR) was 11% (28 of 257) and the incidence of ischemic optic neuropathy was 9.7%.

RESULTS

A diagnosis of GCA was supported in 101 patients with a positive TAB and in 162 patients with an ultrasound. In 70% of cases, the results of the biopsy and ultrasound were consistent. The sensitivity of biopsy was 39%; the sensitivity of ultrasound was 54%. The specificity of biopsy was 100%; the specificity of ultrasound was 81%. One-third of patients had a negative ultrasound and biopsy. The combination of a clinical evaluation plus ultrasound was more sensitive (93% vs. 91%), less specific (77% vs. 81%) and more cost effective (net savings of approximately $600 USD) than the current practice of clinical evaluation paired with a TAB.

The study included an assessment of inter-rater outcomes among 30 selected cases. For ultrasound, the concordance was 0.61; for biopsy, it was 0.62. For biopsy, there was improved concordance when giant cells were present and weaker concordance when more minimal (though not specified) changes were present.

SUMMARY

The most clinically relevant results of the TABUL study are:

1. Ultrasound (temporal + axillary arteries, bilaterally) was more sensitive than unilateral TAB in detecting GCA (54% vs. 39%); the ultrasound method employed in the TABUL study examined long stretches of

the temporal *and* axillary arteries bilaterally, which likely improved diagnostic sensitivity beyond previous studies that did not include such extensive evaluation.

2. The specificity of biopsy was greater than that of ultrasound.

3. Unilateral TAB was more accurate in detecting patients who did *not* have GCA; specifically, 19% of "positive" ultrasound studies were found in patients with negative biopsies.

4. The combination of a clinical assessment performed by a medical doctor and a temporal artery ultrasound identified 93% of patients with GCA and was cheaper (by roughly $600 USD) than clinical assessment and biopsy. The assessment of relative costs included complications thought to occur from corticosteroids, such as bone fractures.

COMMENTARY

The TABUL study was well-designed to compare the relative sensitivities of ultrasound and TAB for patients with suspected GCA. Earlier suspicion and treatment of GCA would have eliminated patients with more obvious findings of GCA on the initial clinical evaluation from the TABUL study. In fact, for this and other reasons, 300 of 730 patients were eliminated from inclusion in the TABUL study, which presumably enhanced the fraction of patients with less severe symptomatology. The *specificity* of ultrasound was less than for TAB, and ultrasound could not, for instance, uncover the inflammation confined to smaller blood vessels in the adventitia that can signal the diagnosis of granulomatosis with polyangiitis.

The *sensitivity* of TAB varies considerably in the reported literature, in some cases exceeding the sensitivity reported in the TABUL study. The authors suggest that the relatively low sensitivity on TABs in the TABUL study could have been due in part to earlier detection of GCA by the referring clinicians given the heightened awareness of the threat posed by untreated GCA.

Notably, the TABUL study did not seek to standardize the diagnostic approach for TABs across the 20 study sites. Our U.S.-based experience is that there can be significant variability in the rendered diagnosis with biopsies despite clear guidance published in the literature. As such, there is some potential that falsely negative interpretations of the TABs could have yielded a comparatively better sensitivity for use of ultrasound.

A major conclusion of the study is that 1/3 of patients believed by a clinician to have GCA had negative results with both TAB and ultrasound, supporting the long-held understanding that the clinical assessment is necessary and integral to the decision--making process about whether patients need to be treated for suspected GCA. Another relevant outcome from the TABUL study is the negative financial implications of obtaining TAB in *all* suspected cases of GCA.

Important caveats to consider are that the value of ultrasound is highly dependent upon the quality of the equipment and most importantly upon the training and experience of the person who performs the ultrasound. (The TABUL study required ultrasound equipment with a grey-scale frequency of 10 MHz or greater and a color Doppler frequency of at least 6 MHz.) Although newer software techniques for MRI provide another diagnostic approach to detect vasculitis, the cost of obtaining an MRI is much higher than either ultrasound or biopsy, or both. The "reference" diagnosis for the TABUL study was made in accordance with American College of Rheumatology classification criteria, which likely would have failed to identify a small fraction of more subtle GCA cases. More than half of the patients in the TABUL study

were recruited by only 2 of the 20 centers, which might have skewed the results in unpredictable ways, including the possibility that the most experienced ultrasound practitioners were in the two centers that recruited the majority of patients. If true, this influence could limit the relevance of these results to other academic centers or private practices with relatively less experienced ultra-sonographers.

The 2023 EULAR Recommendations

In recent years, imaging modalities such as MRI and [^{18}F]-fluorodeoxyglucose positron emission tomography (FDG-PET) have been introduced as important supplementary means of diagnosing GCA. In 2018, the European Alliance of Associations for Rheumatology (EULAR) issued recommendations for the use of imaging in large vessel vasculitis, including GCA [18]; those guidelines were updated in 2023 [19]. They are based on evidence and expert consensus. Compared to the initial 2018 version, ultrasound is now recommended as first-line imaging in all patients suspected of having GCA. In addition, axillary arteries should be included in the standard examination, recognizing the propensity of the disease to involve more than just the cranial arteries.

In line with the EULAR recommendations, and recognizing that ultrasound is a non-invasive and cost-efficient procedure, ultrasound is being more widely used in the diagnosis of GCA worldwide and especially in Europe.

SUMMARY

GCA poses a clinical emergency due to the risk of rapid and irreversible vision loss. Extracranial involvement in large-vessel GCA is not uncommon, and while TAB has been the gold standard for GCA diagnosis, its high false-negative rate has led to exploring alternatives. Temporal artery ultrasound, introduced in 1997, gained support in subsequent meta-analyses, with a sensitivity almost equal to that of TAB, but with a slightly lower specificity.

The TABUL study, published in 2016, emphasized the importance of clinical assessment in conjunction with imaging, as one-third of patients had negative results with both ultrasound and biopsy. However, the study highlighted the negative financial implications of obtaining TAB in all suspected cases of GCA. The study also underlined the significance of the quality of ultrasound equipment and the expertise of the operator.

In 2023, EULAR updated recommendations for large vessel vasculitis imaging, emphasizing ultrasound as the first-line imaging for suspected GCA. Axillary arteries are now included in the standard examination. The trend toward ultrasound for suspected GCA is growing globally, particularly in Europe, acknowledging ultrasound's non-invasiveness and cost efficiency.

CME ANSWERS

1. B
2. C
3. E

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TRAUMATIC BRAIN INJURY (TBI)

TRAUMATIC OPTIC NEUROPATHY: CRASH BEFORE AND BEYOND

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LEARNING OBJECTIVES

1. Describe the different forms of traumatic optic neuropathy including indirect, direct and orbital compartment syndrome and subclinical manifestations of TBI.
2. Review reversible causes of visual loss after TBI and how to address these
3. Review the evidence for the use of corticosteroids in traumatic optic neuropathy.

CME QUESTIONS

1. The CRASH study found which of the following:

    A. Oral corticosteroids are indicated in all patients with suspected traumatic optic neuropathy.
    B. IV corticosteroids are indicated in all patients with suspected traumatic optic neuropathy.
    C. Three days of IV corticosteroids 250 mg q 6 hours for three days followed by an 11-day taper is indicated in all cases of traumatic optic neuropathy
    D. One gram of solumedrol is indicated in emergency room unless the patient has no light perception due to traumatic optic neuropathy.
    E. None of the above

2. Optic nerve trauma can occur due to which of the following causes:

    A. Indirect optic nerve trauma
    B. Direct optic nerve trauma
    C. Optic canal hematoma
    D. Orbital compartment syndrome
    E. All of the above

3. If not decompressed, orbital compartment syndrome may cause irreversible loss of vision within:

    A. 1 minute
    B. 1 hour
    C. 8 hours
    D. 24 hours.

CME ANSWERS

1. E

2. E

3. B

KEYWORDS

1. Traumatic brain injury
2. Traumatic optic neuropathy
3. Indirect traumatic optic neuropathy
4. Direct traumatic optic neuropathy
5. Orbital compartment syndrome

OUTLINE

1. Discuss the pathophysiology of post-traumatic optic neuropathy
   A. Indirect
   B. Direct
   C. Optic nerve sheath hematoma
   D. Compartment syndrome

2. Discuss the treatment options for different forms of optic neuropathy.

   A. Indirect
   B. Direct
   C. Optic nerve sheath hematoma
   D. Compartment syndrome

3. Discuss Findings of the Clinical Trials and implications for Therapeutic Intervention

SUMMARY

Traumatic optic neuropathy is a challenging clinical entity and clinical trials to date have not provided clear direction in therapeutic interventions.

Traumatic brain injury (TBI) may occur after open or closed head injury and is always associated with altered brain function. Closed injury, with intact skin and skull, is most common and the mechanism of injury is acceleration and deceleration of the brain within the skull, twisting, stretching, and damaging the axons and blood vessels. Initial damage with acute injury to the axonal and nerve soma is called primary injury from the physical impact. Secondary injuries may occur from pathophysiological consequences and neurodegenerative processes. (Wang, Yang et al. 2018, Raymont, O'Donoghue et al. 2020) The biochemical reactions taking place after the primary injury and their role in initiating a cycle of neurodegeneration are poorly understood. (Harris, Rickard et al. 2022)

TBI may be categorized as mild, moderate, or severe, although symptom severity does not always coincide with injury severity, making TBI severity difficult to diagnose and manage. Among a wide number of classification systems for TBI severity, the Mayo classification is used most commonly:

Criteria	Mild	Moderate	Severe
GCS score	13-15	9-12	≤ 8
Post-traumatic amnesia	< 24 hours	24 hours to 1 week	> 1 week
Loss of consciousness	Up to 30 minutes	30 minutes to 24 hours	> 24 hours
Alteration of consciousness / mental state	< 24 hours	> 24 hours, severity based on other criteria	> 24 hours, severity based on other criteria

Table 1. The Mayo classification of TBI. (Malec, Brown et al. 2007)

Mild TBI may develop after neuronal stretching and has common symptoms of headache, dizziness, nausea, confusion, and disorientation, which can last indefinitely. (Alexander 1995, Pearn, Niesman et al. 2017) Moderate to severe TBI may be associated with hematomas and tissue necrosis, losing brain functionality, and releasing toxins with more prolonged unconsciousness and long-term neurological impairment. (Pearn, Niesman et al. 2017)

VISUAL LOSS ASSOCIATED WITH TBI

In a sample of 594 TBI patients with ophthalmic signs, 28.0-51.8% suffered eyelid ecchymosis, 38.6-44.4% subconjunctival haemorrhage, 43.1% chemosis, 41.4% lid edema, and 22.5% a lacerated wound.(Blakeslee 1929, Singh and Chawla 1980, Raju 1983, Sharma, Gupta et al. 2014) Classical traumatic optic neuropathy (TON) is described in 0.5-8% of civilian TBI cases. (Steinsapir and A. 1994, Van Stavern, Biousse et al. 2001, Carta, Ferrigno et al. 2003, Kulkarni, Aggarwal et al. 2005, Odebode, Ademola-Popoola et al. 2005, Pirouzmand 2012) TON is more common in combat ocular trauma, with 33% of cases having orbital fractures and 40% being legally blind (Justin, Turnage et al. 2020). In a different series of military trauma, 101 (66%) of 152 cases of eye injury suffered TBI, (Weichel, Colyer et al. 2009) with 20% of ocular trauma patients noted to have TON. (Weichel, Colyer et al. 2008)

Areas of the brain related to vision are vulnerable to TBI, including the long axons between the eye and lateral geniculate body (LGN) and between the LGN and visual cortex, which may be distorted by diffuse axonal injury (DAI) (Alexander 1995) (Capo-Aponte, Jorgensen-Wagers et al. 2017). TBI indicators are therefore found in the retina, with 11-54% of TBI patients suffering visual field defects, and ganglion cell layer (GCL) thinning in 31-47%, which may or may not be associated with visual symptoms and is considered to be subclinical TON (Saliman, Belli et al. 2021, Hepschke, Laws et al. 2023) (Chan, Hills et al. 2019) (Kumar Das and Das 2022) (Lemke, Cockerham et al. 2016). These changes, including visual field defects and classical TON, occur across the range of TBI severity from mild to severe. TON therefore represents a spectrum of ophthalmic TBI manifestations, including subtle chronic neurodegeneration detectable on OCT, (Gilmore, Lim et al. 2020), subacute RNFL and GCL loss weeks to months after injury, and severe and catastrophic visual loss associated with direct or indirect injury to the anterior visual pathways.

ACUTE VISUAL LOSS AFTER TBI

Patients with TBI often suffer from skull and facial fractures and may develop orbital compartment syndrome secondary to intra-orbital hematoma. The timescale within which irreversible retinal ischemia occurs is poorly defined and varies depending on the orbital perfusion pressure (a function of orbital pressure and blood pressure), and pre-existing optic nerve and retinal health. Anecdotal reports indicate that orbital decompression should be performed within 2-4 hours, although irreversible ischemia may occur within less than 60 minutes. (Lima, Burt et al. 2009)

Initial treatment should be immediate lateral canthotomy and cantholysis, followed by administration of intravenous mannitol and acetazolamide if orbital or intraocular pressure remain elevated. If the orbit remains tense and retinal perfusion is impaired, further decompression may be achieved through an upper lid skin crease incision to allow orbital fat prolapse, and bony decompression.

TRAUMATIC OPTIC NEUROPATHY TREATMENT IN INTERNATIONAL PRACTICE

In a survey of 42 medical centers in the United States and around the world, 64% of centers routinely administered systemic corticosteroids for TON in widely varying doses (Table 2).

	N (%)
Routinely administered systemic corticosteroids	21 (63.6%)
IV	12 (36.4%)
Oral	8 (24.2%)
Both IV and Oral	1 (3.0%)
Systemic corticosteroid dosage	
Prednisone 1mg/kg daily (Moderate)	7 (21.2%)
Methylprednisolone 1gm daily (High)	12 (36.4%)
Methylprednisolone >2gm daily (Mega)	1 (3.0%)
Other	1 (3.0%)
Avg. duration of steroid therapy (days)	15.98 ± 11.87

Table 2. International variation in practice of treatment for TON. (Miller, Shah et al. 2022)

EVIDENCE FOR TREATMENT OF TRAUMATIC OPTIC NEUROPATHY

The CRASH1 study, published in 2005 recruited 10,008 patients examined within less than 8 hours after TBI, randomizing them to placebo or 11.6g intravenous methylprednisolone over the first 24 hours, followed by 21.2g over the second 48 hours. Patients were more likely to have an outcome of death or severe disability when treated with corticosteroids than with placebo. That difference in outcome was qualitatively greater in patients with mild and moderate TBI than in patients with severe TBI. (Edwards, Arango et al. 2005)

A single prospective non-randomized study of TON compared three managements: 1) corticosteroids (ranging from megadose to low dose), 2) optic canal decompression and 3) observation. Patients were most likely to recover visual function in the observation group and least likely to recover visual function in the optic canal decompression group. (Levin, Beck et al. 1999) A Cochrane review found no evidence that corticosteroid treatment was of benefit in TON. (Yu-Wai-Man and Griffiths 2013) Another trial that compared megadose corticosteroid treatment to surgical decompression found that there was no difference in visual recovery in the two groups. There was no control group (Chen, Lee et al. 2020) (Wladis, Aakalu et al. 2021). Other studies have looked at treatment with erythropoetin and levodopa, finding no strong evidence of benefit (Chaon and Lee 2015) (Wladis, Aakalu et al. 2021).

There is therefore no evidence of benefit for any pharmacologic or surgical intervention in treatment of TON and strong evidence of harm for treatment with megadose corticosteroids.

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IDEBENONE FOR LEBER HEREDITARY OPTIC NEUROPATHY: FROM RHODOS TO LEROS

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LEARNING OBJECTIVES

1. Review the evidence for the use of idebenone in Leber hereditary optic neuropathy (LHON)
2. Appreciate differences in practice and access to idebenone between North America and other parts of the world
3. Discuss the gaps in our knowledge on the therapeutic indications for idebenone in LHON depending on the patient's characteristics and the causative mitochondrial DNA mutation

CME QUESTIONS

1. All of the following studies have investigated the safety and efficacy of idebenone in LHON except:

    A. RHODOS
    B. Expanded access program (EAP)
    C. LEROS
    D. RESCUE

2. Which of the following are thought to be relevant to the mode of action of idebenone?

    A. Idebenone is a hydrosoluble quinone analogue that can penetrate the blood-brain barrier
    B. Idebenone helps shuttle electrons directly to complex III, bypassing complexes I and II of the mitochondrial respiratory chain
    C. Idebenone increases ATP production and reduces the level of reactive oxygen species
    D. All of the above
    E. None of the above

3. What is the recommended dose of idebenone in LHON?

    A. 150mgs once per day
    B. 300mgs once per day
    C. 300mgs three times per day
    D. 750mgs once per day
    E. 750mgs three times per day

4. Which of the following factors can influence the therapeutic response when treating a patient with idebenone?

    A. Causative mtDNA mutation

B. Duration of visual loss
C. Duration of treatment with idebenone
D. All of the above
E. None of the above

KEYWORDS

1. Leber hereditary optic neuropathy
2. Hereditary optic neuropathy
3. Idebenone
4. Mitochondrial DNA
5. Retinal ganglion cells

HIGHLIGHTS

- LEROS was a phase IV, open-label study to assess the efficacy and safety of long-term idebenone treatment in patients with Leber hereditary optic neuropathy compared to an external natural history control cohort over 24 months of treatment.
- LEROS met its primary endpoint: in subacute/dynamic eyes the rate of clinically relevant benefit from baseline was significantly higher following 12 months of treatment with idebenone versus matched natural history eyes
- Overall, idebenone was able to provide a meaningful treatment benefit in a large proportion of eyes/patients in both the subacute/dynamic and chronic disease phases.
- The treatment effect of idebenone varied depending on the underlying mitochondrial DNA mutation, with particular benefit for patients with the most common mutation at m.11778G>A.

IDEBENONE IN LHON

Leber hereditary optic neuropathy (LHON) is a mitochondrial disease resulting in bilateral vision loss.[1,2] Recovery of functional visual acuity (VA) and/or prevention of further VA worsening are desirable outcomes. Idebenone is a soluble short-chain synthetic benzoquinone that helps shuttle electrons directly to complex III, bypassing complexes I and II of the mitochondrial respiratory chain.[3,4] This compound is hypothesized to restore mitochondrial function via a number of mechanisms, increasing ATP production and reducing the level of reactive oxygen species.[3,4] Idebenone was approved by the European Medicines Agency (EMA) in 2015 for the treatment of LHON at a recommended dose of 300 mg three times/day for patients aged 12 years and older.

In the randomized, double-blind, placebo-controlled Rescue of Hereditary Optic Disease Outpatient Study (RHODOS),[5] patients with LHON and a disease onset ≤5 years prior were treated with idebenone at 300 mg three times/day orally or placebo for 6 months. A trend towards improved VA was observed in idebenone-treated patients. Post-hoc analysis by VA-responder rate showed a meaningful difference in favor of idebenone.[6] An Expanded Access Program (EAP) allowed for analysis of long-term idebenone treatment at 300 mg three times/day in the real world in patients with LHON onset ≤1 year prior. [7] Although uncontrolled, this study indicated a potential benefit of maintaining idebenone therapy for 24–30 months. This approach resulted in a VA stabilization and/or recovery rate that was higher than expected from limited natural history (NH) studies.[8]

Collectively, RHODOS and the EAP showed that idebenone is effective and safe in patients with LHON. However, the limitations of these studies warranted further investigations. The 6-month treatment duration in RHODOS was likely too short to fully capture a potential treatment benefit, and the lack of a control group in the EAP made direct comparisons difficult. In addition, patients in the chronic phase of LHON (>1 year after onset) were underrepresented. The Study to Assess the Efficacy and Safety of Raxone in LHON Patients (aka LEROS, ClinicalTrials.gov: NCT02774005) was designed, in part, to address these limitations and to further enhance the body of evidence supporting the use of idebenone as a treatment for LHON.

LEROS STUDY DESIGN

Conducted from 2016 to 2021, LEROS was a phase IV open-label study with a primary aim of assessing the efficacy of idebenone in providing a clinically relevant benefit in patients with LHON compared to an external NH cohort. VA outcomes were measured over 24 months in 199 patients treated with idebenone at 300 mg three times/day compared to 372 control subjects matched by time since visual loss onset The study included patients aged ≥12 years with a confirmed primary mitochondrial DNA (mtDNA) mutation (m.11778G>A, m.14484T>C or m.3460G>A) in both the subacute/dynamic (≤1 year after onset) and chronic (1-5 years after onset) disease phases. Four VA outcome measures were used to assess efficacy: clinically relevant benefit (CRB), clinically relevant recovery (CRR), clinically relevant stabilization (CRS), and clinically relevant worsening (CRW) (Figure 1). The primary outcome measure was CRB from baseline at 12 months in treated subacute/dynamic eyes compared to matched eyes of the NH cohort.

LEROS STUDY RESULTS

In the subacute/dynamic phase, a higher proportion of idebenone-treated eyes experienced a CRB from baseline compared to matched NH eyes at 12 months (42.3% vs 20.7%; $p = 0.002$ [primary endpoint]) and 24 months (52.9% vs 36.0%; $p = 0.03$) (Figure 2A). The CRB rate in treated eyes was largely driven by an increased frequency of CRS. A CRW was observed in a lower proportion of treated subacute/dynamic eyes compared to matched NH eyes at both 12 months (29.1% vs 58.5%; $p < 0.001$) and 24 months (25.8% vs 51.0%; $p = 0.005$).

In the chronic phase, the frequency of a CRB from baseline was higher in treated eyes compared to matched NH eyes at 12 months (50.3% vs 38.6%; $p = 0.009$) and 24 months (49.1% vs 37.6%; $p = 0.02$) (Figure 2B). This result was driven by an increase in the rate of CRR. A smaller proportion of treated chronic eyes experienced a CRW compared to matched NH eyes at both 12 months (4.9% vs 16.9%; $p = 0.006$) and 24 months (2.9% vs 20.0%; $p < 0.001$).

The benefits of idebenone treatment varied according to mtDNA mutation. The m.11778G>A mutation is the most common and has a poor visual prognosis. In m.11778G>A eyes, at 24 months, the frequency of a CRR was significantly higher in the subacute/dynamic phase (Figure 2A) in treated compared to matched NH eyes and the frequency of a CRW was significantly lower, in both the subacute/dynamic (Figure 2A) and chronic phases (Figure 2B). By month 24, idebenone-treated m.11778G>A eyes could read up to an additional 16 ETDRS chart letters on average compared to matched NH eyes (a relative improvement of -0.32 logMAR [p=0.002] in subacute/dynamic eyes, and a relative improvement of -0.11 logMAR (p=0.04) in chronic eyes. In m.3460G>A eyes, at 24 months, idebenone treatment had little impact on outcomes regardless of disease phase, and CRW rates were significantly higher in treated subacute/dynamic eyes compared to matched NH eyes (Figure 2A, B). In m.14484T>C eyes, at 24 months, idebenone treatment had no significant impact in the subacute/dynamic phase (Figure 2A).

Chronic eyes had a significant increase in the frequency of a CRR, and a significantly decreased frequency of CRW (Figure 2B). By month 24, idebenone-treated m.14484T>C eyes in the chronic phase could read an additional 26 ETDRS chart letters on average compared to matched NH eyes. a relative improvement of -0.52 logMAR [p<0.001]. As in previous studies, idebenone was well tolerated, with few, mostly mild, side effects.

In interpreting the findings of LEROS, it is important to consider the limitations of using a historical NH cohort for comparative analysis. The low number of eyes included in some analyses should also be noted as this reduces the rigor of the data. This is particularly apparent for the m.3460G>A and m.14484T>C subanalyses.

LEROS APPLICATION: NORTH AMERICA vs EUROPE and BEYOND

Do you always use idebenone for LHON patients?
Do you start it only in patients within one year of vision loss? Within 5 years of vision loss?
Do you use it in children under 12 years old?
For how long do you use it?
Do you use it differently depending on the LHON mtDNA mutation?
Do you use it differently depending on the demographics of the patient?
What other trials or experience influences how you use idebenone for LHON patients?
What do other key opinion leaders in North America, Europe and other countries do?

CME ANSWERS

1. **D**
2. **D**
3. **C**
4. **D**

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GLOBAL PERSPECTIVE: LOST IN TRANSLATION? – HOW MAJOR NEURO-OPHTHALMIC TRIALSS ARE APPLIED LOCALLY (US/CANADA) VERSUS INTERNATIONALLY
ONTT

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LEARNING OBJECTIVES

1. The attendee will be able to list the objectives of the Optic Neuritis Treatment Trial
2. The attendee will be able to describe the findings of the Optic Neuritis Treatment Trial
3. The attendee will be able to know the responses of US ophthalmologists and neurologists to the findings of the Optic
   Neuritis Treatment Trial

CME QUESTIONS

1. The primary outcome of the Optic Neuritis Treatment Trial was change in:

   A. Visual acuity
   B. Visual field mean deviation
   C. Contrast sensitivity
   D. Color perception

2. What finding of the Optic Neuritis Treatment Trial was not accepted by many neurologists in the US?

   A. The IV/oral steroid regimen was associated with marked visual improvement compared with placebo or oral Prednisone
   B. The oral steroid regimen was associated with an increased risk of recurrent optic neuritis in the previously affected eye and new episodes of optic neuritis in the fellow eye
   C. The oral steroid regimen was associated with an increase in enhancing white-matter lesions on magnetic resonance imaging
   D. Patients receiving oral placebo had an increased risk of developing multiple sclerosis within the first year after onset of optic neuritis

3. The Optic Neuritis Treatment Trial showed that

   A. Magnetic resonance imaging should be performed in patients with apparent acute optic neuritis to rule out an intracranial mass lesion
   B. Patients with acute idiopathic optic neuritis should undergo an assay for antinuclear antibodies
   C. The visual prognosis for patients with acute idiopathic optic neuritis treated with the IV/oral steroid regimen was the same as that of patients who received placebo.
   D. Patients with acute optic neuritis should be treated with plasma exchange if vision does not improve within 5 days of symptom onset

KEYWORDS

1. Optic neuritis
2. Visual prognosis
3. Contrast sensitivity
4. Steroid treatment
5. Multiple sclerosis

HIGHLIGHTS

1. Treatment of acute idiopathic or MS-related optic neuritis with a combination of intravenous methylprednisolone (1 gm per day) for 3 days followed by oral prednisone (1 mg/kg/day) for about 2 weeks speeds recovery but does not result in improved visual sensory function at 6 months or longer.
2. Treatment of acute optic neuritis with oral prednisone in the dose used in the Optic Neuritis Treatment Trial (1 mg/kg/day) is not warranted as it does not improve visual outcome, does not speed visual recovery, and is associated with an increased incidence of recurrent optic neuritis in the previously affected eye and of new attacks in the fellow eye.
3. MRI is not cost-effective from the standpoint of identifying intracranial mass lesions causing visual loss that mimics acute optic neuritis, although it should be used to assess risk of subsequent multiple sclerosis.
4. In the absence of a history consistent with an underlying connective tissue disorder or a systemic inflammation/infectious disease, laboratory studies to rule out such disorders are not cost-effective in patients with acute optic neuritis.

SUMMARY

In 1949, Hench et al. (1) described the beneficial effects of systemic corticosteroids in the treatment of rheumatoid arthritis. Following this report, physicians began to consider other disorders, including acute optic neuritis, that might respond to similar treatment or to treatment with adrenocorticotrophic hormone (ACTH). The first systematic attempt to address this issue was a double-blind, prospective study of the treatment of 50 patients with acute retrobulbar neuritis with either ACTH or placebo (2,3). The study showed that the group treated with ACTH recovered vision faster than the group give placebo, but at 1 year, the mean visual acuities in the two groups were not significantly different from each other.

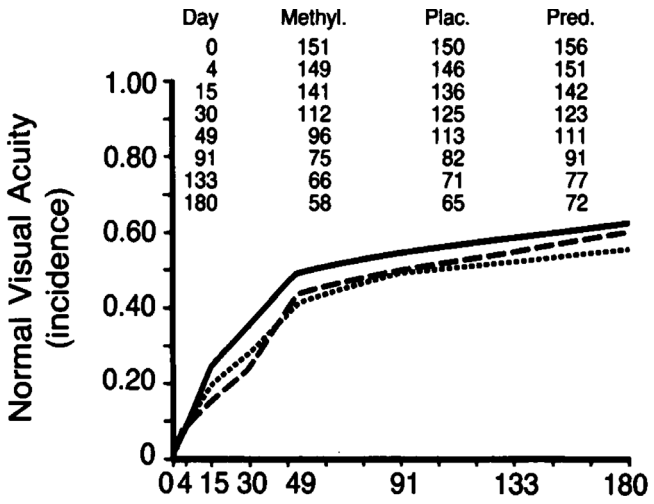
In the subsequent Cooperative Multiple Sclerosis Study (4), the results of which were published in 1970, there were 41 cases in which acute optic neuritis was the primary manifestation of multiple sclerosis (MS) for which patients were entered into the study. The 22 patients treated with ACTH improved faster than the 19 patients treated with placebo, but there was no long-term follow-up. Bowden et al. (5) subsequently performed a prospective clinical trial in 54 patients with acute optic neuritis. The study showed no benefit on visual acuity of ACTH compared with placebo in these patients.

In 1977, Gould et al. (6) performed a prospective single-blind controlled clinical trial in which 74 patients with acute optic neuritis either received a retrobulbar injection of triamcinolone or were randomized to a control group that received no treatment. Visual acuity in the affected eyes of the treated patients improved faster than did visual acuity in the affected eyes of patients who received no treatment, but there was no difference in mean visual acuity between the two groups after 6 months. Trauzettel-Klosinski et al. (7) also performed a study in which 50 patients with acute optic neuritis were randomized

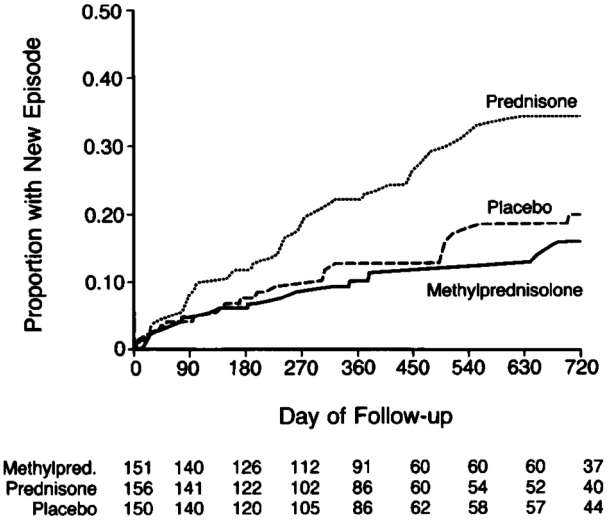
to receive either oral corticosteroids or placebo. There was a suggestion of a slightly more rapid recovery of vision in the patients treated with steroids compared with patients in the placebo group, but there was no difference in vision between groups at 12 months. In the meantime, Spoor (8) and Spoor and Rockwell (9) described rapid recovery of vision in two small series of patients with optic neuritis treated with intravenous methylprednisolone.

By the late 1980s, there was considerable controversy as to whether steroids were useful in the treatment of idiopathic and MS-related acute optic neuritis. Indeed, in 1986, a survey conducted by mail of 112 ophthalmologists and 54 neurologists in Michigan and Florida determined that whereas 65% of ophthalmologists treated patients with acute optic neuritis with systemic steroids, 90% of neurologists did (10). A group of neuro-ophthalmologists decided that it was time to try to answer this question, and the Optic Neuritis Treatment Trial (ONTT) was born.

In this National Eye Institute-supported, prospective, multicenter study, 457 patients with acute optic neuritis whose visual symptoms began within 8 days and who had no systemic disorders known to be associated with optic neuritis other than MS, were enrolled and randomized to one of three treatment groups: (a) oral prednisone (1 mg/kg/day) for 14 days; (b) intravenous methylprednisolone sodium succinate (250 mg qid for 3 days as a hospital inpatient, followed by oral prednisone 1 mg/kg/day) for 11 days; and (c) oral placebo for 14 days. Each regimen was followed by a short oral taper (11,12. It should be noted, particularly with respect to subsequent criticisms of the trial (see below) that it was clear to the investigators that ideally there should have been four treatment groups rather than three, with the fourth being participants who were hospitalized and received intravenous placebo followed by oral placebo as an outpatient; however, the risk: benefit ratio and the cost of having this group made this option untenable. The primary outcome measure was contrast sensitivity assessed using a Pelli-Robson chart (as it was assumed that this would be a more sensitive indicator of visual sensory function than visual acuity); secondary outcomes were best-corrected visual acuity, visual field mean deviation assessed using a Humphrey visual field analyzer, and color vision using the Farnsworth-Munsell 100-hue test. Most patients in all three treatment groups had a good recovery of visual sensory function (12). Indeed, after 6 months of follow up, the median contrast sensitivity, best-corrected visual acuity, and visual field mean deviation were normal in all three groups, and less than 10% of the patients in each group had visual acuity of 20/50 or worse. One year after the onset of visual symptoms, there was still no significant difference in mean contrast sensitivity, visual acuity, visual field mean deviation or color vision among the three groups (13,14). On the other hand, patients treated with the regimen of intravenous methylprednisolone followed by oral prednisone recovered vision considerably faster (about 42 days) than patients treated with oral placebo (12) (Fig. 1). The benefit of this treatment regimen was greatest in the first 15 days of follow up and decreased subsequently.



There was one particularly surprising finding of the ONTT. Not only did patients treated with low-dose oral prednisone alone not recover vision any faster and had no better vision at the end of a 6-month follow-up period than patients treated with oral placebo (8), but also, and quite unexpectedly, these patients had an increased rate of recurrent attacks of optic neuritis in the previously affected eye and an increased rate of new attacks of optic neuritis in the fellow eye compared with patients in the other two groups (12) (Fig. 2)!



Thus, oral prednisone in a dose of 1 mg/kg/day did not speed recovery of vision compared with no treatment, did not improve ultimate visual acuity compared with no treatment, and produced a higher rate of recurrent and new attacks of optic neuritis than did no treatment.

The ONTT also evaluated the rate of development of clinical MS in the three treatment groups and found that the patients treated with the intravenous/oral corticosteroid regimen had a reduced rate of development of clinically definite MS during the first 2 years (15,16). The benefit of treatment was seen

only in patients who had significantly abnormal brain MR imaging at the onset of the optic neuritis (however, neither FLAIR image software nor paramagnetic contrast material been developed at the time the trial began).

Among the 457 patients in the ONTT, only two 2 patients with presumed acute optic neuritis had intracranial mass lesions; 1 patient had a pituitary adenoma and 1 patient had an aneurysm that was identified only on a subsequent MRI performed when the patient's visual acuity continued to worsen (17).

In the ONTT, a comprehensive medical history was obtained from all patients, all of whom underwent blood testing for connective tissue disease (antinuclear antibody assay [ANA]) and syphilis (fluorescent treponemal antibody adsorbent test for syphilis [FTA ABS]), and a chest radiograph to evaluate for sarcoidosis or tuberculosis (18). A lumbar puncture was optional. The key findings from this testing were as follows:

1. The ANA was positive in a titer less than 1:320 in 13% and 1:320 or more in 3%. Only one patient developed a diagnosable connective tissue disease in the first 2 years of follow up. Visual and neurologic outcomes were no different in this subgroup.
2. The FTA ABS was positive in six patients (1.3%), but none had active syphilis.
3. The chest radiograph did not reveal evidence of sarcoidosis or tuberculosis in any patient (12).
4. Analysis of cerebrospinal fluid (CSF) did not yield any unsuspected information in the 131 patients in whom it was performed (19).

Based on the findings of the ONTT, the following recommendations were made (12):

1. Treatment of acute optic neuritis with oral prednisone in the dose used in the study is not warranted as it does not improve visual outcome, does not speed recovery, and is associated with an increased incidence of recurrent optic neuritis in the previously affected eye and of new attacks in the fellow eye.

2. No treatment of acute optic neuritis should be considered for patients with visual acuity of 20/40 or better.
3. MRI is not cost-effective from the standpoint of identifying intracranial mass lesions causing visual loss that mimics acute optic neuritis and, thus, need not be performed in the setting of a clear-cut clinical picture of acute optic neuritis (the importance of MRI as a risk factor for the subsequent development of MS was subsequently reported (20).
4. In the absence of a history consistent with an underlying connective tissue disorder or a systemic inflammation/infectious disease, laboratory studies are not cost-effective in patients with acute optic neuritis.

The results of the ONTT were generally accepted by ophthalmologists in the US, most of whom referred their patients with acute optic neuritis to a local neurologist; however, the recommendations generated considerable controversy among some neurologists who challenged the validity of two findings and the recommendations on which they were based. The first was that visual improvement was more rapid with the intravenous/oral steroid regimen than with oral prednisone alone. The objection was that, as noted above, there was no matched placebo-treated, hospitalized, intravenous/oral regimen treatment arm.

The argument was made that factors other than the treatment may have influenced the rate of recovery in the hospitalized intravenous/oral group compared with the other two groups. Thus, caution was recommended in accepting the recommendation that patients with visual acuity worse than 20/40 receive (high-dose) intravenous methylprednisolone rather than (low-dose) oral prednisone (21-23).

The second and perhaps more controversial issue that concerned neurologists was the finding that recurrent optic neuritis in the previously affected eye and new optic neuritis in the fellow eye occurred more frequently in the oral prednisone group than in the other two groups. The concern here was that there were no data presented on the proportion of patients in the three treatment arms with abnormal brain MRI, abnormal CSF, or particular HLA types. Thus, it was thought that these or other factors could have influenced the rate of recurrent/new optic neuritis in these groups.(21-23) A final point made by some authors was that the recommendations on treatment of acute optic neuritis might not be applicable to children under the age of 14 years, although it was admitted that a randomized study of the same magnitude would be difficult to achieve in children because of the very low incidence of this disease in children (24). These arguments were addressed by the study director and others (25-27) but failed to convince some neurologists.

Following publication of the ONTT results, many physicians elected to treat patients with the intravenous/oral regimen but to do so with a single daily dose of 1 gram of methylprednisolone for three days as an outpatient rather than to hospitalize the patient and treat with divided doses. Although initially this was an extrapolation of the ONTT recommendations, a similar optic neuritis treatment trial performed in Japan in which the intravenous/oral group received a single dose of 1 gm of intravenous methylprednisolone daily for 3 days rather than 250 mg qid, confirmed the results of the US-based ONTT (28).

The usefulness of MRI as a predictor of MS has been confirmed (20). But the results of the ONTT must be viewed based on the subsequent discovery that a small proportion of patients with what previously would have been diagnosed as acute idiopathic optic neuritis have aquaporin-4 antibodies or myelin oligodendrocyte glycoprotein antibodies in their serum, CSF, or both, giving rise to a diagnosis of neuromyelitis optica spectrum disorder (NMOSD) or myelin oligodendrocyte glycoprotein-associated disorder (MOGAD). Current recommendations are that patients with those diagnoses need to be treated aggressively with systemic corticosteroids, plasmapheresis, and/or immunosuppressive agents. For these reasons, the ONTT recommendations are not as useful as they once were. Indeed, most ophthalmologists and neurologists now treat all--or at least most--patients with acute optic neuritis with an intravenous/oral regimen, not just to speed visual recovery but to improve outcome in case blood tests eventually disclose that the patients have NMOSD or MOGAD.

CME ANSWERS

1. C
2. B
3. C

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Platform Session I – Monday, March 4th [2.0 CME]

Moderators: Beau Benjamin Bruce, MD, PhD and Oana Dumitrascu, MD

3:45 pm – 4:00 pm	**Safety and Efficacy of Intravitreal Injection of Pegfilgrastim in Patients with Indirect Traumatic Optic Neuropathy. An open-label phase I trial**, *Rong-Kung Tsai, MD, PhD*
4:00 pm –4:15 pm	**Clinical Features of Black Patients with Non-Arteritic Anterior Ischemic Optic Neuropathy**, *Ana Banc, MD, PhD*
4:15 pm – 4:30 pm	**Paracentral Acute Middle Maculopathy is a Biomarker of Arteritic Anterior Ischemic Optic Neuropathy**, *Steffen Hamann, MD, PhD*
4:30 pm – 4:45 pm	**10-Year Risk of Aortic and Carotid Complications in Patients with Giant Cell Arteritis**, *J. Anthony Chacko, MD*
4:45 pm – 5:00 pm	**Multimodality Imaging in Cranial Giant Cell Arteritis: First Experience with High-resolution T1-weighted 3D Black Blood without Contrast Enhancement Magnetic Resonance Imaging**, *Michael Stormly Hansen, MD, FEBO*
5:00 pm – 5:15 pm	**Efficacy of Intra-Arterial or Intravenous Thrombolytic Therapy Versus Conservative Standard Therapy for Central Retinal Artery Occlusion: An individual patient data meta-analysis**, *Jim Shenchu Xie, MD*
5:15 pm – 5:30 pm	**Visual Outcomes in a Large Cohort of Patients with Acute Central Retinal Artery Occlusion and Initial Insights on Telemedicine-Enabled Intravenous Thrombolytic Treatment**, *Aubrey Gilbert, MD, PhD*
5:30 pm – 5:45 pm	**Diagnosis of Central Retinal Artery Occlusion within 4.5 hours after Visual Loss, Using a Deep Learning Method Applied on Fundus Images**, *Dan Milea, MD, PhD*

Platform Session I – Monday, March 4th

Safety and Efficacy of Intravitreal Injection of Pegfilgrastim in Patients with Indirect Traumatic Optic Neuropathy. An open-label phase I trial

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Introduction:
There is no effective treatment for traumatic optic neuropathy (TON), and the search for treatments for TON is emerging. In preclinical trials, we have demonstrated that intravitreal injection (IVI) of Pegfilgrastim has neuroprotective effects on a TON model. Since Pegfilgrastim is an available drug in the oncology department, we conducted a phase 1 trial of Pegfilgrastim (Neulasta®) use in TON patients.

Methods:
A Unicenter, open-label phase I trial was conducted. Inclusion criteria: Indirect TON patients between 20 to 70 y/o, 7 days to 1 month after trauma, the BCVA ≤20/100, or central visual field (MD ≤ -10 dB). After enrollment and signing the informed consent, patients received a single IVI in the affected eye with a dosage of 0.15 ml of Neulasta®. The primary assessment was safety, and the second assessment was efficacy in BCVA and VF defects. Enrolled patients were evaluated on 1 day, 1 week, 1 month, and 3 months after injection. This trial was approved by the IRB at Tzu-Chi Medical Center and the FDA of the Taiwan government.

Results:
A total of 12 participants (10M and 2F) were enrolled in this trial. The average age was 42.8 y/o. The average duration of treatment post-trauma was 17.4 days. There was no SAE. The IOP was normal at the follow-up time. 100% of participants showed transient leukocytosis post-injection and back to normal at one-month follow-up. Only one patient showed transient systemic soreness (8.3%) and another with sub-conjunctival hemorrhage post-injection (8.3%). The log MAR BCVA was improved in 9 patients (75%) and 8 patients (67%) at one-month and three-month follow-up respectively. the visual field examination also showed improvement in 6 patients (50%).

Conclusions:
In conclusion, the intravitreal injection of Pegfilgrastim was safe for patients with indirect TON. There was no SAE. Certain participants got vision improvement after treatment at three-month follow-ups.

References: None provided.

Abstract Type: Clinical Trial

Keywords: Optic nerve trauma and treatment

Financial Disclosures: The authors had no disclosures.

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Clinical Features of Black Patients with Non-arteritic Anterior Ischemic Optic Neuropathy

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[1] Iuliu Hatieganu University of Medicine and Pharmacy Cluj-Napoca, [2] Emory University School of Medicine, [3] Icahn School of Medicine at Mount Sinai, New York, NY, [4] Emory University

Introduction:
Why non-arteritic anterior ischemic optic neuropathy (NAION) is very rare in persons of Black race compared to those of White race is unknown. Our goal was to analyze the systemic and ocular features of Black NAION patients compared to White patients.

Methods:
Retrospective cross-sectional study from a single neuro-ophthalmology service. Self-reported race was collected from all NAION patients seen between 2014-2022. All Black NAION patients and a randomly selected sample of White NAION patients were included. We collected information on hypertension, hyperlipidemia, diabetes mellitus, hypothyroidism, obesity, ischemic heart disease, atrial fibrillation, pacemaker insertion, chronic kidney disease, dialysis, anemia, obstructive sleep apnea, deep vein thrombosis, stroke, malignancy, use of phosphodiesterase inhibitors, and smoking status. We reviewed color fundus photographs and optic nerve OCT images to measure the optic disc area, adjusted cup-to-disc ratio, and document the presence of optic disc drusen. Counterfactual random forest was used to calculate associations for each characteristic of interest by race controlling for the other exposures.

Results:
We included 32 Black NAION patients (mean age 57±11 years, 38% men) and 69 of 432 White patients (mean age 57±15 years, 59% men). Time between NAION onset and neuro-ophthalmic examination was significantly longer in Black patients (OR 9.98, p=0.007). Chronic kidney disease (OR 7.53, p=0.003) and hemodialysis (OR 13.69, p=0.02) were significantly more frequent in Black patients. No significant differences in adjusted cup-to-disc ratio were present (OR 0.88, p=0.83).

Conclusions:
Referral delay occurs in Black patients with NAION, perhaps due to its relative rarity and concern for alternate diagnoses. Black patients with NAION were substantially more likely to have chronic kidney disease and be on dialysis than White patients. Despite known racial differences in cup-to-disc ratio, we found no difference between Black and White NAION patients, suggesting that the underlying compartment mechanism is the same among races.

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Abstract Type: Epidemiological Study

Keywords: Optic neuropathy

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Grant Support: None.

Contact Information: None provided.

Paracentral acute middle maculopathy is a biomarker of arteritic anterior ischemic optic neuropathy

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Introduction:
Differentiating clinically between arteritic anterior ischaemic optic neuropathy (A-AION) and the nonarteritic variant (NA-AION) may be difficult. Paracentral acute middle maculopathy (PAMM) has recently been associated with giant cell arteritis (GCA). Hence, the purpose of this study was to determine if the observation of PAMM could help differ between the two AION subtypes at an early stage.

Methods:
Macular optical coherence tomography (OCT) scans obtained shortly after initial presentation were graded for the presence of PAMM in 10 patients with A-AION and 25 patients with NA-AION, enrolled in prospective studies of GCA and NA-AION, respectively. The diagnosis of A-AION was ascertained by a positive temporal artery biopsy or positive positron emission tomography / computed tomography, whereas NA-AION required GCA to be ruled out.

Results:
PAMM was found in 60% of patients and 53% of eyes with A-AION and in none of the eyes with NA-AION. In the setting of AION, the sensitivity of PAMM for the diagnosis of A-AION was 60% while the specificity was 100%. This resulted in a positive predictive value for A-AION of 100% and a negative predictive value of 88%.

Conclusions:
PAMM appears to be a biomarker of GCA in patients presenting with AION.

References: None provided.

Abstract Type: Clinical Trial

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Optic neuropathy, Retina

Financial Disclosures: Michael Stormly Hansen: The Danish Rheumatism Association and Synoptik-Fonden; Oliver Niels Klefter: No; Lea Lykkebirk: No; Yousif Subhi: No; Jane Maestri Brittain: No; Mads Radmer Jensen: No; Uffe Døhn: No; Victoria Fana: No; Anne Katrine Wiencke: No; Steffen Heegaard: No; Lene Terslev: No; Steffen Hamann: No

Grant Support: The Danish Rheumatism Association and Synoptik-Fonden

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10-Year Risk of Aortic and Carotid Complications in Patients with Giant Cell Arteritis

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Introduction:
Giant cell arteritis (GCA) is a systemic autoimmune disease that can cause permanent blindness. The development of aortic aneurysm has been reported in patients with biopsy-proven GCA. Recent literature has suggested long-term follow-up with MRA or CTA to monitor for aortic structural damage. We present the first large-scale retrospective study to evaluate the risk of development of aortic aneurysm in patients with biopsy-proven GCA.

Methods:
We included patients with biopsy-confirmed GCA and excluded patients with a history of cerebral infarction, myocardial infarction, deep vein thrombosis, and pulmonary embolism utilizing the TriNetX Research Database. Patients were propensity score matched to a control group of patients with cataracts adjusting for medical comorbidities and demographics. Each patient in the cohort was assigned an index date. We explored the first-time risk of developing aortic aneurysms and carotid artery stenosis.

Results:
There were 7,445 patients included in each cohort. Of the 7,445 patients with biopsy-confirmed GCA, 5,219 (70%) were female with a mean (SD) age at index of 70.3 (10.2). We found that the 10-year risk of developing first time aortic aneurysm was significantly higher in patients with biopsy-confirmed GCA compared to the control group (RR: 1.41; 95% CI: 1.10- 1.82, p< 0.01). There was increased risk in thoracic aortic aneurysms (RR: 1.89; 95% CI: 1.31- 2.73, p< 0.001) compared to abdominal aortic aneurysms (RR: 1.02; 95% CI: 0.74- 1.40, p=0.91) and thoracoabdominal aneurysms (RR: 1.10; 95% CI: 0.47- 2.59, p=0.826). The risk of carotid artery stenosis was higher in patients with GCA (RR: 1.48; 95% CI: 1.24- 1.76, p< 0.0001).

Conclusions:
In patients with biopsy-proven GCA, we found an elevation in the 10-year risk for aortic complications, especially thoracic aortic aneurysms. Given this novel insight from our large-scale study, clinicians should consider incorporating regular vascular assessments with MRA or CTA into the routine care of GCA patients.

References: None provided.

Abstract Type: Basic Science

Keywords: Vascular disorders, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: J. Anthony Chacko, JAChacko@uams.edu

Multimodality Imaging in Cranial Giant Cell Arteritis: First Experience with High-resolution T1-weighted 3D Black Blood without Contrast Enhancement Magnetic Resonance Imaging

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Introduction:
To support or refute the clinical suspicion of cranial giant cell arteritis (GCA), a supplemental imaging modality is often required. High-resolution black-blood Magnetic Resonance Imaging (BB MRI) techniques with contrast enhancement can visualize artery wall inflammation in GCA.

Methods:
We compared findings on BB MRI without contrast enhancement with findings on 2-deoxy-2-[18F]fluoro-D-glucose positron emission tomography/low dose computed tomography (2-[18F]FDG PET/CT), in 10 patients suspected of having GCA and in five control subjects imaged as part of a routine control for malignant melanoma. Final diagnosis was clinical evaluation after six months including findings on vascular ultrasound, 2-[18F]FDG PET/CT, and temporal artery biopsy.

Results:
BB MRI was consistent with 2-[18F]FDG PET in 10 out of 10 cases in the group with suspected GCA. Two out of 10 patients were diagnosed as GCA negative and were correctly identified negative on BB MRI. In four out of five cases in the control group, BB MRI was consistent with 2-[18F]FDG PET/CT.

Conclusions:
To our knowledge, this is the first study to perform BB MRI without contrast enhancement to evaluate cranial vasculitis in GCA patients compared to controls. With high-resolution images, a short scan time of 8 minutes, and no MRI contrast agent administration BB MRI has several advantages compared to other non-invasive imaging modalities used in the diagnostic work-up of GCA. BB MRI without contrast enhancement shows promising performance in the diagnosis of GCA and might be an applicable imaging modality in diagnostic management of GCA.

References: None provided.

Abstract Type: Basic Science

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Neuroimaging, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease, Optic neuropathy

Financial Disclosures: Michael Stormly Hansen: The Danish Rheumatism Association and Synoptik-Fonden; Jane Maestri Brittain: No; Jonathan Frederik Carlsen: No; Andreas Hjelm Brandt: No; Lene Terslev: No; Mads Radmer Jensen: No; Ulrich Lindberg: No; Henrik Bo Wiberg Larsson: No; Steffen Heegaard: No; Uffe Døhn: No; Oliver Niels Klefter: No; Anne Katrine Wiencke: No; Yousif Subhi: No; Steffen Hamann: No; Bryan Haddock: No

Grant Support: The Danish Rheumatism Association and Synoptik-Fonden

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Efficacy of intra-arterial or intravenous thrombolytic therapy versus conservative standard therapy for central retinal artery occlusion: an individual patient data meta-analysis

Jim Xie [1], Kirill Zaslavsky [2], Edward Margolin [2]

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Introduction:
There is a lack of high-quality data supporting thrombolytic therapy for non-arteritic central retinal artery occlusion (naCRAO). We performed an individual participant data (IPD) meta-analysis to compare the efficacy of intra-arterial thrombolysis (IAT) and intravenous thrombolysis (IVT) with conservative standard therapy (CST).

Methods:
Embase, Medline, and CENTRAL were searched from inception to June 2023 and IPD were solicited from original investigations that reported treatment modality and visual acuity (VA) data. The proportion of eyes with severe vision loss (SVL), defined as VA less than 20/200, post-treatment was compared between the IAT, IVT, and CST groups using Fisher's exact test.

Results:
Of 143 studies reporting on 2956 patients with naCRAO, 87 studies provided IPD for 871 eyes (29.5% capture rate). The mean age of included patients was 64.8 years (standard deviation [SD] 14.1) and there were 315 (36.2%) females. IPD were provided for 262/759 IAT eyes, 156/367 IVT eyes, and 453/1830 CST eyes across a mean follow-up of 3628.5 (SD 7906.2) hours. At presentation, the rate of SVL was 95.4% with no differences between groups. Among eyes that received treatment ≤4.5 hours from symptom onset, IAT (61.5% vs. 80.6%, P=0.04) and IVT (63.8% vs. 80.6%, P< 0.01) reduced likelihood of SVL compared to CST. Number needed to treat was 5.2 and 5.9 for the IAT and IVT groups, respectively. There were no significant differences in SVL rate between the CST and IAT or IVT groups when time from symptom onset to treatment was between 4.5 and 12 hours or greater than 12 hours. There were also no significant differences in SVL rate between the IAT and IVT groups at any time threshold.

Conclusions:
Compared to CST for naCRAO, early administration of IAT or IVT is associated with increased likelihood of favorable visual outcome. IVT appears to be non-inferior to IAT.

References: None provided.

Abstract Type: Epidemiological Study

Keywords: Vascular disorders, Stroke

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: Edward Margolin, edmargolin@gmail.com

Visual Outcomes in a Large Cohort of Patients with Acute Central Retinal Artery Occlusion and Initial Insights on Telemedicine-Enabled Intravenous Thrombolytic Treatment

Aubrey Gilbert [1], Amar Patel [1], Ronak Shah [2], Robin Vora [1]

[1] The Permanente Medical Group, [2] Renaissance School of Medicine at Stonybrook University

Introduction:
Central retinal artery occlusion (CRAO) carries a bleak prognosis, and the potential of thrombolytic treatment has drawn significant interest. Building upon our previous work investigating acute CRAO presentation patterns, we reviewed visual outcomes in our large patient cohort. We examined patients managed conservatively and those treated with intravenous tenecteplase through a telemedicine pathway employing fundus cameras in 21 emergency departments.

Methods:
We conducted retrospective analysis of 794 confirmed CRAO cases spanning a decade. Subanalyses focused on patients presenting within 30 days with comprehensive documentation. We cataloged visual acuity (VA) at presentation and follow-up after 90 days, comparing outcomes between untreated patients and those subjected to various conservative measures, such as ocular massage. We also stratified outcomes by presentation time and examined results for 26 patients receiving intravenous tenecteplase within 4.5 hours of vision loss.

Results:
Among the 484 patients meeting inclusion criteria, 92.4% presented with VA worse than 20/200, and 86.2% of the 441 patients with follow-up data did not improve beyond this threshold. No statistically significant differences were observed in visual outcomes between untreated patients and those receiving conservative treatment or between the 244 patients presenting within 4.5 hours and those presenting later. Of the 26 patients treated with intravenous tenecteplase, only one demonstrated improvement beyond 20/200.

Conclusions:
Our study describes visual outcomes for the largest cohort of acute CRAO patients reported to date. It is significantly limited by its retrospective nature. Nevertheless, our findings underscore prior reports of poor visual prognosis and inefficacy of conservative treatments for CRAO. Additionally, we found that patients presenting earlier had similar outcomes to those presenting later. We were able to demonstrate a functional integrated telemedicine pathway for expedited diagnosis and treatment with intravenous thrombolysis, but the results of this treatment were disappointing. Further research is needed to gain more definitive insights into this challenging condition.

References: None provided.

Abstract Type: Epidemiological Study

Keywords: Stroke, Retina, Vascular disorders, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease

Financial Disclosures: Aubrey Gilbert: No; Amar Patel: No; Ronak Shah: No; Robin Vora: Iveric Bio (Speaker Bureau), Outlook Therapeutic (Consultant, Advisory Board), Paradigm Biopharmaceuticals (Consultant) None of these relationships are discussed in this abstract or relate directly to the support of the abstract.

Grant Support: None.

Contact Information: Aubrey Gilbert, Aubrey.L.Gilbert@kp.org

Diagnosis of Central Retinal Artery Occlusion within 4.5 hours after Visual Loss, using a Deep Learning Method Applied on Fundus Images

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Introduction:
Accurate and timely diagnosis of acute Central Retinal Artery Occlusion (CRAO) is essential. However, expert centers able to provide fibrinolytic therapies within the first hours after visual loss often lack ophthalmic expertise. In the era of telemedicine and artificial intelligence, we developed, trained and tested a deep learning system (DLS) able to accurately identify acute CRAO (within 24h and 4.5h after visual loss), based on standard retinal color images.

Methods:
We conducted an international retrospective multicenter study, including 623 patients (185 with CRAO, 110 with central retinal vein occlusion, 189 with non-arteritic ischemic optic neuropathy, 139 controls) from six expert neuro-ophthalmology centers in Europe and the US. The DLS employed a convolutional neural network whose hyperparameters were determined using grid search. Training was based on a multiclass classification approach, with weighted categorical cross-entropy loss, and testing was performed on two independent datasets. The first testing dataset included 35 patients with CRAO imaged within 24h after visual loss (and 43 nonCRAO patients). The second testing dataset included 11 patients with CRAO imaged within 4.5h after visual loss (majority were consecutive patients included in a randomized clinical trial evaluating intravenous thrombolysis vs. placebo).

Results:
For enhanced result demonstration, a binary classification approach was adopted, categorizing the data into "CRAO vs. nonCRAO" groups. The DLS exhibited excellent performance in identifying CRAO, both within the first 24h after visual loss (AUC: 0.88 (CI: 0.87-0.90), sensitivity: 82% (0.67-0.91), specificity: 74% (0.59-0.85), and accuracy: 78% (0.67-0.85)) and at 4.5h (AUC: 0.93 (0.92-0.94), sensitivity: 90% (0.62-0.97), specificity: 81% (0.67-0.90), and accuracy: 83% (0.71-0.91)).

Conclusions:
The preliminary results of this study suggest that a DLS can accurately identify acute CRAO on fundus images within both 24h and 4.5h time windows (based on current acute ischemic stroke references), having a potential impact on patients' selection for fibrinolytic treatments and/or secondary stroke prevention.

References: None provided.

Abstract Type: Epidemiological Study

Keywords: Vascular disorders, Stroke, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease, Neuroimaging, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: The authors had no disclosures.

Grant Support: Research grant, VISIO.

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Platform Session II – Tuesday, March 5th [2.0 CME]

Moderators: Melinda Chang MD and Kimberly K Gokoffski MD, PhD

7:30 am – 7:45 am	**Racial Disparities in the Development of Visual Impairment in Patients with Idiopathic Intracranial Hypertension,** *Patrick Zhang, MS*
7:45 am – 8:00 am	**Raised Intracranial Pressure Alters Cranial Nociception Which Can Be Rescued by Glucagon Like Peptide 1 Receptor Agonism and CGRP Antagonism In Vivo,** *Olivia Grech, MRes*
8:00 am – 8:15 am	**Emergency Department (ED) Non-Mydriatic Fundus Photography Expediates Care for Patients Referred for "Papilledema",** *Amy (Mung Yan) Lin, MD*
8:15 am – 8:30 am	**Optic Nerve Blood Flow by Laser Speckle Flowgraphy in Different Causes of Optic Disc Edema,** *Noor-Us-Sabah Ahmad, MD*
8:30 am – 8:45 am	**FALCON: A Prospective Natural History Study of Patients with OPA1-Autosomal Dominant Optic Atrophy (OPA1-ADOA),** Byron Lam, *MD*
8:45 am – 9:00 am	**Factors Predictive of Recurrence in Myelin Oligodendrocyte Glycoprotein (MOG) Associated Optic Neuritis,** *Virender Sachdeva, MS*
9:00 am – 9:15 am	**Prevalence and Clinical Associations of Peripapillary Hyper-Reflective Ovoid Mass-Like Structures (PHOMS) in Patients with Craniosynostosis,** *Jacqueline Jeon-Chapman, BS*
9:15 am – 9:30 am	**Eye Tracking Measures of Oculomotor Function Are Associated with Improvement in Visual Acuity in Children with Cortical/Cerebral Visual Impairment (CVI),** *Melinda Chang, MD*

Platform Session III – Tuesday, March 5th [2.0 CME]

Moderators: Kenneth S. Shindler, MD, PhD and Hong Jiang MD, PhD

10:00 am – 10:15 am	**Diplopia Improvement with Teprotumumab in Patients with High Inflammation/Recent Onset and Low Inflammation/Longer Duration Thyroid Eye Disease (TED),** *Prem S. Subramanian, MD, PhD*
10:15 am – 10:30 am	**Clinical Activity and Safety of VRDN-001, a Full Antagonist Antibody to Insulin-like Growth Factor-1 Receptor, in Active and Chronic Thyroid Eye Disease,** *Kimberly Cockerham, MD*
10:30 am – 10:45 am	**Binocular Visual Function Testing in an Alzheimer's Disease Research Center (ADRC) Cohort: Low-Contrast Letter Acuity and Rapid Automatized Naming (RAN) Tasks of MULES and SUN,** *Laura J. Balcer, MD, MSCE*
10:45 am – 11:00 am	**Curiouser and Curiouser: A Distributed Brain Network Underlying Alice in Wonderland Syndrome,** *Maximilian Friedrich, MD, PhD*
11:00 am – 11:15 am	**Permanent Transduction of Retinal Ganglion Cells by Injection of rAAV2-retro into the Superior Colliculus,** *Jonathan Horton, MD, PhD*
11:15 am – 11:30 am	**Vision-Related Quality of Life in LHON Patients Treated with Lenadogene Nolparvovec Gene Therapy: Analysis of the VFQ-25 Using Rasch Measurement Theory,** *Benson Chen, MBChB, MSc, FRACP*
11:30 am – 11:45 am	**Neuro-ophthalmological Phenotype and Correlations with Heteroplasmy Levels in MELAS and MERRF Syndromes,** *Giulia Amore, MD, PhD*
11:45 am – 12:00 pm	**Electric Field Stimulation Enhances Ciliary Neurotrophic Factor-Mediated Retinal Ganglion Cell Axon Regeneration After Optic Nerve Crush Injury,** *Connie Huang, BS*

Platform Session II – Tuesday, March 5th

Racial Disparities In The Development Of Visual Impairment In Patients With Idiopathic Intracranial Hypertension

Patrick Zhang [1], Noor Chahal [2], Humzah Iqbal [3], Gisou Mohaddes [1]

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Introduction:
Idiopathic intracranial hypertension (IIH) is a condition characterized by increased intracranial pressure without the presence of an identifiable cause. Complications of IIH include pulsatile tinnitus, severe headaches, impaired vision, and vision loss. Despite these complications, the etiology of IIH remains relatively unknown. However, cases of IIH within the United States have risen annually while being especially prevalent in low-income and black communities. With these trends that suggest a sociodemographic disparity in IIH, it is crucial to further elucidate the populations at greater risk.

Methods:
Patients with a diagnosis of IIH and visual impairment were identified using the 2020 Nationwide Inpatient Sample (NIS). Data regarding age, gender, race, and primary insurance were collected. The relationships between these variables and visual impairment in IIH patients were analyzed using multivariate regression analysis.

Results:
This study comprised 29,309 patients diagnosed with IIH, of which 1,378 (4.7%) developed visual impairment. Within the visual impairment group, 1,051 (76.3%) were female, 650 (47.2%) were white, and 526 (38.2%) had private insurance – representing the largest groups in these respective categories. Multivariate regression analysis showed that black (adjusted odds ratio (AOR) = 1.72, $P < 0.001$) and Hispanic (AOR= 1.40, $P < 0.09$) patients with IIH had increased odds of developing visual impairment compared to white patients.

Conclusions:
Our study reports that, black patients exhibited a substantial 1.72-fold higher odds of developing visual impairment compared to white patients when adjusting for confounders, despite the latter constituting the majority of the visual impairment group. These findings emphasize the need for further investigation into the factors contributing to these disparities, aiming to ensure equitable access to care and reduce the risk of visual impairment across diverse patient populations.

References: None provided.

Abstract Type: Epidemiological Study

Keywords: High intracranial pressure/headache

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: Patrick Zhang, zhang2802@chsu.edu

Raised Intracranial Pressure Alters Cranial Nociception Which Can Be Rescued By Glucagon Like Peptide 1 Receptor Agonism And CGRP Antagonism In Vivo.

Olivia Grech [1], Eloisa Rubio-Beltran [2], Emily Stanyer [3], Alejandro Labastida-Ramirez [2], Daniel Fulton [4], Gareth Lavery [5], Lisa Hill [6], Philip Holland [2], Alexandra Sinclair [1]

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Introduction:
Raised intracranial pressure (ICP) is a feature of Idiopathic Intracranial Hypertension (IIH), however, headache mechanisms are unknown, and targeted therapies are lacking. This study investigated headache mechanisms in raised ICP and the effects of; a) reducing ICP with glucagon-like peptide-1 (GLP-1) receptor agonist Exenatide b) attenuation with calcitonin-gene related peptide (CGRP).

Methods:
Kaolin (or saline) was injected intracisternally in rodents to increase ICP. After 7 days, evoked pain behaviour was assessed. Cortical spreading depression (CSD) was then evalautated as well as the impact on cortical and cerebral blood flow (CBF). Measurements were repeated in elevated ICP animals treated with exenatide, CGRP receptor antagonist Olcegepant or vehicle.

Results:
ICP was higher in kaolin animals (mean(SD) ICP saline=5.46mmHg(1.22) n=6, kaolin=17.72mmHg(10.124) n=8 p=0.001). Periorbital and hind paw thresholds were decreased (periorbital;normal ICP=6.43g(1.88) n=10, raised ICP=2.35g(1.91) n=12 p< 0.001, hind paw;normal ICP=5.16g(1.40), raised ICP=3.34g(2.21) p< 0.001). CSD responses were altered in raised ICP (repolarisation duration;normal ICP=86.96s(140.05), n=9, raised ICP=1824.26s(3499.54) n=12 p< 0.0001, % CBF change normal ICP=217.65%(37.70) n=8, raised ICP=85.55%(30.84) n=9 p< 0.001). In raised ICP, exenatide significantly reduced pressure (vehicle=18.27mmHg(6.67) n=16, exenatide=9.74mmHg(6.09) n=19 p< 0.001). Exenatide prevented changes in periorbital and hind paw thresholds in raised ICP. Exenatide also improved CSD responses (repolarization duration vehicle=800.85s(1988.67), n=6, exenatide=177.55s(562.88) n=7 p=0.002). Olcegepant did not influence ICP or improve CSD responses. Olcegepant did not rescue hind paw thresholds (baseline=5.96g(1.12), day 7=2.49g(1.30) n=10 p< 0.0001), but did prevent changes in periorbital sensitivity.

Conclusions:
Raised ICP led to altered pain behaviour, an indicator of trigeminal sensitivity as well as changes to neurovascular and cortical responses which were reversed by reducing ICP. Additionally, CGRP antagonism reduced markers of cranial trigeminal sensitivity. These studies suggest that raised ICP alters cranial nociception and this can be attenuated by lowering ICP but also though CGRP antagonism.

References: None provided.

Abstract Type: Basic Science

Keywords: High intracranial pressure/headache, Pseudotumor cerebri

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Emergency Department (ED) Non-Mydriatic Fundus Photography Expediates Care For Patients Referred For "Papilledema"

Amy (Mung Yan) Lin [1], Hetal Ray [2], Andrew M. Pendley [3], Avital Lily Okrent Smolar [4], Mariana Rodriguez Duran [5], Mariam Torres Soto [5], Gabriele Berman [6], Beau Bruce [1], David W. Wright [3], Nancy J Newman [7], Valérie Biousse [7]

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Introduction:
Fear of missing neurologic disorders or visual loss from unrecognized papilledema often leads to ED visits for "papilledema" rule-out and workup. Our institution developed an ED "papilledema protocol" which took a median of 27 hours (IQR, 19-33) in 20221. We implemented a non-mydriatic hybrid color fundus camera/OCT (NMFP/OCT) in 06/2023 in our ED with the goal to improve patients' outcomes. Our aim was to evaluate whether the NMFP/OCT could avoid in-person ophthalmology consultations in the ED and accelerate the evaluation of "papilledema" in the ED

Methods:
Prospective collection of consecutive adult patients presenting to our ED for "papilledema"rule-out/workup who had NMFP/OCT obtained in the ED from 06/09/2023-09/23/2023. We collected referral questions, final diagnoses, ED length-of-stay and whether an in-person ophthalmology consultation was performed in addition to remote interpretation of images. We compared ED length-of-stay with data prospectively collected in 2022 prior to installation of the camera in the ED

Results:
Compared to 27 hours (IQR, 19-33; 84 patients) in 2022,1 the ED NMFP/OCT reduced the median ED length-of-stay to 18 hours (IQR, 8-28; 104 patients) for patients referred to the ED for "papilledema". For the 62 patients in whom papilledema was ruled-out by NMFP/OCT, the ED length-of-stay decreased from 15 hours (IQR, 8-26) in 2022 to 10 hours (IQR, 7-24) in 2023; papilledema was ruled out remotely without in-person ophthalmology consultation in 59/62 patients. For patients with previously known IIH, ED-stay decreased from 22hours in 2022 (IQR, 11-28) to 12 hours in 2023 (IQR, 7-32; 26 patients).

Conclusions:
Implementation of NMFP/OCT in our general ED reduced the ED length-of-stay of "papilledema" patients by 33%, and consistently avoided in-person ophthalmology consultations when papilledema was ruled-out remotely on ocular imaging. This confirms the feasibility and cost-effectiveness of implementing NMFP/OCT in the ED. Results of the first 8 months will be presented at the NANOS meeting.

References: 1. Ray HJ, Okrent Smolar AL, Dattilo M, Bouthour W, Peragallo J, Kedar S, Newman N, Biousse V. "Papilledema" Neuro-ophthalmology consultations from the hospital: a prospective study. North American Neuro-Ophthalmology Society Annual Meeting. Orlando, FL. March 14, 2023. Poster. 2. Okrent Smolar AL, Ray, HJ, Dattilo M, Bouthour W, Peragallo J, Kedar S, Newman N, Biousse V. Neuro-ophthalmology emergency department and inpatient consultations at a large academic referral center [published online ahead of print, 2023 Aug 4]. Ophthalmology. 2023;S0161-6420(23)00536-5

Abstract Type: Quality Improvement/Evaluation Study

Keywords: High intracranial pressure/headache, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Pseudotumor cerebri

Financial Disclosures: The authors had no disclosures.

Grant Support: None

Contact Information: None provided.

Optic Nerve Blood Flow by Laser Speckle Flowgraphy in Different Causes of Optic Disc Edema

Noor-Us-Sabah Ahmad [1], Noriyoshi Takahashi [1], Natasha Gautam [2], Jui-Kai (Ray) Wang [3], Julie Nellis [4], Edward Linton [5], Randy Kardon [3]

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Introduction:
Laser speckle flowgraphy (LSFG) measures retinal, optic nerve and choroidal blood flow, and can evaluate flow changes in conditions such as ischemic optic neuropathy, glaucoma etc.1,2 The effect of optic disc edema on optic nerve head (ONH) blood flow by LSFG has not been investigated. We sought to assess whether ONH blood flow differed among controls and eyes with differing causes of ONH edema.

Methods:
We analyzed 105 eyes: control (n=36), acute NAION (n=35), acute AAION (n=15), IIH not taking acetazolamide (n=10), and IIH taking acetazolamide at the time of imaging (n=9). Mean of total ONH blood flow (MA), ONH tissue capillary flow (MT) and retinal arterial and venous flow on the ONH (MV-MT) of each group was compared with controls using ANOVA with Dunnett's multiple comparisons test. A neural network (nnU-Net) was trained to identify ONH margins on LSFG images using ground truth from fundus photos and compared to expert tracing of the ONH borders.

Results:
Blood flow (mean blur rate, MBR) for MA, MT, and MV-MT was significantly lower in patients with acute AAION compared to controls (8.1±2.4 vs 11.5±1.9, p=0.0002; 4.4±1.9 vs 6.3±1.7, p=0.009; and 11.8±4.1 vs 17.0±4.3, p=0.0002). MA and MT were significantly higher in patients with IIH not taking acetazolamide compared to controls (14.3±2.5 vs 11.5±1.9, p=0.016 and 9.9±2.2 vs 6.3±1.7, p< 0.0001). MA and MV-MT were significantly lower in NAION patients compared to controls (9.6±3.3 vs 11.5±1.9, p=0.01 and 14.0±3.5 vs 17.0±4.3, p=0.009); MT was significantly higher (8.5±2.3 vs 6.3±1.7, p< 0.0001). The nnU-Net achieved results equal to expert determination of ONH borders.

Conclusions:
Acute AAION patients had lower ONH tissue capillary and vessel flow, NAION patients had higher tissue capillary flow but lower vessel flow, whereas IIH patients not taking acetazolamide had higher total and tissue capillary flow compared with controls.

References: 1. Maekubo T, Chuman H, Nao-I N. Laser speckle flowgraphy for differentiating between nonarteritic ischemic optic neuropathy and anterior optic neuritis. Jpn J Ophthalmol. 2013 Jul;57(4):385-90. doi: 10.1007/s10384-013-0246-8. Epub 2013 May 22. PMID: 23695410. 2. Calzetti G, Mursch-Edlmayr AS, Bata AM, Ungaro N, Mora P, Chua J, Schmidl D, Bolz M, Garhöfer G, Gandolfi S, Schmetterer L, Wong D. Measuring optic nerve head perfusion to monitor glaucoma: a study on structure-function relationships using laser speckle flowgraphy. Acta Ophthalmol. 2022 Feb;100(1):e181-e191. doi: 10.1111/aos.14862. Epub 2021 Apr 20. PMID: 33880888.

Abstract Type: Epidemiological Study

Keywords: Pseudotumor cerebri, Optic neuritis, Optic neuropathy

Financial Disclosures: Noor-Us-Sabah Ahmad: No; Noriyoshi Takahashi: No; Natasha Gautam: No; Jui-Kai (Ray) Wang: This study was supported, in part, by the Department of Veteran Affairs Center for the Prevention and Treatment of Visual Loss, Rehabilitation Research and Development (RR&D) I50RX003002, RR&D I01RX003797; Julie Nellis: Author is associated with: Center for the Prevention and Treatment of Visual Loss, Iowa City VA Health Care System, Iowa City, IA, USA Department of Ophthalmology and Visual Sciences, The University of Iowa, Iowa City, IA, USA This study was supported, in part, by the Department of Veteran Affairs Center for the Prevention and Treatment of Visual Loss, Rehabilitation Research and Development (RR&D) I50RX003002, RR&D I01RX003797, RR&D I01RX001786, National Institutes of Health (NIH) R01EY031544, and NIH R01EY023279,; Edward Linton: No; Randy Kardon: Affiliations: Center for the Prevention and Treatment of Visual Loss, Iowa City VA Health Care System, Iowa City, IA, USA Department of Ophthalmology and Visual Sciences, The University of Iowa, Iowa City, IA, USA This study was supported, in part, by the Department of Veteran Affairs Center for the Prevention and Treatment of Visual Loss, Rehabilitation Research and Development (RR&D) I50RX003002, RR&D I01RX003797, RR&D I01RX001786, National Institutes of Health (NIH) R01EY031544, and NIH R01EY023279. The New York Eye and Ear Infirmary Foundation, New York, N.Y.; Alfiero & Lucia Palestroni Foundation, Inc. Englewood Cliffs, N.J, National Eye Institute (NEI) EY032522. FaceX LLC (Co-Founder)

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FALCON: A Prospective Natural History Study of Patients with OPA1-Autosomal Dominant Optic Atrophy (OPA1-ADOA)

Byron Lam [1], Patrick Yu-Wai-Man [2], Y. Joyce Liao [3], Raghu Mudumbai [4], Marcela Votruba [5], Kelly Saluti [6], Yue Wang [6], Barry Ticho [6], Steven Gross [6]

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Introduction:
Autosomal Dominant Optic Atropy (ADOA) is the most common inherited optic neuropathy seen in the general population, presenting in early childhood with slowly progressive visual loss. Over half of all patients are registered legally blind by the fifth decade of life. Most patients carry mutations in the OPA1 gene resulting in loss-of-function with ~ 50% reduction in cellular OPA1 protein level. OPA1 is a dynamin-related GTPase that localizes to the mitochondrial inner membrane and reduced levels precipitate the loss of retinal ganglion cells secondary to mitochondrial dysfunction. There is limited prospective data on the natural history of OPA1-ADOA, which is essential to determine the best outcome measures for treatment trials.

Methods:
FALCON is a multicenter, prospective study of OPA1-ADOA patients (ages ≥8 to ≤60 years(y)) with a confirmed pathogenic heterozygous OPA1 variant. Clinical and ocular assessments from baseline to 24m include changes in best-corrected visual acuity, visual field and optical coherence tomography parameters.

Results:
FALCON has completed enrollment with 48 patients (16 (8-17y), 22 (18-40y), and 10 (41-60y)) across UK, US, Italy, and Denmark. At baseline, 46% were female and 96% were white. Across all patients, at baseline, mean (SD) LogMAR (25%) was 0.57 (0.335) and visual acuity was 56.75 (16.739). Results will provide a dynamic picture of disease progression in OPA1-ADOA allowing structural and functional correlations with the causative OPA1 genotype.

Conclusions:
There are currently no approved treatments for OPA1-ADOA. FALCON will provide data to support the development of the antisense oligonucleotide (STK-002) as the potential disease-modifying treatment for patients with OPA1-ADOA and initiation of the OSPREY phase 1 clinical trial.

References: Yu-Wai-Man P et al. Ophthalmology, 2010; Yu-Wai-Man P, Chinnery PF. Ophthalmology, 2013; Amati-Bonneau P et al. The International Journal of Biochemistry & Cell Biology, 2009.

Abstract Type: Clinical Trial

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Pediatric neuro-ophthalmology, Genetic disease, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease, Retina

Financial Disclosures: Byron Lam: Stoke Therapeutics Consultant; Patrick Yu-Wai-Man: Received research support and/or personal compensation from Santhera Pharmaceuticals, Chiesi, and GenSight Biologics.; Y. Joyce Liao: No; Raghu Mudumbai: No; Marcela Votruba: Stoke Therapeutics; Kelly Saluti: Stoke Therapeutics; Yue Wang: Stoke Therapeutics; Barry Ticho: Stoke Therapeutics; Steven Gross: Stoke Therapeutics

Grant Support: None.

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Factors predictive of recurrence in myelin oligodendrocyte glycoprotein (MOG) associated optic neuritis

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Introduction:
Recurrences may occur in about one third of patients with Myelin Oligodendrocyte Glycoprotein (MOG) associated optic neuritis. However, there is limited prior literature regarding this. The purpose of this study is to identify the factors predictive of recurrences in patients with MOG associated optic neuritis.

Methods:
We reviewed records of patients with seropositive MOG optic neuritis seen at our institute from June 1, 2019, to June 1, 2023. Patients were classified into 2 groups (recurrent, group 1) and non-recurrent (group 2). Data was collected regarding patient demographics, clinical presentation, neurological symptoms, visual function at presentation, neuroimaging findings, and treatment given. We analyzed the difference in factors predictive of recurrence in optic neuritis patients.

Results:
Results: A total of 27 and 21 patients were identified in group 1 (recurrence) and 2 (non-recurrent) respectively. Patients in group 1 tended to be slightly older, median age 37(IQR: 22-48) years vs. 23 (IQR:12-40) years in group B, p=0.07. At presentation, best corrected visual acuity BCVA was 2.5 (IQR: 0.7-3) logMAR and 2 (IQR:0.1-3) logMAR in groups 1 and 2 respectively, (p= 0.88). Pain on eye movements was noted in 64% in group 1 vs. 33% in group 1 (p=0.04). There was no significant difference in frequency of neurological symptoms (12% group A vs. 28% group B, p=0.16), associated papillitis at presentation (p=1), long segment optic nerve involvement (84.2%, group 1 vs. 93.3% group 2, p-0.42) and posterior optic nerve involvement (84.2% group 1 vs. 86.7%, group 2, p=0.84). Univariate analysis showed pain on eye movements, unilateral involvement, not starting immunosuppression at first episode were more frequent in recurrent group.

Conclusions:
Current study suggests that pain on eye movements, unilateral involvement and not starting immunosuppression initially were associated with increased risk of recurrence in MOG associated optic neuritis. However, larger studies are needed to validate these observations.

References: 1. Satukijchai C, Mariano R, Messina S, Sa M, Woodhall MR, et al. Factors Associated With Relapse and Treatment of Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease in the United Kingdom. JAMA Netw Open. 2022 Jan 4;5(1):e2142780. doi: 10.1001/jamanetworkopen.2021.42780. 2.Huda S, Whittam D, Jackson R, Karthikeayan V, Kelly P, et al. Predictors of relapse in MOG antibody associated disease: a cohort study. BMJ Open. 2021 Nov 30;11(11):e055392.

Abstract Type: Epidemiological Study

Keywords: Optic neuritis, Demeylinating disease, Optic neuropathy, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: Inhouse support, no specific funding

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Prevalence and clinical associations of peripapillary hyper-reflective ovoid mass-like structures (PHOMS) in patients with craniosynostosis

Jacqueline Jeon-Chapman [1], Tais Estrela [1], Yoon-Hee Chang [1], Linda Dagi [1], Ryan Gise [1]

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Introduction:
Patients with craniosynostosis are at high risk of developing intracranial hypertension(IH) causing papilledema and secondary optic atrophy. Diagnosing and monitoring optic neuropathy-related vision loss can be challenging because many patients with craniosynostosis have cognitive delay limiting accuracy of testing and competing causes of vision loss. PHOMS are an optical coherence tomography(OCT) feature, possibly a marker of optic neuropathy. In this study, we investigated the prevalence of PHOMS in patients with craniosynostosis and its relationship with visual function and OCT parameters.

Methods:
This retrospective study included 108 eyes(54 patients) with craniosynostosis that had optic nerve head volumetry. OCT volumes were reviewed by two neuro-ophthalmologists, and prevalence of PHOMS was reported. In 56 eyes with two or more OCT volumes at least 6 months apart, univariate generalized estimating equations logistic regression was used to assess the relationship between PHOMS at initial OCT and logMAR visual acuity(VA), spherical equivalent(SE), retinal nerve fiber layer thickness(RNFL), ganglion cell layer volume(GCL), history of IH, and optic nerve fundus findings at the last follow-up.

Results:
The mean age at initial OCT date was 8.9±5.4y.o. and 37/54(68.5%) were female. The prevalence of PHOMS was 31.5%(17/54 patients, 34/108 eyes). Among patients with multiple OCTs, 53.3% of the PHOMS initially observed resolved by last follow-up; these patients were followed for an average of 4.7 years, range 0.6-10.7. PHOMS was significantly associated with history of IH(p=0.037, OR 9.0 95%CI1.1-70.7) and the presence of pallor at the last follow-up (p< 0.001, OR 45.0 95%CI 4.7-428.4).

Conclusions:
Our results showed that eyes with craniosynostosis have a higher prevalence of PHOMS than healthy eyes as shown in a previous study (8.9%). We also demonstrated that PHOMS could disappear over time and we found a significant association between PHOMS and the history of IH and the presence of pallor, supporting an association of PHOMS and prior papilledema.

References: Behrens CM, Malmqvist L, Jørgensen M, et al. Peripapillary Hyperreflective Ovoid Mass-like Structures (PHOMS) in Children: The Copenhagen Child Cohort 2000 Eye Study. Am J Ophthalmol. 2023;245:212-221. doi:10.1016/j.ajo.2022.09.003

Abstract Type: Epidemiological Study

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Optic neuritis, Pediatric neuro-ophthalmology, High intracranial pressure/headache

Financial Disclosures: The authors had no disclosures.

Grant Support: Children's Hospital Ophthalmology Foundation

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Eye Tracking Measures of Oculomotor Function Are Associated with Improvement in Visual Acuity in Children With Cortical/Cerebral Visual Impairment (CVI)

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Introduction:
Cortical/cerebral visual impairment (CVI) is a leading cause of pediatric visual impairment, but limited tools are available for prognostication. The purpose of this study was to evaluate whether eye tracking parameters are predictive of longitudinal changes in visual acuity (VA) in children with CVI.

Methods:
Children with CVI (ages 12 months to 12 years) without nystagmus were prospectively recruited. Participants underwent eye tracking at baseline, 1 month, 6 months, and 12 months. VA was assessed using preferential looking. Oculomotor parameters calculated by the eye tracking software included fixation and saccade latency, duration, and frequency. Hierarchical clustering was used to group recordings based on oculomotor parameters that were significantly associated with VA. Mann-Whitney tests were used to compare VA in the oculomotor groups.

Results:
37 patients (mean age 4.6 years) underwent 106 eye tracking visits; 25 completed at least 6 months of visits. Clustering analysis resulted in 2 oculomotor groups (A and B), which differed significantly in fixation latency (605 vs. 992 ms, $p< 0.0001$), fixation frequency (4.5 vs. 2.5 fixations per trial, $p< 0.0001$), and saccade duration (139 vs. 254 ms, $p< 0.0001$). Oculomotor group was also significantly associated with VA (0.86 vs. 1.3 logMAR, $p=0.0003$). Finally, there was a borderline significant association between oculomotor group and change in visual acuity between the initial and final visits at 6 or 12 months (-0.47 vs. +0.23 logMAR, $p=0.05$).

Conclusions:
Eye tracking analysis of oculomotor function in children with CVI correlates with VA and may predict changes in VA over 6 to 12 months.

References: None provided.

Abstract Type: Epidemiological Study

Keywords: Pediatric neuro-ophthalmology

Financial Disclosures: The authors had no disclosures.

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Platform Session III – Tuesday, March 5th

Diplopia improvement with teprotumumab in patients with high inflammation/recent onset and Low inflammation/longer duration thyroid eye disease (TED)

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[1] Sue Anschutz-Rodgers University of Colorado Eye Center, [2] Amgen Inc

Introduction:
TED often causes diplopia and visual impairment that may worsen without effective treatment. We assessed teprotumumab diplopia responses vs placebo, regardless of baseline diplopia.

Methods:
Data included: phase2/3 (high inflammation TED, CAS≥4/onset ≤9 months) and phase4 (long duration(2-10yr)/low inflammation (CAS≤1) trial subjects, who received teprotumumab/placebo. Baseline change as ordinal response in Gorman diplopia categories with/without baseline diplopia to Week24 noted as improvement (by 1 grade), significant improvement (2-3 grades), no change, worsening (1 grade) or significant worsening (2-3 grades). Proportional Odds Model and Cochran-Mantel-Haenszel tests compared teprotumumab and placebo with any improvement/worsening in the trials.

Results:
Acute/high inflammation TED patients (N=79) were five times more likely to have diplopia improvements vs placebo patients (N=80, Week24): Odds Ratio (OR) 5.17, 95% CI (2.73, 9.78), P<.0001. Significant improvement was observed in 25 (31.6%) vs 6 (7.5%), improvement in 21 (26.6%) vs 12 (15%), no change in 29 (36.7%) vs 44 (55%), worsening in 3 (3.8%) vs 12 (15%) and significant worsening in 1 (1.3%) vs 6 (7.5%) patients. Long duration/low inflammation TED diplopia baseline change at Week24 favored teprotumumab (N=39) over placebo (N=20) but was not significant (OR 2.26, 95% CI (0.42, 12.22), P=.344). For all teprotumumab (N=118) vs placebo (N=100) patients, significant improvement occurred in 27 (22.9%) vs 7 (7%), improvement in 25 (21.2%) vs 13 (13%), no change in 62 (52.5%) vs 61 (61%), worsening in 3 (2.5%) vs 13 (13%) and significant worsening in 1 (0.8%) vs 6 (6%) patients. Diplopia responder rate was significantly higher in teprotumumab vs placebo (difference 28.2%, CI (16.6%, 39.7%), P<.001).

Conclusions:
Combined diplopia teprotumumab/placebo trial data suggests significantly less diplopia worsening and more improvement vs placebo. Comparing trials, significant improvements were observed in the high inflammation patients with teprotumumab vs placebo; improvements in the low inflammation patients were not significant, possibly due to low numbers.

References: None provided.

Abstract Type: Clinical Trial

Keywords: Graves' disease, Orbit/ocular pathology, Adult strabismus with a focus on diplopia

Financial Disclosures: Prem Subramanian: P.S. Subramanian is a consultant for ACELYRIN, GenSight, Horizon (now Amgen), Tourmaline Bio, and Viridian.; Qianhong Fu: Q. Fu is an employee of Amgen (formerly Horizon) and owns stock.; Robert Holt: R.J. Holt is an employee of Amgen (formerly Horizon) and owns stock.

Grant Support: Horizon Therapeutics plc (now Amgen Inc) was the study sponsor, and contributed to study design, data collection, analysis and interpretation, writing, review, approval of final version.

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Clinical Activity and Safety of VRDN-001, a Full Antagonist Antibody to Insulin-like Growth Factor-1 Receptor, in Active and Chronic Thyroid Eye Disease

Kimberly Cockerham [1], Roger Turbin [2], Michael Yen [3], Navdeep Nijhawan [4], Jody Abrams [5], Andrea Kossler [6], Rosa Tang [7], Chantal Boisvert [8], David Kaufman [9], Wendy Lee [10], Raghu Mudumbai [11], Madhura Tamhankar [12], Michael Yoon [13], Shoaib Ugradar [14], Cathy Michalsky [15], Barrett Katz [15]

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Introduction:
Clinical activity and safety of 2 infusions of VRDN-001 were tested in both active thyroid eye disease (TED) and longer-persisting, more refractory chronic TED in phase 2 proof-of-concept studies.

Methods:
Adults with moderate-to-severe active TED (≤12 months, CAS ≥4, n=21) and chronic TED (>12 months, any CAS, n=12) were randomized to 2 infusions 3 weeks apart of VRDN-001 (3, 10, or 20 mg/kg in active TED; 3 or 10 mg/kg in chronic TED). Clinical outcomes were assessed at 6 weeks from preliminary data cuts.

Results:
All doses of VRDN-001 showed clinically meaningful improvements in outcome measures in both TED populations. The exophthalmometry proptosis responder rate (% of patients with ≥2-mm reduction) was 71% (15/21, active) and 42% (5/12, chronic), with a mean proptosis reduction of 2.3 mm (active) and 1.6 mm (chronic). In patients with interpretable scans, MRI/CT measurement showed mean proptosis reduction of 2.8 mm (active, n=16) and 2.0 mm (chronic, n=8). Improvement in diplopia ≥1 on Gorman score occurred for 85% (11/13, active) and 20% (1/5, chronic). VRDN-001 was generally well tolerated with no serious or severe AEs, discontinuations due to AEs, or infusion reactions.

Conclusions:
In active and chronic TED, just 2 infusions of VRDN-001 led to improvements in TED signs and symptoms at 6 weeks. Both datasets are promising given that clinically meaningful changes were observed with a low antibody dose and only 2 infusions. The clinical improvement observed in the chronic cohort is particularly encouraging given the longer duration of disease of 7.8 years. Safety and efficacy of VRDN-001 (5 infusions) will be further assessed in the ongoing THRIVE (active TED ≤15 months, NCT05176639) and THRIVE-2 (chronic TED >15 months, NCT06021054) phase 3 placebo-controlled trials (both allow for non-responders at 15 weeks to roll-over to an open-label treatment study).

References: None provided.

Abstract Type: Clinical Trial

Keywords: Graves' disease, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Orbit/ocular pathology

Financial Disclosures: Kimberly Cockerham: Research support (IIT), medical advisory board and honoraria for speaking: Horizon Therapeutics Phase 1 Clinical Trial PI and medical advisory board: Viridian Pharmaceuticals; Immunovant consultant/advisor and researcher; Roger Turbin: Is a research investigator for Viridian Therapeutics and has received honoraria from Horizon Therapeutics; Michael Yen: Research Investigator for Viridian Therapeutics and consultant/advisor for Ipsen Innovations and Sling Therapeutics; Navdeep Nijhawan: Research investigator for Viridian Therapeutics; Jody Abrams: Clinical research investigator for Viridian Therapeutics and speaker/advisor for Horizon Therapeutics; Andrea Kossler: Research investigator for Viridian Therapeutics, Horizon Therapeutics, and Sling Therapeutics. Consultant/advisor for Horizon Therapeutics, Immunovant, Genetech, Argenx, Acelyrin, Axogen Inc.; Rosa Tang: Viridian research investigator and consultant Horizon research investigator Serono EMD speaker honoraria ALEXION consultant; Chantal Boisvert: Research investigator for Viridian Therapeutics and OVID Therapeutics; David Kaufman: Research investigator for Viridian Therapeutics; Wendy Lee: Research investigator for Viridian Therapeutics; Raghu Mudumbai: No; Madhura Tamhankar: Clinical research investigator for Viridian Therapeutics and Horizon Therapeutics; consultant for UptoDate; Michael Yoon: Research investigator for Viridian Therapeutics; Shoaib Ugradar: Consultant for Viridian Therapeutics and was a consultant for Valenza Bio within past 24 months but not currently; Cathy Michalsky: Employee of Viridian Therapeutics; Barrett Katz: Employee of Viridian Therapeutics

Grant Support: None.

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Binocular Visual Function Testing in an Alzheimer's Disease Research Center (ADRC) Cohort: Low-Contrast Letter Acuity and Rapid Automatized Naming (RAN) Tasks of MULES and SUN

Lauren Seidman [1], Sara Hyman [1], Steven Galetta [1], Arjun Masurkar [1], Laura Balcer [1]

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Introduction:
Binocular vision testing, performed with both eyes uncovered, is useful for reflecting daily activities. Low-contrast letter acuity (LCLA), the Mobile Universal Lexicon Evaluation System (MULES, rapid picture naming) and the Staggered Uneven Number (SUN, rapid number naming) have been used successfully in studies of multiple sclerosis, concussion and Parkinson's disease. We determined the capacity for LCLA, MULES and SUN, to distinguish patients with mild cognitive impairment (MCI) due to Alzheimer's disease and Alzheimer's dementia (AD) vs. cognitively normal controls.

Methods:
Participants were invited at a single-institution ADRC; all had diagnoses of MCI or AD by NIA-AA criteria, or were cognitively-normal controls. Low-contrast acuity was tested at 2.5% and 1.25%. MULES and SUN were administered using paper/pencil and computerized tablet (Mobile Integrated Cognitive Kit [MICK] app).

Results:
There were 75 participants (31 MCI, 10 AD, 34 controls; aged 74±6 years). LCLA scores at 2.5% were significantly lower (worse) in MCI vs. controls (28 vs. 36 letters, p=0.02, two-sample t-test); this was similar for 1.25% (5 letters for MCI vs. 12 for controls, p=0.004). MULES times were slower (worse) in MCI compared with controls using the tablet (75 sec for MCI vs. 60 for controls, p=0.03), and for AD vs. controls for both paper/pencil (152 vs. 59 sec, p=0.0001) and tablet (100 vs. 60 sec, p=0.003). SUN test scores, on the other hand, did not differ between MCI and controls, but better distinguished AD vs. controls for both paper/pencil (84 vs. 56 sec, p=0.0001) and tablet (85 vs. 60 sec, p=0.003).

Conclusions:
Binocular low-contrast acuity, MULES and SUN have potential roles in MCI and AD in a manner similar to multiple sclerosis and are analogous to patient-specific measures such as cognition. MULES, SUN and LCLA likely complement eye-specific measures and may promote identification of MCI for early participation in clinical trials and for disease-modifying therapies.

References: Park G, Balcer MJ, Colombo JR, Hasanaj L, Joseph B, et al.; The MICK (Mobile Integrated Cognitive Kit) App: Digital rapid automatized naming for visual assessment across the spectrum of neurological disorders, J Neurol Sci, 434, 120150, 2022. Dahan N, Moehringer N, Hasanaj L, Serrano L, Joseph B, et al.; The SUN test of vision: Investigation in healthy volunteers in comparison to the Mobile Universal Lexicon Evaluation System (MULES), J Neurol Sci, 415, 116953, 2020. Conway J, Ilardi M, Gonzalez C, Dahan N, Fallon S, et al.; Rapid picture naming in Parkinson's disease using the Mobile Universal Lexicon Evaluation System (MULES), J Neurol Sci, 410, 116953, 2020. Balcer LJ, Raynowska J, Nolan R, Galetta SL, Kapoor R, et al.; Validity of low-contrast letter acuity as a visual performance outcome measure for multiple sclerosis, Mult Scler 23, 734-747, 2017. Balcer LJ, Galetta SL, Calabresi PA, Confavreux C, Giovannoni G, et al.; Natalizumab reduces visual loss in patients with relapsing multiple sclerosis, Neurology, 68, 1299-1304, 2007.

Abstract Type: Epidemiological Study

Keywords: Higher visual functions, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease

Financial Disclosures: Lauren Seidman: No; Sara Hyman: No; Steven Galetta: No; Arjun Masurkar: No; Laura Balcer: Editor in Chief, Journal of Neuro-Ophthalmology

Grant Support: None.

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Curiouser and curiouser: a distributed brain network underlying Alice in Wonderland syndrome

Maximilian Friedrich [1], Jared Nielsen [2], Amalie Chen [1], Michael Ferguson [1], Michael Fox [1], Sashank Prasad [3]

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Introduction:
Inspired by the Lewis Carroll classic, the term Alice in Wonderland syndrome (AIWS) refers to a fascinating disorder characterized by altered perception of the dimensions of one's body and objects in surrounding space. Migraine is a frequent cause, but similar symptoms can occur following focal brain lesions, providing a unique window into the neuroanatomical localization of higher order perceptual functions. Here, we sought to test whether lesions causing AIWS map to a common neuroanatomical substrate.

Methods:
36 cases of AIWS associated with a focal brain lesion were identified in a systematic literature search. Lesions were mapped onto a reference brain atlas. The distributed functional network associated with the lesion location from each case was computed using a database of resting state fMRI derived from 1000 subjects. Regions of overlap across the structural lesions and the associated lesion-based functional network maps were identified. To establish specificity, the resulting lesion networks were compared to >800 individual lesion-based networks associated with >30 other neuropsychiatric disorders.

Results:
While only 11% of structural lesions demonstrated spatial overlap, >85% of lesions were functionally connected to the same distributed brain network. This network was centered on the fusiform gyrus, frontal cortex, and parietal cortex, regions known to play a role both in visual perception and body image. This connectivity pattern was specific to AIWS when compared to control lesion networks from other neuropsychiatric conditions (voxel-wise FWE $p < .05$).

Conclusions:
Despite phenotypical and neuroanatomical diversity, lesion-induced AIWS maps to a common and specific neural network. These findings lend new insight into the integrated and interdependent nature of visual and bodily perception.

References: None provided.

Abstract Type: Clinical Trial

Keywords: Higher visual functions, Neuroimaging

Financial Disclosures: Maximilian Friedrich: No; Jared Nielsen: No; Amalie Chen: No; Michael Ferguson: No; Michael Fox: M.D.F. was supported by the Nancy Lurie Marks Foundation, the Mather's Foundation, the Ellison/Baszucki Foundation, the Kaye Family Research Endowment and National Institutes of Health grants R21 MH126271, R56 AG069086, R01 MH113929, R01 MH115949, and R01 AG060987. M.D.F. is a consultant for Magnus Medical and Soterix and holds intellectual property on using connectivity imaging to guide brain stimulation; Sashank Prasad: No

Grant Support: None.

Contact Information: Dr. Maximilian U. Friedrich, MD, mfriedrich1@bwh.harvard.edu

Permanent Transduction of Retinal Ganglion Cells by Injection of rAAV2-retro into the Superior Colliculus

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Introduction:
Injection of rAAV2-retro into the superior colliculus offers a potential route for delivery of therapeutic genes to ganglion cells. This approach eliminates the barrier posed by the internal limiting membrane, a major problem following intravitreal virus injection. However, it is unknown for how long the gene product continues to be expressed by ganglion cells.

Methods:
4 rats received bilateral injections of a 1:1 mixture of rAAV2-retro-hSyn-EGFP and rAAV2-retro-hSyn-mCherry into the superior colliculus under electrophysiological guidance. Serial fundus imaging was performed with a Micron IV camera to compare ganglion cell labelling at 14, 45, 211, and 375 days after injection.

Results:
The number of ganglion cells labeled by EGFP and/or mCherry in baseline fundus images obtained after virus injection ranged between 59 and 1474. Variability occurred because tracer injection sites varied in size and location within the retinotopic map. At day 375 a mean of 93% of EGFP-positive cells and 96% of mCherry-positive cells imaged at baseline were still brightly fluorescent and unequivocally identifiable (n = 8 retinas).

Conclusions:
The expression of reporter genes by ganglion cells transduced by rAAV-2 retro is essentially perpetual, at least in the context of a rat's lifespan. Serial imaging of labeled ganglion cells showed a slight decline (4-7%) over a year. However, fundus pictures showed that in every case, apparent loss of a labeled cell could be attributed to slight image defocus or incorrect light exposure. No convincing example was detected of a ganglion cell that had ceased to be labeled by EGFP or mCherry. This result suggests that a therapeutic gene, if effective, would likely convey long-lasting benefit following delivery via injection of rAAV-2 retro into a retinal target nucleus.

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Abstract Type: Basic Science

Keywords: Genetic disease, Optic neuropathy, Retina

Financial Disclosures: The authors had no disclosures.

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Vision-Related Quality Of Life In LHON Patients Treated With Lenadogene Nolparvovec Gene Therapy: Analysis Of The NEI-VFQ-25 Using Rasch Measurement Theory

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Introduction:
The impact of gene therapy on vision-related quality of life (VRQoL) in Leber hereditary optic neuropathy (LHON) was previously investigated in three pivotal Phase III clinical trials (RESCUE, REVERSE, REFLECT) using the National Eye Institute Visual Function Questionnaire (NEI-VFQ-25). The purpose of this study was to use Rasch measurement theory to evaluate changes in VRQoL in participants of RESCUE, REVERSE, and REFLECT.

Methods:
Rasch analysis was conducted using NEI-VFQ-25 responses from participants at baseline (n=174) and two years after treatment (n=153). The scoring structure of the NEI-VFQ-25 at baseline was assessed to determine the fit of the data to the Rasch model. A post-hoc revision of the scoring structure was created and psychometrically re-evaluated. Finally, stacked analysis in the Rasch model was conducted to compare Rasch-revised scores at baseline and two years.

Results:
Using the original scoring structure, the mean composite VFQ-25 score significantly improved by 7.2±1.9 after gene therapy, from 45.1±15.5 at baseline [95%CI: 3.4-10.9, P< 0.0001)]. However, the NEI-VFQ-25 exhibited multiple issues including limitations in response functioning and scale dimensionality, making the composite VFQ-25 score misleading. These issues were rectified by revising the NEI-VFQ 25 into two unidimensional scales measuring “Vision-related Activity Limitation” [VAL] and “Socioemotional Functioning” [SEF]. Participants’ mean VAL score at baseline on a Rasch-transformed 0-100 scale was 50.9, improving to 52.7 at two years after treatment [F(1, 325) = 1.62, P=0.20]. On the SEF scale, there was a significant difference two years after treatment, with participants improving from a mean score of 39.4 at baseline to 45.9 [F(1, 325) = 16.97, P< 0.001].

Conclusions:
The scoring structure of the original NEI-VFQ-25 has limitations that undermine its psychometric validity as a measure of VRQoL. Using the Rasch-revised NEI-VFQ-25, we determined that improvement in VRQoL after treatment with lenadogene nolparvovec was driven predominantly by an improvement in socioemotional functioning.

References: None provided.

Abstract Type: Clinical Trial

Keywords: Genetic disease, Optic neuropathy

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Grant Support: None.

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Neuro-ophthalmological Phenotype And Correlations With Heteroplasmy Levels In MELAS And MERRF Syndromes.

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Introduction:
A critical threshold of mutant mtDNA is necessary to manifest symptoms both in carriers of the Mitochondrial myopathy, Encephalopathy, Lactic Acidosis and Stroke-like episodes (MELAS)-associated m.3243A>G/MT-TL1 mutation and Myoclonic epilepsy with ragged-red fibers (MERRF)-associated m.8344A>G/MT-TK mutation. However, a correlation between heteroplasmy and specific clinical phenotypes is poorly documented. We performed a prospective study to compare neuro-ophthalmological features in MELAS and MERRF and correlate them with heteroplasmy levels.

Methods:
We evaluated 33 MELAS and 8 MERRF patients. Mutant load was assessed on peripheral blood, urinary sediment and skeletal muscle. A comprehensive neuro-ophthalmological assessment included Optic Coherence Tomography (OCT) to measure retinal nerve fiber layer (RNFL) and ganglion cell layer (GCL) thickness. Demographic data and heteroplasmy levels were compared using Mann-Whitney test. Neuro-ophthalmological results were analyzed with Clustered Wilcoxon rank-sum test. Pearson's correlation was used to relate heteroplasmy to neuro-ophthalmological data.

Results:
Retinopathy was the most common neuro-ophthalmological manifestation in 17/33 (51%) MELAS patients, while optic atrophy was present in 7/8 (87%) MERRF patients, reflecting in significantly thinner RNFL compared to MELAS (p=0.021). Heteroplasmy in MERRF was significantly higher than MELAS in blood (p< 0.001) and muscle (p=0.049). A significant negative correlation between blood heteroplasmy with age was confirmed in MELAS (p=0.011), warranting for a correction, but not in MERRF (p=0.430). We failed to demonstrate significant correlations between heteroplasmic mutant load and neuro-ophthalmological findings in MELAS, while heteroplasmy was negatively correlated with both RNFL (p=0.002) and GCL (p=0.030) thickness in MERRF.

Conclusions:
MELAS and MERRF patients present a distinct ocular phenotype, respectively retinopathy in MELAS and optic atrophy in MERRF, the latter correlating with mtDNA heteroplasmy levels. This may reflect a selective susceptibility of different retinal cell types, photoreceptors in MELAS and retinal ganglion cells in MERRF, in possible relation to a global energy defect in MELAS as opposed to predominant oxidative stress in MERRF.

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Abstract Type: Epidemiological Study

Keywords: Genetic disease, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Optic neuropathy, Retina

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Electric Field Stimulation Enhances Ciliary Neurotrophic Factor-Mediated Retinal Ganglion Cell Axon Regeneration After Optic Nerve Crush Injury

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Introduction:
Neuro-restoration requires strategies that both promote neuronal survival and direct axon growth—processes that are independently regulated. Phase I trial recently demonstrated safety with chronic administration of neuroprotective molecule ciliary neurotrophic factor (CNTF). Our prior work showed that electric field (EF) stimulation directs target-specific regeneration of retinal ganglion cell (RGC) axons after crush injury. Here, we evaluated for synergistic effects from CNTF and EF stimulation on RGC axon regeneration.

Methods:
Adult Long-Evans rats underwent optic nerve crush injury (ONC) with electrode implantation. AAV2-CNTF, CNTF protein, and cAMP were administered intravitreally after ONC. One week later, EF stimulation was initiated and continued for 30 days. RGC survival, RGC axon regeneration, RGC electrophysiologic function, and recovery of visual behaviors were assessed. Four groups are assessed in this study: CNTF+EF (n=3), CNTF alone (n=2), EF alone (n=3), and untreated (n=3).

Results:
CNTF+EF treatment demonstrated 3.77% ± 1.86% axon regeneration 250µm past the crush site (n=3), compared to CNTF alone with 1.5% ± 1.84% (n=2). EF alone demonstrated 20.13% ± 1.86% (n=3) while 0.56% ± 0.9% was observed in untreated rats (n=3). Normalized N95 peak amplitude on pattern electroretinogram (PERG) was 0.23 ± 0.18 in CNTF+EF (n=3), 0.38 ± 0.007 in CNTF only (n=2), 0.66 ± 0.14 in EF only (n=3), and 0.30 ± 0.16 in untreated (n=3).

Conclusions:
Preliminary data show that EF application enhances gains mediated by CNTF but combinatorial treatment is not superior to EF alone. Optical medial opacity due to intravitreal injections likely contributed to the findings. More data is currently being collected.

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Abstract Type: Basic Science

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295	Prognosis of Non-Arteritic Anterior Ischemic Optic Neuropathy (NAION)	Meital Ben Dov	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
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306	The natural history of Leber hereditary optic neuropathy in the subacute/dynamic phase: Visual acuity outcomes from the historical Case Record Survey-2 (CRS-2)	Diviya Gorsia	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
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330	Outcomes Of Idiopathic Intracranial Hypertension Patients on Glucagon-Like Peptide-1 Receptor Agonist Therapy	Matthew Elitt	Idiopathic Intracranial Hypertension (IIH)
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361	T2-Lesion analysis in Myelin Oligodendrocyte Glycoprotein Associated Disease Optic Neuritis	Deena Tajfirouz	Neuro-Imaging
362	A Comparison of Outcomes Between Two Techniques for Optic Nerve Sheath Fenestration	Kendall Hughes	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
363	Analysis of clinical features and outcomes in patients with ocular myasthenia gravis according to anti-acetylcholine receptor antibody-seropositivity: a retrospective cohort study	Byung Joo Lee	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
364	Analysis of Peripapillary Vessel Density in Ethambutol-induced Optic Neuropathy Using Optical Coherence Tomography Angiography	Donghun Lee	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
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Ocular Post-Mortem Analyses with Histopathological and Molecular Assessments in Leber Hereditary Optic Neuropathy Following AAV2 Gene Therapy

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Introduction:
Leber hereditary optic neuropathy (LHON) is a rare disease that causes severe vision loss. Lenadogene nolparvovec is a novel AAV2 gene therapy for LHON patients carrying the m.11778G>A MT-ND4 mutation.

Description of Cases:
Two patients with MT-ND4 LHON, participating in the RESCUE clinical study, received an intravitreal injection of AAV2-ND4 in one eye and a sham injection in the other. During the study, both patients developed intraocular inflammation in the treated eye within 2 months of gene therapy: one patient had moderate inflammation in the anterior chamber and vitreous, while the other had mild vitritis; both events resolved within months. Patient 1 died of acute alcohol toxicity and the other (patient 2) of cardiac arrest. Post-mortem molecular (ddPCR) analyses of the eyes were conducted. For patient 1, there was noted an angiocentric lymphocytic chronic inflammation at the optic nerve head and in the temporal retina. This was not seen in patient 2. In patient 1, AAV2-ND4 distribution was asymmetric in the treated eye, most prevalent in temporal retinal ganglion cells, sparse in photoreceptors, and absent in optic nerve, vessels, retinal pigmented epithelium, and choroid. A much lower level of AAV2-ND4 was detected in the retina of the untreated eye.

Conclusions, including unique features of the case:
This is the first postmortem study of human eyes unilaterally injected with AAV2-based gene therapy. In one patient, there was persistent inflammation and AAV2-ND4 retinal transfection was evident in the injected eye and detected at a much lower level in the contralateral eye. The analysis of eyes, nerves, optic chiasm and optic tracts, available from patient 2, may confirm and better characterize this transfer.

References: None provided.

Keywords: Optic neuropathy, Retina, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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Association Between Childhood Vision Impairment and Dementia Onset in Later Life

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Introduction:
To examine the association between childhood visual impairment (VI) and a positive screen for dementia in adulthood.

Methods:
Screening data for dementia was collected from survey respondents who were 65 years old or older in the 2017 wave of the Panel Study of Income Dynamics (PSID). The study included 1,029 eligible participants who also had information on VI, which included having trouble seeing even when wearing glasses before the age of 17, as part of the Childhood Retrospective Circumstances Survey supplement. Data was gathered on dementia screening using the AD8 test, which has 8 questions that help distinguish between normal cognition and dementia. We used adjusted logistic regression models to determine the ability of childhood VI to predict dementia while adjusting for race, education, income, overall health status, heart disease, smoking history, alcohol use, and physical activity.

Results:
Our analysis included 1,029 participants (37.61% females). All participants were over the age of 65. A majority of the participants were white (74.44%) with an average household income of $68,820. We found that 11.18% of patients reported trouble seeing even when wearing glasses before the age of 17 with 21.09% having a positive dementia screen in adulthood. We found that a significantly greater number of patients with a history of VI in childhood went on to have a positive dementia screen in adulthood than those without a history of VI (30.43% vs 19.91%, $p< 0.01$). A logistic regression model adjusting for confounders found that there was a 1.62 increased odds (CI, 1.05-2.50) of developing dementia in those with a history of VI in childhood ($p=0.03$).

Conclusions:
The findings suggest a correlation between childhood VI and the later onset of dementia. This underscores the potential utility of early-life impairment as predictors for dementia in adulthood. Further research is required to explore underlying mechanisms.

References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Miscellaneous

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Retinal Color Fundus Photography and Machine Learning can Discriminate Alzheimer's Disease

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Introduction:
Alzheimer's disease (AD) has rising incidence and vast socio-economic impact. We have previously shown that certain retinopathy features are associated with AD-specific cognitive decline and neuroimaging measures. To overcome the subjectivity and inefficiency of color fundus photographs (CFP) manual analysis, we employed a deep neural network approach to classify and extract AD biomarkers from CFPs. We further enhanced our automated AD discrimination tool by comparing the accuracy of neural networks using images from single versus both eyes and employing vessel segmentation versus binary vessel segmentation.

Methods:
A pre-trained U-Net-based architecture was used to segment the 45-degree macula and optic disc-centered CFPs from 118 AD and 129 cognitively intact individuals. The segmented vessel results, and binary vessel segmentation results were imputed into the U-Net encoder for feature extraction. Weakly supervised localization and Gradient-weighted Class Activation Mapping were used to determine the AD classification performance (AUC-ROC). AD-specific biomarkers were extracted from the CFPs-derived heat-maps.

Results:
After data curation, we obtained 318 binary vessel segmentation images and 338 vessel segmentation images (116 AD subjects). The control group included 259 images (129 subjects). The overall vessel segmentation group' accuracy was 95% (120 testing, 476 training images) and binary vessel segmentation group' accuracy was 88% (116 testing, 460 training). The accuracy of the segmented and binary segmented images in the right eye (97.7% and 90.7%) was similar with the left eye (86.4% and 97.7%). Vessel segmentation for both eyes had an accuracy of 97.7%. The generated heatmaps pointed-out to vascular changes in the retinal mid-periphery in AD.

Conclusions:
In a large dataset of AD-derived CFPs, no significant differences were noted between single versus both eyes, favoring vessel segmentation (maximal accuracy 97.7%) over binary vessel segmentation. This multiple group analysis mitigates the impact of fortuitous occurrences in neural networks, enhancing our results accuracy.

References: None provided.

Keywords: Neuroimaging, Retina, Higher visual functions

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Retinal microstructural changes and ApoE polymorphism in predicting treatment-associated cognitive dysfunction in patients with low-grade gliomas

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Introduction:
Treatment-associated cognitive dysfunction (TACD) is the most common neurologic sequelae in patients with low-grade gliomas (LGGs). Retinal microvascular changes can reflect cognitive status. ApolipoproteinE (ApoE) ε4 polymorphism is the most susceptible genetic factor for dementia. This study explores the role of retinal features and ApoE polymorphism in predicting TACD in LGG patients.

Methods:
We assessed Montreal Cognitive Assessment (MoCA) scores in a cohort of LGG patients in 6 months intervals. ApoE genotyping was performed, and retinal nerve fiber layer (RNFL), ganglion cell complex (GCC) thicknesses, radial peripapillary capillary density (RPC), inner and outer retinal microvasculature densities, and foveal avascular zone (FAZ) were obtained. A machine learning (ML) algorithm was established to predict the development of TACD using ApoE and ophthalmic features. Normal controls were recruited from convenient sampling.

Results:
15/44 patients with LGGs were eligible and consented. 12/15 (80%) had frontotemporal tumors. Median time from diagnosis to the first eye exam was 35 months (2-266) and 27.5 months (0-219) from radiation. MoCA was normal (≥26/30) in 7/15 (46.7%) patients; scores varied significantly based on tumor location (frontal vs. temporal, p=0.0054) and pathology (oligodendroglioma vs. astrocytoma, p=0.0012). ApoE genotyping showed: two ε2/ε3 (13.3%), six ε3/ε3 (40%), one ε3/ε4 (13.3%). 13/15 (86.7%) had normal visual acuity (>20/40), 6/15 (40%) had a visual field defect (MD<-2.0). 14/15 patients had normal RNFL and 6/15 (40%) had GCC thinning. Decreased RPC was seen in LGG patients than controls ($p < 0.0001$). The eye ipsilateral to radiation field in frontotemporal lobe tumors demonstrated significantly enlarged FAZ 3 years after radiotherapy ($p< 0.05$), suggesting radiation spilling over effect. Linear regression ML model identified FAZ as a standout MoCA score predictor.

Conclusions:
Retinal changes and ApoE polymorphism can serve as potential surrogate markers to predict TACD. A larger study is warranted to validate the model and inform management of LGG patients.

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Keywords: Chemotherapy and radiation injury, Tumors, Genetic disease, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease

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Adolescent traumatic optic neuropathy: Recognizing a role for glia in axon injury signaling using a murine model of brain injury.

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Introduction:
Traumatic brain injuries (TBI) comprise 1/3rd of all injury related deaths in the United States, with traumatic axonal injury (TAI) as one of the most devastating underlying pathologies. Traumatic optic neuropathy (TON) is a type of TAI that occurs with high incidence after TBI and can result in irreversible visual dysfunction. TON involves both oxidative and endoplasmic reticulum (ER) stress that is more severe in adolescent mice.1, 2 While secondary mechanisms of distal axon injury and somal responses are well studied (e.g., Wallerian degeneration3, 4), little is known about signaling between the axonal injury site and the soma.5 We hypothesize is that ER and OxStress influence each other in a reciprocal relationship that is unique to the proximal axon vs. the soma.

Methods:
Using an adolescent mouse model of closed-head weight-drop TBI, we prevented ER (Salubrinal & ISRIB [insert dose]) or oxidative stress (Edaravone 3mg/kg ip) then separately dissected retinal ganglion cell soma, proximal optic nerves, and distal optic tracts.

Results:
Western blotting revealed ER stress in the retina and optic nerve; however, immunofluorescent assessment clarified that “nerve” ER stress is primarily isolated to the soma of glial cells (grp78 and ATF4) while oxidative stress (MitoSOX Red) is more abundant in axons. Preliminary results suggest that microglia express higher levels of ER stress while oligodendrocytes contain almost no positive signal; and there is significantly less ER stress present in TUJ1+ RGC axons. We are still determining whether interventions alter glial vs. axonal responses in the retina and how interventions alter this.

Conclusions:
Although RGC axons are injured after TBI, glial cells appear more responsible for ER stress in the nerve. After analysis of how interventions alter these pathologies between regions, we hope to explain why some therapies do not work as well when translated from bench to bedside.

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Keywords: Optic nerve trauma and treatment, Optic neuropathy, Pediatric neuro-ophthalmology, Retina, Trauma

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Contact Information: None provided.

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Aging is Associated with Increased Reactive Gliosis and Accelerated Retinal Ganglion Cell loss after Optic Nerve Crush Injury.

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Introduction:
Mechanisms related to aging and astrocyte reactivity in optic neuropathies are poorly understood. Astrocytes, which interact closely with retinal ganglion cells (RGC), can produce a maladaptive microenvironment in response to injury and exacerbate RGC death and axonal loss. Here, we utilized an optic nerve crush (ONC) injury model to test the hypothesis that aging increases susceptibility to RGC loss and retinal glial cell reactivity after optic nerve injury.

Methods:
Young (3-month-old) and aged (16-month-old) wild-type mice (n=6/group) underwent unilateral ONC by implementation of self-closing forceps 1mm posterior to the globe for 1 second. Injured and fellow uninjured eyes were collected on post-injury day (PID)-3 and PID-7. Retinal whole mounts were prepared and stained for RGC-specific marker Rbpms and glial-specific markers S100B and GFAP. To investigate candidate pathways and mechanisms for differentiated injury response in aged animals, whole retina transcriptomics were performed on PID-3.

Results:
Cell counts revealed a significant decrease in RGC density after ONC injury on PID-3 among aged but not young mice. By PID-7, young and aged animals both demonstrated significant loss of RGC, without significant difference between age groups. At uninjured baseline, aged animals demonstrated a significant decrease in S100B cell density and GFAP reactivity compared to young animals. In response to injury, significant increases were seen in S100B cell density on PID-7 in both young and aged animals, but GFAP reactivity was significantly increased on PID-7 in aged animals alone. Whole retina transcriptomics on PID-3 revealed early differential molecular changes that occur in aged animals in response to injury, with notable differences in chemokine signaling pathways mediated specifically by glial cells.

Conclusions:
Age-related acceleration of neurodegenerative RGC loss after optic nerve injury is associated with increased reactive gliosis. Compelling molecular transcriptomic changes in the retina after optic nerve injury suggest an interaction between RGC and glial cell responses.

References: None provided.

Keywords: Optic neuropathy, Optic nerve trauma and treatment

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Cerebral angiographic features of Ophthalmic Artery in patients with central retinal artery occlusion and its influence on intra-arterial thrombolysis

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Introduction:
In this study, cerebral angiography was used to observe the features of the OphA in CRAO patients.

Methods:
There were 56 patients with non-arterial CRAO who underwent cerebral angiography consecutively included, and the demographic characteristics, vascular risk factors, and cerebral angiographic of the patients were recorded in detail. The course of the OphA was classified as type A, type B and type C according to its cerebral angiographic morphology. It was divided into the proximal group and the distal group depending on whether the OphA originated from the proximal opthalmic segment of theinternal carotid artery(ICA), and the differences in the OphA-ICA angle, the course and the diameter of theOphA, and the proportion, the operation time and the complications of the IAT between the two groups were compared.

Results:
Analysis of the cerebral angiographic features showed that the OphA was supplied by the ICA in 50 cases and the external carotid artery (ECA) in 6 cases, respectively, among which 45 cases were treated by anterograde IAT via the ICA (including 21 caseswith proximal OphA microcatheterization) and 2 cases by retrograde IAT via the ECA. Further analysis of the cerebral angiographic features of the OphA originating from the ICA, the results showed that the mean OphA-ICA angle was 81.8±25.2°, the course was type A, type B and type C in 26, 16 and 8 cases, and the OphA had no stenosis, mild-grade stenosis and moderate to high-grade stenosis in 36, 9 and 5 cases, with a mean diameter of 1.0±0.3mm. Compared with the distal group, patients in the proximal group had a larger OphA-ICA angle, a more varied course, and a shorter operation time.

Conclusions:
To recognize the cerebral angiographic features of the OphA in CRAO patientsis helpful to identify the blood supply of the OphA and select an individualized surgical path for IAT.

References: None provided.

Keywords: Interventional neuroradiology, Stroke, Vascular disorders, Retina

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Grant Support: None.

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Challenging ICD-10 Search Methodology in the Context of Sequential Ischemic Optic Neuropathy

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Introduction:
The validity of clinical research conducted with healthcare claims databases depends on the accuracy of the applied ICD (International Classification of Diseases) codes.

Methods:
Medical records from January 2016 to February 2023 in a U.S. tertiary care center were retrospectively analyzed. The selection criteria identified patients with ICD codes for ischemic optic neuropathy “H47.013”, “H47.012,” and “H47.011” and records with the keywords "ischemic optic neuropathy" or "NAION". Manual review of these records confirmed the diagnosis of sequential non-arteritic anterior ischemic optic neuropathy (sNAION). The results of the manual review were compared to those found by the more broad ICD codes and text-based searches. A sensitivity analysis of accuracy and precision compared the two methodologies.

Results:
A total of 1720 cases with ICD code H47.011 (right eye optic neuropathy) were found (467 unique patients). Similarly, for H47.012 (left eye optic neuropathy), we identified 1562 cases, (417 unique patients). Bilateral ischemic optic neuropathy (H47.013) revealed 1191 cases, (305 unique patients). Text-based searches identified 317 unique patients for each term. In total, we identified unique 462 unilateral and 198 sequential NAION cases. Using ICD codes alone, we would have missed 33 (of 198) sNAION. The errors were due either to wrong-eye eye codes or lack of assigning the correct code; the latter were found via our text-based search. The results of our sensitivity analysis showed an accuracy of 0.83 [95% CI of 0.774, 0.883] and p value of 0.5463, i.e. the ICD code method was precise but not accurate.

Conclusions:
Our study underscores the limitations of using only ICD codes and the value of performing a comprehensive manual search. This lack of accuracy with ICD searches would be compounded with extremely large databases, like the Medicare database.

References: None provided.

Keywords: Optic neuropathy

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Contact Information: None provided.

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Circadian rhythm disruption in bilateral optic neuropathies

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Introduction:
Recent work has indicated that optic neuropathies can cause death of melanopsin-expressing photosensitive retinal ganglion cells (pRGCs), which entrain mammalian circadian rhythms and align the sleep-wake cycle. It remains unknown whether optic neuropathies cause measurable disruption of sleep or circadian rhythms in humans. We performed a cross-sectional study to evaluate the impact of bilateral optic neuropathies, on subjective and objective measures of sleep quality and circadian rhythms.

Methods:
Adult patients with confirmed diagnoses of unilateral or bilateral optic neuropathies were recruited. Subjective sleep quality was evaluated using the Pittsburgh Sleep Quality Index (PSQI), a validated sleep questionnaire. Participants were asked to complete ≥ 14 days of continuous non-invasive wristwatch actigraphy, which measures locomotor activity as a surrogate for sleep and activity rhythms. Interdaily stability, which measures the degree of regularity in the activity-rest cycle, was measured from 0 to 1. A value of 0 indicates a total lack of regularity, while 1 indicates a perfectly stable rhythm. Total sleep time, sleep efficiency (total sleep time/time in bed), sleep latency, fragmentation index (degree of sleep fragmentation), and intra-daily variability (degree of fragmentation of activity-rest periods) were also assessed.

Results:
19 patients with bilateral optic neuropathies (mean age 48±22 years, 50% female) and 12 patients with unilateral optic neuropathies (mean age 54±16 years, 58% female) completed actigraphy. Bilateral patients (n=19) demonstrated significantly lower interdaily stability than unilateral patients (n=10) (mean difference -0.111; 95% CI: -0.196 to -0.026; p=0.013). Total sleep time, sleep efficiency, sleep latency, fragmentation index, intra-daily variability and PSQI scores were not significantly different between groups. Linear regression analysis confirmed the difference in interdaily stability after adjustment for age and gender.

Conclusions:
Bilateral optic neuropathy patients demonstrated significantly reduced interdaily stability compared to unilateral optic neuropathy patients, indicating measurable circadian rhythm dysfunction.

References: None provided.

Keywords: Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Clinical Characteristics and Treatment Effects of Chronic Immunotherapy in Idiopathic Recurrent Papillitis and Idiopathic Recurrent Neuroretinitis: A Multi-center Retrospective Analysis

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Introduction:
Idiopathic recurrent neuroretinitis is described by recurrent attacks of optic disc edema and macular star. Idiopathic recurrent papillitis presents with recurrent attacks of disc edema without macular star. We sought to better characterize the clinical features of idiopathic recurrent papillitis in comparison to idiopathic recurrent neuroretinitis, including the treatment effects of chronic immunotherapy.

Methods:
This is a multi-center retrospective review of 30 patients with either idiopathic recurrent papillitis or idiopathic recurrent neuroretinitis (all without retrobulbar enhancement of the optic nerve during the acute attack). Gender, race, age at first attack, number of attacks, and number of attacks on chronic immunotherapy were recorded. For patients who started immunotherapy, annualized relapse rates (ARR) on and off chronic immunotherapy were calculated.

Results:
Among 30 patients, 18 (60.0%) patients had neuroretinitis attacks at least once, and 12 (40.0%) patients had only papillitis attacks. Among patients with neuroretinitis, 10 (55.6%) patients also had attacks of papillitis without neuroretinitis. The median number of attacks for all patients was 4 (IQR 2, 3-5). Twelve (66.6%) patients in the neuroretinitis group were female compared to four patients (33.3%) in the papillitis group (p=0.07). The average age at first attack was 37.3 years for the neuroretinitis group and 37.7 years for the papillitis group (p=0.95). Nineteen (63.3%) patients were initiated on chronic immunotherapy, of which nine (47.4%) relapsed with an average ARR of 0.40 attacks/year. This was lower than the average ARR off chronic therapy (0.84 attacks/year), but not statistically significantly different (p=0.08).

Conclusions:
We describe the clinical features of idiopathic recurrent papillitis in comparison to idiopathic recurrent neuroretinitis, which may be the same disease process with some patients having both papillitis and neuroretinitis. There was a trend toward chronic immunotherapy reducing the number of relapses in idiopathic recurrent papillitis/neuroretinitis.

References: None provided.

Keywords: Optic neuropathy, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Comparison of OCT Findings in Compressive Optic Neuropathy and Primary Open Angle Glaucoma

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Introduction:
Primary open angle glaucoma (POAG) and compressive optic neuropathy (CON) may present similarly with painless, slowly progressive visual field loss, thinning of the retinal nerve fiber layer (RNFL), and lack of optic disc edema. This study compares RNFL optical coherence tomography (OCT) characteristics in patients with CON versus POAG.

Methods:
An electronic medical record from an academic tertiary care center was queried for ICD-10 diagnosis of POAG, peri-optic mass lesions, or cerebral aneurysm among patients over age 50 years who underwent brain MRI, visual field, and OCT of the optic nerve. Records were manually reviewed to confirm diagnoses of POAG or CON. POAG was defined using United Kingdom Glaucoma Treatment Study (UKGTS) criteria; CON was defined using the UKGTS visual field criteria or intra-eye GC+IPL thickness asymmetry in corresponding sectors, inter-eye asymmetry in GC+IPL or RNFL, or RNFL < 70 microns. Objective OCT measurements were compared between the two groups.

Results:
Preliminary analysis identified 47 patients with POAG (93 data points) and 28 patients with CON (44 data points). Vertical cup-to-disc ratio (CDR) < 0.77 carried the highest relative risk (RR) for CON (RR 32.5, mean CON = 0.6, mean POAG = 0.8, $p< 0.001$) followed by RNFL x Rim Area >102 (RR 16.3, mean CON = 90, mean POAG = 58, $p< 0.001$). Other distinguishing factors included Rim Area >1.14 (RR 7.3, mean = CON 1.2, mean POAG 0.9, $p< 0.001$) and RNFL x vertical CDR < 68 (RR 7.2, mean CON = 44, mean POAG = 55, $p< 0.001$).

Conclusions:
Several objective OCT measures were significantly different in POAG versus CON eyes. As anticipated, less cupping on OCT may suggest a compressive lesion instead of glaucomatous optic neuropathy, signaling clinicians to consider neuroimaging studies. Future directions include creating an evidence-based calculator to help predict risk of CON based on OCT features.

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Keywords: Optic neuropathy, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Neuroimaging, Tumors, Perimetry

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Comparison of Visual Outcomes and Optic coherence tomography (OCT) in acute or sub acute Non-Arteritic Ischemic Optic Neuropathy (NAAION) with and without Bevacizumab treatment

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Introduction:
To compare visual outcomes and Optical coherence tomography (OCT) changes in patients with intravitreal Bevacizumab vs. no treatment in patients with acute or sub-acute non-arteritic ischemic optic neuropathy (NAAION).

Methods:
Retrospective review of records of patients with acute (< 15 days) or sub-acute NAAION who were treated with intravitreal Bevacizumab injection (group A) versus no treatment (group B) from January 1, 2020, to December 31, 2023, at our institute. Data was collected regarding patient demographics, visual function, and OCT parameters at presentation and follow-up visits.

Results:
A total of 39 eyes of 37 Patients with NAAION (26 group A and 13 group B) were identified. Median age of patients was 50 (IQR:43-58) years and 44 (IQR: 42-53) years in groups A and B respectively, p (0.25). There was no statistically significant difference in gender, presenting visual acuity, disc edema grade, visual field mean deviation, coexisting macular edema. However, the average duration of symptoms was 7 days vs 20 days in groups A and B respectively. The average thickness of peripapillary RNFL was more in group A (312: IQR: 198-356 microns) vs. 140 (IQR: 117-265) microns, p-0.008. The average improvement in best corrected visual acuity, BCVA was 0.2 (IQR:0.1-0.5) logMAR in group A vs. 0(IQR: -0.3 to 0) logMAR in group B. p=0.0008. Improvement in foveal sensitivity was 4.5(IQR: 0 to 9) db in group A vs. -3(-8 to 2 dB) in group B, p =0.008. Regression analysis showed intervention (bevacizumab vs. no treatment) and presenting visual acuity were the only factors that affected improvement in BCVA and visual field foveal sensitivity. .

Conclusions:
The current study suggests that patients with acute/subacute NAAION treated with intravitreal Avastin might have a greater improvement in final BCVA and foveal sensitivity. However, prospective more robust studies might be needed to validate these results.

References: None provided.

Keywords: Optic neuropathy, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Vascular disorders, Miscellaneous

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Demographic And Epidemiological Profile Of Optic Neuritis In Colombia: A Retrospective Study Using Data From The Comprehensive Information System For Social Protection.

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Introduction:
Optic neuritis (ON) comprises a group of entities leading to the demyelination of the optic nerve. The prevalence of ON has not been studied in Latin-American countries. We aim to describe the demographic characteristics of ON in Colombia from 2015 to 2021.

Methods:
This is a descriptive cross-sectional study collecting data from individual health service records within the Integrated Social Protection Information System (SISPRO) of the Colombian health system, from January 1, 2015, to December 31, 2021. ON data was classified in SISPRO according to the International Statistical Classification of Diseases and Related Health Problems (ICD-10). We conducted descriptive analyses to delineate geographical patterns, age, and gender as well as estimate the prevalence of ON in Colombia.

Results:
22,525 ON cases were identified. 6,336 (28.12%) had a diagnosis of neuromyelitis optica spectrum disorder (NMOSD) and 16,189 (71.88%) with a diagnosis of non-NMOSD divided into multiple sclerosis (MS) and non-NMOD/non-MS cases. The incidence of non-NMOSD and NMOSD was calculated at 7.29 and 2.05 cases per 100,000 individuals, respectively. 78.5% of NMOSD patients were female, with a higher prevalence in Risaralda, Sucre, and Bogotá. For MS associated ON, 64.1% of patients were female, with a higher prevalence in Antioquia, Sucre, and Tolima. For non-NMOSD/non-MS cases, 55.3% of cases were female, with a higher prevalence in Bogotá.

Conclusions:
This is the first epidemiological study of ON conducted in Colombia. Diagnosis of MS was more frequently made in regions with a larger Caucasian population, while NMOSD and non-NMOSD/non-MS diagnosis were more prevalent in more racially diverse states. Other types of specific antibodies are of limited availability in Colombia.

References: None provided.

Keywords: Optic neuritis

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Determinants of Pulse Steroid Therapy Acceptance Among Patients Presenting Clinically with Optic Neuritis

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Introduction:
Optic neuritis (ON) research has focused on corticosteroid treatment efficacy, however there is a knowledge gap as to how many patients accept steroid therapy based on efficacy data alone. Many patients presenting with first time ON require ample information to make an informed decision on proceeding with steroids or not. We aim to identify factors influencing treatment decisions in patients with ON considering pulse steroid therapy, enhancing the informed consent process.

Methods:
Patient data between 2013-2023 from the electronic medical records of the University of British Columbia Hospital Multiple Sclerosis Clinic will be reviewed. Two-hundred patients presenting with primary ON, with exclusion criteria applied to patients with a previous diagnosis of MS, are expected to be included. Data including demographic information, comorbid medical problems, time to diagnosis, severity of acuity and color vision loss, and occupational information will be reviewed. Comparative statistics will be used, utilizing means, standard deviations, frequencies, and percentages. A significance level of < 0.05 will be used, and one-way analysis of variance tests will assess differences in patient characteristics between those consenting to pulse steroid therapy and those declining it.

Results:
We expect a total of 200 participants from 2013- 2023. We hypothesize that a significant percentage of patients with optic neuritis will consent to receive pulse steroid therapy. We anticipate that patients with poor visual acuity or color perception at presentation, younger patients, patients presenting early and prior to any spontaneous improvement, and patients who have occupations that are dependent on high visual acuity will be more likely to consent to this treatment.

Conclusions:
This comprehensive analysis will shed light on how individual patient characteristics and course of presentation can influence their decision to proceed with pulse steroid therapy. This will help to guide patients who are having difficulty making the decision based on steroid efficacy alone.

References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Optic neuritis

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Emergency Department Presentations of Bilateral Optic Nerve Head Edema in an Australian Tertiary Hospital

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Introduction:
Increasing awareness of idiopathic intracranial hypertension (IIH) has changed the referral pattern of patients with incidental bilateral optic nerve head oedema (BONHE), resulting in rising Emergency Department (ED) referrals. We aim to review these cases to streamline the management pathway.

Methods:
A retrospective review of patients referred to a tertiary centre ED with concerns for BONHE between 2017 to 2022.

Results:
Ninety-six patients were identified, with a trend of increasing referrals over five years. 54 patients were referred by optometrists, and 17 were referred by General Practitioners. 54 patients were admitted ('admission group') and 38 were discharged from ED ('discharge group'). The mean ED length of stay was approximately 5 hours, and the average hospital stay was 3.7 days in the admission group. Discharge group had similar visual acuity (VA) to admission group, however, were less likely to have formal visual field tests (OR 38.722, 95%CI 10.95 to 136.86, P< 0.01), or fundoscopy exams (OR 25.95, 95%CI 1.43 to 469.86, P=0.0275). The most common diagnosis for both groups was IIH (41.3% for discharge group, 54.7% for admission group). Nine patients from admission group and one patient from discharge group required venous stenting for IIH. Compared to patients without stent, patients who received stent had a lower mean visual field index (VFI) (87.5% compared to 94.5%, P=0.04), but a comparable opening pressures and mean VA. On initial follow up, the mean VFI of both groups were similar, however the admission group had a higher average RNFL thickness (P = 0.0002). Parameters of visual function (VA and VFI) were similar in both groups at initial and 6 months follow up.

Conclusions:
This study indicates that a rapid access clinic will provide a safe and cost-effective management for patients with BONHE, with timely neuro-ophthalmic assessment and necessary investigations.

References: None provided.

Keywords: High intracranial pressure/headache, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Pseudotumor cerebri, Optic neuritis

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Evidence-based, risk-stratified monitoring protocol for optic pathway late toxicity following for head and neck & CNS radiotherapy

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Introduction:
CNS tissues such as optic nerves and chiasm are sensitive to late toxicity from radiation therapy (RT). Treatment with systemic bevacizumab may stabilize but rarely improve vision in radiation-induced optic neuropathy (RION), indicating the need for early identification. We aim to develop an evidence-based, risk-stratified monitoring protocol.

Methods:
Pubmed database was searched for manuscripts with primary data on rates of radiation optic neuropathy. Articles lacking patient level data on dose to optic structures were excluded (those with only median, mean, range of dose if non-uniform doses were given). Individual patients were excluded if they had vision of Counting Fingers or worse prior to RT, vision loss within the first 6 months following RT, follow-up < 2 years, received stereotactic radiosurgery or hypofractionated RT (dose of >3 Gy per fraction, or < 20 fractions), or had unclear cause for decline in vision. Patients were included and deemed at risk for RION if they received > 50 Gy to an optic structure.

Results:
Fifty-three manuscripts met inclusion & exclusion criteria with a total of 3155 patients deemed to be at risk of RION. The overall rare of RION was 4.4%. A dose-dependent relationship was noted with increasing rate per 5 Gy intervals (50 – 54.9 Gy: 2.4%; 55 – 59.9 Gy: 3%; 60 – 64.9 Gy: 4.6%; 65 – 69.9 Gy 5.3%; 70 Gy and above 10.1%) as well as per 10 Gy intervals (50-59.9 Gy: 2.6%; 60-69.9 Gy: 4.9%; 70 Gy and above: 10.1%).

Conclusions:
With the advancement of Level 1 evidence from randomized controlled trials for the use of bevacizumab for CNS radiation necrosis and evidence for benefit in RION, early detection is key to vision preservation. For patients with less than 5% risk we propose annual monitoring, 5-10% risk monitoring every 6 months, and those with 10% or higher risk quarterly monitoring.

References: None provided.

Keywords: Optic neuropathy, Skull base, Chemotherapy and radiation injury

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Generating Physiologic Electric Fields Along the Human Optic Nerve

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Introduction:

Significant interest exists in developing electric field (EF) application into a technology to direct target-specific neuronal regeneration. We have shown that in vivo EF stimulation of the rat optic nerve (ON) after crush injury directed full-length regeneration of retinal ganglion cell axons and partial restoration of vision. Whether EFs can successfully direct axon regeneration in humans is unknown. Here, we pair 3D computational modeling experiments with cadaveric measurements to interrogate the optimal electrode configuration for generating an EF along the human ON.

Methods:

High-resolution 3D image of the adult head and orbit was developed using computed tomography, then discretized and imported into the Admittance Method computational platform. Various combinations of stimulating electrodes (SE) and ground electrodes (GE) were modeled and the field gradient estimated. Electrodes were then surgically placed in cadavers. SEs considered included a contact lens (CL) or intraorbital J-electrode, needle electrode, or cuff electrode. GEs included a needle electrode on the optic chiasm, intranasal electrode, and small (4x4cm) or large patch (9x9cm) along the occiput. Eight measuring electrodes were placed at intervals along the ON.

Results:

3D modeling predicted that direct electrodes placed along the optic nerve will generate a larger electric gradient than indirect electrodes placed on the surface of the head. Cadaveric experiments (n=2) accordingly showed a 1.54 V/m gradient with direct stimulation, compared to 1.16 and 0.9 V/m with indirect stimulation. This was similar to prior rat measurements which demonstrated a gradient of 1.4 - 1.7 V/m.

Conclusions:

Given that we were able to generate similar EF gradients in human cadavers as rats, we are optimistic about the potential for translation. Further work will be aimed at development of wearable devices for EF stimulation of the human ON.

References: None provided.

Keywords: Optic neuropathy, Optic nerve trauma and treatment

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Idebenone for patients with Leber hereditary optic neuropathy: Results from the PAROS post-authorization safety study

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Introduction:
Idebenone has been approved in Europe for the treatment of Leber hereditary optic neuropathy (LHON), a rare mitochondrial disorder in which patients present with severe, bilateral vision loss. PAROS was a phase IV post-authorization study to further evaluate the long-term safety profile of idebenone treatment in patients with LHON under conditions of routine clinical care.

Methods:
PAROS was a multicenter, prospective, non-interventional safety study, conducted at 26 centers across 6 countries in Europe. Safety was assessed by the collection and analysis of adverse event (AE) reports. The primary endpoints included: frequency of treatment-emergent AEs (TEAEs) and serious TEAEs; frequency of adverse drug reactions (ADRs) and serious ADRs; and frequency of AEs of special interest (AESIs), including abnormal liver function tests (LFTs) and hepatitis, blood count abnormalities, cases of Wolff-Parkinson-White (WPW) syndrome, and atrial fibrillation.

Results:
Of 229 patients originally enrolled in the study, 224 received treatment with idebenone and comprised the safety population. The mean treatment duration was 765.4 days (SD 432.6 days). A total of 130 (58.0%) patients reported 382 TEAEs, and 25 (11.2%) patients reported 31 serious TEAEs. Fifty (22.3%) patients reported 82 ADRs, including two serious ADRs in two patients, both of which were reported as lack of treatment effectiveness leading to permanent discontinuation. Regarding AESIs, 15 (6.7%) patients each reported increased alanine aminotransferase (ALT) or gamma-glutamyltransferase (GGT), 9 (4.0%) patients reported increased aspartate aminotransferase (AST), and 1 patient (0.4%) reported an unspecific abnormality in LFT. Ten events related to blood count abnormalities were reported for 9 (4.0%) patients. There were no events related to WPW syndrome or atrial fibrillation.

Conclusions:
This real world, long-term study confirms the known safety profile of idebenone and does not raise any additional safety concerns regarding abnormal LFTs, hepatitis, and blood count abnormalities.

References: None provided.

Keywords: Optic neuropathy, Genetic disease, Retina

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Grant Support: None.

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Ischemic Optic Neuropathy: Analysis of Distribution and Etiologies in a Tertiary Care Center

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Introduction:
The spectrum of diseases responsible for ischemic optic neuropathies varies, yet the vast majority of these conditions stem from a relatively limited set of underlying causes. The main objectives of this study were to examine the distribution of various causes of ischemic optic neuropathy and the prevalence of cases where the cause of optic neuropathy could not be determined.

Methods:
This cross-sectional study examined patients who underwent evaluation at the Neuro-Ophthalmology service at a tertiary care center in the U.S. from January 2016 to February 2023 with queries of the electronic health record (EHR) for encounters with ICD-10 code for “ischemic optic neuropathy” (right, left, bilateral, or unspecified). The prevalence of etiologies was determined, including special cases and those where the cause of optic neuropathy could not be determined.

Results:
A total of 1197 records were reviewed. The most common cause of ischemic optic neuropathy was NAION in 721 (72%) of cases, of which 221(30.6%) were sequential NAION. Recurrent NAION and NAION with quasi-simultaneous bilateral optic nerve edema were identified in 8 (1.1%) and 10 (1.3%) cases, respectively. Incipient NAION (nerve head swelling without visual loss) was identified in 23 (3.2%) patients. Giant cell arteritis accounted for 69 (7%) of cases. Optic disk drusen and shock-induced ischemic optic neuropathy were observed in 19 (2%) and 28 (3%) cases, respectively. We diagnosed posterior ischemic optic neuropathy in only 16 (2%) patients. A substantial proportion of the cases (131, 13%) were classified as idiopathic.

Conclusions:
The findings underscore the varied nature of optic neuropathies, ischemic and otherwise. Notably, 13% of our optic neuropathies were of unknown etiology, which offers insight into the magnitude of the diagnostic vacuum and provides some perspective of direction for future research.

References: None provided.

Keywords: Optic neuropathy, Vascular disorders

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Grant Support: None.

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Long-term efficacy of idebenone in Leber hereditary optic neuropathy in the LEROS study: Analyzing visual acuity change according to mitochondrial DNA mutation and disease phase

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Introduction:
Leber hereditary optic neuropathy (LHON) is a mitochondrial disease resulting in progressive, painless, bilateral vision loss. The causative mitochondrial DNA (mtDNA) mutation impacts disease progression, and, potentially, treatment response. In LEROS, a Phase IV, open-label interventional study (ClinicalTrials.gov NCT02774005), visual acuity (VA) outcomes following 24 months of idebenone treatment were compared to those of an external Natural History (NH) cohort.

Methods:
Patients with LHON and a m.G11778A, m.T14484C or m.G3460A mutation were enrolled and stratified by time since onset: subacute/dynamic (≤1 year) and chronic (>1 but ≤5 years). Data from 181 patients were compared to retrospective data from the NH cohort (N=372), matched by time since symptom onset. We compare the difference in least squares (LS)-mean VA change (delta VA) from baseline to Month 24 in treated versus untreated eyes (a negative value favors idebenone treatment).

Results:
In subacute/dynamic m.G11778A eyes, delta VA from baseline to Month 24 was -0.32 logMAR (idebenone: n=60; NH: n=47; p=0.0024). In chronic m.G11778A eyes, delta VA was -0.11 logMAR (idebenone: n=82; NH: n=51; p=0.0434). In subacute/dynamic m.T14484C eyes, delta VA was +0.20 logMAR (idebenone: n=35; NH: n=10; p=0.2854). However, in chronic m.T14484C eyes, delta VA was -0.52 logMAR (idebenone: n=11; NH: n=18; p< 0.0001). In subacute/dynamic m.G3460A eyes, delta VA was +0.53 logMAR (idebenone: n=26; NH: n=18; p=0.0012). In chronic m.G3460A eyes, delta VA was -0.13 logMAR (idebenone: n=23; NH: n=24; p=0.1618).

Conclusions:
Idebenone can improve VA in a large proportion of LHON patients, although these benefits manifest to varying degrees depending on disease stage and/or causative mtDNA mutation. Patients with the most prevalent mutation, m.G11778A, saw a consistent treatment benefit regardless of disease stage. Results for m.T14484C and m.G3460A should be interpreted with caution in some cases due to the relatively low number of eyes; further investigation is warranted.

References: None provided.

Keywords: Optic neuropathy, Genetic disease, Retina

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Mitochondrial Stress in Optic Disc Drusen Skin Fibroblasts: A Multiomic Analysis

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Introduction:
Optic disc drusen (ODD) are yellowish calcified concretions in the unmyelinated optic nerve, commonly causing pseudopapilledema or optic nerve ischemia(1-3). ODD occur in ~2% of general population, sometimes in autosomal dominant fashion. Ultrastructurally, ODD are associated with mitochondrial calcification(4). Our study analyzed cellular energy metabolism and key molecular changes in skin fibroblasts from patients with ODD.

Methods:
We recruited patients with ODD and other optic neuropathies and performed clinical, imaging, whole genome sequencing, and skin punch biopsies. We assessed cellular energy metabolism of passage-0 skin fibroblasts to examine mitochondrial respiration and glycolytic activity (Seahorse Analyzer, Agilent) and performed multiomic analysis.

Results:
We collected skin biopsies from patients with ODD (N=20, 13 with autosomal dominant disease), autosomal dominant optic atrophy (ADOA) (N=3), and healthy controls (N=5). Analysis of skin fibroblast energy metabolism revealed that, compared with controls, ODD fibroblasts exhibited evidence of increased mitochondrial stress, but the bioenergetics were less severe than that of ADOA. We focused our analysis on one family with autosomal dominant ODD (6 affected members, ages 7-76 years) with complete clinical, genomic, and multiomic data. Analysis of over 7500 proteins in fibroblasts showed that the most significantly decreased molecules in this family are involved in different aspects of mitochondrial function, lipid metabolism, and solute transport. A heatmap of the 21 most decreased mitochondrial proteins revealed that the 2 most severely affected members of the family had the lowest protein levels. In contrast, a healthy control from the same family had values similar to those of controls. The top increased molecules are involved in modification of the extracellular matrix and fibrosis, like those in age-related macular degeneration and other neurodegenerative diseases.

Conclusions:
Bioenergetic and multiomic analysis of autosomal dominant ODD skin fibroblasts revealed evidence of mitochondrial stress and downregulation of key molecules important in mitochondrial function, lipid metabolism, and solute transport.

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Natural course of clinically isolated optic neuritis: Implications for trial design

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Introduction:
Optic neuritis is the most common optic neuropathy in young adults and a frequent manifestation of multiple sclerosis. Its natural course is pertinent to the design of visual pathway neuroprotection trials.

Methods:
Treatment-independent analysis of the TONE trial cohort (NCT01962571), including 103 patients with acute optic neuritis and baseline high contrast visual acuity < 0.5 dec. We analyzed study visits at baseline and weeks 1, 4, 16, and 26 with mixed effects linear piece-wise models to describe the dynamics of low contrast letter acuity, contrast sensitivity, visual fields, visually evoked potentials, and macular and peripapillary retinal layer thicknesses. Sample size estimates are based on a two-sided t-test with α=0.05, power 80%, and treatment effects equal to 50% of the mean diseased induced change.

Results:
After baseline visual loss, there was improvement of visual function with thinning of inner- and swelling of outer retinal layers. Clinical trials could reduce their required size by more than half when using macular ganglion cell and inner plexiform layer thinning (33 patients/group) over peripapillary retinal nerve fiber layer thinning (79/group) as the primary outcome. Similarly, trials of functional neuroprotection could reduce their size by more than 40% when employing the inter-eye delta of 2.5% low-contrast letter acuity (109/group) over the affected eye's value alone (189/group) as their outcome. The respective associations to vision-related quality of life (NEI-VFQ overall score) were similar (Pearson's $|r|$ =0.08 vs 0.15 and 0.38 vs 0.39). Because inner retinal layer thicknesses remained stable after four months but functional improvements continued up to month six, trials should follow up accordingly.

Conclusions:
The negative results of the TONE trial make its participants one of the best-characterized and largest cohorts of acute optic neuritis. Our data show that future trials may benefit from substantial efficiency gains.

References: None provided.

Keywords: Optic neuritis, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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Non-arteritic anterior ischemic optic neuropathy as a potential connection between vascular insufficiency and increased dementia risk: a nationwide, population-based cohort study

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Introduction:
This retrospective, nationwide population-based cohort study conducted in South Korea investigated the association between non-arteritic anterior ischemic optic neuropathy (NAION) and the risk of dementia.

Methods:
This study examined 120,501 patients diagnosed with NAION between 2010 and 2017 and followed until 2018. Upon excluding patients with histories of optic neuropathies other than NAION, like optic neuritis, multiple sclerosis, brain injuries, or increased intracranial pressure, 14,709 cases remained. Further refinement excluded those under 40 years or lacking a National Health Screening Program registration two years before their NAION diagnosis, leaving 46,807 patients. After further exclusions like prior dementia and missing data, 42,943 patients remained, matched with 214,715 age- and sex-matched controls without NAION. The average follow-up period was 2.69 years (SD, 1.96).

Results:
Newly diagnosed NAION was associated with an elevated risk of all-cause dementia (ACD; HR=1.281, 95% CI: 1.204-1.363), Alzheimer's disease (AD; HR=1.267, 95% CI: 1.182-1.357), and vascular dementia (VaD; HR=1.311, 95% CI: 1.087-1.581), independent of potential confounding factors. In subgroup analysis, the younger age group exhibited a stronger association between NAION and ACD (HR=1.833 [< 65 years] versus 1.225 [≥ 65 years]; P for interaction < 0.0001). Stronger associations were observed between NAION and all-cause dementia among younger patients and current smokers.

Conclusions:
Our research indicates NAION as an independent risk factor for ACD, AD, and VaD. Ophthalmologists should recognize this risk particularly in younger, smoking NAION patients, and consider referrals. The study emphasizes CNS vascular insufficiency's role in cognitive decline, necessitating prevention strategies focused on cardiovascular risk. Further studies are needed to establish a clear causal relationship between NAION and dementia.

References: None provided.

Keywords: Optic neuropathy, Vascular disorders

Financial Disclosures: The authors had no disclosures.

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Optic Nerve And Optic Nerve Sheath Biopsy Indications And Outcomes

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Introduction:
Optic nerve and nerve sheath biopsy (ONB/ONSB) are diagnostic tests considered for optic nerve disease when other investigations have failed to provide a diagnosis. This study aimed to describe the clinical presentation, diagnostic yield and outcomes of patients undergoing ONB/ONSB.

Methods:
Retrospective multicenter study including patients undergoing an ONB/ONSB at a tertiary medical center. We searched the pathology database for optic nerve or optic nerve sheath biopsies performed between 1/1/04 and 6/1/23. Charts were reviewed to confirm the diagnoses and review the patient's presentation, clinical course, investigations, and indication for biopsy.

Results:
A total of 74 patients were included in this study, (23 ONB, 51 ONSB). The median age at biopsy was 42 years (range, 7 month-81 years) and 44 (59%) were female. The most common indication for biopsy was an unexplained optic neuropathy in 60 (81%), followed by extrinsic pathology to rule out optic nerve sheath involvement in 14 (19%). Surgical approaches included orbitotomy (35, 47%), craniotomy (31, 42%), and trans nasal/sinus (8, 11%). In the unexplained optic neuropathy cohort, a specific diagnosis was made in 40(67%) cases. In the remaining 20 cases, the biopsy was non-specific (10) or normal (10) and aided the clinical impression by ruling out causes. The most common definitive diagnoses were optic nerve sheath meningioma(20), neurosarcoid(7), optic nerve glioma(7), lymphoma(2) and germinoma(2). Among the non-diagnostic biopsies, chronic inflammatory orbital disease was commonly diagnosed in 6 patients, followed by idiopathic intracranial hypertension(3), idiopathic granulomatous disease(2), presumed tacrolimus toxicity(2) and presumed non-arteritic anterior ischemic optic neuropathy(2). Of the 23 ONBs performed, the diagnosis was most commonly glioma(6), followed by meningioma(5), non-specific inflammatory disease(4), sarcoidosis(3), germinoma(2), and salivary gland choristoma, hemangiopericytoma, and presumed tacrolimus toxicity(1 each).

Conclusions:
This study showed that ONB/ONSB was helpful in establishing the diagnosis in a wide range of pathologies.

References: None provided.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Optic neuropathy

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Outer Retinal Assessment Of Patients With Temporal Hemianopia from Chiasmal Compression Using Spectral-Domain Optical Coherence Tomography

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Introduction:
Patients with chiasmal compression from pituitary tumors have retinal nerve fiber layer and ganglion cell layer thinning that are correlated with visual field (VF) defects. Few studies have evaluated the outer retinal layers in these patients, with contradicting conclusions. The purpose of this study is to investigate outer retinal parameters in patients with pituitary tumors and VF loss.

Methods:
In this retrospective cross-sectional study, 20 eyes of 10 patients with temporal hemianopia due to pituitary tumors and 20 healthy control eyes were included for analysis. All patients underwent VF and spectral-domain OCT testing prior to resection of the tumor. OCT scans were segmented using a machine learning-enabled platform with manual correction. Output metrics included thickness of the inner retina (internal limiting membrane to outer plexiform layer), middle retina (outer nuclear layer [ONL] to ellipsoid zone), outer retina (ONL to retinal pigment epithelium), and photoreceptor outer segment (OS). These layers were further segmented into nasal and temporal hemiretinas.

Results:
The inner retina (p=0.005) and middle retina (p=0.028) were statistically significantly thinner in patient eyes compared to control eyes. There was no significant difference between the outer retinal thickness of the 2 groups; however, when isolating the nasal outer retina, the patient group was found to be significantly thinner (p=0.007). This difference was not seen in the temporal outer retina (p>0.5). The difference between the mean thickness of the 2 groups was 16.9µm in the nasal outer retina compared to 0.49µm in the temporal outer retina. There was no significant difference in the OS thickness or nasal OS thickness between the two groups.

Conclusions:
This is the first study to demonstrate thinning of the outer retina in patients with visual field loss from chiasmal compression. Longitudinal analysis and correlation with other clinical and testing parameters are needed to further evaluate the significance of these findings.

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Keywords: Tumors, Visual fields, Retina, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease

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Patterns and Prognosis of Visual Field Changes in Patients with Traumatic Optic Neuropathy

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Introduction:
To analyze visual field patterns in traumatic optic neuropathy(TON) patients and investigate factors related to the prognosis of visual acuity and visual field.

Methods:
The authors conducted a retrospective analysis of medical records from 54 patients diagnosed with TON between 2014 and 2023. Various factors, including gender, age, trauma mechanism and timing, treatment methods, visual acuity, visual field, and intracranial hemorrhage, were examined. The study classified visual field patterns based on 17 mutually exclusive patterns from OHTS investigated related factors

Results:
Of the 54 patients, 43 (79.6%) were male, and head trauma (42.3%) and falls (22.2%) were the most common locations and causes, respectively. Intracranial hemorrhage was present in 61.1% of patients. The most common initial visual field defects were total loss (63.0%) and altitudinal loss (25.9%). During the final visual field test, similar patterns of total and altitudinal losses were observed. 59.3% of patients received steroid treatment, and among all patients, those who received high-dose steroids treatment within 24 hours had a final visual acuity of 0.1 or more more than those who did not (OR=4.286, p=0.017). An initial visual field index(VFI) was associated with a final visual acuity of 0.1 or more (32.1%) (OR=1.06, p=0.032). Cases where final VFI maintaining over 80% of the initial VFI were linked to early high-dose steroid treatment (OR=5.00, p=0.039). However, the visual field pattern had no relationship with the final visual acuity or VFI improvement

Conclusions:
TON commonly resulted in altitudinal visual field defects and total loss. However, existing classification criteria for visual field defects had limited applicability. Factors influencing visual acuity and visual field prognosis included the initial VFI and administration of high-dose steroids treatment within 24 hours. The study highlights the importance of evaluating initial visual field test and promptly administering high-dose steroids in patients with TON

References: None provided.

Keywords: Trauma, Visual fields

Financial Disclosures: The authors had no disclosures.

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Contact Information: None provided.

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Peripapillary Retinal Nerve Fiber Layer Thickness As A Prognostic Factor Of Visual Outcomes In Nonarteritic Anterior Ischemic Optic Neuropathy

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Introduction:
Nonarteritic anterior ischemic optic neuropathy (NAION) is the most common cause of acute optic neuropathy in patients older than 50 years. Currently, there is no proven therapy for this condition. Therefore, this study aimed to evaluate the prognostic ability of peripapillary retinal nerve fiber layer thickness (pRNFLT) for predicting visual outcomes, including visual acuity (VA) and visual field (VF), of subjects with acute NAION.

Methods:
This 12-year retrospective study was performed at a single university hospital in Bangkok, Thailand. Sixty eyes of 60 subjects with acute NAION were included. The pRNFLT was measured globally and in the four quadrants, using optical coherence tomography. Multivariate analysis and area under the curve (AUC) were used to evaluate the prognostic ability of pRNFLT for predicting visual outcomes, including favorable VA (VA better than or equal to 20/25) and favorable VF (visual field index (VFI) ≥ 90%), at 6-month follow-up visit.

Results:
The median VA and mean VFI at 6-month follow-up visit were 0.30 (interquartile range: 0.00, 0.70) logarithm of the minimum angle of resolution and 69.27% ± 28.94%, respectively. Multivariate analysis for all 60 eyes showed that thinner temporal-quadrant pRNFLT was associated with favorable VA (odds ratio 0.98; p = 0.042) with a cut-off value of 128 µm (AUC = 0.839, 95% CI: 0.732-0.947, sensitivity 77.27% and specificity 84.21%). Among the 30 eyes with both reliable VFI at initial and at 6-month follow-up visits, thinner nasal-quadrant pRNFLT was associated with favorable VF (odds ratio 0.97; p = 0.047) with a cut-off value of 105 µm (AUC = 0.780, 95% CI: 0.612-0.948, sensitivity 90.00% and specificity 70.00%).

Conclusions:
The pRNFLT offers a clinical utility for predicting visual outcomes in acute NAION. Temporal-quadrant pRNFLT ≤ 128 µm and nasal-quadrant pRNFLT ≤ 105 µm predicted favorable VA and VF at 6-month follow-up visit, respectively.

References: None provided.

Keywords: Optic neuropathy, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)

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Plasma Limitrin Level as a Diagnostic Biomarker and Predictor of Recurrence for Double-seronegative Idiopathic Optic Neuritis

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Introduction:
To evaluate the clinical relevance of the plasma limitrin level in patients with double-seronegative idiopathic optic neuritis (DS-ION).

Methods:
Peripheral blood samples were collected from 27 patients with DS-ION and 30 healthy controls. Plasma limitrin levels were measured using an enzyme-linked immunosorbent assay. The correlation between plasma limitrin levels and recurrence was analyzed. A receiver operating characteristic (ROC) curve was constructed to assess the ability of plasma limitrin levels to predict recurrent ION.

Results:
The mean plasma limitrin level was significantly higher in patients with DS-ION (1.94 vs. 0.74 ng/mL, $p = 0.0007$). Plasma limitrin level and visual acuity at diagnosis were significantly correlated ($r = 0.42$, $p = 0.029$). The area under the ROC curve of plasma limitrin level was 0.765 ($p = 0.0065$). The cut-off plasma limitrin level of 1.37 ng/mL predicted recurrence with a sensitivity and specificity of 70.0% and 76.5%, respectively. Patients with plasma limitrin level > 1.37 ng/mL showed significantly higher recurrence rates (63.6% vs. 18.8%) and shorter intervals (median interval 4 vs. 51 months) than patients with plasma limitrin level ≤ 1.37 ng/mL.

Conclusions:
Patients with DS-ION demonstrated significantly higher plasma limitrin levels than controls, and those with plasma limitrin level >1.37 ng/mL demonstrated worse vision at diagnosis and higher recurrence rates. Thus, plasma limitrin level could serve as diagnostic biomarker and predictor of recurrence for DS-ION.

References: None provided.

Keywords: Optic neuritis, Demeylinating disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Prevalence and Clinical Profile of Isolated Syphilitic Optic Disc Swelling in a Tertiary Eye Care Center.

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Introduction:
Optic disc edema is a common presenting sign in neuro-opthalmology services, however there is no data regarding the frequency of syphilitic infection as the cause of this clinical scenario, we strived to determine the prevalence of this etiology among the population that presents with unilateral or bilateral isolated optic disc edema at a tertiary eye care center, and describe the clinical, perimetric and radiologic profile in these patients.

Methods:
We conducted a search in the institutional database for all patients assessed for active optic disc edema from January 2021 to September 2023, including subjects of any sex and age group, without intraocular or orbital inflammation, clinical proptosis, or retinal arterial or vein occlusions. We excluded patients with pseudopapilledema or when treponemal (FTA) and non-treponemal (NTT) serologic tests or magnetic resonance (MRI) were not available. Patients with macular edema were not excluded.

Results:
There were 327 subjects that met the study criteria, excluding 48 cases of pseudopapilledema and 15 with an incomplete clinical record, we analyzed 264 subjects. Active syphilitic infection (positive FTA and NTT) was present in 3.4% patients (9). Mean age was 46.6 years compared to 44.8 years in the other etiologies (p=0.51). 88.8% were male and 55.5% bilateral, compared to 38.4% (p=0.03) and 41.5% (p=0.7) in the remaining etiologies, respectively. Pain with eye movements was present in 22.2%. Mean VA acuity at presentation in affected eyes (14) was 0.73 logMAR. Frequent Goldmann perimetry defects are described. MRI showed enhancement and T2 hiperintensity in only one eye. Post-treatment follow-up was available in 7 eyes showing a mean post-treatment visual acuity of 0.07 logMAR compared to an initial of 0.54 logMAR (p=0.11).

Conclusions:
One in every 29 patients with isolated optic disc swelling seen in neuro-opthalmology services may have syphilis infection, most present without pain or changes in MRI.

References: None provided.

Keywords: Neuro-ophth & infectious disease (eg, AIDS, prion)

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Prevalence and Severity of Vision Loss in Wolfram Syndrome

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Introduction:
Wolfram syndrome is a predominantly autosomal recessive condition with classic symptoms consisting of juvenile-onset diabetes mellitus, diabetes insipidus, sensorineural hearing loss, and optic atrophy. Not all patients with Wolfram syndrome will present with the full spectrum of symptoms, resulting in delays in diagnosis.

Methods:
Retrospective chart review was performed on 18 patients with Wolfram Syndrome confirmed by genetic testing, who presented to the Wolfram Center and the Neuro Ophthalmology Clinic at Washington University in Saint Louis. All patients underwent complete neuro-ophthalmic exams by a single attending physician. OCT was performed on a Zeiss machine at a single testing center and interpreted by the same attending. Linear regression with slope fitting was done using Prism. Statistical significance was defined as $P < 0.05$.

Results:
Among this cohort of 18 patients, only 13 had diabetes mellites, and only 6 presented with the full spectrum of classic Wolfram symptoms. 3 patients only had vision loss and no other major symptom. 10 out of 18 patients had best corrected vision in at least one eye better than 20/100, and 2 patients had 20/20 vision despite optic nerve pallor. The severity of visual impairment was inversely correlated with ganglion cell complex but not retinal nerve fiber layer thickness, age of visual symptom onset, or duration of optic atrophy.

Conclusions:
The majority of Wolfram patients in this cohort have mild to moderate visual impairment. Many patients with Wolfram Syndrome do not display the full spectrum of Wolfram symptoms, and some patients only have vision loss. therefore, it is important to consider screening for Wolfram syndrome in patients with unexplained central vision loss and optic nerve pallor, even if they lack other cardinal Wolfram symptoms.

References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Optic neuropathy, Pediatric neuro-ophthalmology

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Prevalence of Anatomic Narrow Angle in Patients with Non-Arteritic Anterior Ischemic Optic Neuropathy

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Introduction:
Non-arteritic anterior ischemic optic neuropathy (NAION) is an optic neuropathy thought to be related to diminished blood flow to the anterior optic nerve. This has been associated with obstructive sleep apnea, hypertension, and diabetes. However, the association between NAION and narrow ocular drainage angle is not well-established. There are 9 reported cases in literature of patients with NAION with concomitant narrow angle or increased intraocular pressure from angle-closure. To date, no large study has assessed the prevalence of narrow angles in NAION patients. Our study serves as a pilot study to determine whether there is increased prevalence of narrow drainage angle in patients with NAION compared to the general population.

Methods:
This is a cross-sectional study. Patients will be recruited from a neuro-ophthalmology clinic in a tertiary academic center. Anterior segment optic coherence tomography will be performed to determine the drainage angle of eyes with NAION. The prevalence of narrow angle in the study population will be calculated.

Results:
Prospective power analysis indicates that at least 34 eyes with NAION will need to be analyzed in the manner described above to detect a six-fold increase in prevalence of narrow angle in the study population compared to the general population (3.8% according to Leibowitz et al.). It is anticipated that more than 34 eyes will be recruited.

Conclusions:
The association between NAION and narrow drainage angle has not been established. If there is a greater prevalence of narrow angle in the study population, there may be a causal relationship between the two that warrants further investigation. There is a 15% risk of subsequent development of NAION in the second eye. If further studies establish a causal relationship, there may be a role for screening and prophylactic treatment of narrow angle when managing patients with unilateral NAION.

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Keywords: Optic neuropathy, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)

Financial Disclosures: The authors had no disclosures.

Grant Support: None

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Prognosis of neurosyphilis presenting with optic atrophy

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Introduction:
Neurosyphilis, a condition caused by Treponema pallidum infection of the central nervous system, has seen a resurgence in recent years. This study focuses on the prognosis of optic atrophy (OA) associated with neurosyphilis, which can lead to irreversible vision loss and visual field (VF) defect.

Methods:
This retrospective case series study included the patients seen between 2015 and 2023. We collected and analyzed gender, age, symptom duration, comorbidity, treatment, follow-up time, complete ophthalmic examination, VF testing, OCT examination, and laboratory tests of serum and cerebral spinal fluid (CSF). A change ≥ 0.2 on the logMAR visual acuity (VA) indicated improvement or deterioration, or otherwise it was stable.

Results:
Seventeen patients (33 eyes) were included, with mean age of 58 years. Thirteen patients had Argyll-Robertson pupils. Fifteen patients received aqueous penicillin intravenously. One patient received ceftriaxone intravenously and another patient received oral doxycycline. The mean titers of serum toluidine red unheated serum test and CSF venereal disease research laboratory (VDRL) decreased by 4-folds after treatment. The visual acuity increased by 2 lines after treatment and then decreased by 3 lines during follow-up. Patients with older age, worse initial VA, and higher CSF VDRL and total protein tended to a worse prognosis. The eyes with initial thinner retinal nerve fiber layer in inferior quadrant on OCT and worse mean sensitivity and mean deviation of VF test had a worse prognosis.

Conclusions:
Neurosyphilis patients with OA tended to have a bad prognosis in the long term despite the temporary improvement after treatment.

References: None provided.

Keywords: Adult strabismus with a focus on diplopia, Ocular motility, Optic neuritis, Optic neuropathy, Orbit/ocular pathology

Financial Disclosures: The authors had no disclosures.

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Contact Information: None provided.

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Prognosis of Non-Arteritic Anterior Ischemic Optic Neuropathy (NAION)

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Introduction:
This study aims to identify patients with NAION who experienced a decline in vision over time and investigate potential risk factors associated with a poor prognosis.

Methods:
A retrospective chart review was conducted for NAION patients diagnosed between June 1, 2022, and June 10, 2023. Included adults (≥18 years) with at least two clinic visits, acute painless vision loss in one eye, and optic disc swelling. Patients with high inflammatory markers or positive temporal artery biopsy were excluded. Epidemiological, clinical, and ancillary data, including visual field testing, optical coherence tomography, and fundus images, were reviewed. Patients were assessed within two weeks of symptom onset and followed up for up to three months from presentation.

Results:
Included 9 patients (4 males). Among them, 5 patients (55.5%) had worsening vision (unstable group, UG) with mean age of 68, while the stable group (SG) mean of 66. Four UG and 2 SG patients had prior NAION, with no significant differences in comorbidities. UG patients were seen at a mean of 9.5 days after presentation (9 days for SG patients), with UG follow-ups at 18.75 days (SG at 21.2 days). UG's mean visual acuity at follow-up was 20/125, while SG had 20/30. Visual field testing MD showed UG at -8.1 (acute) and -18.6 (follow-up) and SG at -8.96 (acute) and -8.17 (follow-up). IOP was slightly higher in UG (15.6/16.4 mmHg, acute/follow-up) than SG (13.3/13.25 mmHg, acute/follow-up). Fundus revealed prolonged swelling in UG and earlier pallor development in SG, with a smaller c/d ratio in UG.

Conclusions:
We identified 2 groups: stable and unstable vision loss. Risk factors for unstability encompass prior fellow eye NAION and elevated IOP. The UG displayed lower color plate scores, smaller cups, and persistent edema. Studying this subgroup can yield valuable insights into the factors underlying vision deterioration in specific NAION subgroups.

References: None provided.

Keywords: Optic neuropathy, Vascular disorders

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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PYC-001, a Peptide Conjugated Oligonucleotide for the Treatment of Autosomal Dominant Optic Atrophy

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Introduction:
Autosomal dominant optic atrophy (ADOA) is the most common form of inherited optic neuropathy, characterized by a progressive degeneration of the retinal ganglion cells, leading to bilateral vision loss. Mutations in the optic atrophy 1 (OPA1) gene account for 57-89% of ADOA cases, resulting in haploinsufficiency and inadequate OPA1 protein expression, which is essential for mitochondrial function. Antisense oligomers (AOs) designed to modify pre-mRNA splicing or protein expression for treatment of genetic diseases present suboptimal AO delivery to target cells, which limits their therapeutic potential for disease correction. PYC-001 is designed to overcome this major unmet need, the optimal delivery to the target cells. Phosphorodiamidate morpholino oligomers (PMOs) are neutrally charged AOs that offer potential for enhanced AO delivery when conjugated with a cell penetrating peptide to facilitate transport through the cell membrane. This study aims to demonstrate that PYC-001, a cell penetrating peptide-PMO (PPMO) conjugate targeting OPA1, is a potential treatment for ADOA.

Methods:
Improvement in OPA1 protein levels in PYC-001 treated patient derived cell models (PDMs) was assessed by Western blot. Impact of upregulated OPA1 protein levels was measured by improvements in oxygen consumption rate and mitochondrial networks and structure in PDMs.

Results:
PYC-001 treatment showed a consistent and broad range of upregulation of OPA1 protein in multiple ADOA PDMs. Results from PDM show both improvements in mitochondrial network structure as well as in bioenergetics.

Conclusions:
The ability of PYC-001 to maintain OPA1 isoform balance in treated cells is a key differentiator from other therapies and is potentially required to obtain full restoration of mitochondrial function. Alleviation and restoration of mitochondrial pathways has been obtained on ADOA PMDs upon PYC-001 treatment. PYC-001 leverages PYC's ocular PPMO platform and is currently under investigation in IND-enabling studies, which will support clinical trials that are expected to commence in 2024.

References: None provided.

Keywords: Genetic disease, Retina, Optic neuritis, Optic neuropathy

Financial Disclosures: Sri Mudumba: All thy authors are employed by PYC Therapeutics; Janya Graynok: Works for PYC Therapeutics; Sasiwimon Utama: Employed by PYC Therapeutics; Tracy Chai: Employed by PYC Therapeutics; Emily Woodward: Employed by PYC Therapeutics; Danie Champain: Employed by PYC Therapeutics; Ferrer Ong: Employed by PYC Therapeutics; Megan Thorne: Employed by PYC Therapeutics; Munik Tian: Employed by PYC Therapeutics; Grace Liu: Employed by PYC Therapeutics; maria Kerfoot: Employed by PYC Therapeutics; adam martin: Employed by PYC Therapeutics; Paula Cunningham: Employed by PYC Therapeutics; Dean De Alvis: Employed by PYC Therapeutics

Grant Support: None.

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Reducing Neuro-Inflammation in a Mouse Model of Mitochondrial Optic Neuropathy

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Introduction:
Effective, mutation-independent treatment for mitochondrial optic neuropathies is an important unmet need. In our Vglut2-Cre;ndufs4loxP/loxP preclinical mouse model with RGC-specific deletion of the mitochondrial complex I subunit NDUFS4, RGC degeneration develops rapidly between postnatal day 45 (P45) and P90, accompanied by inner retinal accumulation of Iba1+ mononuclear inflammatory cells as a sign of retinal neuro-inflammation. Based on reports of significant improvement in neurological function and lifespan when the colony stimulating factor-1 receptor inhibitor pexidartinib is used to deplete mononuclear cells from the brains of mice with global loss of NDUFS4, we hypothesized that pexidartinib may similarly deplete retinal mononuclear cells while slowing RGC degeneration and preserving vision in Vglut2-Cre;ndufs4loxP/loxP mice.

Methods:
Wild-type C57Bl/6 mice received control or pexidartinib-infused chow (400 mg/kg) beginning at P25 (n=10 male and 10 female mice per treatment). Retinal tissue was harvested after one week (P32) and an additional month of treatment (P60). Retinal flat mounts were stained for Iba1 and Tuj1 to label mononuclear cells and RGCs, respectively, and their abundance was quantified by confocal microscopy.

Results:
Compared to control mice, one week of pexidartinib treatment (P32) produced a depletion of Iba1+ cells from 114.4±6.6 to 0.4±0.7 cells/mm2 ($p < 0.0001$). Inner retinal mononuclear cell depletion remained complete at P60 (118.1±18.6 vs 0.0±0.0 cells/mm2, $p < 0.0001$). No evidence of RGC neurotoxicity was observed in pexidartinib-treated mice at P60 (RGC abundance 3073.2±374.6 cells/mm2 in controls vs. 3167.9±367.5 in pexidartinib-treated mice; $p=0.66$). These observations were consistent in male and female mice and in central, mid, and peripheral locations of the retina.

Conclusions:
Pexidartinib efficiently and durably depletes retinal mononuclear cells in wild-type mice of both sexes, without inducing RGC toxicity. Ongoing experiments will determine whether combatting neuro-inflammation in Vglut2-Cre;ndufs4loxP/loxP mice with pexidartinib can reduce RGC soma and axon degeneration while preserving visual function in optomotor and electrophysiological assessments.

References: None provided.

Keywords: Genetic disease

Financial Disclosures: The authors had no disclosures.

Grant Support: NANOS Pilot Research Grant

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Retinal Nerve Fiber Layer Thickness Fluctuation and its Effect on Macular Ganglion Cell Layer Volume in Asymptomatic Adolescent Optic Disc Drusen Patients.

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Introduction:
Introduction: Optic disc drusen (ODD) are acellular calcified deposits in the optic nerve head. In adolescent ODD patients, we have observed that RNFL thickness may fluctuate between visits raising concern of intracranial hypertension. Optical coherence tomography (OCT) can measure peripapillary retinal nerve fiber layer (RNFL) thickness and macular ganglion cell layer (GCL) volume as visual function parameters. This study aimed to investigate the fluctuation of RNFL thickness and its effect on GCL in asymptomatic adolescent ODD patients.

Methods:
Methods: Observational cohort study of 39 eyes from 22 asymptomatic adolescents with ODD who underwent Heidelberg OCT examination in at least 3 consecutive visits in the clinic. We classified participants into two groups based on the degree of RNFL thickness fluctuation (< 20µm or ≥20µm) and compared their demographic, clinical, and OCT data.

Results:
Results: Participant mean age was 14 years (range 10-17 years) and mean follow-up time was 3.9 years (range 5 months to 8 years). Brain magnetic resonance imaging was performed on 11 and lumbar puncture on 4 participants. None was diagnosed with intracranial hypertension. 7 patients had low RNFL thickness fluctuation (< 20µm) and 15 had high fluctuation (≥20µm). The high fluctuation group had significantly longer follow-up (P=0.01), more RNFL measurements (P=0.001), and higher mean RNFL thickness (P< 0.05) than the low fluctuation group. No significant difference in GCL volume change was observed between the two groups. A mixed effects model including all eyes showed that GCL volume decreased significantly for each year of follow-up (P< 0.05), whereas RNFL fluctuation did not influence mean GCL volume.

Conclusions:
Conclusion: Fluctuations in RNFL thickness were observed in adolescent ODD patients, but RNFL thickness fluctuation did not seem to affect GCL volume in the short term. This indicates that fluctuation of RNFL thickness might not be a worrying phenomenon in asymptomatic adolescent ODD patients.

References: None provided.

Keywords: Pediatric neuro-ophthalmology, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)

Financial Disclosures: The authors had no disclosures.

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REUNION: Registry of patients with Inherited Optic Neuropathies (IONs) in the United Kingdom, a five-year single-centre study.

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Introduction:
Inherited optic neuropathies (IONs) constitute a large group of rare monogenic disorders that primarily affect the optic nerve. In the last decade there has been increased access to genetic testing in the United Kingdom (UK), facilitating an earlier diagnosis of an ION. The purpose of this study was to determine the epidemiology of patients with IONs seen at a specialised referral clinic for IONs at Cambridge University Hospitals, Cambridge, UK.

Methods:
This retrospective cohort study reviewed the medical records of all consecutive ION patients seen at Cambridge University Hospitals between August 2017 and September 2022. Analysis was based on age, sex, diagnosis (including genetic diagnosis) and change in visual parameters over time.

Results:
A total of 172 patients (56% men; mean age 34 ± 18 years at first consultation; range 1-80 years) attended the IONs service. Leber hereditary optic neuropathy (LHON) was the most prevalent ION (N=75), including asymptomatic LHON mutation carriers (N=6), followed by dominant optic atrophy (N=18). Patients with symptomatic LHON were typically younger men (67% men; mean age at diagnosis 25.8 ± 13.7 years; range 1 – 60 years). The most common mutation was m.11778G>A, which comprised 66.7% LHON cases. Best corrected visual acuity (BCVA) followed up over the five-year period tended to remain static in patients regardless of mutation with a few notable exceptions, including one of three patients with LHON-Multiple Sclerosis overlap whose BCVA improved from count finger to 0.0 logMAR following treatment with idebenone. Mean BCVA at most recent follow-up in LHON patients was 1.72 logMAR bilaterally.

Conclusions:
With greater access to genetic testing, new epidemiological data demonstrates the cross-section of patients seen with IONs. However, questions remain surrounding the natural history of these conditions. This study offers context for prospective ION natural history studies, of relevance to ongoing gene therapy trials.

References: None provided.

Keywords: Optic neuropathy, Genetic disease, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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Grant Support: None.

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Risk Of Clinical And Sub-clinical Radiation-induced Optic Neuropathy Following High-dose Irradiation In Chinese Patients With Nasopharyngeal Carcinoma: A Case Control Study

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Introduction:
Nasopharyngeal carcinoma (NPC) is common in southeast Asia. NPC is highly radiosensitive, but its deep-seated location renders neighboring optic apparatus susceptible to radiation injury. Older literature based mainly on conventional radiotherapy reported a drastic increase of radiation-induced optic neuropathy (RION) when the point maximum dose of radiation (Dmax) to optic apparatus exceeded 55 Gy, a threshold often used as the safety limit during radiation planning. Intensity-modulated radiation therapy (IMRT) is a newer enhanced radiation delivery system, providing precise radiation to tumor while reducing harm to surrounding structures. This study aims at determining the risks of clinically manifested and subclinical RION following high dose IMRT for NPC.

Methods:
Consecutive NPC patients who received IMRT, with Dmax >54 Gy to the optic apparatus (any part of the optic nerves, chiasm or globes) at a tertiary center between 2010-2016 were recruited. Clinical findings and ophthalmic imaging were compared with age and gender-matched controls.

Results:
36 eyes of 18 patients with a mean age of 59.0 ± 13.4 years were examined at a mean of 6.9 years following radiotherapy. All tumors received 69.96-70 Gy of radiation. The incidence of clinically manifested RION was 2.8%. Excluding the eye with clinical RION, irradiated eyes had significantly thinner average and inferior peripapillary retinal nerve fiber layer (pRNFL) ($p< 0.01$) and macular ganglion cell-inner plexiform layer (GCIPL) in all quadrants (all $p< 0.001$). The inferior quadrant of pRNFL, inferotemporal sector of GCIPL and the inferotemporal peripapillary vessel density (PPVD) were significantly correlated with the maximum dose (Dmax) to the optic apparatus (all $p< 0.05$).

Conclusions:
Our study demonstrated significant, dose-dependent reductions in optic nerve fiber thickness after irradiation. Despite anatomical alterations, no functional deficit could be detected. Clinically manifested RION remained rare. A higher threshold for radiation to chiasm or optic nerves may be adopted for better disease control.

References: None provided.

Keywords: Chemotherapy and radiation injury, Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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Risk of Mortality Following Non-arteritic Ischemic Optic Neuropathy

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Introduction:
Systemic (diabetes mellitus, obstructive sleep apnea) and ophthalmic (crowded optic disc) risk factors are associated with non-arteritic anterior ischemic optic neuropathy (NAION). Risk of mortality following unilateral or bilateral NAION are not known.

Methods:
In this retrospective study, we identified new onset NAION diagnosed by experienced neuro-ophthalmologists at our tertiary care center from 1/1/2015-12/31/2016 (n =81). Age, race, and gender-matched patients who underwent cataract surgery during the same period served as controls (n = 81). Charlson comorbidity index was calculated from comorbid conditions. CDC National Death Index was queried to determine vital status on January 1, 2022, date and primary cause of death for both cohorts. Kaplan Meier survival analysis and Cox Regression modeling was performed to identify clinical characteristics associated with mortality risk.

Results:
Of 81 unique cases of new onset NAION, 13 (16%) developed bilateral NAION and 11 (14%) were deceased over 5- years. The proportion of deceased were higher for bilateral NAION (4/13; 31%) compared to unilateral NAION (7/68; 10%) and matched control (6/81; 7%) (p=0.04, Chi-square test). Charlson comorbidity index was higher for the bilateral NAION group compared to unilateral and control groups (p=0.05; ANOVA). Kaplan Meier analysis showed differences in mean survival time (in months) between controls (79.5□1), unilateral NAION (76.7□2) and bilateral NAION (69.8□7) (p=0.04, Mantel-Cox Log Rank). Multivariate Cox regression model showed older age at diagnosis, male gender, and higher comorbidity index was significantly increased risk for mortality. Higher comorbidity index was also a significant risk factor for development of bilateral NAION.

Conclusions:
We report increased mortality risk following NAION particularly bilateral NAION. This risk may be related to frailty from older age and underlying systemic comorbidities. Comorbidities also increase risk of bilateral NAION. Neuro-ophthalmologists must recommend aggressive management of systemic comorbid conditions to reduce mortality risk and fellow eye involvement following NAION

References: None provided.

Keywords: Optic neuropathy

Financial Disclosures: Kirstyn Taylor; Deepta Ghate; Sachin Kedar: Consultant for Astra-Zeneca

Grant Support: None.

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Sequential NAION: Associated Risks and Temporal Distribution of Events

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Introduction:
Non-arteritic anterior ischemic optic neuropathy (NAION) is the most common acute optic neuropathy in patients over age 50, and there is a 15-25% risk of a sequential (sNAION) event in the fellow eye. The Ischemic Optic Nerve Decompression Trial reported 326 patients with NAION (mean follow-up: 5.1 years) with a 14.7% incidence of sNAION; median time between study enrollment and sNAION was 1.2 years.

Methods:
Retrospective query of the electronic health record (EHR) at a specialty eye hospital for encounters with ICD-10 code for “ischemic optic neuropathy” (right, left, bilateral, or unspecified), text phrase “NAION”, or “ischemic optic neuropathy”. With manual chart review, 451 patients with other diagnoses were excluded (search methodology evaluated in companion abstract) and date of vision loss, rather than ICD-10 code association, was recorded.

Results:
A total of 672 patients were identified with at least unilateral involvement. Kaplan–Meier survival analysis (12 month censure) revealed that 31% of patients had sNAION. Mean age at first NAION episode was 59.5 ±12.7 years. Median time between sNAION episodes was 19.5 months. The probability of remaining event-free at 12 months was 57% (95% CI: 50%-65%), with a cumulative incidence of the sequential NAION of 43% at 12 months. Age at first NAION episode ($p < 0.0001$), hyperlipidemia ($p=0.0076$), systemic hypertension($p=0.0013$), and cardiovascular risk ($p=0.021$) were each associated with shorter time between NAION episodes.

Conclusions:
This study assessed risks of sNAION derived from the largest cohort of patients with sNAION ever reported. The risk of sNAION is higher than previously reported. And, this study is the first to document that specific systemic factors influenced the timing between events.

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STOP-BANG Questionnaire for Obstructive Sleep Apnea Screening in Patients with Non-Arteritic Anterior Ischemic Optic Neuropathy

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Introduction:
Non-arteritic anterior ischemic optic neuropathy (NAION) is an acute optic neuropathy that results in permanent vision loss. One risk factor that has been demonstrated for the development of NAION is obstructive sleep apnea (OSA). The gold-standard diagnostic test for OSA is in-laboratory polysomnography (PSG). Screening tools aid in evaluating which patients should receive PSG, which can be done either at home or in-lab. One such screening tool is the STOP-BANG screening questionnaire, which is a set of eight yes or no questions that has been validated to stratify patients based on risk for OSA. We hypothesized that increasing STOP-BANG score is correlated with increasing severity of diagnosis of OSA among NAION patients.

Methods:
We conducted a retrospective analysis of 20 adult patients at a neuro-ophthalmology clinic who received a diagnosis of NAION. Variables collected from patient charts were STOP-BANG score, diagnosis, and severity of OSA (low, intermediate, and high). Multivariable logistic regression was used to evaluate the relationship between STOP-BANG score and severity and diagnosis of OSA. Statistical analysis was performed using R (Vienna, Austria) software.

Results:
Five patients had low risk STOP-BANG scores (score < 2) , 11 had intermediate risk (score 3-4), and 4 had high risk (score 5+). Sixteen of 20 patients were diagnosed with OSA. Of these, 5 had mild OSA, 6 moderate, and 4 severe. One patient's OSA severity level was unknown. Multivariate logistic regression found no statistically significant relationship between STOP-BANG scores and diagnosis of OSA (p=0.162).

Conclusions:
Our analysis did not find a statistically significant relationship between STOP-BANG scores and severity and diagnosis of OSA. Future analyses with larger patient samples may further elucidate these findings.

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Structural changes in axon initial segments of ON-sustained alpha retinal ganglion cells in retinal degeneration (rd10) mice

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Introduction:
The axon initial segment (AIS) is a portion of the proximal axon underlying action potential ("spike") initiation and back propagation. Its structural properties, such as length and distance from the soma, are tailored to optimize the input/output properties of individual neurons and can be altered in response to changes in network excitability. Spontaneous spiking activity of retinal ganglion cells (RGCs) increases early during retinal degeneration, then declines over time. While alterations in synaptic input contribute to this increased spiking, whether such changes result in alterations to the AIS has not been well studied. Here, we examined AIS properties in a single type of RGC, the ON-sustained alpha cells, known to exhibit significantly increased rates of spontaneous spiking during degeneration, and compared results in the rd10 mouse model of retinal degeneration to those from age-matched wild type (wt) animals.

Methods:
We used specific strains of both mouse models that express GFP in subpopulations of RGCs (GFP-Thy1-EGFP-M). The AIS was identified by immunolabeling with a pan-sodium channel (pan-Nav) antibody, a widely used marker for the AIS, in GFP-expressing RGCs, followed by confocal microscopy and morphometric analysis of fluorescent AIS markers. ON-sustained alpha RGCs were identified using previously described morphological features: soma and dendritic field sizes, and the location of the terminal dendrites within the inner plexiform layer (IPL).

Results:
Both the length of the AIS and its distance from the soma were significantly reduced in rd10 RGCs compared to wt. Our results indicate that AIS properties are indeed altered in at least some RGC types. We have begun examining separate multi-electrode recordings for potential correlations with spiking patterns of these and other RGC types.

Conclusions:
Based on previous studies outside the retina, the changes we observed may help reduce excitability, and thus may compensate for the network hyperactivity arising as photoreceptor degeneration progresses.

References: None provided.

Keywords: Retina, Genetic disease, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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305 Structure-Function Correlates in Myelin Oligodendrocyte Glycoprotein Antibody Disease Optic Neuritis

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Introduction:
Myelin oligodendrocyte glycoprotein antibody disease (MOGAD) is a demyelinating disorder that most commonly presents with optic neuritis (ON), and affects children more often than adults. We report patients with MOG-associated ON and characterize longitudinal focal optical coherence tomography (OCT) and visual function abnormalities.

Methods:
This is a retrospective case series of eight young patients with MOG-associated ON (MOG titer ≥1:100) who were referred for neuro-ophthalmic evaluation. Data for history, physical exam, and OCT obtained for clinical evaluations were collected via medical record review. Stata statistical software was used to calculate Spearman correlations between visual function and OCT parameters.

Results:
Patients demonstrated acute peripapillary retinal nerve fiber layer (RNFL) thickening followed by steady RNFL thinning, with 9/16 and 11/16 eyes reaching significantly low RNFL thickness and papillomacular bundle (PMB) thickness, respectively ($P< 0.01$). Concurrently, there was recovery of high-contrast visual acuity (HCVA) in all 5 affected eyes without recovery of contrast sensitivity (CS) in all but 1 of 11 affected eyes. There was no correlation between HCVA and any OCT measure. By contrast, lower global RNFL thickness was associated with worse CS (ρ=+0.36) and visual field depression (ρ=+0.66). Lower PMB thickness was associated with worse CS, color vision by Ishihara plates, and visual field depression (ρ=+0.42, +0.41, +0.38, respectively). Higher nasal/temporal ratio was associated with worse CS and less visual field depression (ρ=-0.42, +0.48, respectively).

Conclusions:
MOG shows a pattern of prominent retinal atrophy, as demonstrated by global RNFL thinning, with remarkable preservation of HCVA but concurrent deficits in CS, color vision, and visual fields. These tests may be better clinical markers of vision changes secondary to MOG-ON. Of the OCT parameters measured, PMB thickness demonstrated the most consistent correlation between structural and functional measures. Thus, it may be a more sensitive marker of clinically significant retinal atrophy in MOG-ON than global RNFL thickness.

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Keywords: Optic neuritis, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Demeylinating disease, Pediatric neuro-ophthalmology, Optic neuropathy
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The natural history of Leber hereditary optic neuropathy in the subacute/dynamic phase: Visual acuity outcomes from the historical Case Record Survey-2 (CRS-2)

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Introduction:
Leber hereditary optic neuropathy (LHON) is a rare mitochondrial disorder resulting in severe bilateral vision loss. The natural history of LHON is influenced by the age of onset and the causative mitochondrial DNA (mtDNA) mutations, among other factors. The Case Record Survey-2 (CRS-2; ClinicalTrials.gov NCT02796274) was conducted to establish the clinical course in patients with a genetically confirmed diagnosis of LHON.

Methods:
Retrospective clinical data was extracted from case records between May 2016-March 2018 from 20 sites in 7 European countries. Patients carrying one of the three common LHON mtDNA mutations (m.11778G>A, m.3460G>A, or m.14484T>C) aged ≥12 years, with onset of symptoms after 1999, and with at least two visual acuity (VA) assessments within 5 years of symptom onset and prior to any potential idebenone use, were eligible for enrolment. Outcome measures were: (i) clinically relevant recovery (CRR): improvement from 'off-chart' VA to ≤1.6 logMAR, or an improvement of ≥0.2 logMAR if on-chart; (ii) clinically relevant stabilization (CRS): maintenance of VA < 1.0 logMAR; (iii) clinically relevant benefit (CRB): reaching a CRR, a CRS, or both; and (iv) clinically relevant worsening (CRW): worsening to 'off-chart' or a VA loss of ≥0.2 logMAR if on-chart. The baseline was defined as the first VA assessment after symptom onset.

Results:
CRS-2 included data from 219 patients. In eyes with symptom onset ≤1 year prior to baseline, the following outcome rates were observed at 12 months from baseline: CRB: 20.8% (20/96 eyes; primary endpoint); CRR: 12.5% (12/96 eyes); CRS: 26.2% (11/42 eyes); CRW: 52.1% (50/96 eyes). The following outcome rates were observed at 24 months from baseline: CRB: 43.2% (19/44 eyes); CRR: 27.3% (12/44 eyes); CRS: 45.5% (10/22 eyes); CRW: 36.4% (16/44 eyes).

Conclusions:
CRS-2 provides important insight into the natural history of LHON, which is essential for the interpretation of clinical trials for this rare disease.

References: None provided.

Keywords: Optic neuropathy, Genetic disease, Retina

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Therapeutic intervention in Leber Hereditary Optic Neuropathy: later is better?

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Introduction:
Therapeutic intervention in Leber Hereditary Optic Neuropathy (LHON) is thought to obey the rule earlier is better. However, recent results from gene-therapy clinical trials highlighted that the best visual outcome occurred when therapy was administered during LHON dynamic-phase. We investigated the visual outcome of idebenone-treated and untreated LHON eyes in relation to timing of idebenone administration from the disease-onset.

Methods:
This retrospective and exploratory study investigated the effect of idebenone-therapy on final functional and structural ocular outcomes of treated and untreated patients with asynchronous/synchronous LHON-onset.

Results:
Globally, 116 eyes of 58 LHON patients (50 males; 8 females) carrying the 11778G>A/MT-ND4 mutation with average disease-duration of 15.9±12.3 years and follow-up time of at least 3-years after disease-onset were included. Outcome measures were final best-corrected visual acuity (VA, LogMar), final average and superior/nasal quadrant peripapillary-retinal nerve fiber layer (RNFL, µm) thicknesses measured by SS-OCT (DRI Triton, Topcon). Of 58 patients, 37 (64%) were treated with idebenone at different dosage and interval from disease-onset and 21 (36%) were never treated. At last visit, eyes treated in dynamic/chronic-phase (n=22) showed a significant VA increase compared to the ones treated in subacute-phase (n=48) (p=0.02) and untreated ones (n=41) (p=0.004). Concerning OCT outcomes, different comparison groups did not show statistically significant differences.

Conclusions:
These preliminary results suggest that LHON visual outcomes might be better in eyes treated in dynamic/chronic disease-stage, thus matching the results from gene-therapy clinical trials. The reason for this counterintuitive observation with different types of therapy needs further investigation in larger cohorts of treated patients.

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Keywords: Optic neuropathy, Genetic disease

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Visual Acuity Outcomes in Post-Cataract Surgery Optic Neuropathy

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Introduction:
Post-cataract surgery optic neuropathy (PCSON) is a rare, but serious complication occurring weeks to months after cataract surgery. Multiple studies have previously evaluated the timing and incidence of PCSON, including in comparison to spontaneous non-arteritic anterior ischemic optic neuropathy (sNAION) and control populations. However, visual acuity (VA) outcomes in PCSON are not known. Therefore, evaluated the long-term VA outcomes in patients with PCSON compared with sNAION.

Methods:
A retrospective cohort study was conducted using chart review of Mayo Clinic patients who underwent cataract surgery and subsequently developed PCSON within 1 year of surgery and compared to Mayo Clinic patients with sNAION . Final VA, at 6 months or greater following diagnosis, was compared using logMAR conversion and student t-test.

Results:
The PCSON group (N = 17) had a mean final VA of 20/150, compared with 20/110 in the NAION group (N = 86) (p = 0.46). In the PCSON group, 1 of 17 patients achieved final VA of 20/20 (5.8%), while 16 of 86 (18.6%) sNAION patients had a final VA of 20/20 (p = 0.20). Approximately half of the patients in each group achieved VA of 20/50 or better (p = 0.86). In the PCSON group, 9 of 17 (53%) patients had final VA of < 20/200, compared to 27 of 86 (32%) of sNAION patients (p = 0.10). Mean follow up time was 97.65 months (range, 7-277) and 144.2 months (range, 13-1264) in the sNAION and PCSON groups, respectively.

Conclusions:
Our study demonstrated that the mean final VA difference was not statistically significant between PCSON and sNAION; however, the distribution of VA showed a non-significant trend towards worse outcome in PCSON.

References: None provided.

Keywords: Optic neuropathy, Optic neuritis, Optic nerve trauma and treatment

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A Pilot Study of Optical Filters to Improve Vision-Related Quality of Life in Patients with Visual Snow Syndrome

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Introduction:
Visual Snow Syndrome (VSS) is characterized by persistent perception of visual static with at least one associated symptom of palinopsia, photopsia, photophobia, nyctalopia, or entoptic phenomena. Currently, there is no effective treatment. Individuals with migraine and blepharospasm have used filtered lenses to manage symptoms of photophobia. The purpose of this investigation is to determine if filtered lenses that maximally block light at 480 nm and 590 nm improve vision-related quality of life.

Methods:
A cross-sectional web-based invitation was sent on a social media site dedicated to VSS. Eligible subjects completed five validated questionnaires: Utah Photophobia Symptom Impact Scale (UPSIS-12), National Eye Institute Visual Function Questionnaire (VFQ-25), the 10- item Neuro-Ophthalmic supplement (VFQ- 10), General Anxiety Disorder-2 (GAD-2), and Personal Health Questionnaire Scale -2 (PHQ-2). Participants received glasses fitted with filtered lenses. After wearing them for 6 weeks, participants completed the same questionnaires. Individuals could keep the glasses or exchange them for a $100 gift card.

Results:
Of the 28 recruited participants, 26 completed the 6-week study, and 10 have returned the post-filter survey. The mean pre-filter VFQ-25 score was 67.2 and the mean post- filter score was 71.1. The mean pre-filter UPSIS-12 score was 41.9 and the mean post-filter score was 35.0. The mean score of the VFQ-10 was 27.2 pre-filter and 26.5 post-filter. The PHQ-2 pre-filter mean was 3.4 and post-filter 1.8. The GAD-2 pre-filter mean was 3.4 and 1.8 post-filter. All mean scores for the surveys showed improvement in symptoms, but only the GAD-2 improvement was statistically significant. 7/10 patients have decided to keep the glasses; 3/10 patients chose the gift card. Results will be updated in advance of the Annual Meeting.

Conclusions:
Filtered lenses show promise in improving VSS patients' overall vision-related quality of life. Further studies are needed to definitively determine if these lenses are effective.

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Assessing Visual Photosensitivity in Subjects with and without Traumatic Brain Injury Using the Ocular Photosensitivity Analyzer

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Introduction:
Visual photosensitivity is an incapacitating symptom of traumatic brain injury (TBI). We assessed photosensitivity in healthy and TBI subjects with and without light filtering lenses by using the validated Ocular Photosensitivity Analyzer (OPA) (PMID:30460148) and Visual Light Sensitivity Questionnaire-8 (VLSQ-8) (PMID:28845363).

Methods:
46 healthy subjects (age 32.5±13.4 years, 26 females) and 46 TBI subjects (age 42.0±15.0 years, 11 females) were administered VLSQ-8 before OPA testing. The OPA automated audio instructed the subject to press a button when light stimulus is “uncomfortable”. The visual photosensitivity thresholds (VPT) is calculated from the mean of ten response reversals. A lower VPT and a higher VLSQ-8 score indicate more photosensitivity. Each subject completed two, five-trial study visits, one month apart (V1 and V2). The five trials were performed with no lens (NL), followed by plano lens (PL), blue-light blocking lens (BL), FL-41 (FL), and gray filtering lens (GL) glasses.

Results:
Test-retest reproducibility for all trials between visits showed good reliability (ICC=0.79-0.92). NL and PL lenses produced comparable VPT values within healthy and TBI subjects. FL and GL lenses improved light tolerance in healthy and TBI subjects significantly, more than the NL, PL, and BL light filtering lenses ($p< 0.05$). The VPT of healthy and TBI subjects at V1 were 2.5±0.8 and 1.7±0.9 log lux, respectively ($p< 0.01$). The VLSQ-8 scores of healthy and TBI subjects at V1 were 11.5±3.4 and 21.1±8.3, respectively, (< 0.01). The VPT scores were negatively correlated with the VLSQ-8 scores ($r=-0.61$, $p< 0.01$).

Conclusions:
The OPA and VLSQ-8 are reliable tool for quantifying visual photosensitivity in TBI with TBI subjects having lower VPT and higher VLSQ-8 scores compared to healthy subjects. FL and GL lenses increased VPT and improved photosensitivity in healthy and TBI subjects. FL lenses are preferred to GL lenses given potential dark adaptation with long-term use of GL lenses.

References: None provided.

Keywords: Trauma, Higher visual functions, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease

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Evaluating Visual Snow Symptoms and Severity Using the Colorado Questionnaire and Visual Snow Simulator in Koreans

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Introduction:
This study aims to assess the symptoms of visual snow syndrome (VSS) among Koreans utilizing the Colorado questionnaire (CQ) and to determine the severity of the condition through the visual snow simulator.

Methods:
From May 2021 to July 2023, 53 individuals diagnosed with VSS at Konkuk University underwent a thorough examination focusing on the density, speed, and size of the visual snow simulator which is a specialized tool used to replicate and quantify the visual disturbances experienced by individuals with VSS. In conjunction with the simulator evaluation, participants were requested to complete the CQ, which was designed to gauge the intensity and impact of VSS on individuals' daily lives. spectrum of experiences related to the condition.

Results:
The mean age of the 53 patients (58.8%, 31 males, age=11-50) in the study was 28±11.11 years. Among the various items assessed in the CQ, the results revealed that the symptom with the most significant impact on patient's daily lives was "floater." Following closely after "floater" were two other impactful symptoms: "anxiety" and "blue field entoptic phenomenon." On the other hand, the symptoms with the lowest impact on patients' daily lives were "The feeling of detachment," "Tinnitus," and "Palinopsia," in that order. The average density, speed, and size in the visual snow simulator were measured to be 0.48, 34.38, and 1.84, respectively. There was no significant correlation between the severity of the visual snow simulator and Colorado questionnaire scores.

Conclusions:
These results suggest that it is the subjectivity of individuals' perception of VSS, rather than the severity itself, that has a greater impact on their quality of life. Also, by quantifying parameters related VSS, researchers can offer a more comprehensive understanding of VSS and its impact on life on the Korean population.

References: None provided.

Keywords: Non-organic visual disorders, Higher visual functions, Pediatric neuro-ophthalmology, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Ocular motility

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Human Astrocyte Matrisome Enhances Neural Network Formation for Use in Transplant Therapy in Cortical Vision Loss

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Introduction:
Damage to the occipital cortex disrupts established neural tracks and networks resulting in poor vision processing and blindness. Regeneration of these networks are inherently slow; thus, expediting recovery of synapses in this region is imperative. Here, we demonstrate the use of synapse-promoting mechanisms of astrocytes in human organoid systems to develop rapid and mature neural networks within 28 days.

Methods:
Transgenic stems cells engineered for rapid maturation into neurons and astrocytes were differentiated in 3 and 12 days respectively and were combined in 3-dimensional organoid coculture (Asteroids) versus monocultures of neurons-only (Neurospheres).

Results:
Asteroids showed increased synchronicity and frequency of neural burst activity seen both in multi-electrode array (MEA) analysis and Ca2+-imaging when compared to neurospheres. To further specify the mechanism, transcriptome analysis of stem-cell derived astrocytes compared to neural progenitor cells identified known synaptogenic matricellular protein Thrombospondin-1 (THBS1) and multiple matrix chondroitin sulfate (CS) proteoglycans to be uniquely secreted by astrocytes. Immunohistochemistry imaging of asteroids confirmed that astrocytes secrete significantly more proteoglycans than neurospheres. To test these components upon neural networks, exogenous addition of THBS1 to neurospheres showed increased frequency of synaptic bursts on Ca2+-imaging and increased spike frequency on MEA. This effect was blocked with cotreatment of gabapentin, an anticonvulsant known to antagonize THBS1 at its receptor, α2∂1. Chondroitin sulfate treatment of neurospheres also increased Ca2+ bursts. Thus, astrocyte-mediated synaptogenesis offers therapeutic potential to restore neural networks in injured and diseased areas; therefore, we genetically engineered human asteroids to overexpress THBS1 via lentivirus transduction. Encapsulation of these asteroids in alginate hydrogel capsules provide a non-immunogenic and non-motile environment permitting transplantation of capsules to an injured occipital cortex in vivo.

Conclusions:
Overall, we identified and characterized the role of astrocytes in generating robust neural networks and propose a therapy to regenerate networks after occipital neurotrauma or stroke to expeditiously restore visual function.

References: None provided.

Keywords: Trauma, Stroke, Higher visual functions, Miscellaneous

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Neural network correlates of anosognosia for visual loss

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Introduction:
The phenomenon of anosognosia, the lack of recognition of a neurological deficit, remains one of the great mysteries of neurology. Among patients with complete visual loss from occipital lesions, it is not known why some report awareness of the deficit while others do not. The topology of structural lesions alone does not account for the presence or absence of awareness of the deficit.

Methods:
Through a PRISMA systematic literature search, we identified 24 reports of patients with unawareness of complete vision loss (i.e., Anton syndrome). An ideal comparator group – namely, a cohort of patients with occipital lesions causing complete visual loss but spared consciousness – was not available. We therefore used an available control group consisting of 69 individuals with lesions causing partial visual field loss with awareness. For each case of Anton syndrome, we determined the distributed functional network of brain regions connected with the structural lesion location using a database of resting-state functional connectivity collected from 1000 healthy subjects. By identifying regions of overlap across these lesion-based network maps, we identified brain areas implicated in determining awareness of a visual deficit. We also conducted the same analyses using a dataset of individuals with lesions producing hemiparesis with awareness (n=79) or hemiparesis without awareness (n=95). We thus determined areas implicated in anosognosia of a neurological deficit regardless of its specific modality.

Results:
Anosognosia in Anton syndrome is strongly associated with lesions involving brain regions that have functional connectivity to visual association areas and the posterior cingulate. More generally, anosognosia for deficits that are either visual or motor is associated with lesions that have connectivity to the hippocampus and precuneus (FDR $p < 0.05$).

Conclusions:
Lesion-based network analysis demonstrates that anosognosia may be accounted for by functional impairment in distributed networks including memory circuits in the brain.

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Keywords: Higher visual functions, Neuroimaging

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Visual Imagery in Posterior Cortical Atrophy and Visual Agnosia

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Introduction:
Visual imagery has a close overlapping relationship with visual perception. Posterior cortical atrophy is a degenerative syndrome marked by early impairments in visuospatial processing and visual object recognition. We asked whether this disorder would therefore also be marked by deficits in visual imagery, as probed by objective forced-choice questionnaires, and whether imagery deficits were more prominent for certain types of visual stimuli.

Methods:
We recruited five patients with visual agnosia, four with posterior cortical atrophy and one patient with bilateral occipitotemporal strokes. We administered a battery of nine tests probing imagery for object shape or size, colour lightness or hue, upper-case or lower-case letters, word shape, letter construction, and famous faces. Findings were contrasted with those of eleven patients with adult-onset ocular blindness and four subjects with congenital blindness.

Results:
All agnosic subjects showed a marked impairment in visual imagery. Imagery for lower-case letters was most likely to be spared, while several agnosic subjects found the word shape and letter construction tests too difficult to complete, likely reflecting the more complex demands of these tasks. In some tasks their performance was similar to that of subjects who had never been able to see. In contrast, patients with acquired ocular blindness had better preserved visual imagery, even after decades of visual loss in some cases.

Conclusions:
Subjects with posterior cortical atrophy can show severe deficits in visual imagery. This likely reflects the degradation of stored information about visual properties when high-level object-processing networks are damaged. Further work is needed to establish how frequently and how early this occurs in the course of posterior cortical atrophy. A practical short test for visual imagery may be a useful screening tool.

References: Dietz C, Malaspina M, Albonico A, Barton JJS. The persistence of remote visual semantic memory following ocular blindness. Neuropsychologia 2022; 165: 108110.

Keywords: Higher visual functions, Stroke

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A Retrospective Chart Review Assessing The Outcomes of Dural Venous Sinus Stenting in Idiopathic Intracranial Hypertension Patients

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Introduction:
Idiopathic intracranial hypertension (IIH) is a condition characterized by elevated intracranial pressure that predominantly affects women of childbearing age. This study aims to analyze the post-operative effect of dural venous sinus stenting (DVSS) on quality of life of patients with IIH through assessment of symptoms and acetazolamide dosage and to add to the pool of existing literature on DVSS for IIH.

Methods:
Charts of 15 patients who have undergone DVSS from April 2020 to April 2023 were retrospectively reviewed. Acetazolamide dosages in mg/day and retinal nerve fiber layer (RNFL) thickness in µm were recorded at baseline, pre-stent, and post-stent. Patient symptoms such as headaches, migraines, transient visual obscurations (TVOs), papilledema, and pulsatile tinnitus were recorded and deemed worsened, stable, or improved compared to baseline. The Wilcoxon signed-rank test was performed to determine the significance of acetazolamide dosage and OCT RNFL thickness at post-stent compared to baseline and pre-stent.

Results:
There was a statistically significant difference in acetazolamide dosage between baseline and post-stent measurements ($p=0.02$) as well as between pre-stent and post-stent measurements ($p=0.025$). There was also a statistically significant difference in OCT RNFL right eye thickness between baseline and post-stent measurements ($p=0.0069$) as well as between pre-stent and post-stent measurements ($p=0.028$). The difference between baseline and post-stent OCT RNFL left eye thickness was significant ($p=0.018$), but the difference between pre-stent and post-stent OCT RNFL left eye thickness was not significant ($p=0.36$). Post procedurally, headaches improved in 78.6%, migraines improved in 37.5%, papilledema improved in 100%, pulsatile tinnitus improved in 45.4% of patients, and TVOs improved in 100% of patients who had these symptoms prior to stenting.

Conclusions:
This study supports the use of DVSS as a tool to improve quality of life of people with IIH through the decrease or cessation of acetazolamide therapy and the improvement in symptoms seen.

References: None provided.

Keywords: Pseudotumor cerebri, High intracranial pressure/headache

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Grant Support: None.

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Accuracy Of Fundoscopic Evaluation Of Papilledema Compared To Indirect Neuro-Radiological Signs Of Intracranial Hypertension

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Introduction:
Papilledema refers to optic disc edema secondary to raised intracranial pressure which can lead to irreversible blindness and death if not recognized promptly. However, several benign entities can mimic papilledema on fundoscopy, including optic disc drusen or tilted nerves. Magnetic resonance venography can reveal indirect signs of intracranial hypertension such as bilateral transverse sinus stenosis (TVSS), with a sensitivity and specificity of 93%. This study sought to quantify the accuracy of neuro-ophthalmologists in their ability to discern true papilledema based on fundoscopy alone.

Methods:
This was a prospective chart review of all patients referred to a tertiary university-affiliated neuro-ophthalmology practice for query papilledema between 2022-2023. Clinical and neuro-radiological data was collected. Fundus photography was evaluated by 3 independent neuro-ophthalmologists and their assessments of papilledema were compared to neuro-radiologic reports of TVSS.

Results:
36 patients were analyzed. 21 demonstrated neuro-radiologic signs of intracranial hypertension. The overall accuracy of each rater was 33.3%, 44.4%, and 41.7% (rater 1, 2, and 3) respectively in discerning true papilledema. 7 patients (19.4%) were correctly graded by all three neuro-ophthalmologists and 16 (44.4%) were incorrectly graded by all three. The positive predictive value of fundoscopy was 23.8%, 28.6%, and 19.0% by each rater respectively. The negative predictive value was 46.7%, 66.7%, and 73.3% respectively. There was no significant difference in symptoms, visual acuity, visual field mean deviation, RNFL thickness, or Frisen grading among those correctly and incorrectly diagnosed by all three neuro-ophthalmologists, and within each rater. Inter-rater reliability was poor.

Conclusions:
Fundoscopy alone does not allow for sufficient distinction of papilledema from pseudopapilledema, highlighting the importance of neuroimaging in confirming the diagnosis. Thus, in cases with sufficient clinical suspicion, MRV should be considered the gold standard to rule out intracranial hypertension.

References: None provided.

Keywords: High intracranial pressure/headache, Pseudotumor cerebri, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease

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Grant Support: None.

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An Update on Fulminant Idiopathic Intracranial Hypertension: From Potential Risk Factors to Visual Outcomes

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Introduction:
Limited research is available to guide the management of patients with fulminant idiopathic intracranial hypertension (FIIH), with the most robust data derived from the sixteen patients reviewed in the Thambisetty et al. landmark publication from 2007. We aimed to conduct an updated study that would include venous sinus stenting, which has since become an accepted interventional treatment for IIH.

Methods:
Patients with fulminant presentation who met the Dandy Criteria and received an ICD code for IIH or papilledema at a single tertiary care center from June 1, 2012 to April 1, 2022 were included in this IRB approved study.

Results:
FIIH had a prevalence of thirty-two patients or 4.2% within the IIH population at a single tertiary care center. 3 (9.4%) patients were men, mean age at diagnosis was 27.98 (SD 8.84), and mean BMI was 40.0 (SD 7.94). 15 were black, 15 were white, and 2 were Hispanic. Twenty-three (71.9%) underwent surgical and/or interventional procedure within 3 months of diagnosis (mean of 13.9 days). Visual field (VF) mean deviations (MD) at baseline were -16.61 OD, -14.03 OS compared to -14.93 OD, -15.70 OS at follow up 3 months to 1 year after diagnosis. Patients who underwent ventriculoperitoneal shunt or optic nerve sheath fenestration (ONSF) had the worst average VF MD, with the greatest improvement seen after ONSF. As compared to our cohort of 734 IIH patients, multiple potential risk factors for a fulminant presentation were found, including history of anemia (2.67, CI 95%: 1.26, 5.66), having a Black race (2.42 CI: 1.26, 4.64) compared to white race, and being a current smoker (2.31 CI: 1.09, 4.89) compared to never smoker.

Conclusions:
To our knowledge, this is the largest FIIH cohort that has been reported. It provides potential risk associations for fulminant presentation and updated visual outcome data in FIIH.

References: None provided.

Keywords: Pseudotumor cerebri, High intracranial pressure/headache, Visual fields

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Grant Support: None.

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Application Of Novel Non-invasive Ophthalmic Imaging To Elucidate The Impact Of Elevated Intracranial Pressure On The Ultrastructure Of The Retina And Optic Nerve Head

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Introduction:
Elevated intracranial pressure (ICP) is an important diagnostic parameter for which non-invasive measures have been elusive. Previous studies have investigated potential non-invasive surrogate measures, but they all have their limitations. Our aim was to identify novel non-invasive biomarkers of ICP using multimodal imaging of the ultrastructure of the retina and optic nerve head in subjects with elevated ICP and evaluate the feasibility of implementing these biomarkers in clinical practice and in further scientific research.

Methods:
This single-center pilot study included subjects with untreated or incompletely treated high ICP (idiopathic intracranial hypertension (IIH) or secondary pseudotumor cerebri (SPTC)). Optical coherence tomography (OCT) and adaptive optics-scanning laser ophthalmoscopy (AO-SLO) images were used to assess the volume of peripapillary hyperreflective ovoid mass-like structures (PHOMS), hyalocyte distribution and peripapillary wrinkles (PPW)/retinal folds (RF). The time needed to acquire and process these images was estimated.

Results:
6 subjects with high ICP (5 IIH, 1 medication induced SPTC, 30.8 ± 8.6 years, 75% female, 5 with papilledema) and 1 control (25 years, female) were included. PHOMS, PPW and RF were present in all subjects with papilledema, but neither the high ICP subject without papilledema nor the control subject. Averaged en-face OCT scans and AO-SLO were more sensitive for PPW and RF than OCT B-scans and SLO scans. Hyalocyte distribution was difficult to evaluate due to the presence of PPW/RF. The time spent on image acquisition (30-90 minutes) and image processing (30 minutes up to 2 weeks) varied between imaging modalities.

Conclusions:
PHOMS and PPW/RF have potential as non-invasive biomarkers of ICP. However, lack of automated image acquisition and processing limits widespread adoption in clinical settings. Further research is needed to validate these structures as biomarkers for elevated ICP.

References: None provided.

Keywords: Pseudotumor cerebri, Retina

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Clinical Profile and Etiologies of Papilledema in Tertiary Eye Care Centre

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Introduction:
Papilledema is a bilateral optic disc oedema due to transmission of elevated raised intracranial pressure (ICP) to the surrounding subarachnoid spaces thus hindering axoplasmic transport within ganglion cell axons. Pathological culprits include idiopathic causes, conditions that decrease cerebrospinal fluid (CSF) outflow and rarely by conditions that increase CSF production. This study aims to explore the clinical profile and various etiologies of papilledema.

Methods:
A retrospective cross-sectional study analyzing the electronic medical records of all diagnosed cases of papilledema from Jan 2021 to Jun 2023 with Magnetic Resonance Imaging (MRI) of Brain and Venography (MRV) reports was done. The parameters studied include presenting history, co-existing illness, visual acuity, colour vision, fields, pupils, extraocular movements, and fundus evaluation

Results:
In total, 97 participants were included for this analysis. Among them ,61(62.88%) patients were women and 36 (37.11%) were men with mean (SD) age of 31.25 (12.21). Among them, 50 patients (51.6%) had Idiopathic Intracranial Hypertension (IIH), 23 patients (23.7%) had Cerebral Venous Sinus Thrombosis (CVT), 19 patients (19.6%) had Tumour with mass effect, 5 patients (5.15%) had Meningitis. Double vision (39.2%) was the commonest presenting symptom and extraocular muscle palsies were found in 30.9 % of the subjects, especially in cases with IIH and CVT. Co-existing illnesses like menstrual irregularities, hypothyroidism and anemia were found in 38% of the IIH cases. The median Body Mass Index (BMI) of IIH patients was 31.45 (27.06 – 37.29). Colour vision (26.3%), field (31.6%) and pupil (21.1%) abnormalities were noted more in cases with mass effects.

Conclusions:
Though the most common cause is IIH, non-idiopathic causes contribute to half of the rest. Higher BMI, alterations in the menstrual cycle, thyroid profile and anemia favour the likelihood of IIH. Papilledema due to IIH and mass effects can present with asymmetric disc oedema

References: None provided.

Keywords: High intracranial pressure/headache, Pseudotumor cerebri

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Contact Information: None provided.

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Correlation Between Glymphatic Flow and Intracranial Pressure in Idiopathic Intracranial Hypertension: Preliminary Findings

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Introduction:
The mechanism by which intracranial hypertension develops in idiopathic intracranial hypertension (IIH) remains unclear. The recently identified glymphatic system is a novel and compelling candidate mechanism. A preliminary gadolinium-based study described glymphatic dysfunction in IIH, but it remains unclear whether glymphatic dysfunction causes or results from elevated intracranial pressure (ICP).

Methods:
3-Tesla MRI was employed to derive indices of glymphatic flow (ALPS-index) in IIH patients and controls pre and post-lumbar puncture (LP), using a previously-validated method involving 12-direction diffusion tensor imaging in voxels located along the perivascular space (DTI-ALPS). Lower ALPS-indices suggest attenuated glymphatic function.

Results:
4 overweight female participants underwent pre-and-post-LP imaging, 1 with active, untreated IIH, 1 with long-resolved IIH, and 2 controls. The participant with active IIH exhibited the lowest ALPS-index (1.1), indicative of least glymphatic function, and the highest opening pressure (24cm H2O). Conversely, the participant with long-resolved IIH had the highest ALPS-index (1.56) and lowest opening pressure (14cm H2O). The ALPS-index increased in all patients post-LP. The patient with active IIH exhibited the largest reduction in ICP pre/post-LP (24 to 10 cm H2O) and exhibited the largest increase in ALPS index (1.1 to 1.24), though this remained at the low end of the range of ALPS-indices.

Conclusions:
Preliminary findings suggest an inverse relationship between glymphatic function and ICP among IIH patients and controls. However, glymphatic flow may represent more than a byproduct of elevated ICP; the participant with active IIH, despite showing the most significant post-LP rise in the ALPS-index, demonstrated persistently low flow upon re-imaging immediately post LP. Our study has been active for 1 month and comprises 11 controls, 4 patients with new IIH, and 2 with a past IIH diagnosis but resolved papilledema. We anticipate presenting data from 40 controls (not all will undergo LP) and 10 IIH patients at the NANOS meeting.

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Keywords: Pseudotumor cerebri, High intracranial pressure/headache, Neuroimaging

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Eating Behaviors in Idiopathic Intracranial Hypertension

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Introduction:
Despite the centrality of weight loss in the management of idiopathic intracranial hypertension (IIH), little research has examined eating behaviors or the role of nutritional counseling in this population. We conducted two studies to address these gaps: 1) a cross-sectional analysis of eating behaviors in patients with IIH vs. controls and 2) a comparison of weight loss in patients with IIH who received counseling from a nutritionist and neuro-ophthalmologist compared to those who received neuro-ophthalmic counseling alone.

Methods:
We conducted a cross-sectional study administering the EAT-26, a validated eating disorders screening questionnaire, to patients with IIH and controls matched for gender, age, and habitus. Prospective follow-up EAT-26 surveys with IIH patients are underway and will be available by January 2024. To examine the influence of nutritional counseling on weight loss in an IIH cohort, change in weight between the first and most recent neuro-ophthalmic encounter was compared between patients who had received formal nutritional counseling vs. those who received physician-only counseling.

Results:
14 participants with IIH and 11 controls participated in the baseline EAT-26 questionnaire. Patients with IIH scored significantly higher on the EAT-26 than controls (8.6 vs 4.4, p=0.032) despite a similar BMI. Weight loss was compared between 12 IIH patients who received nutritional counseling and 23 who did not; over the follow-up period (mean 6 months), weight loss was not significantly different between groups (p=0.43).

Conclusions:
The prevalence of ego-dystonic body attitudes is higher in patients with IIH than in controls. The follow-up period will clarify whether these attitudes correlate (positively or negatively) with weight loss or increase in prevalence over time, possibly as an unintended result of counseling. Conventional nutritional counseling did not augment physician-only guidance in achieving weight loss in IIH and underscores the need for developing weight loss strategies specific to this population.

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Factors associated with vision loss in idiopathic intracranial hypertension (IIH) patients with severe papilledema

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Introduction:
Vision loss from papilledema, the most serious complication of IIH, is difficult to predict at initial diagnosis, but only occurs in patients with high-grade papilledema for whom deciding whether aggressive treatment at presentation is necessary. We compared patients with severe papilledema and poor or good visual outcomes.

Methods:
Retrospective review of consecutive IIH patients (1/1/2013-6/10/2023). Severe papilledema: Frisén 4-5/±atrophy in ≥1 eye. Poor visual outcome: VA ≤20/200 or HVF-MD <-15.00 or < 10º GVF III4e/V4e in ≥1 eye; good visual outcome: VA ≥20/40 OU, and HVF-MD >-15.00 on HVF or >20º GVF III4e/II4e/I4e. Follow-up >6 months for medically-treated patients; >3 months for surgically-treated patients.

Results:
Of 134 IIH patients with severe papilledema, 70 had poor and 64 had good visual outcomes. No significant differences existed for age, gender, race, hypertension, hemoglobin, CSF-OP. Poor-outcome group had significantly greater BMI (mean 39.2 vs 35.1 kg/m2, p=0.004), diplopia (23.4% vs 8.6%, p=0.03), and worse initial HVF-MD (-20.04 vs -5.81 dB, p< 0.0001). Poor-outcome patients saw more prior health-care providers (4.7 vs 2.4, p< 0.0001), with delayed neuro-ophthalmology encounters (58.5 vs 15.2 weeks, p=0.001). 41.4% of poor-outcome patients were initially seen in outside emergency departments (ED) (vs 14.1% of good-outcome group, p=0.0005), while only 27.1% were seen by eye-care providers (vs 53.1% of good-outcome group, p=0.0027). No poor-outcome patients initially consulted our ED vs 7.8% of good-outcome patients. 71.4% of poor-outcome patients underwent at least one surgery vs 20.3% of good-outcome patients (p< 0.0001).

Conclusions:
Factors associated with poor visual outcome among IIH patients with severe papilledema at presentation included higher BMI, diplopia, and generalized depression on initial HVF/GVF. Most poor-outcome patients had delayed diagnosis/treatment related to prior outside ED visits and lack of prior eye-care provider evaluations, suggesting that early diagnosis and management of papilledema is essential for patients with symptoms of intracranial hypertension.

References: None provided.

Keywords: Pseudotumor cerebri, High intracranial pressure/headache, Visual fields

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Five Years of a Multidisciplinary Intracranial Hypertension Clinic

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Introduction:
Patients diagnosed with intracranial hypertension often have complex medical needs necessitating multiple regular physician appointments and close collaboration among specialties to adequately treat the root cause and associated symptoms. We have been operating a monthly multidisciplinary intracranial hypertension clinic with a neurosurgeon, headache specialist, cerebrospinal fluid (CSF) specialist and neuro-ophthalmologist since March 2017. Here we present demographics and outcomes from this clinic after reviewing the first 5 years of clinics held.

Methods:
This multidisciplinary intracranial hypertension clinic saw 196 unique patients on 58 clinic dates with 6 physicians in 4 specialties over 5 years. Information was collected on demographics, diagnoses, testing conducted, interventions performed, and specialists seen.

Results:
Patients ranged from 18 to 77 years old, with an average age of 40 and 87% of patients were female. Patients identified as 78% white, 11% black, 4% Asian, 2% Native Hawaiian or Pacific Islander, 2% American Indian or Native Alaskan, 2% Hispanic and 8% Declined to Answer, with overlap for patients identifying as mixed race. Patients traveled from across the northwest for this clinic, including from Alaska, Hawaii, Idaho, Montana, and Washington. Of these patients, 15% were seen by a neurosurgeon, 45% by a headache specialist, 70% by a CSF specialist and 99% by a neuro-ophthalmologist. Conditions seen in this clinic include idiopathic intracranial hypertension, hydrocephalus, venous sinus thromboses, meningiomas, dural arteriovenous fistulas, and primary headache. Additional outcomes data from the clinic will be presented.

Conclusions:
Hosting monthly intracranial hypertension clinics improves patient access to multiple specialties, augments collaboration between subspecialty providers and has the potential to improve the patient experience.

References: None provided.

Keywords: High intracranial pressure/headache, Pseudotumor cerebri

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Frequency of Medication-Induced Intracranial Hypertension and Odds of Fulminant Presentation of Disease

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Introduction:
Idiopathic Intracranial Hypertension (IIH) is defined as elevated intracranial pressure in the absence of an identifiable cause. IIH can lead to serious neuro-ophthalmic manifestations including vision loss. Tetracyclines and retinoids can cause secondary IH, also known as medication-induced IH. We aimed to determine the frequency of medication-induced IH among patients diagnosed with IIH in a large referral center.

Methods:
This retrospective study was performed at a tertiary care center. Data was collected from the electronic medical records of patients diagnosed with IIH (ICD-9: 348.2; ICD-10: G93.2) from 6/2012-6/2022. Patients with an identified structural cause of elevated intracranial pressure were excluded. Medication-induced IH patients were compared to IIH patients who met the Dandy criteria. Data collection included demographics, disease characteristics (papilledema, neuroimaging, lumbar puncture, visual field testing), and treatments.

Results:
858 patients with IIH were identified, of which 82 (9.6%) had exposure to tetracyclines (64.6%), retinoids (24.4%), or both (11%). The mean age was 26.24, mean body mass index (BMI) was 33.31, and 89% were female. Four patients (4.9%, 3 female) had a fulminant presentation, including two taking retinoids and two taking both retinoids and tetracyclines. Patients exposed to retinoids had a 4.85 (95% CI 1.55-15.24) times increased odds of having a fulminant presentation compared to patients not exposed to retinoids. While patients taking both tetracyclines and retinoids had 5.32 (95% CI 1.07-26.49) times increased odds of having a fulminant presentation compared to IIH patient exposed to neither drug.

Conclusions:
Medication-induced IH constitutes about 10% of all IIH diagnoses. These patients have increased chances of fulminant disease compared to idiopathic IH. This study suggests that tetracyclines are a more common exposure although retinoids are more likely to cause fulminant presentation. Ophthalmic monitoring for patients started on these medications should be considered going forward, with earlier referral to neuro-ophthalmology clinics.

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Keywords: Pseudotumor cerebri, High intracranial pressure/headache

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Idiopathic Intracranial Hypertension Relationship with Pregnancy and Associations with Hypertensive Disorders

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Introduction:
Idiopathic intracranial hypertension (IIH) mainly occurs in women of a reproductive age who are overweight or obese (1,2). As pregnancy occurs in this age group and is associated with weight increases, this is an important part of IIH healthcare needs. The purpose of this study was to determine the incidence of IIH development during a pregnancy and if IIH is associated with hypertensive disorders of pregnancy.

Methods:
In this retrospective cohort analysis, patients electronic health records who had a diagnostic code for IIH or papilledema from June 1st 2012 through April 1st 2022 were observed for IIH. After meeting the Dandy Criteria (2,3), patients were evaluated for a history of pregnancy before, during, or after their IIH diagnosis and hypertensive disorders including preeclampsia/eclampsia, HELLP syndrome, gestational diabetes, and hypertension. Incidence and risk ratios (RR) were calculated comparing IIH patients to tertiary care center of pregnant women using ICD coding during the same time period.

Results:
312 patients with IIH were found to have a history of pregnancy of which IIH was diagnosed during pregnancy in 7.1%, after 33.7%, and before 49.0%. IIH patients had an increased risk of having a hypertensive disorder in pregnancy with a RR of 1.83 (95% CI 1.43, 2.33) compared to control pregnancies without IIH. This included an increased risk of eclampsia at 9.91 (4.37, 22.44) and HELLP syndrome at 5.42 (1.34, 21.98). This increased risk was comparable if a patient had a pregnancy before or after their IIH diagnosis.

Conclusions:
Hypertensive disorders of pregnancy including eclampsia and HELLP syndrome were associated with IIH and had a higher incidence among this population compared to controls. As hypertensive disorders in pregnancy are associated with future metabolic syndromes (4), this further illustrates IIH as a potential neuro-metabolic disease.

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Keywords: Pseudotumor cerebri, High intracranial pressure/headache, Miscellaneous

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Long Term Changes In The Ganglion Cell Layer–Inner Plexiform Layer Thickness In Patients With Papilledema

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Introduction:
Optical coherence tomography (OCT) is a useful tool to monitor the long term consequences of papilledema resulting from intracranial hypertension (IIH) and hydrocephalus. The purpose of this study is to evaluate the impact of papilledema on ganglion cell layer–inner plexiform layer (GCL-IPL) in subjects with IIH and hydrocephalus post treatment.

Methods:
It is a retrospective study of 24 eyes of 12 patients with papilledema (11 patients with IIH and 1 with communicating hydrocephalus) who were monitored with serial spectral domain optical coherence tomography. The mean follow up of the patients was 18.56 months.(1-72 months).The intracranial pressure (ICP) was recorded for all the patients (except one with communicating hydrocephalus).The difference between the GCL-IPL in six sectors recorded after the lumbar puncture (baseline) and the GCL-IPL at the final follow up was analysed. The mean of difference from the baseline ,in all six sectors was calculated.Thinning of the GCL-IPL was defined as GCL-IPL value less than the fifth percentile of the GCL-IPL value derived from age-matched Zeiss normative scans.

Results:
Twenty four eyes of 12 patients were included. The age range was 17-43 years . All the eyes had a best corrected visual acuity of 6/9 or better.The mean ICP was 334.55mm H2O.The mean GC-IPL difference from the baseline was -6.17 in superior sector,-6.38 superonasal sector,-5.67 inferonasal sector,-4.67 inferior sector,-6.67 inferotemporal sector and -6.08 superotemporal sector .Ten eyes out of 24 (41.7%) showed thinning of the GCL-IPL at the final follow up.

Conclusions:
GCL-IPL thinning is noted in more than one third of the treated patients of papilledema on long term follow up.

References: None provided.

Keywords: Pseudotumor cerebri, High intracranial pressure/headache, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease

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Outcomes Of Idiopathic Intracranial Hypertension Patients on Glucagon-Like Peptide-1 Receptor Agonist Therapy

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Introduction:
Obesity is a major risk factor for the development of idiopathic intracranial hypertension (IIH), as well as recurrence after remission.1,2 While weight loss can induce remission and decrease risk of recurrence, diet and exercise often fail to achieve sustained weight reductions, and weight loss surgeries, while effective, carry significant risks.2-6 Glucagon-like peptide-1 receptor agonists (GLP-1-RAs), which have demonstrated profound weight loss in obesity, as well as the ability to directly lower intracranial pressure in IIH, may represent a potential new therapeutic option for IIH.7-10

Methods:
We conducted a multicenter, retrospective chart review of IIH patients treated with standard medical therapy and GLP-1-RAs during active disease or after resolution of papilledema (remission) (n=42). Patients with other causes of optic neuropathy, or a history of surgical management for IIH or obesity were excluded (n=14). Papilledema grade, retinal nerve fiber layer (RNFL) thickness, ganglion cell complex (GCC) thickness, patient weight, time to remission were collected.

Results:
GLP-1-RA use during remission: There were no recorded recurrences of papilledema for patients using GLP-1-RA therapy (n=17) for a median of 287 days (IQR:79-444). Last recorded patient weight declined by a median of 12% (IQR:2-14%,n=7) compared to their initial presentation with papilledema. GLP-1-RA use during active disease: Median documented peak papilledema was Frisen grade 2 (IQR:1-3, n=8). Median peak RNFL thickness decreased from 133µ (IQR:101-157µ) during active disease to 93µ (IQR:79-98µ) after remission (n=9). Post-remission median GCC thickness was 77µ (IQR:74-81µ). Patient weight declined by a median of 7% (IQR:2-11%, n=6) from initial presentation of active disease to remission. Compared to patients who began GLP-1-RAs after remission (n=13), patients who used GLP-1-RAs during >50% of their active disease period (n=6) achieved remission on average 103 days earlier (219d, SD:120 vs. 322d, SD:218; p value 0.3).

Conclusions:
Treatment augmentation using GLP-1-RAs may represent a promising new therapeutic approach for IIH.

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Peripapillary retinal pigment epithelium shape improves with venous sinus stenting in idiopathic intracranial hypertension

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Introduction:
Papilledema in idiopathic intracranial hypertension (IIH) has been shown to correlate with several findings on optical computed tomography (OCT), including anterior displacement of the retinal pigment epithelium/Bruch's membrane (RPE/BM). The angle of this anterior displacement has been shown to improve after treatment with acetazolamide, but improvement after stenting, to our knowledge, has not been previously evaluated.

Methods:
In a retrospective cohort study of patients treated by the neuro-ophthalmology group at our center since 2013, patients with papilledema who underwent transverse sinus stenting for treatment of IIH were included. Patients who underwent other interventions for IIH, had more than one stenting procedure, or who did not have both a pre- and post-treatment raster scan were excluded. Descriptive statistics were performed, and Wilcoxon signed-rank test was performed for the paired, non-normally distributed data.

Results:
Twenty patients were included, of whom 18 (90%) were female. Mean age was 34.5 years (SD 10.7). The median pre-treatment and post-treatment RPE/BM angles were 4.5 degrees (IQR 1.55 to 8.1) and -3.85 degrees (IQR -6.25 to 2.7), respectively ($p < 0.001$).

Conclusions:
In a retrospective cohort of IIH patients undergoing stenting, the angle of anterior displacement of Bruch's membrane was positive prior to the procedure and significantly decreased following the procedure. This accords with prior work demonstrating a similar decrease following treatment with acetazolamide. To our knowledge, this is the first paper demonstrating that stenting is associated with a decrease in the angle of anterior displacement of the retinal pigment epithelium/Bruch's membrane on OCT.

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Keywords: Pseudotumor cerebri, Interventional neuroradiology, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease

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Persistence Of Pulsatile Tinnitus After Resolution Of Papilledema In Idiopathic Intracranial Hypertension

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Introduction:
Papilledema is commonly used to diagnose and monitor progression and treatment of Idiopathic Intracranial Hypertension (IIH). While papilledema is expected to resolve with sufficient reduction of intracranial pressure, associated symptoms of intracranial hypertension may persist, such as headache and pulsatile tinnitus. These persistent symptoms may affect quality of life. We wish to evaluate the persistence of pulsatile tinnitus in IIH patients after resolution of their papilledema.

Methods:
This is a retrospective chart review of patients seen in our tertiary academic neuro-ophthalmology clinic for management of IIH between September 2019 and October 2023. Data regarding demographics, BMI, presenting symptoms (headache, transient visual obscurations, pulsatile tinnitus, binocular diplopia), Frisen grade for papilledema, RNFL thickness, MRV findings, pharmaceutical treatments, surgical treatments, and resolution of symptoms are being collected. Resolution of papilledema was determined by fundus exam and optical coherence tomography.

Results:
To date, 80 patient charts have been reviewed. 10 were excluded for lack of papilledema or insufficient documentation. Of the remaining patients with initial papilledema in the setting of IIH, 77.1% (54/70) presented with pulsatile tinnitus. 29 of these 54 (53.7%) demonstrated resolution of papilledema as of their most recent clinical visit, of which 65.5% (19/29) were documented to have ongoing symptoms of pulsatile tinnitus. Additionally, 28 of these patients initially presented with concomitant headaches, of which 67.9% (19/28) had persistent headaches after the resolution of papilledema. We intend to continue reviewing a total of 247 charts and resubmit a more developed abstract before the deadline for producing the syllabus. We also intend to review MRV results to identify potential associations between pulsatile tinnitus and venous sinus stenosis.

Conclusions:
The majority of patients continue to experience pulsatile tinnitus even after resolution of papilledema. These findings suggest IIH pathology may continue to affect quality of life even after papilledema resolution.

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Presenting Characteristics of Patients with Idiopathic Intracranial Hypertension from Different Racial, Ethnic, and Insurance Groups

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Introduction:
Idiopathic intracranial hypertension (IIH) has been characterized by previous studies as a disease that disproportionately affects young, Black, female patients. However, there is limited data that characterizes differences in initial presentation of IIH across groups. This study aimed to compare presenting features of IIH from different racial, ethnic, and insured groups.

Methods:
A retrospective chart review was conducted on patients with IIH seen at an academic tertiary care center between 7/1/2016 and 7/10/2023. Patient characteristics included self-reported race and ethnicity, insurance status, age, and sex. Clinical features included lumbar puncture opening pressure, body mass index (BMI), visual acuity, visual field mean deviation, retinal nerve fiber layer (RNFL) average thickness, and presence of symptoms (headaches, diplopia, transient vision obscurations, and pulsatile tinnitus). Patients were excluded if they were already treated for IIH prior to initial presentation or if diagnostic data were incomplete. Linear, mixed effect, and logistic regression models were used to evaluate differences between racial, ethnic, and insurance status groups. Statistical significance was set at $p< 0.05$.

Results:
Our study included 241 patients. One-hundred twenty-five were black, 107 white, 4 Asian, 1 Native Hawaiian/Pacific Islander, and 3 other. Two-hundred thirty-five were non-Hispanic and 6 were Hispanic. One-hundred thirty-six had private insurance, 63 Medicaid, 29 Medicare, 10 no insurance/self-pay, and 3 military insurance. There were no statistically significant differences in BMI, presence of symptoms of high intracranial pressure, visual function, or RNFL thickness at initial presentation between groups stratified by race, ethnicity, and insurance status. Black patients were more likely to have Medicaid coverage, whereas White patients were more likely to have private insurance (Medicaid 38% vs 14%; private 47% vs 67%, $p< 0.001$).

Conclusions:
There were no statistically significant differences in presenting IIH features based on race, ethnicity, or insurance status. Further work will characterize treatment course and outcomes.

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Prevalence and Geographic Variation of Idiopathic Intracranial Hypertension in the United States

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Introduction:
The prevalence of idiopathic intracranial hypertension (IIH) is increasing1, but previous studies have not considered geographic variation in disease prevalence or health outcomes.2

Methods:
To measure state-level variation in IIH prevalence, we used Medicaid claims data to identify all female Medicaid beneficiaries with at least two diagnosis codes for IIH and a prescription for acetazolamide or methazolamide in 2018. Medicaid beneficiaries represent a subset of all IIH patients. To determine the extent of this subset, we used two large nationwide electronic health record registries (IRIS® Registry [Intelligent Research in Sight] and SOURCE) to calculate the proportion of all actively treated IIH patients who were insured by Medicaid. Dividing the number of Medicaid beneficiaries by this proportion estimates the total number of treated IIH patients in each state. To validate this approach, we obtained linked medical records for a single U.S. county and identified women aged 18-54 with confirmed IIH who had a prescription for acetazolamide or methazolamide in 2014. Prevalence was calculated using U.S. Census Bureau data from with direct standardization to the U.S. population.

Results:
There were an estimated 37,000 Medicaid beneficiaries with at least one diagnosis code for IIH in 2018. In the IRIS Registry and SOURCE, 22% of all IIH patients were insured by Medicaid (95% CI 13-34%). Once we receive complete Medicaid claims data, we will combine these to estimate the nationwide and state-level prevalence of IIH in the U.S. By comparison, in 2014 there were 11 women in a single county undergoing treatment for IIH, and the age-standardized prevalence of IIH was 4.6 per 10,000 (95% CI: 3.5-5.7).

Conclusions:
Our research will provide estimates of IIH prevalence that incorporate a diverse nationwide population and produce novel data on state-level variation in IIH, which will identify areas with the greatest need for neuro-ophthalmic expertise.

References: 1. Kilgore KP, Lee MS, Leavitt JA, et al. Re-evaluating the Incidence of Idiopathic Intracranial Hypertension in an Era of Increasing Obesity. Ophthalmology. 2017;124(5):697-700. 2. Lochner KA, Goodman RA, Posner S, Parekh A. Multiple chronic conditions among Medicare beneficiaries: state-level variations in prevalence, utilization, and cost, 2011. Medicare Medicaid Res Rev. 2013;3(3):mmrr.003.03.b02.

Keywords: Pseudotumor cerebri, High intracranial pressure/headache, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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Prevalence Of Choroidal Neovascularisations In Spectralis Optical Coherence Tomography Angiography Of The Optic Nerve Head in Idiopathic Intracranial Hypertension Patients At Debut

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Introduction:
We aimed to establish how many patients with newly diagnosed idiopathic intracranial hypertension (IIH) that represent with choroidal neovascularisation (CNV) or retinal vein occlusion (RVO) near the optic nerve head in spectralis optical coherence tomography angiography (OCTA). This to help ensure early diagnosis of patients debuting with IIH. IIH could be a possible differential diagnosis when representing with CNVs in clinic as seen in a case report.

Methods:
The study was prospective including all patients with IIH referred to Copenhagen University Hospital in Denmark year 2020-21. Alle patients went through a systematic neuro- and ophthalmological clinical work up and a standardized OCT protocol including spectralis OCTA was obtained.

Results:
We included 37 IIH patients. For this abstract preliminary data of 10 IIH patients (20 eyes) were included. All patients were female, mean age 27.7 years, mean body mass index 36.2, mean opening pressure 39.5 cm cerebrospinal fluid. Three (30%) patients presented with Frisén grade 1 papilledema, 3 (30%) with Frisén grade 2, 1 (10%) with Frisén grade 3 and 3 (30%) patients with Frisén grade ≥ 4. Octopus mean perimetric mean deviation and retinal nerve fiber layer volume were -5.1 dB and 217 µm, respectively, and mean ganglion cell layer was 1.22 mm3. No CNV's and no retinal vein occlusions were identified in this small cohort. PHOMS were seen in all patients and appeared as bulging capillary networks.

Conclusions:
No CNV or RVO were seen in debuting IIH patients in this pilot analysis. Further analysis of a larger data set is ongoing to reveal the prevalence of CNVs possibly caused by axonal stasis in relation to high intracranial pressure.

References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Pseudotumor cerebri

Financial Disclosures: The authors had no disclosures.

Grant Support: Fight For Sight, Denmark Synoptikfonden, Denmark

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Quality, Reliability, and Readability of Online Information on Idiopathic Intracranial Hypertension

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Introduction:
To evaluate the quality & reliability, technical quality, and readability of online information about idiopathic intracranial hypertension.

Methods:
A cross-sectional study. We searched Google search engine for the phrases "idiopathic intracranial hypertension" and “pseudotumor cerebri”. We evaluated the first 50 search outcomes of each search term in terms of their quality, dependability, technical precision, and comprehensibility. We omitted peer-reviewed papers, discussions on patient forums, dictionary explanations, and websites that were either non-English or unrelated to human subjects. Two independent reviewers assessed each website for: 1) quality and reliability through the application of DISCERN, HONcode, and JAMA criteria; 2) technical quality based on eleven criteria; and 3) readability using six distinct measures (Flesch-Kincaid reading ease score and grade level, Gunning fog, Simple Measure of Gobbledygook index, Coleman–Liau index, and automated readability index).

Results:
The mean scores for the DISCERN, HONcode, and JAMA criteria were 3.6±1 (1-5; 1: worse, 5: best), 11.4±2.9 (0-16; 0: worse, 16: best), and 2.5±1.3 (0-4; 0: worse, 4: best), respectively. The mean technical quality score was 0.8±0.1(0-1). Readability was poor among most websites, with 92.6% having a Flesch Kincaid Reading Ease Score of < 59. The mean Flesch Kincaid Grade Level Score was 9.6±3.6 (1-16). No statistically significant difference was present between institutional and private websites in any readability criteria.

Conclusions:
We found that while online information on IIH had poor to moderate quality and reliability, their technical quality was good. Most websites’ readability was above the layman person, 7th-8th grade, reading level.

References: None provided.

Keywords: Pseudotumor cerebri, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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The Clinical Course and Prognosis of Incidental Idiopathic Intracranial Hypertension (IIH) Patients: The Ottawa Experience

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Introduction:
A subset of patients with IIH are diagnosed after incidental detection of optic nerve edema, without symptoms of increased intracranial pressure. Information about this population's clinical presentation and characteristics is limited in literature. The objectives of this study were to compare the patients with incidental presentation of IIH to those who present with symptoms of high intracranial pressure.

Methods:
This was a retrospective cross-sectional study of all patients who were referred to the Eye Institute for a possible diagnosis of IIH.

Results:
One-hundred twenty-four patients were included: twenty-four had a diagnosis of incidental IIH while a hundred were diagnosed with symptomatic IIH. The mean age was 35.9 (SD 4.5, n=24) in the incidental IIH (IIIH) and 30.3 (2.3, 100) in the symptomatic IIH (SIIH) group (P< 0.001). In the IIIH group, 0% were female, and in the SIIH group, 5% were female (P=0.26). The proportion of patients with Frisen grade edema of 0-2 was 81.3% and 61.6% for the IIIH and SIIH groups respectively (P=0.14). 50% and 80% of the IIIH and SIIH groups respectively required medical treatment (0.0006). None required surgical treatment in the IIIH group but 9% of the SIIH group did (P=0.13). Among IIIH patients, the LP opening pressure was 28.95mmH2O (6.4) and 29.745mmH2O for the IIIH group (10.4) (P=0.82). 83.3% of patients with IIIH had features of high ICP on MRI, versus 82.0% of SIIH patients (P=0.88).

Conclusions:
Patients with incidentally detected IIH are older than those who present because of symptoms of high ICP, however have similar rates of optic disc edema, neuroimaging findings of high ICP, and high opening pressure on LP. Incidentally detected IIH patients are less likely to require medical treatment. Future work will compare visual outcomes between groups.

References: None provided.

Keywords: High intracranial pressure/headache, Neuroimaging, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Visual and pharmacotherapy outcomes after transverse sinus stenting for idiopathic intracranial hypertension

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Introduction:
Transverse sinus stenting (TSS) is an increasingly commonly used treatment for patients with idiopathic intracranial hypertension (IIH). However, detailed neuro-ophthalmic evidence on visual and pharmacotherapy outcomes after TSS is scarce and heterogeneous. This study aimed to describe the visual outcomes of patients undergoing TSS for IIH and to ascertain the proportion of patients who could be weaned off intracranial pressure (ICP)-lowering medication after this procedure.

Methods:
A retrospective chart review of all patients with IIH from two tertiary academic neuro-ophthalmology practices who underwent TSS between 2016 and 2022 was performed. Indications for stenting included failure of pharmacotherapy, intolerance of pharmacotherapy, and acute vision loss from severe papilledema.

Results:
Of 435 patients with IIH, 15 (13 women, median age 27 years with interquartile range [IQR] 22 to 32) met inclusion criteria. After TSS, ICP-lowering pharmacotherapy was discontinued in 10 patients and decreased in 4; one patient was not on ICP-lowering medication before TSS. All patients experienced resolution or improvement of symptoms (10 resolution, 4 improved, 1 asymptomatic before TSS) and papilledema (11 resolution, 4 improved) after stenting. Papilledema resolution was confirmed with optical coherence tomography-measured peripapillary nerve fibre layer thickness (median decrease 147 µm, IQR 41.8 to 242.8). Median change in VA and VFMD between the baseline and most recent visit was 0 logMAR (IQR -0.1 to 0) and 3.0 dB (IQR 2.0 to 4.2), respectively. No patient developed transverse sinus restenosis nor in-stent thrombosis postoperatively across a median follow-up of 20.8 weeks (11.3 – 49.8) and no patient required subsequent surgical intervention for IIH.

Conclusions:
In this cohort of patients with IIH and fulminant presentation, medication resistance, or medication intolerance, TSS was an effective and safe treatment modality. Most patients were able to stop ICP-lowering medications while demonstrating striking improvement in symptomatology and visual field function.

References: None provided.

Keywords: High intracranial pressure/headache, Interventional neuroradiology, Pseudotumor cerebri

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Visual Outcomes of Optic Nerve Sheath Fenestration versus Dural Venous Sinus Stenting for Pseudotumor Cerebri

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Introduction:
Current treatment options for pseudotumor cerebri (PTC) include medical therapy, cerebrospinal fluid shunting, dural venous sinus stenting (DVSS) and optic nerve sheath fenestration (ONSF). Extensive evidence exists showing that surgical procedures effectively protect visual function, but there remains a paucity of literature comparing the visual outcomes of ONSF and DVSS. In this study, we evaluate the therapeutic effects in PTC patients who underwent either ONSF or DVSS for neuroprotection from papilledema.

Methods:
A total of ninety PTC patients who underwent either ONSF (46 patients) or DVSS (44 patients) between January 2017 and March 2023 underwent a retrospective review. Preoperative and postoperative ICP, visual acuity (VA), mean deviation (MD) on automated perimetry, as well as retinal nerve fiber layer (RNFL) and ganglion cell layer (GCL) thickness measured by optical coherence tomography (OCT) were assessed in addition to Frisén papilledema grading during a 3-month period.

Results:
VA and MD, the primary outcomes, significantly improved following ONSF (0.10 to 0.01 logMAR, p=0.027; -10.44 to -8.23 dB, p< 0.001) and DVSS (0.05 to 0.00 logMAR; -4.37 to -2.59 dB, p< 0.001). The papilledema grade and RNFL thickness reduced following ONSF (Frisén 3 to 2; 159.0 to 119.0 µm, p< 0.001) and DVSS (Frisén 3 to 0; 134.0 to 98.0 µm, p< 0.001). ICP significantly decreased after DVSS (322.5 to 280.0 mmH2O, p< 0.001). GCL thickness did not deteriorate after ONSF (89.0 to 87.0 µm, p=0.06), in contrast to DVSS (96.0 to 93.0µm, p=0.001). Significant difference were observed in postoperative papilledema grade (Z=-6.070, P< 0.001) and RNFL thickness (Z=-3.137, P< 0.001) between the two groups.

Conclusions:
Both ONSF and DVSS can improve visual outcomes in PTC patients. ONSF demonstrated superior efficacy in neuroprotection, while DVSS effectively reduces ICP and alleviates papilledema to a greater extent. The neuroprotection benefits of ONSF may serve as an effective complement to DVSS.

References: None provided.

Keywords: Pseudotumor cerebri, High intracranial pressure/headache, Optic neuropathy, Visual fields, Vascular disorders

Financial Disclosures: The authors had no disclosures.

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A Survey of Fellows and Fellowship Directors On Their Experience With the NANOS Illustrated Curriculum (IC)

Meagan Seay [1], Sachin Kedar [2], Bryan Hull [1], Nancy Lombardo [1], Kathleen Digre [1]

[1] University of Utah, [2] Emory University Hospital

Introduction:
The North American Neuro-Ophthalmology Society's (NANOS) neuro-ophthalmology curriculum created in 2006 and revised in 2020, provides a framework that defines the scope of knowledge expected of a practicing neuro-ophthalmologist. This curriculum forms the structure of the NANOS Illustrated Curriculum (IC) which is comprised of up-to-date, high-yield, multimedia learning materials. In February 2022, the NANOS IC was adopted by the NANOS Board as the official curriculum of AUPO-compliant neuro-ophthalmology fellowships. The NANOS IC is freely available to NANOS members on the NANOS website, however, a more sophisticated version is available via subscription on STAT!Ref. The purpose of this study is to report the results of a survey of fellows and fellowship directors about their experience with the NANOS IC after the 2022-2023 academic year.

Methods:
An email containing a survey was sent in July 2023 to all fellowship directors and recently graduated fellows of AUPO-compliant neuro-ophthalmology fellowship. Survey results were analyzed.

Results:
Twenty-eight participants (20 fellowship directors and 8 fellows) completed the survey. Sixteen respondents (57%) reported that NANOS IC was a required educational resource for their program and 89% confirmed having access to NANOS IC. Most (43%) accessed NANOS IC on the NANOS website, 30% accessed through STAT!Ref and 22% used both. Participants felt positively about the educational effectiveness, comprehensiveness, and methods of presentation, while ease of search and organization of the NANOS IC were felt to be weaker. 56% agreed/strongly agreed the NANOS IC was their go-to resource.

Conclusions:
Overall, the opinions from fellowship directors and fellows regarding the NANOS IC were positive. It is seen as an effective and comprehensive resource for neuro-ophthalmology education. Further efforts to improve the NANOS IC, particularly the organization and searchability may lead to an improved user experience. Future plans are to expand this survey more broadly to NANOS members.

References: None provided.

Keywords: Miscellaneous

Financial Disclosures: Meagan Seay; Sachin Kedar: Consultant for Astra-Zeneca; Bryan Hull; Nancy Lombardo; Kathleen Digre

Grant Support: None.

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Assessing Antiplatelet Agents' impact on Retinal Artery Occlusion Patient Recurrence

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Introduction:
Retinal Artery Occlusion (RAO), regarded as an ophthalmic emergency and the ocular analog of stroke, lacks established secondary prevention guidelines. This study examines the potential benefits of using antiplatelet agents in patients with RAO to prevent its recurrence.

Methods:
This study was a retrospective, population-based cohort study using the dataset from the health insurance review and assessment service-National patient sample (HIRA-NPS) between January 1, 2018 and December 31, 2018 in South Korea. During this period, the study included patients who had been diagnosed with retinal artery occlusion (H340, H341, H342). Patients who used any antiplatelet agents (aspirin, clopidogrel, cilostazol, dipyridamole, ticlopidine) and those who had not were assessed for their clinical characteristics and evaluated based on RAO recurrence as the outcome. Propensity score matching was conducted to adjust for the baseline comorbidities of the patient groups.

Results:
The analysis included the antiplatelet user group (n = 1,732) and the non-user group (n = 1,732), with mean ages of 68.3 and 66.5 years, respectively. The group of patients using antiplatelet agents exhibited higher proportion of Myocardial infarction (5.4% vs 0.6%, $p < 0.001$), cerebrovascular accidents (37.0% vs 20.4%, $p < 0.001$), moderate to severe renal disease (9.9% vs 6.8%, $p < 0.001$), and peripheral arterial disease (15.8% vs 7.5%, $p < 0.001$). Recurrence of RAO occurred in 28 patients in the antiplatelet user group and 16 patients in the non-user group (OR = 1.76, 95% CI 0.92-3.50, $p = 0.069$)

Conclusions:
In this study aimed at assessing the preventive effect of antiplatelet use in RAO, it was demonstrated that the use of antiplatelet agents does not have a significant impact on secondary prevention. However, caution is warranted in interpreting the findings due to limitations in HIRA-NPS data and the inability to control for various covariates. Further research is needed in the future.

References: None provided.

Keywords: Stroke

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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Assessment of ChatGPT For Production Of Neuro-Ophthalmology Patient Educational Handouts

Brendan Tao [1], Armin Handzic [2], Nicholas Hua [2], Amir Vosoughi [3], Edward Margolin [2], Jonathan Micieli [2]

[1] University of British Columbia, [2] University of Toronto, [3] University of Manitoba

Introduction:
Patient education in ophthalmology poses a challenge for physicians due to time and resource limitations. ChatGPT (OpenAI, San Francisco) may assist with automating production of patient handouts on common neuro-ophthalmic diseases. This study sought to determine the quality of such handouts, as assessed by a neuro-ophthalmologist, and their readability for patients.

Methods:
We queried ChatGPT-3.5 to generate 51 patient education handouts across 17 conditions. We devised the "Quality of Generated Language Outputs for Patients" (QGLOP) tool to assess handouts on the domains of accuracy/comprehensiveness, bias, currency, and tone, each scored out of 4 for a total of 16. A fellowship-trained neuro-ophthalmologist scored each passage. A total score of 70% out of 16 was considered to support the application of ChatGPT in producing patient handouts. Handout readability was assessed using the Simple Measure of Gobbledygook (SMOG), which estimates years of education required to understand a text.

Results:
The QGLOP scores for accuracy, bias, currency, and tone were found to be 2.43, 3, 3.43, and 3.02 respectively. The mean QGLOP score was 11.9 [95% CI 8.98, 14.8] out of 16 points, indicating a performance of 74.4% [95%CI 56.1%, 92.5%]. The mean SMOG across responses as 10.9 [95%CI 9.36, 12.4] years of education.

Conclusions:
The mean QGLOP score surpassed the threshold of 70%, indicating a generally acceptable quality of generated handouts. However, given that the lower bound of this estimate fell below 70%, some handouts may require more involved revision. As well, the mean SMOG score exceeded the accepted upper limits of grade 8 reading level for health-related patient handouts. In its current iteration, ChatGPT should be used as an efficiency tool to generate an initial draft for the neuro-ophthalmologist, who may then refine the accuracy and readability for a lay readership.

References: None

Keywords: Miscellaneous, Optic neuropathy, Optic neuritis, Pseudotumor cerebri, Graves' disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None

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Medical Trainee Survey of Comfort with Fundoscopy using Traditional Direct Ophthalmoscopy versus a Novel Direct Ophthalmoscopy technique with a Loose 13-diopter Lens

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Introduction:
We propose a novel technique of ophthalmoscopy with use of a direct ophthalmoscope and +13.00 diopter (D) loose lens. Currently, direct ophthalmoscopy (DO) is the preferred method taught in healthcare training to visualize the optic disc and retina. However, this technique is difficult to learn and students and practitioners alike report low confidence with DO. Furthermore, DO can be uncomfortable to perform, since the practitioner's face must be extremely close to the patient's face and necessitates using the non-dominant eye for half of the exam. Other alternatives for visualizing the fundus such as imaging, indirect ophthalmoscopy, slit-lamp ophthalmoscopy and smartphone attachments are costly and rarely found outside of ophthalmology clinics.

Methods:
Approved by IRB, we taught a group of medical students and neurology residents both the traditional DO method and the novel lens method. Pre and post instruction questionnaires were administered to compare the student's ability and comfort level visualizing and describing the disc and preferred method. Students performed undilated exams on each other.

Results:
20 surveys met criteria for inclusion. 17 students (85%) preferred the novel lens method, while 3 students (15%) preferred the traditional method (Chi-Squared = 8.45, df=1, p=0.004). Students reported a slightly higher comfort level with the novel lens method compared to DO but this result was not statistically significant (Wilcoxon rank signed rank test p=0.7).

Conclusions:
Preference for the novel lens method may be because the novel method allows students to be more physically comfortable and properly positioned to observe the fundus. A +13.00-diopter lens also allows for slightly increased magnification of the fundus compared to DO. With training, this cost-effective technique may be used by healthcare providers regardless of specialty or clinical setting to more accurately screen for ocular disease.

References: None provided.

Keywords: Neuroimaging, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Miscellaneous

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Grant Support: None.

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Monoclonal Antibodies against Calcitonin Gene-Related Peptide for the Prophylaxis of Visual Aura

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Introduction:
Monoclonal antibodies to CGRP or its receptor (anti-CGRP mAbs) are a novel class of migraine-specific prophylaxis. Theoretically, the high molecular weight of anti-CGRP mAbs prevents them from crossing the blood-brain barrier and does not inhibit cortical spreading depression, which is the underlying mechanism of a visual aura (VA). Furthermore, no randomized controlled trials have evaluated their efficacy in migraine with aura (MA), which occurs in up to one-thirds of migraine patients. Here, we prospectively evaluated the changes in days with VA after 3 months of anti-CGRP mAb treatment.

Methods:
Patients with migraine according to ICHD-3 who had been treated with anti-CGRP mAbs for 3 months were included in the study. Patients were included if they had at least one VA attack per month. Data were collected at baseline and at the third month of treatment. The efficacy of anti-CGRP mAbs in VA was compared with that in migraine without aura (MO). The number of headache and VA days was assessed using a headache diary.

Results:
Of the 332 patients with migraine who were treated with anti-CGRP mAbs (galcanezumab or frenezumab), 26 had MA. All MA patients reported VA and two of them also had sensory and aphasic aura. The mean age of the patients was 33.7 years and 69.2% were female. The mean age at the onset of the visual aura was 24.8 years. At month 3, 65.4% and 42.3% of patients achieved at least a 50% and 75% reduction in monthly VA days, respectively, which was not statistically different from the monthly headache days in the MO group (75.2% and 46.4%). No serious adverse events were observed regardless of the presence of VA.

Conclusions:
This study supports that the efficacy of anti-CGRP mAbs is not limited to the incidence of headache, but is also effective in VA attacks that precede headache.

References: None provided.

Keywords: Non-organic visual disorders, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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National Football League (NFL) Game Officials' Self-Rating of Knowledge in Neuro-ophthalmic Principles and Practice: Pilot Program to Improve Precision and Accuracy of Game Official Calls

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Introduction:
To determine if a neuro-ophthalmic curriculum would improve National Football League (NFL) game officials' self-rated knowledge of neuro-ophthalmic principles applicable to NFL play-calling.

Methods:
The formalized neuro-ophthalmic principles (NOP) curriculum was introduced to 121 National Football League (NFL) game officials, 17 replay officials, and 4 officiating staff who attended the NFL Official Training Camp in Irving, Texas on September 8th-9th, 2023. Before and after the curriculum was introduced, participants completed a feedback form pertaining to self-reported NOP knowledge, likelihood of using said terms, and interest in future content. Paired two-tailed t-tests were used for statistical analysis to directly compare the self-reported knowledge before and after neuro-ophthalmic curriculum introduction.

Results:
142 participants completed the feedback forms. There was a statistically significant improvement in the mean ratings of the pre- versus post-lecture understanding of the specific neuro-ophthalmic terms pertinent to NFL game officials (2.6 [95% CI, 2.3-3.0] versus 7.9 [95% CI, 7.6-8.2], $p< 0.001$) and 2.7 [95% CI, 2.3-3.0] versus 7.7 [95% CI, 7.4-8.0] respectively. There was a statistically significant greater likelihood of using said terms pre- versus post-lecture (2.9 [95% CI, 2.4-3.4] versus 7.5 [95% CI, 7.2-7.9], $p< 0.001$). The curriculum was "highly relevant" to their officiating in real-time games, with an average rating of 8.8 (95% CI, 8.5-9.1). NFL officials had an average rating of 8.2 (95% CI, 7.8-8.6) for interest in future content.

Conclusions:
This study found a statistically significant improvement in neuro-ophthalmic knowledge and a greater likelihood of using NOP terms following the NOP curriculum. NFL game officials, replay officials, and staff are interested in expanding their knowledge in the vision science of neuro-ophthalmic concepts and applications involved in play calling. We hope that our pilot data will lead to a model of education that will improve the precision and accuracy of NFL play calls by officials on game days.

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Keywords: Miscellaneous, Miscellaneous

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Optimization of Patient Education Materials in Neuro-Ophthalmology

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Introduction:
Generative Language Models (GLMs), including OpenAI's ChatGPT, have vast utility. This includes the simplification of complex medical resources to create patient educational material (PEM) — especially for rare conditions that do not have information tailored to a patient's level of understanding. This study compares the readability of PEMs created by the North American Neuro-Ophthalmology Society (NANOS) and ChatGPT-transformed StatPearls (T-SP) articles.

Methods:
Eleven PEMs from NANOS's website and their associated StatPearls articles were collected for analysis. The StatPearl articles were transformed with GPT-4 using the following prompt: "Please rewrite this text to be readable at a 5th grade level. Do not include information not contained in the original text, and do not exclude information contained in the original text." Both the PEMs and T-SPs were analyzed using Flesch-Kincaid Grade Level (FKGL) and Reading Ease (FKRE) scores. Latent Semantic Analysis (LSA) verified content similarity which was further validated by a Neuro-Ophthalmologist to ensure no content was added or omitted.

Results:
In the twelve NANOS PEMs, the average FKGL and FKRE were 11.22 ± 0.71 and 47.4 ± 2.71, respectively. Within the twelve transformed StatPearls, the average FKGL and FKRE were 6.71 ± 0.81 and 74.45 ± 5.27, respectively. FKGL scores in the transformed StatPearls articles were significantly decreased (45.11, %, $p < .001$) and FKRE scores significantly increased (57.07, %, $p < .001$) compared to the NANOS PEMs. The LSA was 0.976 ± 0.002.

Conclusions:
While StatPearls articles offer great comprehensive synopsis for medical professionals, they are written with complex medical terms and jargon which are not understood by the general public. The use of GLMs, like ChatGPT, show potential to enable physicians to rapidly transform complex medical articles and provide their patients with accurate, up-to-date summaries which may not yet be available; therefore, further research into GLMs and prompt-refinement should be conducted.

References: None provided.

Keywords: Miscellaneous

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Performance of Generative Artificial Intelligence Platforms in Developing Differential Diagnoses of Neuro-ophthalmology Cases

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Introduction:
Artificial intelligence (AI) has revolutionized health care in recent years. Large language models (LLMs), a subset of AI capable of understanding and generating data, have shown promise in medicine, particularly in medical problem-solving. This study aimed to evaluate LLMs' performance in correctly diagnosing neuro-ophthalmology cases.

Methods:
This cross-sectional study compared the diagnostic accuracy of four different LLMs (ChatGPT-3.5, ChatGPT-4, Glass.health, Google Bard) using neuro-ophthalmology cases selected from the section "Unknown Patients for Residents in Ophthalmology or Neurology Training" (UPFRONT), publicly available on the Journal of Neuro-Ophthalmology website. From the 27 cases available, 3 were excluded for not presenting a list of differential diagnoses that could serve as ground-truth. Each case was reorganized as a structured clinical vignette. Ancillary testing data was not included. The clinical vignettes were pasted into the chat box of the various LLMs without prior training (zero-shot) and preceded by the statement: "Please develop a list of 5 differential diagnoses for the following medical case. Please list the diagnoses in the order of most likely to least likely." Preliminary analysis employed a Chi-squared test for independence on the three categories of outcomes: the provided list contained the correct diagnosis; the provided list contained a partially correct diagnosis (e.g., correct localization or categorization); and the list did not contain the correct diagnosis. P-values < 0.05 were considered statistically significant. All statistical analyses were performed using Microsoft Excel.

Results:
Among the four models, ChatGPT-4 demonstrated statistically significant superior performance in diagnostic accuracy (correct diagnosis 42% and partially correct 25%), compared to ChatGPT-3.5, Glass.health and Google Bard (25% and 8%, 25% and 8%, 25% and 17%, respectively; $P < 0.00001$).

Conclusions:
ChatGPT-4 was the most reliable among the evaluated LLMs for generating differential diagnoses for neuro-ophthalmology clinical vignettes. However, the overall accuracy in diagnosis was still below 50%.

References: None provided.

Keywords: Miscellaneous

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Grant Support: None.

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Peri-operative Retinal Artery Occlusion in Cardiac Surgery: Predictive Models From Longitudinal Medical Claims Database

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Introduction:
Perioperative retinal artery occlusion (RAO) is a devastating complication of cardiac surgery whose risk factors are scarcely studied in the literature. The purpose of this study is to develop a predictive model for RAO using a longitudinal medical administrative claims database, which provides temporal sequence of RAO and potential risk factors.

Methods:
Participants in Clinformatics® Data Mart medical claims database (2007−2017) with hospitalization involving cardiac surgery and no history of prior RAO were included. 827 cases and 141,321 controls were identified. Matched controls (n=1218) were selected based on year of surgery and zip-code. Chronic and perioperative variables were assigned based on medical claims codes. Least absolute shrinkage and selection (LASSO) penalized conditional logistic regression with 10-fold cross validation was used to select variables for the optimal predictive model from the subset of variables with $p< 0.15$ between cases and matched controls (unadjusted conditional logistic regression). Receiver operating characteristic (ROC) curves were generated for the strata-independent matched and full samples.

Results:
The predictive model included age >57 years, male gender, atherosclerosis, pre-existing cerebrovascular disease, carotid artery stenosis, (peri-operative) stroke, open cardiac procedures including ventricular assist device, heart transplant and septal defect repair, as well as ophthalmic conditions including age-related macular degeneration, cataracts, glaucoma and hypertensive retinopathy. Area under ROC curve was 0.687 (95% confidence interval [CI]: 0.668, 0.707) for the matched sample and 0.690 (95% CI: 0.672, 0.708) for the full sample.

Conclusions:
This predictive model for RAO in cardiac surgery considers chronic and perioperative conditions, and is unique to date in its use of longitudinal medical claims data, inclusion of ICD-10 codes and study of ophthalmic conditions as risk factors. Similar to other studies, the multivariable model included coronary artery stenosis, open cardiac surgeries, stroke and cerebrovascular disease as predictive factors, but identified age, atherosclerosis and degenerative ophthalmic conditions as new predictive factors.

References: None provided.

Keywords: Stroke, Vascular disorders, Retina

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Contact Information: None provided.

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The impact of brain damage on driving skills in patients with visual field defects.

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Introduction:
We previously reported the binocular visual fields and the amount of eye movements were associated with the number of accidents in a driving simulator (DS). However, the residuals of the actual number of accidents from the estimated number were still high in some patients. In this study, to evaluate the impact of brain damage on driving skills, we evaluated the differences in the number of accidents in DS according to with or without brain damage.

Methods:
Patients who had undergone a driving risk assessment with DS and binocular Esterman visual field test between April 2021 and July 2023 were included in this study. The cause of visual field loss was collected from the medical records. A single trial of DS contains 15 scenarios of an accident that is avoidable by braking, and patients were instructed to avoid the accident by using the foot brakes. During the simulation, the eye movements were monitored with an infrared eye-tracking system. We compared the differences in the actual number and the estimated number with a generalized linear model by the visual fields and eye movements of the accidents in DS between the patients with and without brain damage.

Results:
8 out of 27 patients had visual field loss due to brain damage (4 cerebral infarctions, 3 brain tumors, and 1 brain hemorrhage). Once we set the threshold as 1 standard deviation of the residuals, 1 out of 19 in the non-brain damage group and 3 out of 8 in the brain damage group had more accidents than estimated. This was significantly different between the groups. ($P = 0.03$, chi-squared test)

Conclusions:
When patients have brain damage, we can't judge whether they can drive safely or not just from the visual acuity and/or visual field. DS will be effective for such patients to assess the risks of driving.

References: None provided.

Keywords: Miscellaneous, Visual fields, Stroke, Tumors

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Artificial Intelligence Deep Learning Model for the Radiological Diagnosis of Typical and Antibody-Mediated Optic Neuritis

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Introduction:
Optic neuritis exhibits increased T2 signal and/or enhancement on MRI orbits (1). These findings can be subtle at times(2). Machine learning, a branch of artificial intelligence, is a statistical technique that enables predictive models to learn from data, and deep learning (DL) is a subtype that leverages neural networks to make clinical predictions(3). The primary objective of this study is to create a DL model that can detect the presence of optic neuritis on MRI orbits. Secondary objectives are to determine 1) if the model can detect more subtle cases than a skilled professional, 2) if gadolinium is required for accuracy, and 3) if the model can differentiate typical versus antibody-mediated optic neuritis.

Methods:
This is a single-centre retrospective proof-of-concept study involving patients with a clinical diagnosis of optic neuritis from January 2012-September 2023. One-hundred and fifty-eight patients had MRI orbits with T2 coronal images available for review. Age, sex, affected eye(s), visual acuity, testing for MOG/NMO antibodies, administration of gadolinium, and presence/absence of optic neuritis on the radiologist's report were recorded for each patient. Next steps are for two neuro-radiology fellows to assess all scans for presence/absence of increased signal and/or enhancement. Labelled MRI images will then be administered to a supervised DL algorithm.

Results:
Of the 158 patients identified, 72% were female, mean age at presentation was 38.5 years, and 17% had bilateral involvement. Regarding visual acuity, 75% had ≤20/40 at presentation and 63% had final vision ≥20/25. MOG antibodies were positive in 23%; NMO in 2.5%. Gadolinium was administered to 90.5% of patients. The radiologist identified optic neuritis in 64% of cases. Results from the DL model are expected by March 2024.

Conclusions:
Findings from this study will dramatically advance the radiological diagnosis of optic neuritis and likely facilitate more rapid and accurate diagnosis of typical versus antibody-mediated optic neuritis.

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Keywords: Optic neuritis, Neuroimaging, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Demeylinating disease

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Contact Information: None provided.

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Challenges in MRI Diagnosis of Optic Perineuritis

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Introduction:
Optic perineuritis (OPN) is a broad category of optic nerve sheath inflammation in which outcomes depend upon timely diagnosis and treatment. Given the importance of MRI in the diagnosis of OPN, this project investigates the accuracy of neuroradiologists in recognizing this condition as compared to the more common finding of optic nerve sheath meningioma (ONSM) and controls with no structural abnormality.

Methods:
MRI studies were excluded if they lacked contrasted or orbital sequences. Two neuroradiologists, both masked to clinical history and other identifiers, individually reviewed studies from patients with OPN (n=10), ONSM (n=10), and controls (n=10) after which they reported their suspected diagnosis and key imaging findings. Based on preliminary data suggesting an association between OPN and intraconal fat enhancement, a second round of interpretations was performed on studies from patients with OPN (n=6), ONSM (n=9), and normal controls (n=8) with instructions to regard fat enhancement as a potential indicator of OPN. For both rounds, diagnostic accuracy was tabulated and interrater agreement was determined using Cohen's kappa.

Results:
Masked interpretation was significantly less accurate in detecting OPN (50%) as compared to ONSM (90%) and normal controls (95%). When neuroradiologists were instructed to approach intraconal fat enhancement as an indicator of OPN, the accuracy of OPN diagnosis increased (75%) but the accuracy of ONSM diagnosis markedly decreased (44%) with most of the missed cases inaccurately interpreted as OPN (n=7). Interrater agreement for the two rounds of interpretations was 0.55 and 0.41, respectively.

Conclusions:
Optic perineuritis represents a significant diagnostic challenge for neuroradiologists. Although attention to intraconal fat enhancement increases the sensitivity of radiological interpretation for this condition, this comes at the cost of specificity with many cases of ONSM misrecognized as OPN. A final phase of the project, which is currently ongoing, evaluates how the inclusion of clinical history affects diagnostic accuracy.

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Keywords: Neuroimaging, Optic neuritis, Optic neuropathy, Orbit

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Comparing Leber Hereditary Optic Neuropathy and Optic Neuritis Manifestation Diseases: Brain Imaging Findings.

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Introduction:
The purpose of this cohort study was to classify brain imaging findings in affected subacute/dynamic LHON patients in comparison to Optic Neuritis patients secondary to Multiple Sclerosis (MS), Myelin Oligodendrocyte Antibody Disorder (MOG), and Neuromyelitis Optica (NMO).

Methods:
MRI images were obtained from various time points within the first year of visual loss from a cohort of genetically confirmed LHON patients between Jan 1st, 2013, and Mar 31st, 2023. MRI images from the LHON group were compared to a sex and age-matched Optic Neuritis (ON) group and were scored on pre-set criteria by masked neuro-radiologists. The white matter and the following optic nerve segments were assessed: orbital, canalicular, intracranial, chiasm, and optic tract.

Results:
Sixteen image sets (LHON, MS, and MOG patients) were analyzed. LHON patients (mean age 30.6 years) were compared with age and sex-matched MS patients (mean age 31.8 years), and MOG patients (mean age 31.2 years). Unpaired t-test comparison indicated a statistically significant difference ($p = 0.04$) in the orbital and chiasmal segments between LHON and MOG patients. In addition, LHON patients did not exhibit any white matter involvement, but this was observed in 100% of the MS and MOG patients.

Conclusions:
Our results illustrate that chiasmal involvement is more common in LHON patients than in ON patients (specifically in the MOG group) during the first year of vision loss. White matter involvement was not seen in any of the LHON patients but was seen in all the MS and MOG groups. Further data analysis is ongoing, including comparison to subjects with clinical isolated syndrome (CIS) presenting with optic neuritis.

References: None provided.

Keywords: Neuroimaging, Optic neuritis, Optic neuropathy, Genetic disease, Demeylinating disease

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Degree of Optic Nerve Enhancement in MOG-ON as a Predictor of Visual Outcome

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Introduction:
The prognostic value of radiologic findings in myelin oligodendrocyte glycoprotein-related optic neuritis (MOG-ON) has not been well described. We investigated the hypotheses that a lesser degree of optic nerve enhancement is correlated with poorer visual outcome, and specifically that subtle canalicular enhancement correlates with poor visual outcome due to a canalicular compartment syndrome which prohibits contrast leakage.

Methods:
This was a retrospective chart review of patients from three tertiary neuro-ophthalmology practices with a diagnosis of MOG-ON confirmed by positive antibody titers obtained through cell-based assay. Poor visual outcome (VA or VFMD worse than 20/40 and -5.0 dB) at a minimum follow-up of 3 months was compared to radiological features on enhanced MRI orbit studies (degree of enhancement of the orbital and canalicular portions of the involved optic nerve) using Mann-Whitney U test and Fisher's exact test.

Results:
A total of 151 eyes with MOG-ON were analyzed, of which 6% demonstrated poor VA outcome and 24.0% demonstrated poor VFMD outcome. All eyes with poor VA outcome also had poor VFMD outcome. The median time from symptom onset to MRI was 7 days. Patients with mild orbital enhancement had worse VA (median 0 logMAR [0, 0.1] vs. 0 logMAR, [0, 0], P=0.013; mean 0.22 logMAR vs. 0.05 logMAR) and a higher proportion of poor VFMD outcome (36.4% vs. 16.9%, P=0.044) than patients with moderate-severe enhancement. Patients with mild canalicular enhancement had a higher proportion of poor VA outcome (14.9% vs. 1.8%, P=0.022) than patients with moderate-severe enhancement.

Conclusions:
We found evidence that lesser degree of optic nerve enhancement correlated with poorer visual outcome in MOG-ON. We also found that subtle canalicular enhancement correlates with poor visual outcome in MOG-ON. This finding supports the existence of a canalicular compartment syndrome which could be investigated with diffusion restriction sequences.

References: Handzic, Naidu, Brossard-Babosa, Margolin; Poor Visual Outcome After First Attack in a Cohort of Patients With Myelin Oligodendrocyte Glycoprotein-Related Optic Neuritis, Journal of Neuro-ophthalmology, currently in print

Keywords: Neuroimaging, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Optic neuritis, Optic neuropathy

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Detailed Analysis of Intraretinal Layers and their Relationship to Brain Structures in Normal Healthy Aging

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Introduction:
The retina has been employed as a proxy for investigating cerebral alterations in conditions like Alzheimer's disease and has demonstrated changes as a component of the typical aging process. Nevertheless, there is a need for more extensive investigation into the intricate connection between retinal structures and brain structures. This project was undertaken with the objective of clarifying the correlation between retinal and cerebral structures in individuals with normal, healthy conditions.

Methods:
Eighty-four subjects were recruited were recruited. The retina of one eye from each subject was imaged using Optical Coherence Tomography (OCT) to get intraretinal tissue volumes in various layers, including total retinal thickness (TRT), retinal nerve fiber layer (RNFL), ganglion cell inner-plexiform layer (GCILP), inner nuclear layer (INL), outer nuclear layer (ONL), outer plexiform layer (OPL), photoreceptor layer (PR), and retinal pigment epithelium (RPE) were obtained utilizing OCT. Each subject underwent brain magnetic resonance imaging (MRI) to analyze brain structure. Two hundred different brain regional tissue volumes were obtained with Magnetic Resonance Imaging (MRI). The MRI mapping was done using the Schaefer 2018 200 regions x 17 networks atlas.

Results:
All eight retinal layers were related to tissue volumes in some regions of the brain ($P< 0.05$). The most related parts of the retina were TRT, RNFL, and GCILP ($r=0.57, 0.62, 0.63$ for most related regions, respectively; $P< 0.05$ for all). In addition, age was found to be related to structures in the retina and brain. TRT, RNFL, GCILP, and PR demonstrated correlations with age ($P< 0.01$). The majority of the 200 regions of the brain examined demonstrated a negative relationship with age ($P< 0.05$).

Conclusions:
This study, for the first time, employed meticulous segmentation of retinal layers and brain regions to illustrate the connection between retinal layers and specific brain areas, with age serving as an intermediary factor.

References: None provided.

Keywords: Neuroimaging, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease

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Frequency of Non-specific Optic Nerve Sheath Enhancement on Magnetic Resonance Imaging

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Introduction:
Optic nerve sheath enhancement (ONSE) on magnetic resonance imaging (MRI) is thought to be a sign of pathogenic disease, but anecdotally is sometimes incidentally seen in normal individuals. We examined the frequency, sensitivity, and specificity of ONSE in a cohort of patients with and without pathologic ONSE and evaluated for possible factors associated with nonspecific ONSE, such as age and tesla (T) strength.

Methods:
Patients at a single institution who had an MRI orbits with and without contrast between 01/10/2010 and 06/01/2023 and were seen by neuro-ophthalmology were collected. A total of 250 patients were randomly selected and manually reviewed to identify 100 controls without pathology affecting the optic nerve or sheath, and 15 patients with pathologic ONSE, which included etiologies such as optic nerve sheath meningioma, giant cell arteritis, and optic perineuritis. A neuroradiologist blinded to clinical diagnosis and MRI field strength (1.5 or 3T) interpreted the scans as either with or without ONSE.

Results:
Of 115 total patients, 68% were female, 90% were white, median age was 63.2 years (range 14.7-84.3), and 42% had 3T MRIs. Of the 100 controls, 7 were interpreted as enhancing (false positives) with a median age of 66.3 years (range 37.8-74.7), 4 of which (57%) were 3T MRIs, while the 93 true negative scans had a median patient age of 63.2 years (range 14.7-87.9) (p=0.81), 37 of which (40%) were 3T MRIs (p=0.37). Of the 15 pathologic scans, 2 (13%) were interpreted to be not enhancing (false negatives) , while 13 (87%) were interpreted as enhancing (true positives), thus providing a sensitivity of 87% and specificity of 93%.

Conclusions:
ONSE can be seen in 7% of normal individuals and missed in subtle optic nerve sheath pathology. Patient age and MRI field strength were not strongly correlated with MRI interpretation concordance of ONSE in our cohort.

References: None provided.

Keywords: Neuroimaging

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Ocular Itch Potentiates Reactivity of Pain Processing Brain Regions in Chronic Ocular Pain

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Introduction:
Ocular pain and itch are both multidimensional sensations with overlapping features in terms of quantitative, qualitative, and motor aspects. To further elucidate differences in neurophysiology, we used functional magnetic resonance imaging (fMRI) to explore whether pain and itch are processed in separate or identical cerebral networks.

Methods:
30 subjects with ocular pain (OP+, worst pain rating 1 week recall>1) were split into two groups based on ocular itch (23 cases with McGill questionnaire≥2, OP+Itch+; 7 controls with McGill≤1, OP+Itch-). Using fMRI, blood oxygen level-dependent (BOLD) responses to light stimuli were measured and analyzed to identify brain regions related to pain processing. Subjects reported light-evoked unpleasantness after each scan.

Results:
Unpleasantness ratings were comparable in both groups. OP+Itch+ individuals had greater BOLD activity in the left primary somatosensory (S1), bilateral secondary somatosensory (S2) and left insular cortices compared to OP+Itch- patients.

Conclusions:
Individuals with ocular pain and itch have greater BOLD activation in areas involved in sensory (S1) and emotional (S2 and insula) pain processing than ocular pain alone. Brain processing of ocular itch and pain overlap and appears additive.

References: None provided.

Keywords: Neuroimaging

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Optic nerve T2 signal intensity and caliber reflect clinical severity in genetic optic atrophy

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Introduction:
Genetic optic atrophies comprise phenotypically heterogenous disorders of mitochondrial function. We aimed to correlate quantitative neuroimaging findings of the optic nerves in these disorders with clinical measures.

Methods:
A subset of a retrospective database of 111 patients with bilateral optic atrophy referred for genetic testing who had accessible magnetic resonance (MR) images of the orbits and/or brain were analyzed. T2 STIR signal and optic nerve caliber were quantified according to a standardized protocol and normalized to internal standards. Inter-reader reproducibility was assessed. Clinical features were analyzed according to MR imaging features.

Results:
Within our database, 7 patients with pathogenic variants in OPA1, 3 patients with Wolfram syndrome, and 3 patients with Leber hereditary optic neuropathy had MRI orbital imaging available for analysis. No patient had MRI findings suggestive of a cause of optic atrophy aside from their respective genetic diagnoses. Compared to control patients, optic atrophy patients had significantly increased T2 STIR signal and decreased optic nerve caliber after internal normalization (p=0.0016 and 0.00012 respectively). Imaging metrics significantly correlated with degree of visual acuity, cup/disc ratio, and abnormal visual field testing. Inter-reader reliability correlation coefficients were 0.98 (p=0.00036) and 0.74 (p=0.0025) for normalized STIR and nerve caliber, respectively.

Conclusions:
This study uniquely demonstrates that normalized optic nerve STIR signal and optic nerve caliber significantly correlate with visual acuity, cup/disc ratio, and perimetric performance in patients with genetic optic atrophy. A formalized protocol as specified in this manuscript to characterize these differences on MR imaging may help to guide accurate and expedient diagnostic evaluation of optic neuropathy in the future.

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Prediction of Increased Intracranial Pressure Using Quantitative Features on MRI

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Introduction:
MRI signs of raised intracranial pressure (ICP) are clinically relevant and have been included in the diagnostic criteria of Idiopathic Intracranial hypertension (IIH) (1). The most common MR signs include enlargement of the optic nerve sheath, flattening of the posterior sclera, protrusion of the optic papilla into the globe, tortuosity of the optic nerve and empty sella (2). Clinical utility of these signs has its challenges because these signs when reported by radiologist are often subjective and, in isolation, not highly specific (3,4). Question arises whether an artificial intelligence-based algorithm can be applied to robustly differentiate patients with raised ICP.

Methods:
We did a proof-of-concept study using MRI orbit or brain images to evaluate which quantitative features could be manually extracted and analyzed to develop a model to diagnose raised intracranial pressure. We used an internally developed and validated image analysis and Graphic User Interface tool to extract these features from MRI images of two retrospective cohorts: 10 patients with securely diagnosed IIH and 10 patients without IIH or raised intracranial pressure.

Results:
The features reliably extracted included ratio of pituitary volume to intrasellar CSF volume and ratio of intrasellar CSF height to entire sella height, optic nerve sheath diameter, perioptic CSF space width, flattening of the sclera and protrusion of optic nerve head into the globe. We are using these features to develop a model to diagnose raised intracranial pressure. The model's diagnostic accuracy will be reported.

Conclusions:
Manual extraction of quantitative features representing the typical MRI findings in raised intracranial pressure can be used to develop predictive models. Future direction will focus on validating the predictive models on a larger number of cases using radiomic features and deep learning models to automatically identify the MRI findings of raised ICP.

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Keywords: Neuroimaging, Pseudotumor cerebri, High intracranial pressure/headache, Orbit/ocular pathology

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Predictive Ability of Orbital Apex Crowding Index for Dysthyroid Optic Neuropathy in Comparison with Barrett's Index

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Introduction:
The most widely accepted theory of Dysthyroid optic neuropathy (DON) is direct compression of the optic nerve by enlarged extraocular muscles at orbital apex. Barrett's index (BI)1, measuring muscle crowding at mid-retrobulbar level on coronal orbital Computed Tomography (CT), helps in identifying DON. Recent study defined the orbital apex as the posterior ⅕ of retrobulbar space2. This study aims to evaluate and compare the predictive potential of BI to the new indexes measured at orbital apex, called Orbital Apex Crowding Index (OACI), in distinguishing TED with DON from those without DON.

Methods:
Between 2010 and 2022, 101 TED patients (193 eyes) were retrospectively reviewed and categorized into TED with and without DON. A blinded radiologist calculated BI and two new indexes i) OACI-2M (greater value between ratio of horizontal rectus muscles diameters to horizontal orbital apex width and vertical rectus muscles diameters to vertical orbital apex width ii) OACI-4M (ratio of entire four rectus muscles diameters to the sum of horizontal and vertical orbital apex widths). These parameters were assessed for their predictive capability in identifying DON.

Results:
This study included 71 eyes of TED with DON and 122 eyes without DON. OACI-2M, OACI-4M and BI exhibited significantly higher mean values in the TED with DON groups ($p< 0.001$), with distinct differences in the area under the ROC curve ($p=0.0014$): 0.887, 0.923, and 0.8818 (95% CI), respectively. Optimal cut-off values for diagnostic accuracy were as follows: OACI-2M at 53.5% (sensitivity: 95.8%, specificity: 67.2%, accuracy: 81.5%), OACI-4M at 54% (sensitivity: 84.5%, specificity: 84.4%, accuracy: 84.5%), and BI at 51% (sensitivity: 91.5%, specificity: 75.4%, accuracy: 83.5%). All three parameters exhibited a strong correlation with best-corrected visual acuity (BCVA) ($p< 0.001$).

Conclusions:
Both OACI demonstrate higher prediction performance for DON compared to BI and are potentially applied in clinic as alternative methods for screening DON.

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Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Graves' disease, Neuroimaging, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease, Orbit

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Spatial Frequency Domain Imaging of a Facial Tissue Phantom of Known Optical Properties

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Introduction:
Spatial frequency domain imaging (SFDI) is a wide-field optical imaging modality that applies patterned illumination at multiple center wavelengths (470-851 nm) to quantify the properties and chromophore concentrations of sub-surface tissue. Its application to the periocular region facilitates mechanistic understanding of inflammatory conditions such as thyroid eye disease (TED) by quantifying parameters such as tissue oxy- and deoxy hemoglobin concentrations (hence oxygen saturation). The periocular anatomy is unique due to complex ocular adnexal anatomy. We, therefore, explored the potential geometric impact of neighboring bony (nasal process of the maxilla, nasal bone, supraorbital rim, lateral zygoma) and soft tissue (nasal cartilage and anterior projection, brow ptosis) regions on the validity of SFDI measurements by imaging a fabricated facial phantom.

Methods:
We cast a polydimethylsiloxane-based tissue-simulating facial phantom having homogeneous known optical properties. The phantom was placed on a chin rest and imaged nine times from two positions; 'en face' and 'side profile'. Between each pair of measurements, the phantom was removed and replaced on the chin rest. The flat back of the phantom was measured after being removed and replaced on a cart 15 times. Mean optical properties were calculated for 4 5x5 mm regions of interest (ROIs): inferior temporal, inferior nasal, superior temporal, and forehead control.

Results:
The measured absorption and reduced scattering coefficients are reproducible when comparing the facial phantom to those of its flat posterior surface. ROIs were not distinct (two sample test p-value >0.05), and the imaging orientation ('en face' vs. 'side profile') did not impact the measurements.

Conclusions:
This study demonstrates that the periocular profile with its elevation and adjacent structures does not impact, or bias SFDI measurements at the ROI locations selected, suggesting promise for imaging the periocular region of human subjects and obtaining biological indices of tissue optical characteristics and chromophore distribution.

References: None provided.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Orbit/ocular pathology, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: Stephanie Kirk; Shijun Sung; Kaylyn Mattick; Miranda An; Divya Devineni; Gordon Kennedy; Anthony Durkin: Dr. Durkin has a financial interest in Modulating Imaging, Inc., which developed the Reflect RS(TM). However, Dr. Durkin does participate in the management of Modulated Imaging and has not shared these results with that company. Conflicts of interest have been disclosed and managed in accordance with the University of California and NIH Policies.; Lilangi Ediriwickrema

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T2-Lesion analysis in Myelin Oligodendrocyte Glycoprotein Associated Disease Optic Neuritis

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Introduction:
The rate and timing of T2-lesion resolution of optic nerves on magnetic resonance imaging (MRI) has not been explored in patients with optic neuritis (ON) in myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD).

Methods:
This was a retrospective observational study of MOGAD patients 1 with ON and available T2 sequence orbital MRI studies. Medical records were reviewed for demographic information, details of ON attacks, and visual outcomes. A blinded neuroradiologist reviewed the MRI scans: T2 lesions were analyzed at the time of ON and with follow-up orbital MRIs obtained at least six months later. Patients with recurrent ON attacks before the follow-up MRI scan were excluded. Visual acuity outcomes were compared between those with persistent T2 lesions to those without.

Results:
There were 392 MRIs evaluated (160 unique patients, 59% female), 195 of which were obtained at the time of ON (within 30 days of ON onset). T2-lesion of the optic nerves was present in 144 of 195 (73%) sequences with acute ON. Furthermore, 35 unique patients (60% female) had follow-up orbital MRIs ≥ 6 months after initial ON onset (median one year). Resolution of T2-lesions was present in 21/35 (60%) patients. Long-term visual outcomes were not significantly different in patients with persistent T2-lesions, with most patients in both groups improving to 20/20.

Conclusions:
T2 lesions of the optic nerves were present in a majority of patients at the time of acute ON. A subset of patients without recurrent ON attacks had available follow-up orbital MRIs, which showed resolved T2 lesions in 60% of cases. These findings are important for understanding the natural history of MOGAD and suggest that T2-lesions of the optic nerves persist in some patients but without significant impact on visual outcomes.

References: None provided.

Keywords: Demeylinating disease, Neuroimaging, Optic neuritis, Optic neuropathy

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A Comparison of Outcomes Between Two Techniques for Optic Nerve Sheath Fenestration

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Introduction:
Patients with increased intracranial pressure (ICP) and papilledema are at risk for vision loss. Increased ICP may be managed medically, however, severe cases often require surgical intervention such as optic nerve sheath fenestration (ONSF).1-3 ONSF has been shown to stabilize vision and in some cases improve visual acuity and reverse visual field loss.4-7 At our institution, two different surgical techniques have been employed for ONSF—the medial upper lid crease orbitotomy (MULC), and the superior nasal transconjunctival approach (SNTC).8-10 In the literature, there are no direct comparisons of outcomes between these techniques, particularly by the same surgeon. We compared these two techniques to determine if there is a difference in visual field mean deviation, visual acuity, and surgical complications after ONSF.

Methods:
A retrospective chart review included 164 eyes from 89 patients who underwent ONSF from a single surgeon from 2014 through 2023 using either the SNTC approach (34 eyes) or the MULC approach (130 eyes). Patients undergoing prior ONSF were excluded from the study.

Results:
Eighty of 89 patients (90%) were female with a mean age 29.8 (± 10.6) years. There were no significant differences in pre-operative ($P = 0.36$) and post-operative ($P = 0.36$) visual acuity between groups or changes in visual acuity from baseline ($P = 0.75$). Additionally, there were no significant changes in visual field mean deviation between groups pre-operatively or post-operatively. There were minimal complications from ONSF and there were no statistically significant differences in complications between groups.

Conclusions:
Overall, visual outcomes (change in visual acuity, change in visual field) were similar between both ONSF approaches without either group having an increased rate of complications. Based on this data, we suggest that either surgical technique is suitable for ONSF, and that surgeons should choose their surgical approach based on their own preference and individual patient factors.

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Keywords: Pseudotumor cerebri, Orbit, Pseudotumor cerebri, Visual fields

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Analysis of clinical features and outcomes in patients with ocular myasthenia gravis according to anti-acetylcholine receptor antibody-seropositivity: a retrospective cohort study

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Introduction:
There are several previous studies on the clinical features of seronegative generalized myasthenia gravis. However, the clinical implication of seropositivity against acetylcholine receptors remains to be delineated in OMG. In this study, we comparatively analyzed the clinical feature of acetylcholine receptor antibody-positive patients with OMG with that of the seronegative group.

Methods:
Medical records of patients with OMG who presented to a tertiary eye care center between 2003 and 2020 were retrospectively reviewed. Demographics, ophthalmologic characteristics, response to medical treatment, presence of autoimmune thyroid disease and thyroid autoantibody were compared between the AchR Ab seropositive and seronegative groups.

Results:
A total of 130 patients with OMG were identified; among them, 46 patients (35.4%) had autoantibody against acetylcholine receptors. The mean age at symptom onset was 42.4±18.9 years. There were no differences in mean age at symptom onset, gender ratio, and mean follow-up period between patients with seropositive and seronegative OMG. Graves ophthalmopathy was significantly more frequent in seronegative patients ($p=0.04$), while thymic disease ($p< 0.01$) was in seropositive patients ($p< 0.01$). Among patients with seropositive OMG, 52.3% showed a good response to medical treatment, while only 31.4% of the seronegative patients were classified as good responders ($p=0.01$). Thyroid dysfunction was found in 27.4% patients with OMG and the proportion of thyroid dysfunction was not different according to anti-acetylcholine receptor antibody-seropositivity.

Conclusions:
Seropositivity to acetylcholine receptor antibody is associated with a better response to medical treatment and lower risk of concomitant autoimmune thyroid disease in patients with OMG.

References: None provided.

Keywords: Myasthenia, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Adult strabismus with a focus on diplopia

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Analysis of Peripapillary Vessel Density in Ethambutol-induced Optic Neuropathy Using Optical Coherence Tomography Angiography

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Introduction:
To investigate the changes in peripapillary and macular vessel density in ethambutol-induced optic neuropathy using optical coherence tomography angiography (OCTA).

Methods:
The medical records of patients diagnosed with ethambutol-induced optic neuropathy were analyzed retrospectively. Patient age, sex, daily dose (mg/day/kg), treatment duration, best-corrected visual acuity (logMAR), color vision (Ishihara color plate tests), and mean deviation of visual field test were evaluated in non-pathological individuals with age and sex controlled as the normal control group. Peripapillary retinal nerve fiber layer (RNFL) thickness, macular ganglion cell/inner plexiform layer (GC/IPL) thickness, radial peripapillary capillary (RPC) density, and macular superficial capillary plexus (SCP) density were also compared between the patient and control groups.

Results:
The medical records of patients diagnosed with ethambutol-induced optic neuropathy were analyzed retrospectively. Patient age, sex, daily dose (mg/day/kg), treatment duration, best-corrected visual acuity (logMAR), color vision (Ishihara color plate tests), and mean deviation of visual field test were evaluated in non-pathological individuals with age and sex controlled as the normal control group. Peripapillary retinal nerve fiber layer (RNFL) thickness, macular ganglion cell/inner plexiform layer (GC/IPL) thickness, radial peripapillary capillary (RPC) density, and macular superficial capillary plexus (SCP) density were also compared between the patient and control groups.

Conclusions:
Patients with ethambutol-induced optic neuropathy had significantly lower temporal RPC and macular SCP densities. Ethambutol toxicity may affect not only axonal degeneration but also peripapillary and macular vascular function.

References: None provided.

Keywords: Neuroimaging, Optic neuropathy

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Characteristics and Disparities of Participants with Retinal Artery Occlusion in the NIH All of Us Research Program

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Introduction:
Associations between social determinants of health and retinal artery occlusion (RAO) are unclear. This study investigated medical and sociodemographic factors associated with RAO diagnosis in underrepresented U.S. populations using the NIH All of Us Research Program.

Methods:
Retrospective cohort study of participants with RAO from 2018 to 2023 using the All of Us Research Program, an NIH initiative that has recruited participants from historically underrepresented groups to create a diverse representative U.S. population sample. Main outcome measures included medical and socioeconomic factors associated with RAO diagnosis.

Results:
Among 329,023 participants overall, 384 (0.12%) were diagnosed with RAO including 114 diagnosed with central RAO. Females accounted for 172 (45.6%) of RAO diagnoses, 83 (24.9%) were Black, and 50 (13.3%) were Hispanic. Frequent medical comorbidities included hypertension (N=275; 71.6%), diabetes mellitus (N=153; 39.8%), atrial fibrillation (N=48; 12.5%), stroke (N=66, 17.2%), smoking/tobacco use (N=156; 41.2%), and glaucoma (N=86; 22.4%). Most patients reported having health insurance (N=365; 97.6%) which was most commonly Medicare (N=143; 40.6%). In an unadjusted analysis comparing central RAO to branch RAO, there were non-significant trends toward developing central RAO in participants with higher age (OR=1.21, p=0.06), Medicare insurance (OR=1.97, p=0.06), and glaucoma (OR=1.56, p=0.08). In participants who completed health disparity survey data, 24.3% reported inability to see an eye doctor within the past 1 year, 6.9% reported inability to afford seeing a specialist, 12.6% reported delaying care due to out-of-pocket expenses, 29.5% reported inquiring about alternative medications to lower cost, and 31.8% reporting sometimes/never seeing health care providers who were similar to them.

Conclusions:
These findings highlight medical and sociodemographic factors associated with RAO diagnosis in a diverse U.S. sample, which is imperative to understanding health disparities in ophthalmology and addressing gaps in eye care for underrepresented populations.

References: None provided.

Keywords: Stroke, Vascular disorders, Retina

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Characterization of HLA Class II Alleles in Patients with Neuromyelitis Optica in Colombia: A Multicentric Study

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Introduction:
Neuromyelitis Optica (NMO) is a demyelinating disease with a low prevalence in Latin America. International studies have found associations between the risk of NMO and alleles of the human leukocyte antigen (HLA) class II complex. To date, there are no studies in Colombia. Our objective was to characterize the HLA class II alleles in patients with NMO and a control population in Colombia.

Methods:
This case-control study used blood samples to isolate and purify genomic DNA. HLA-DRB1 and DQB1 allele genotyping was done using SSP-PCR. Mitochondrial hypervariable region 1 was amplified and haplogroups were determined using HaploGrep software. The allele frequencies were analyzed and differences between the groups were determined by bivariate and multivariate logistic regression analysis.

Results:
60 patients with NMO (mean age 44.5 ± 12.2 years; 83% females) and 93 healthy controls (mean age 37.6 ± 12.4 years; 85% females) were enrolled. Mitochondrial haplogroup frequencies did not differ between the groups. HLA-DRB1*16 (odds ratio [OR] = 2.93, 95% CI: 1.13 - 7.59, p=0.026), DRB1*11 (OR = 3.02, 95% CI: 1.26 - 7.20, p = 0.013) and DQB1*05 (OR= 5.29, 95% CI: 1.37 - 20.44, p=0.016) were significantly associated with NMO in our population. By contrast, HLA-DRB1*04 (OR = 0.48, 95% CI: 0.23 - 0.96, p =0.038) and DQB1*04 (OR = 0.33, 95% CI: 0.16 - 0.69, p= 0.003) alleles were more common in the control group than in NMO patients. After the multivariate regression analysis, all these associations remained statistically significant (p< 0.05).

Conclusions:
This study provides new insights into the genetic characterization of NMO in Colombia. Our findings suggest that HLA-DRB1*16, DRB1*11, and DQB1*05 alleles confer susceptibility to NMO, while HLADRB1*04 and DQB1*04 alleles may exert a protective effect in our population

References: None provided.

Keywords: Demeylinating disease, Genetic disease, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Optic neuritis

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Clinical Profile and Outcomes of Ocular Myasthenia Gravis: A Retrospective Study at Tertiary Eye Care Centre in India

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Introduction:
While several epidemiological studies have been conducted on MG patients, these have mainly involved those with generalised myasthenia gravis (GMG.) The purpose of this study is to evaluate the clinical profile and treatment outcomes of Indian patients who presented solely with ocular myasthenia gravis (OMG) with a modest follow up of 18 months .

Methods:
A total of 40 patients diagnosed with purely OMG were included in the study after excluding patients who did not meet the inclusion criteria. All patients underwent comprehensive eye evaluation and diagnostic electrophysiological tests. Steroids and acetylcholine esterase inhibitors were prescribed to all patients, and treatment outcomes and adverse effects were evaluated at 3, 6, 12, and 18 months of follow-up from the initial clinical presentation. Categorical variables were presented in number and percentage (%) and , continuous variables were presented as mean ± SD and median.

Results:
Males had a definite preponderance in OMG, with ptosis positive in 97.5% of patients, ICE test positive in 82.35% of patients, and Neostigmine test positive in 97.22% of patients. All patients were treated with steroids except for 3 patients, and only 5% of patients needed immunomodulatory therapy in the form of Azathioprine. None of the patients developed new-onset diabetes mellitus or hypertension. Systemic steroids were well-tolerated with few adverse effects on moderately long-term follow-up of patients.

Conclusions:
Patients with variable and fatigable ptosis should be evaluated further to rule out OMG, and office-based tests like the ICE test and fatigue test should be performed routinely while evaluating patients of OMG suspect .Early treatment with anticholinesterase agents along with corticosteroids leads to good clinical outcomes over a moderately long follow-up period. However, relapse or persistence of symptoms even after therapy with steroids may require the use of additional immunosuppressants.

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Keywords: Myasthenia, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Ocular motility

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Comparison of number and type of ophthalmic surgeries in patients treated with Teprotumumab versus those who were treated with steroids and/or orbital radiation alone.

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Introduction:
Teprotumumab reduces proptosis, improves diplopia and clinical activity score (CAS) in active TED patients, though its impact on TED-related surgeries remains unexplored.1,2 We evaluated surgeries including eyelid surgery (ES), strabismus surgery (SS), and orbital decompression (OD) in TED patients treated with Teprotumumab versus those who were not; >/=two-wall OD was considered severe.

Methods:
Retrospective chart review of patients seen by TED clinicians was performed. Active TED patients treated with steroids and/or orbital radiation (S/OR) between 02/01/2017-01/31/2020 were compared to active TED patients treated with Teprotumumab with/without S/OR between 05/1/2020-04/30/2023. Primary outcomes were number of surgeries (OD, SS, ES), and surgery severity (OD).

Results:
106/486 charts reviewed had active TED. Of the 106, 21/32 non-Teprotumumab group patients received S/OR while 37/74 Teprotumumab group patients received Teprotumumab with/without S/OR. Demographics were similar between non-Teprotumumab and Teprotumumab groups: age (65 (SD+/-15.5) vs. 56 (SD+/-14.0) years), gender (M:28%, F:72% vs M:32%, F:68%), average follow-up (29.5 vs 22.5 months), average CAS at presentation (3.9 vs. 4.1), and patients receiving no treatment (34% vs. 35%). Nine eyes of 21 S/OR-treated non-Teprotumumab patients underwent OD vs. three eyes of 37 Teprotumumab-treated patients (p = 0.04). Of these nine non-Teprotumumab eyes that underwent OD, three eyes underwent severe OD compared to zero Teprotumumab-treated eyes (p = 0.045), and six eyes underwent one-wall OD compared to three Teprotumumab-treated eyes (p = 0.15). The difference in SS, ES, and total surgery numbers between groups was not significant (SS: 6 vs. 5, p = 0.16; ES: 5 vs. 8, p = 0.85; total surgeries: 10 vs. 14, p = 0.47).

Conclusions:
Teprotumumab treatment led to significantly reduced number and severity of OD surgeries for active TED patients. Teprotumumab may better control active TED and ultimately lead to fewer and less-severe OD surgeries, though patients may still require similar numbers of ES and SS.

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Keywords: Graves' disease, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Orbit

Financial Disclosures: Taylor Linaburg; Tejus Pradeep; Yuanyuan Chen; Brian Rinelli; Yineng Chen; Gui-Shuang Ying; Cesar Briceno; Madhura Tamhankar: Clinical research investigator for Viridian Therapeutics and Horizon Therapeutics; consultant for UptoDate

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Consensus Disease Definitions for the Spectrum of Neuro-ophthalmic and Orbital Immune-Related Adverse Events

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Introduction:
Expanding indications for immune-checkpoint inhibitors in oncology have resulted in both therapeutic success and immune-related adverse events (irAEs). There is growing recognition of afferent and efferent neuro-ophthalmic irAEs. Lack of standardized disease definitions and accurate phenotyping leads to syndrome misclassification and impedes treatment and research progress. The objectives of this study were to develop consensus guidance for an approach to neuro-ophthalmic and orbital irAEs including disease definitions and severity grading. This was performed as part of a larger effort to develop consensus-based ophthalmic irAE criteria.

Methods:
Four ophthalmologists and neuro-ophthalmologists drafted consensus guidance and definitions, which were reviewed by the Ophthalmic irAE Disease Definition Panel, consisting of ophthalmologists, neuro-ophthalmologists, neurologists, and oncologists. A modified Delphi consensus process was used, with 2 rounds of anonymous ratings by panelists and 2 virtual meetings to discuss areas of controversy. Panelists rated content for usability, appropriateness and accuracy on 9-point scales in electronic surveys and provided free text comments. Consensus was based on numeric ratings using the RAND/UCLA Appropriateness Method with pre-specified definitions.

Results:
Of 34 Delphi panel participants, 29 completed round 1: neuro-ophthalmologists (12), oncologists (2), ophthalmologists (11), other subspecialists (4); 22 completed round 2. In round 1, of 66 Neuro-ophthalmology/Orbital statements, 86.4% (57/66) reached consensus. Round 2 included 12 revised components; 93.9% (62/66) reached final consensus: 4 afferent disorders (optic neuritis, optic perineuritis, inflammatory optic nerve edema, arteritic ischemic optic neuropathy) and 7 orbital/efferent disorders (orbital inflammation, orbital myositis, thyroid eye disease-like inflammation, cavernous sinus syndrome, and ocular motor mononeuritides). For each disorder, 5 sub-classifications are described: possible symptoms, supportive examination findings, laboratory & imaging tests, diagnostic certainty and treatment.

Conclusions:
These disease definitions standardize neuro-ophthalmic and orbital irAE classification. Given consensus on their accuracy and usability from a representative panel group, we anticipate that they can be used broadly across clinical and research settings.

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Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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Grant Support: None.

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Correlation between central retinal artery blood flow and visual recovery in traumatic optic neuropathy surgery

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Introduction:
Changes in blood flow in the central retinal artery in patients with traumatic optic neuropathy (TON) were examined by OCTA with a view to predicting the correlation between optic nerve blood flow and visual recovery and whether it could be used as a predictor of best corrected visual acuity (BCVA) outcome.

Methods:
OCTA was used to detect changes in blood flow at the optic papilla/retinal macula in TON patients in the immediate and recovery periods of injury, and electrophysiologic and visual function changes were observed during the same period to study the correlation between blood flow and visual function. The correlation between blood flow changes and visual function recovery was tested by binary regression logistic method.

Results:
After optic canal decompression surgery, BCVA improved in 80/138 (57.9%) patients with TON, whereas the improvement rate in patients with BCVA at or better than light perception was only 0.1%. Posterior ethmoid and/or pterygoid sinus hemorrhage, orbital fracture, time interval between trauma and treatment, and pretreatment BCVA were predictors of postoperative BCVA improvement in TON patients. Macular blood flow was not associated with visual acuity.

Conclusions:
Surgery has a positive outcome in patients with TON, especially those with good pretreatment BCVA, a short interval between trauma and treatment, and no orbital fracture or posterior ethmoid and/or pterygoid sinus hemorrhage.

References: None provided.

Keywords: Trauma, Optic neuropathy, Retina

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Delay in Diagnosis of Giant Cell Arteritis in Veterans: A Nationwide Study

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Introduction:
The initial diagnosis of Giant cell arteritis (GCA) is often challenging due to the nonspecific nature of the symptoms.1 Moreover, the elderly population invariably has co-existing symptoms that confound GCA diagnosis such as arthritis, dental issues, and a history of headaches. The United States Veterans Health Administration (VHA) holds the nation's largest electronic medical database.2 Consequently, we leveraged the VHA database to identify clinical factors that led to a delay in GCA diagnosis.

Methods:
Using a pre-defined cohort of 2285 patients diagnosed with biopsy-proven GCA since 1/1/2001 within the national VA Informatics and Computing Infrastructure (VINCI) database3, individual chart reviews were conducted on Veterans Information Systems and Technology Architecture Joint Legacy Viewer databases. Initial clinical presentation, type of initial healthcare provider, and the duration from initial GCA symptom to time of treatment were collected for each case. A logistic regression model will be developed to compare the number of days between initial patient evaluation to treatment among various healthcare providers.

Results:
The results of the initial 50 patients are highlighted. The mean age at diagnosis was 74.7 (range of 58 – 91) years. The median days from initial GCA symptoms to the first healthcare presentation were 14, with an interquartile range (IQR) of 43 days. Twenty-five patients presented initially with temple tenderness. Patients who initially presented with visual symptoms were treated earlier than those who presented with temple tenderness (median of 3 versus 26 days). Patients who initially presented to ophthalmology received GCA treatment the most rapidly (median of zero versus 5 days).

Conclusions:
Our findings underscore that patients often present to a healthcare provider months after the onset of the initial GCA symptom. Patients who presented to ophthalmology were expediently diagnosed and treated. This is encouraging as early treatment is paramount in preventing GCA complications.

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Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Optic neuropathy, Vascular disorders

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Double seronegative, non-multiple sclerosis demyelinating optic neuritis- clinical profile and outcomes

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Introduction:
TO Study the clinical profile, radiological characteristics and treatment outcomes of rare entity of double seronegative, non MS optic neuritis patients

Methods:
Retrospective study of patients with demyelinating optic neuritis negative for multiple sclerosis, neuromyelitis optica (NMO) and myelin oligodendrocyte glycoprotein (MOG) antibody seen at our institute from June 1, 2019, to December 31, 2022. Data was collected regarding demographics, laterality, neurological symptoms, visual function, neuroimaging findings, treatment and final visual outcomes.

Results:
Non-MS double seronegative, demyelinating optic neuritis occurred in 67/ 330 patients during this period. 98 eyes of 67 patients [31 males:36 females; median age:33+/-17.8 (IQR:14-44) years] were enrolled. 35/67(52%) patients had unilateral optic neuritis. Associated symptoms were: ocular pain: 44.7%, headache:26.8%, and ataxia in 4.4% patients. At presentation 25% had papillits, 29% had disc pallor, and remaining 46% had retrobulbar neuritis.Magnetic resonance imaging (MRI) of brain and orbits with contrast showed optic nerve enhancement as short segment : 34.3% , long segment: 11.9%, posterior optic nerve (intracanalicular and intracranial): 31.3% and long segment with chiasm involvement in 13.4% patients. MRI brain lesion was seen in only one patient. All patients were treated with IV methylprednisolone. 9 patients were treated with immunosuppressive agents (1Mycofenolate mofetil and 8 Azathioprine). Median visual acuity improved from 1.7 LogMAR units(IQR 0.48- 3) LogMAR units) at presentation to 0.1(IQR:0 to 0.7) logMAR units($p< 0.001$)Median visual field mean deviation improved from -18.3 dB(IQR: -6.33 to -27.1) to -5.dB (IQR:-- -3.6 to -10.2 db), $p >0.0001$.Recurrence occurred in only 3/67 patients, no predisposing factors were noted. Improvement in visual function was irrespective of segment of the optic nerve affected.

Conclusions:
Double seronegative, non-MS optic neuritis occurred in 20.3%% patients. Radiologically majority had short segment optic neuritis and posterior optic nerve involvement. In majority, visual acuity and visual fields recovered well, irrespective of the optic nerve segment involved

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Keywords: Optic neuritis, Demeylinating disease, Visual fields

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Efficacy and Safety of Lenadogene Nolparvovec Gene Therapy for Leber Hereditary Optic Neuropathy in the Real-Life Setting

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Introduction:
Through early access programs, patients with Leber hereditary optic neuropathy (LHON) can benefit from lenadogene nolparvovec, an as yet unapproved gene therapy for LHON due to the m.11778G>A ND4 mutation.

Methods:
Lenadogene nolparvovec was provided based on unsolicited requests and its use was authorized by local regulations. Patients received lenadogene nolparvovec in 4 countries (France, Italy, UK and US) as a unilateral or bilateral intravitreal injection at a dose of 9x10^10 viral genomes/eye.

Results:
A total of 63 ND4-LHON patients received lenadogene nolparvovec in early access programs, mainly in France (35 [55.6%]) and the US (18 [28.6%]). Overall, 42 (66.7%) patients received a bilateral injection; all but one received both injections on the same day. At the time of the first injection of lenadogene nolparvovec, patients were on average (SD) 33.7 (16.6) years old, with 6 (9.5%) children aged < 15 years. The mean (SD) duration of disease at the first injection was 11.4 (9.6) months. Most (81.0%) patients were treated with idebenone therapy at the time of or after the gene therapy injection. BCVA values at 1 year were obtained from 50 patients; the mean (SD) change in BCVA from nadir to 1 year was -0.43 (0.54) LogMAR (+22 ETDRS letters equivalent). An improvement of at least 0.3 LogMAR from nadir was observed in 63.0% patients. The safety of lenadogene nolparvovec was comparable to those of the 189 patients from clinical studies, with an intraocular inflammation rate of 51.4% and no difference in the incidence of intraocular inflammation between patients treated bilaterally and unilaterally.

Conclusions:
Preliminary analyses show that injection of lenadogene nolparvovec in the real-life setting was associated with a clinically meaningful improvement in visual acuity from nadir and a favorable safety profile similar to that observed in the clinical studies.

References: None provided.

Keywords: Optic neuropathy, Genetic disease, Retina

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Evaluation of Horner Syndrome in Acute Stroke Patients by Pupillometry versus Clinical Examination – a Blinded Prospective Clinical Trial

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Introduction:
Horner syndrome, comprising of ptosis, miosis, and anhidrosis, is considered the first sign of potentially life-threatening conditions, such as carotid artery dissection in acute stroke. Current literature estimates the incidence of Horner syndrome in cervical artery dissection to be almost 40%. We prospectively investigated the incidence of Horner syndrome in acute stroke patients with and without cervical artery dissection using automated pupillometry, comparing it to a blinded standard clinical evaluation.

Methods:
82 patients under 60 years of age who were admitted to the acute stroke unit at a large University Hospital in Switzerland between 2017 and 2020 were examined for Horner syndrome clinically and using binocular pupillometry by two different physicians within 72 hours of admission. The presence of a dilation lag in pupillometry was measured as the change of anisocoria between 3 to 4 seconds after light-off compared to baseline anisocoria at light-on. A dilation lag of ≥0.4 mm was classified as Horner syndrome. The clinical evaluation consisted of testing for ptosis, miosis, and anhidrosis.

Results:
24 acute stroke patients with cervical artery dissection and 58 patients without dissection were included in the preliminary evaluation. Using pupillometry, we found a dilation lag defining Horner syndrome in 29% of patients with and in 19 % of patients without dissection. Strokes with Horner syndrome without dissection were mostly localized in the pontomedullary region. With pupillometry set as a reference standard, clinicians reached a 44% percent sensitivity and a 94% specificity for detecting Horner syndrome in acute stroke patients.

Conclusions:
Clinical evaluation of Horner syndrome to detect cervical artery dissection in acute young stroke patients is unreliable as its sensitivity is very low compared to digital binocular pupillometry. Nevertheless, a positive clinical sign is very specific. Therefore, binocular pupillometry can serve as a helpful tool for identifying Horner syndrome in acute stroke patients.

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Keywords: Pupil, Stroke, Vascular disorders

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Factors Predicting Favorable Visual Outcomes In Posterior Reversible Encephalopathy Syndrome

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Introduction:
Posterior reversible encephalopathy syndrome (PRES) is a clinico-radiological syndrome characterized by headaches, seizures, altered mentation, and visual disturbances. This paper investigates which factors portend favorable outcomes and analyzes visual field (VF) and optical coherence tomography (OCT) data. The present retrospective study at a single center aims to shed light on the aforementioned clinical research inquires.

Methods:
Electronic medical record database was searched using following criteria: diagnosis of PRES with evidence of VF/OCT testing using SlicerDicer in EPIC (2013-2023), patients were excluded for age < 18 and central variant PRES. Factors analyzed included age, gender, medical history, presence of seizure, and presentation of visual loss. Patients with at least 20 days of follow-up were evaluated for visual outcome, visual acuity of 20/40 or better was deemed good outcome. A p-value of < 0.1 was considered statistically significant.

Results:
Forty seven charts were identified, 21 were included for baseline analysis: 52% were female and mean age at onset of PRES was 51 years The most common pre-existing medical conditions were cardiovascular disease (CVD) in 62%, autoimmune disease (AD) in 33%, chronic kidney disease (CKD) in 29%, and hematologic disease in 24%. Seizure occurred in 52%, 33% reported vision loss. 15 patients (46% female) had follow-up of 20 at least days: 80% of patients had good visual outcome. Good visual outcome was associated with female gender (58% vs 0%, p=0.002, endocrinologic disease (25% vs 0%, p=0.08), symptomatic vision loss (42% vs 0%, p=0.02). CVD, hematologic disease, CKD, seizure, and postpartum status did not correlate with visual outcome.

Conclusions:
Majority of PRES patients recovered (VA 20/40 or better) seen at least 20 days after diagnosis. Favorable factors include: female gender, endocrinological abnormalities.

References: None provided.

Keywords: Higher visual functions, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Visual fields, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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Frequency of Increased Intracranial Pressure in MOGAD

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Introduction:
There are a few case reports of bilateral optic disc edema and raised opening pressure (OP) on lumbar puncture (LP) in myelin-oligodendrocyte-glycoprotein-antibody-associated-disease (MOGAD), which could cause diagnostic confusion between MOGAD with bilateral optic neuritis (ON) and pseudotumor cerebri. We evaluated the frequency of increased intracranial pressure (ICP) in a large cohort of MOGAD.

Methods:
Cross-sectional study of MOGAD patients at a tertiary institution with LP OP within 30 days of attack onset.

Results:
From 321 MOGAD patients, 109 LPs were included from 104 patients. The frequency of increased ICP (OP >250 mmH2O in adults or >280 mmH2O in children) was 26% (28/109) in MOGAD attacks (25% [26/104] in MOGAD patients). Patients with increased ICP were slightly younger (median age at LP 23 [IQR 11-40] vs. 35 [IQR 17-49], p=0.050), more often male (58% vs. 35%, p=0.038), and obese (54% vs. 32%, p=0.043). The median OP was 350 [IQR 296-400] mmH2O during increased-ICP attacks and 172 [IQR 140-210] during normal-ICP attacks (p< 0.001). The median CSF white cell count was 33 (IQR 5-134) cells/mm3 in increased-ICP attacks vs. 8 (IQR 2-43) in normal-ICP attacks (p=0.022) with CSF pleocytosis (>5 cells/mm3) in 75% vs. 54% (p=0.063). CSF protein was comparable. Increased ICP was most commonly observed during acute disseminated encephalomyelitis (ADEM: 44%; 10/23), cerebral cortical encephalitis (67%; 2/3), and ON with myelitis attacks (33%; 3/9). Among 28 increased-ICP attacks, 32% (9/21) had bilateral disc edema (2 papilledema from increased ICP alone; 7 bilateral ON), while 33% (7/21) had no disc edema, and 64% (18/27) had headache. Three (11%) attacks initially treated as pseudotumor cerebri had bilateral ON and CSF pleocytosis.

Conclusions:
Increased ICP can be observed in a quarter of MOGAD attacks, particularly ADEM and cerebral cortical encephalitis. The cause is uncertain but potential etiologies include MOGAD inflammation, coinciding pseudotumor cerebri, and spuriously elevated OP.

References: None provided.

Keywords: Demeylinating disease, High intracranial pressure/headache, Pseudotumor cerebri, Optic neuritis

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Genetic variants affecting NQO1 protein levels impact on efficacy of idebenone treatment in Leber's hereditary optic neuropathy

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Introduction:
Idebenone, a synthetic analogue of CoQ10 approved by the European Medicines Agency for Leber's hereditary optic neuropathy (LHON), significantly increases to 50% the proportion of LHON patients with clinically relevant recovery. However, about half of LHON patients remain unresponsive and there is no clear explanation for why idebenone may be ineffective in these patients. Upon reduction by NAD(P)H oxidoreductase (NQO1), a cytosolic homodimeric flavoprotein that catalyzes the reduction of highly reactive quinones, idebenone can be oxidized by complex III, thus reactivating downstream electron flow, mitochondrial respiration, and ultimately cellular ATP level. Thus, idebenone reduction is key, as in its oxidized form may exert a deleterious inhibitory effect on both the redox and proton pumping activity of complex I.

Methods:
We investigated the role of NQO1 expression and activity on the efficacy of idebenone treatment in LHON cell models (cybrids, fibroblasts and iPSCs-derived neurons), LHON post-mortem ocular tissues, and in treated patients.

Results:
We document that common NQO1 polymorphic variants (NM_000903.3: c.559C>T, p.P187S - NQO1*2 and NM_000903.3: c.415C>T, p.R139W - NQO1*3) present in the general population lower consistently the NQO1 protein levels in human cells when homozygote or compound heterozygote. This reflects on the therapeutic effect of idebenone to bypassing defective complex I in LHON, both in vitro using patient-derived cells, and in vivo in treated patient's visual outcome, particularly targeting the LHON patients carrying the m.3460G>A/MT-ND1 mutation.

Conclusions:
The current results have critical clinical implications for the future use of idebenone therapy in LHON, including the possibility that in certain subgroups of patients idebenone might be not only ineffective but perhaps detrimental. In fact, our results may provide an explanation to the negative results of the LEROS trial in m.3460G>A/MT-ND1 LHON patients. Future strategies aimed at increasing NQO1 expression may ultimately optimize therapeutic efficiency of idebenone in LHON.

References: None provided.

Keywords: Genetic disease, Optic neuropathy

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Is Methotrexate More Cost-Effective Than Tocilizumab as an Adjunctive Treatment for Giant Cell Arteritis?

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Introduction:
Treatment for giant cell arteritis (GCA) is corticosteroids. Tocilizumab is the only steroid-sparing agent approved by the FDA for GCA. That therapy has a far higher cost than conventional immunosuppressives. The average estimated cost is $866/year for methotrexate and $37,067/year for tocilizumab [1,2]. In the literature, there is no prospective, randomized, head-to-head comparison of these treatments. This retrospective pilot study aims to determine if there is a significant difference between these two agents regarding efficacy and side effects.

Methods:
Fifty-one consecutive patients with a GCA diagnosis within the last 6 years were reviewed for their demographic characteristics, clinical features, laboratory studies, treatments, and relapses. Descriptive analysis and subgroup comparisons were made to evaluate treatment strategies. We analyzed the thirty patients with biopsy-proven diagnoses of GCA.

Results:
Among the fifteen cases requiring adjunctive treatment, there were eight methotrexate and seven tocilizumab-treated patients. Corticosteroid side effects were the top cause of adding steroid-sparing therapies. Patients treated with adjunctive immunosuppressives had a higher rate of ischemic optic neuropathy at presentation (p=0.028). Patients requiring additional immunosuppressives were on higher oral prednisone in the 3rd month than the rest of the cohort (mean 39.1 vs. 26.2, p=0.031). Relapse rates were statistically not different between the patients requiring adjunctive immunosuppressives and those not (p=0.108). There was also no difference regarding the relapse rates between methotrexate or tocilizumab-treated patients (p=0.199). However, two patients had relapses while on methotrexate and none on tocilizumab. Neither lost further vision. One was then switched to tocilizumab and the other one to rituximab.

Conclusions:
In this pilot series, the difference in costs is substantial between methotrexate and tocilizumab. A randomized trial aimed at the comparison of these steroid-sparing agents would be valuable to determine cost versus efficacy between treatment strategies [3,4].

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Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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Long-Term Comparative Efficacy of Inebilizumab in the AQP4+ Subpopulation from N-MOmentum Open-Label Extension Versus Azathioprine and Immunosuppressive Therapies and Versus Placebo in Patients with NMOSD

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Introduction:
Inebilizumab (INEB), an anti-CD19 B cell-depleting antibody, is approved for the treatment of neuromyelitis optica spectrum disorder (NMOSD) in adults seropositive for aquaporin-4 antibody (AQP4+). N-MOmentum (NCT02200770) consisted of a 28-week randomized-controlled period (RCP) and an optional open-label extension period (OLP) (>2 years) in which all participants received treatment with INEB. The aim is to evaluate the long-term comparative efficacy of INEB over N-MOmentum OLP vs. azathioprine and other immunosuppressive therapies (AZA/IST) and vs. historical PBO in participants with NMOSD.

Methods:
Two historical comparator groups (HCGs) of participants who received AZA/IST (N=132) or PBO only (N=106) were derived using data from published NMOSD studies and were used to evaluate the comparative efficacy of INEB (N=208) over the OLP. Hazard ratios (HR) for INEB vs HCGs were estimated using a Cox proportional hazards (PH) regression. Time to NMOSD attack was analysed using parametric and flexible survival (spline) models that were fit to INEB and HCGs.

Results:
The HR(95% CI) of time to NMOSD attack for the N-MOmentum PBO group compared to PBO groups was 1·15(0.67–1.91); P=0.58. The HR(95% CI) for time to NMOSD attack for INEB vs AZA/IST and PBO groups were 0.29(0.17,0.42); P< 0.001 and 0.15(0.10,0.21); P< 0.001, respectively. A time-varying spline with two internal knots and normal linear predictor provided the best fit. At 4 years, the model estimated an attack-free probability (95% CI) of 77%(71,83) for INEB, 36%(27,46) for AZA/IST, and 12%(7,20) for PBO. Results indicate a greater difference in efficacy for INEB vs PBO compared to AZA/IST vs PBO, suggesting a significant reduction in risk of attack for INEB vs both AZA/IST and PBO.

Conclusions:
INEB was associated with a statistically significant reduction in risk of an NMOSD attack and provided a long-term attack-free probability over the OLP compared to the relative short-term benefit observed with AZA/IST.

References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Optic nerve trauma and treatment, Optic neuritis

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Mitochondrial Dysfunction in OPA1-Autosomal Dominant Optic Atrophy (OPA1-ADOA) Assessed in FALCON, A Non-interventional, Natural History Study

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Introduction:
Autosomal Dominant Optic Atrophy (ADOA) is the most common inherited neuro-ophthalmic disorder. Patients typically present in the first decade of life and over half of all patients are registered as legally blind by the fifth decade of life. Most cases are caused by a heterozygous mutation in the nuclear gene OPA1, often leading to OPA1 protein haploinsufficiency. Reduced OPA1 protein levels are associated with impaired mitochondrial function in retinal ganglion cells leading to apoptosis causing progressive and irreversible vision loss. The natural history of OPA1-ADOA visual neurodegeneration is understudied and mitochondrial dysfunction has not been studied in vivo. In the presence of retinal oxidative stress, mitochondrial flavoproteins, when stimulated by blue light, display increased fluorescence measured as green light. Ocumet Beacon leverages this by quantitating this light emission, generating a retinal flavoprotein fluorescence (FPF) score. FPF functions as a biomarker of mitochondrial dysfunction in vivo. Here we present initial baseline data from FALCON from a patient subset who completed the Beacon.

Methods:
FALCON is a multicenter, prospective study of patients who are ≥8 to ≤60 years (y) old and have a confirmed heterozygous OPA1 gene variant. FALCON includes 48 patients, of which 19 (8 (8-17y), 6 (18-40y), and 5 (41-60y)) completed baseline Beacon.

Results:
For the subset of 19 patients, the mean duration since OPA1-ADOA onset was 16.0y (SD 13.71) with the mean (SD) LogMAR (25%) of 0.7 (0.37); and average reading speed of 96.4 (38.39) words per minute. FPF is being analyzed and will be reported at presentation time.

Conclusions:
FPF may add to current diagnostic tools for earlier detection of OPA1-ADOA mitochondrial dysfunction and may help to inform future studies as a measure of treatment response.

References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Pediatric neuro-ophthalmology, Retina, Genetic disease, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease

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Optic Nerve Sheath Enhancement On Orbital Magnetic Resonance Imaging In Giant Cell Arteritis: A Case-Control Study

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Introduction:
Differentiating arteritic anterior ischemic optic neuropathy (A-AION) due to giant cell arteritis (GCA) from non-arteritic anterior ischemic optic neuropathy (NA-AION) is challenging, particularly since systemic symptoms are absent in occult GCA. Many case reports of A-AION patients report MRI enhancement of the optic nerve sheath (ONS) but whether there are differences in ONS enhancement between A-AION and NA-AION remain unclear. This study aimed to assess the utility of ONS enhancement on dedicated orbital MRI in distinguishing A-AION from NA-AION.

Methods:
This case-control study included 26 patients (12 A-AION, 14 NA-AION) who underwent contrast-enhanced orbital MRIs within 3 months of symptom onset. Diagnosis of GCA was determined by temporal artery biopsy and/or ACR-EULAR classification criteria. Two radiologists blinded to clinical data independently evaluated MRIs for ONS enhancement. Groups were compared using Fisher's exact test and diagnostic performance was assessed. Cohen's kappa measured inter-reader agreement.

Results:
Patients with A-AION were significantly older and had more extra-ocular cranial symptoms, but had no difference in visual acuity compared to NA-AION patients. On orbital MRI, ONS enhancement was more common in A-AION than in NA-AION (reader 1: 75% vs. 29%, P = 0.04; reader 2: 75% vs. 7%, P < 0.01), with moderate inter-reader agreement (kappa = 0.46, 73% agreement). Pallid disc edema or retinal ischemia was seen on ophthalmologic exam in 50% of A-AION vs 0% in NA-AION (P < 0.01). Among A-AION patients without pallid disc edema or retinal ischemia, ONS enhancement was seen in 75% (reader 1) and 50% (reader 2).

Conclusions:
GCA patients with A-AION are more likely to have optic nerve sheath enhancement on MRI compared to NA-AION, highlighting the potential value of orbital MRI in distinguishing these two conditions. Future studies are needed to validate these results and demonstrate that orbital MRI improves diagnostic accuracy and patient outcomes.

References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Optic neuropathy

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Grant Support: Research grant from the Rheumatology Research Foundation

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Optic Neuropathy in the Hospital Setting: a Single Tertiary Care Center Retrospective Cohort Study

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Introduction:
Patients with vision loss secondary to optic neuropathy of any cause frequently present through the emergency department for urgent evaluation and inpatient management. Neurologists and neuro-ophthalmologists are often the primary physicians that manage these hospitalized patients. Timely diagnostic and treatment decisions in the acute hospitalized setting can preserve visual function and expedite recovery[1], particularly in arteritic ischemic neuropathy and optic neuritis. Optic neuropathy is well characterized in the outpatient setting, but there is limited data on the spectrum of disease in the hospital setting, as well as the heterogenous practices for its inpatient management [2-4]. Furthermore, prior studies suggest a high rate of misdiagnosis of neuro-ophthalmologic conditions when the patient reaches the outpatient setting[2, 5]. Our retrospective study aims to clinically characterize the hospitalized optic neuropathy patients and investigate factors that predict changes in diagnosis and visual acuity outcomes.

Methods:
We included all patients over the age of 18 with suspected optic neuropathy evaluated in the ER or inpatient services at a large urban tertiary care center between June 2018 and June 2023. Our patient query defined optic neuropathy by ICD 10 codes H46, H47 and H48. Patients with history of optic neuropathy were included if their presenting complaint is related to optic neuropathy. Medical record review will be completed to characterize patient demographics, diagnostics, therapeutics, outpatient follow-up and clinical outcomes. Statistical analysis will be performed to identify variables that predict changes in diagnosis and clinical outcome.

Results:
Our initial query identified 309 patient encounters with 233 unique patients coded for optic neuropathy over 5 years. In the following 6 months, 108 patients had follow-up with ophthalmology clinic while 137 with neurology clinic. In-depth chart review is taking place following IRB approval to identify the clinical spectrum of optic neuropathy and variables that predict changes in diagnosis and clinical outcome.

Conclusions:
TBD

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Keywords: Optic neuropathy, Neuroimaging, Optic neuritis, Miscellaneous

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Optical Coherence Tomography In Patients With Repetitive Head Trauma; A Case-Control Analysis Of Probable Traumatic Encephalopathy Syndrome

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Introduction:
Traumatic encephalopathy syndrome (TES) is the clinical condition associated with chronic traumatic encephalopathy (CTE); an autopsy diagnosed tauopathy associated with repetitive head trauma (RHT). The effect of RHT on Optical Coherence Tomography (OCT) measures such as Retinal Nerve Fibre Layer (RNFL) thickness remains poorly understood, yet progressive RNFL thinning has been found in neurodegenerative disease. We sought to investigate the presence of OCT abnormalities in patients with probable TES (pTES).

Methods:
32 patients with a history of RHT from sport or military service underwent neurological and ophthalmological assessment. Preliminary analysis of OCT measures was undertaken from five patients with features consistent with pTES (Katz, 2021). Other neurological causes of TES symptoms were reasonably excluded using clinical evaluation, neuroimaging, neuropsychological measures and follow up progression.

Results:
Mean OCT measures were compared between the pTES and control group using an independent one-tailed t test. The control group (n=5) was selected with comparable average age (51 years control; 54 years pTES), years exposed to RHT (24 years control; 21 years pTES) and number of concussions (18 control; 15 pTES); TES was formally excluded using the same measures. The average RNFL was significantly thinner in the pTES group for both right (P=0.023) and left (P=0.033) eyes compared to control group. Pearson product-moment correlation demonstrated no significant correlations between OCT measures and extent of RHT exposure, number of self-reported concussions or age first exposed to RHT.

Conclusions:
Preliminary analysis suggests patients with pTES may have RNFL thinning relative to non-TES patients also exposed to RHT. This implies that the changes seen are not merely a reflection of direct mechanical trauma to the optic nerve secondary to the RHT, but may be a reflection of the underlying neurodegeneration in TES/CTE. OCT is an inexpensive, non-invasive modality that may be a suitable biomarker for TES and CTE in the future.

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Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Retina, Trauma

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Population-Based Performance of Inflammatory Markers in Giant Cell Arteritis

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Introduction:
Inflammatory markers are an important screening tool for the diagnosis of giant cell arteritis (GCA), available literature is based on tertiary centers which are susceptible to referral bias. The purpose of this study was to determine the population-based sensitivities and specificities of various inflammatory markers for the diagnosis of GCA.

Methods:
Retrospective population-based cohort study. Patients who underwent temporal artery biopsy (TAB) from 01/01/1995 through 12/31/2019 in a single county in the United States were identified. Subjects were categorized under the GCA cohort if they met classification criteria for GCA(1), and a sex-matched non-GCA control cohort was randomly selected from the TAB-negative patients. Sensitivity and specificity of inflammatory markers obtained prior to steroids were determined using the following criteria for elevation: CRP >8mg/L, ESR >age/2 male or >(age+10)/2 female, platelets >317x10^9/L male or >371x10^9/L female.

Results:
143 GCA patients were identified and compared with 143 non-GCA control patients. Median age at time of TAB was 76 years (range 50-97) and 203(71%) were female. The GCA cohort had higher median CRP (68 vs 20 mg/L, p=< 0.001), ESR (62 vs 40 mm/hr, p=< 0.001), and platelets (363 vs 268 x10^9/L, p=< 0.001) than the control cohort. Sensitivity was 97% for CRP, 78% for ESR, and 63% for platelets. Specificity was 23% for CRP, 50% for ESR, and 78% for platelets. Specificity did not significantly improve when combining individual inflammatory markers beyond the specificity of platelets: 55% for combined ESR and CRP and 78% for combined ESR, CRP, and platelets. Normal inflammatory makers, including ESR, CRP, and platelets, were observed in 2(3%) GCA patients.

Conclusions:
This population-based study evaluated the performance of various inflammatory markers in the diagnosis of GCA, which confirms that CRP is the most sensitive. Inflammatory markers are helpful in the diagnosis of GCA, but normal values do not exclude the diagnosis.

References: 1. Ponte C, Grayson PC, Robson JC, et al. 2022 American College of Rheumatology/EULAR classification criteria for giant cell arteritis [published correction appears in Ann Rheum Dis. 2023 Feb;82(2):e52]. Ann Rheum Dis. 2022;81(12):1647-1653. doi:10.1136/ard-2022-223480

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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Contact Information: None provided.

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Prevalence and Trends of Cranial Nerve Palsies: A Nationwide Analysis from 2016 to 2020

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Introduction:
Cranial nerve III, IV, and VI palsies can profoundly impact ocular motility and vision and can be indicative of underlying systemic or neurologic diseases. Moreover, given the potential for these palsies to serve as clinical indicators, understanding their prevalence and trends becomes paramount. This knowledge is foundational for effective diagnosis, management, and delineating research directions in neuro-ophthalmology.

Methods:
National data from January 2016 to December 2020, inclusive of the early COVID-19 pandemic phase, were retrospectively analyzed. Sourced from the HCUP National Inpatient Sample, the study focused on oculomotor, trochlear, and abducens nerve palsies. Categorizations were based on unspecified, right, left, and bilateral presentations, with chi-squared tests for statistical analyses.

Results:
- Oculomotor nerve palsy: Predominated with an annual average of 1,110 cases (range: 985-1,230), with no significant yearly fluctuation ($p=0.11$). - Trochlear nerve palsy: Less frequent, averaging 35 cases annually (range: 20-50), stability observed over the years ($p=0.14$). - Abducens nerve palsy: Accounted for an average of 933 cases yearly (range: 860-1,000), with consistent prevalence ($p=0.12$). Differences in prevalence among the palsies were statistically significant ($p < 0.001$).

Conclusions:
There was an observed consistent prevalence of oculomotor nerve palsy, which underscores its significance in neuro-ophthalmology. Early identification and intervention of these nerve palsies are crucial, given the potential association with life-threatening conditions, such as intracranial aneurysms, and their role as early indicators of underlying neurological disorders. This study fills gaps in neuro-ophthalmological literature, emphasizes the importance of vigilant monitoring of symptoms, and lays a foundation for future research. For more information contact Rami Ghanem at ghanemr@amc.edu

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Keywords: Optic neuropathy, Optic nerve trauma and treatment, Miscellaneous

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Prevalences Of Other Non-Thyroid Autoimmune Diseases And Factor Associated With Their Presence In Ocular Myasthenia Gravis

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Introduction:
Myasthenia gravis (MG) is an autoimmune disease that affects neuromuscular junction resulting in fluctuation of muscle weakness and fatigability. Approximately half of the patients present with only ocular symptoms, classified as ocular MG (OMG). Many studies have evaluated the prevalences of other thyroid autoimmune diseases in MG patients. However, only a few studies have reported the prevalences of other non-thyroid autoimmune diseases, particularly in OMG patients. Therefore, this study aimed to report prevalences of other non-thyroid autoimmune diseases and identify factors associated with their presence in OMG subjects.

Methods:
A total of 208 subjects with OMG diagnosis were included. Demographic data, clinical characteristics, ice-pack test, acetylcholine receptor (AChR) antibody test, edrophonium chloride test, electrophysiology tests, presence of thymoma, generalized MG conversion, and presence of other non-thyroid autoimmune diseases (defined as the presence of at least 1 other non-thyroid autoimmune disease) were retrospectively reviewed. Univariate and multivariate logistic regression analyses were used to identify associated factors.

Results:
Of the total 208 subjects, there were 21 subjects (10.10%) with the presence of other non-thyroid autoimmune diseases (19 and 2 subjects had 1 and 2 other non-thyroid autoimmune diseases, respectively) and systemic lupus erythematosus (SLE) was diagnosed in 9 subjects (4.33%), followed by Sjogren's syndrome (7 subjects, 3.37%), rheumatoid arthritis (6 subjects, 2.88%) and ankylosing spondylitis (1 subject, 0.48%). Positivity of AChR antibody was the only significant factor associated with the presence of other non-thyroid autoimmune diseases (odds ratio 4.60, 95% CI 1.46-14.49, p = 0.009).

Conclusions:
Presence of other non-thyroid autoimmune diseases was found in approximately 10% of OMG subjects, with SLE being demonstrated the highest prevalence. We recommend screening and monitoring for other non-thyroid autoimmune diseases, particularly those with positivity of AChR antibody.

References: None provided.

Keywords: Myasthenia, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Miscellaneous, Miscellaneous, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Quantification of changes in ocular misalignment in thyroid eye disease patients treated with teprotumumab via objective sensorimotor examination and cover-uncover testing.

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Introduction:
Several studies have evaluated the effect of teprotumumab therapy on binocular diplopia in thyroid eye disease (TED) patients using subjective measures (e.g. Bahn-Gorman Scale), however, few if any studies have objectively quantified these associations. The current study investigated changes in ocular misalignment in TED patients with binocular diplopia after receiving teprotumumab therapy via quantitative sensorimotor and prism examination.

Methods:
In this retrospective chart review, 12 TED patients treated with teprotumumab reported symptoms of binocular diplopia at presentation and demonstrated quantifiable ocular misalignment via sensorimotor exam. These subjects underwent comprehensive eye examinations, including sensorimotor exam and cover-uncover testing in cardinal and primary fields of gaze, before and after therapy. Groups were divided in a pre-post study design that compared ocular misalignment measures before and after treatment.

Results:
All patients with baseline vertical tropias in primary gaze demonstrated significant improvement with therapy (N = 5, post-treatment mean change = -10.00 D +/- 7.48, $p = 0.041$). Six of 8 patients (75%) with horizontal tropias in primary gaze also showed improvement (mean change = -5.00 D +/- 2.76, $p = 0.007$). Horizontal tropias were also significantly reduced in all cardinal fields of gaze (post-treatment mean change > -8.56 D, $p < 0.039$), whereas vertical tropias were reduced only in up- and right-gaze (post-treatment mean change > -8.60 D, $p < 0.044$). Thyroid-stimulating immunoglobulin (TSI) correlated with the mean change in vertical tropias in primary gaze and in all fields of cardinal gaze except up-gaze ($R2 > 0.66$, $p < 0.047$), but not with mean change in horizontal tropias in any fields of gaze. Pre-treatment clinical activity score (CAS) did not correlate with any mean changes in ocular misalignment.

Conclusions:
Teprotumumab significantly improved signs of ocular misalignment when measured objectively with sensorimotor testing. Pre-treatment TSI, but not CAS, correlated with the degree of improvement.

References: None provided.

Keywords: Graves' disease, Adult strabismus with a focus on diplopia, Ocular motility, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Orbit/ocular pathology

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Retinal artery occlusion and risk of stroke.

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Introduction:
Retinal artery occlusions (RAO) are rare diseases that can induce severe irreversible visual loss. Indeed, patients with central retinal artery occlusion (CRAO) or a branch retinal artery occlusion (BRAO) have a risk of stroke. Our study aimed to assess the risk of stroke in patients presenting with CRAO, BRAO or paracentral acute middle maculopathy (PAMM) and to evaluate the risks factors for stroke in these patients.

Methods:
We conducted a retrospective, monocentric review of patients diagnosed with RAO at the Rothschild Fundation in Paris, France, between January 2010 and January 2022. Patients were identified via electronic medical records. Their ophtalmological and neurological records, as well as their imaging, were reviewed.

Results:
703 patients with RAO were identified. 54 were excluded (36 had giant cell arteritis and 18 had PAMM with central retinal vein occlusion). Among the remaining 649 RAO cases, 122 had concomitant stroke. CRAO and BRAO patients had a significantly higher risk to develop a stroke than PAMM patients. Associated risks factors to develop a stroke were male sex and homolateral carotid stenosis. In fact, the risk of stroke in RAO patients was doubled when they had a carotid stenosis. Stroke risk was higher after vascular surgery (p=0,008), carotid dissection (p=0,0001), in atherosclerosis (p=0,02) or emboli (p=0,02). Patients treated with anti-platelets drugs had the same risk of stroke than patients without.

Conclusions:
The risk of stroke in RAO depends of the type of retinal vascular insult. CRAO and BRAO represent a much higher risk than PAMM. There were few associated risks factors, namely male gender and homolateral carotid stenosis. Patients should systematically be referred to a neurovascular unit or have, at the very least, a supra-aortic Doppler ultrasounds examination, specifically when magnetic resonance imaging (MRI) is not available. A brain MRI should systematically be performed in case of a significant carotid stenosis.

References: None provided.

Keywords: Vascular disorders, Neuroimaging, Retina

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Contact Information: None provided.

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Retinal Mitochondrial Function in Patients with Multiple Sclerosis

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Introduction:

Multiple sclerosis (MS) is a leading cause of disability in young individuals.1 Despite current treatment options, approximately half of patients with relapsing-remitting MS (RRMS) get into the progressive stage, whereas the efficient clinical biomarkers for monitoring the disease progression remain elusive.2 Notably, mitochondrial dysfunction has been reported in patients with MS.3, 4 The retina, a valuable tool for MS research,2 is now accessible for such investigations. The retinal and optic nerve head (ONH) mitochondrial function can be assessed by analyzing flavoprotein fluorescence (FPF).5-6 This pilot study explored the retinal and ONH mitochondrial function in patients with RRMS and their correlations with the retinal nerve fiber layer (RNFL) and ganglion cell-inner plexiform layer (GCIPL).

Methods:

Retinal Metabolic Analysis (RMA) (OcuMet Beacon, OcuSciences, Inc. Ann Arbor, MI) was used to measure FPF. After lens compensation, the mean FPF in the macula and ONH were measured. In addition, mitochondrial stress calculated as FPF heterogeneity was also measured with the value > 1 indicating disease suspected. RNFL and GCIPL were measured using optical coherence tomography. 28 eyes of 14 patients with RRMS and six normal controls were recruited, and both eyes were imaged.

Results:

The mean FPF in the macula and ONH were significantly higher in patients with RRMS than normal controls ($P < 0.05$). In addition, the ONH mitochondrial stress index was also significantly higher in RRMS compared to normal controls ($P < 0.05$). The macular mitochondrial stress index was negatively related to the average GCIPL ($r = -0.42$, $\beta = 0.03$).

Conclusions:

This is the first study to determine retinal and ONH mitochondrial function in patients with RRMS. Mitochondrial dysfunction measured as the increased FPF in the macula and OHN could be a biomarker of disease progression, while the continuing study with a large sample may provide detailed characteristics of retinal mitochondrial stress in MS.

References: 1. Wallin MT, Culpepper WJ, Campbell JD, et al. The prevalence of MS in the United States: A population-based estimate using health claims data. Neurology 2019;92:e1029-e1040. 2. El Ayoubi NK, Sabbagh HM, Bou Rjeily N, Hannoun S, Khoury SJ. Rate of Retinal Layer Thinning as a Biomarker for Conversion to Progressive Disease in Multiple Sclerosis. Neurol Neuroimmunol Neuroinflamm 2022;9. 3. Mao P, Reddy PH. Is multiple sclerosis a mitochondrial disease? Biochim Biophys Acta 2010;1802:66-79. 4. Blagov AV, Sukhorukov VN, Orekhov AN, Sazonova MA, Melnichenko AA. Significance of Mitochondrial Dysfunction in the Progression of Multiple Sclerosis. Int J Mol Sci 2022;23. 5. Muste JC, Russell MW, Chen AX, et al. Functional Imaging of Mitochondria in Age-Related Macular Degeneration Using Flavoprotein Fluorescence. Ophthalmic Surg Lasers Imaging Retina 2023;54:24-31. 6. Chen AX, Conti TF, Hom GL, et al. Functional imaging of mitochondria in retinal diseases using flavoprotein fluorescence. Eye (Lond) 2021;35:74-92.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Retina, Demeylinating disease

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Risk of Cranial Nerve Palsies and Double Vision Following CSF Diversion Procedures for Normal Pressure Hydrocephalus: A Large Database Study

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Introduction:
This study investigates the repercussions of cerebrospinal fluid (CSF) diversion procedures in patients with Normal Pressure Hydrocephalus (NPH), focusing on the risks of cranial nerve palsies and diplopia.

Methods:
We grouped patients with NPH who underwent CSF diversion procedures and matched them by demographics (age, race, and sex) to NPH patients without the procedures. Additionally, we compared these groups to patients without NPH history who had an eye exam, examining the 6-month risk of developing diplopia and CN palsies (III, IV, and VI).

Results:
6,432 NPH patients underwent CSF diversion and were matched to NPH patients without procedures. The 6-month risk of diplopia was significantly higher in the surgical group (RR: 2.37, CI: 1.66-3.38, $p< 0.0001$) as was the risk of CN VI palsies (RR: 3.70, CI: 1.84-7.43, $p< 0.0001$), with no elevated risk for CN III or CN IV palsies. Compared to patients with no NPH history, significant elevations in risks of double vision (RR: 2.12, CI: 1.51-2.98, $p< 0.0001$) and CN VI (RR: 2.71, CI: 1.31-5.59, $p< 0.0001$) were noted.

Conclusions:
Post-CSF diversion, NPH patients exhibit elevated risks of developing diplopia and CN VI palsies within six months, necessitating enhanced clinical monitoring. These risks could be due to traction on CN VI resulting from brain displacement after the loss of CSF support in the basal cisterns. Such insights are vital for performing thorough risk-benefit analyses before undertaking CSF diversion procedures.

References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Ocular motility

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Temporal Artery Biopsy: Powerful In the Right Hands

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Introduction:
Giant cell arteritis (GCA) is the most common form of vasculitis in older populations and has devastating sequelae if untreated. Temporal artery biopsy (TAB) is the longstanding gold standard diagnostic tool: reportedly highly specific, but plagued by low sensitivity, which can be improved by increased biopsy length, with >1.8 cm being recommended in the literature. However, frequently, TABs are performed by numerous providers and both surgical technique and targeted specimen length vary. We sought to evaluate how biopsy length and resulting diagnostic sensitivity vary by surgical specialty.

Methods:
A retrospective chart review was performed of all TABs reported in our catchment area of 1.3 million people over a three year period (2019-2022). We subclassified specimens by specialty of performing surgeon; biopsy length and clinical-pathological concordance were documented. Analysis was performed by way of unpaired t-test using a commercially available analytic suite (GraphPad Prism).

Results:
219 TABs (161 female) were performed. 50 biopsies were positive for GCA, 155 negative, and 14 were classified as indeterminate. 26 patients were given a clinical diagnosis of GCA with a negative TAB. Plastic Surgery performed 164 TABs and Ophthalmology performed 55. We found specimens performed by Ophthalmologists were, on average, longer than those performed by Plastic Surgeons (Ophthalmology 21.3 +/- 8.5mm, Plastic Surgery 14.7 +/- 6.1mm, $p< 0.0001$). Likewise, test sensitivity of TAB was higher in the Ophthalmology group (Ophthalmology 80%, Plastic Surgery 53%).

Conclusions:
Our findings support the existing dogma that biopsy sensitivity is positively correlated with specimen length; in our institution, biopsy length differed significantly by surgical discipline. It is unclear whether these differences are due to variable surgical technique, divergent teaching as to acceptable minimum biopsy length, or another factor. This highlights the importance of liaising with your local surgical provider to discuss length targets to maximize the utility of this invasive test.

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Keywords: Vascular disorders, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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The efficacy of contrast sensitivity test to the early prediction of optic chiasmal damage in pituitary adenoma

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Introduction:
Pituitary adenoma results in bitemporal hemianopia but some show normal visual field even chiasmal involvement. The contrast sensitivity test in normal visual field was conducted to find the early optic damage in pituitary adenoma.

Methods:
We prospectively reviewed 70 eyes of 35 patients with pituitary adenoma and 36 eyes of 18 controls. Best corrected visual acuity, Visual field, Spectral-domain optical coherence tomography, contrast sensitivity test (GCT-2000, contrast glaretester, Takagi Co., Nagano-shi, Japan) were performed, and the results were compared with the patient group and the control group.

Results:
In the optical coherence tomography test, macular thickness did not show a significant difference between patient group[250.00(237.00~262.00)] and control group[243.50(232.50~262.75)] (P=0.629), and the average GCL layer thickness did not show a significant difference between patient group[80.00(75.00~84.00)] and control group[80.50(76.25~83.75)] (P=0.607). In the contrast sensitivity test, there was no significant difference between both groups in photopic condition (P>0.05). There was a significant difference in a mesopic condition at a long distance (5 meters) in the left eye (P< 0.05). The presence of glare did not have an effect on difference between both groups.

Conclusions:
There may be a change in contrast sensitivity prior to visual field defect in pituitary adenoma patients, which can help to predict disease progression and suggest early treatment.

References: None provided.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Tumors

Financial Disclosures: The authors had no disclosures.

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The Eyes Have It: Factors Influencing Temporal Artery Biopsy Sensitivity

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Introduction:
There is emergent disagreement in the literature regarding the broad implementation of temporal artery biopsy (TAB) in the assessment of suspected giant cell arteritis (GCA), as it has variable sensitivity based on many factors, and is limited by logistical constraints including barriers to access and the invasive nature of the test. However, TAB unequivocally remains the gold standard diagnostic for GCA. Although the classic features of GCA are well established, identifying the relative contribution of individual features to test positivity may better guide its clinical deployment.

Methods:
A retrospective chart review was performed of all TABs reported in our catchment area of 1.3 million people over a three year period (2019-2022). We classified the clinical presentation of query GCA patients based on the EULAR criteria, subclassifying into high and low pre-test probability based on the number of features present (high: two or more features). In addition, the ordering physician's specialty was documented. Analysis was performed by one-way ANOVA using a commercially available analytics suite (GraphPad Prism).

Results:
235 TABs from 230 patients (168 female) were performed. 54 biopsies were positive for GCA, 163 negative, and 14 were classified as indeterminate. The sensitivity of TAB was higher in patients referred from an Ophthalmologist (79%) when compared to a Neurologist (75%) or Rheumatologist (50%). This cannot be attributed to pretest probability, which varied minimally with no clear trend over the groups (p=0.54). On subgroup analysis, we identified visual symptoms to be strongest single predictor of a positive TAB: when present, TAB sensitivity was 78% vs 53% when absent.

Conclusions:
Our data suggest that visual symptoms are the most important symptom when predicting likely TAB outcome. These findings may help inform the relative weight to place on the EULAR criteria when deciding to perform a biopsy and thereby optimize the cost-benefit ratio in its clinical implementation.

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Keywords: Vascular disorders

Financial Disclosures: The authors had no disclosures.

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Contact Information: None provided.

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The Prevalence and Clinical Characteristics of MOGAD Presenting with Optic Neuritis: A Single-Center Experience

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Introduction:
Optic neuritis (ON) is an inflammatory disease of the optic nerve characterized by a sudden monocular or binocular visual disturbance, which can also manifest as part of inflammatory diseases of the central nervous system (CNS).

Methods:
A total of 113 patients who initially presented with ON were investigated. Patients were classified into two groups: those with only optic nerve involvement (pure-ON) and those diagnosed with inflammatory CNS disease. The latter group was further categorized as MOG antibody-associated disease (MOGAD)-ON, multiple sclerosis (MS)-ON, neuromyelitis optica (NMO)-ON, and unclassified-ON. A comparative analysis of the clinical features between pure-ON and MOGAD-ON was performed.

Results:
62 (54.9%) patients were classified as having pure-ON. Among the 51 (45.1%) patients with inflammatory CNS diseases, there were 25 (22.1%) cases of MOGAD-ON, 12 (10.6%) cases of NMO-ON, 10 (8.8%) cases of MS-ON, and 4 (3.5%) cases of unclassified-ON. There were no differences in age or gender between Pure-ON and MOGAD-ON groups, but MOGAD-ON group showed a higher tendency for recurrence (28.0% vs. 4.8%, p=0.022). The proportions of bilateral optic nerve involvement (bONi), optic disc swelling (ODS), contrast enhancement of the optic nerve on orbit MRI, and concurrent brain lesions in the MOG-ON group were significantly higher than in the pure ON group (p=0.001, p< 0.001, p< 0.001, p=0.011, respectively). The bONi and ODS were the independent factors predictive of MOGAD on multivariate logistic regression analysis (odd ratio, 13.2 and 23.0; 95% confidence interval, 2.394-73.298 and 2.442-217.184; p=0.003 and p=0.006, respectively).

Conclusions:
A significant proportion of patients with ON were diagnosed with inflammatory CNS demyelinating diseases, and it is remarkable that approximately 50% of them were confirmed as MOGAD. To differentiate MOGAD in ON patients without concurrent brain or spinal cord lesions, it may be crucial to consider factors beyond MOG antibody testing, including the presence of bONi and ODS.

References: None provided.

Keywords: Demeylinating disease, Optic neuritis, Neuroimaging, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Treatment Options For Acute/Subacute Patients With m.11778G>A MT-ND4 Leber Hereditary Optic Neuropathy: A Meta-Analysis.

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Introduction:
We assessed the visual outcomes of patients with Leber hereditary optic neuropathy (LHON) harboring the m.11778G>A MT-ND4 mutation with no treatment (natural history), idebenone therapy, and lenadogene nolparvovec gene therapy intravitreal injection.

Methods:
Based on a pre-defined statistical analysis plan, three independent meta-analyses were performed on these three groups of patients, with efficacy outcome being the clinically relevant recovery (CRR; on-chart best-corrected visual acuity [BCVA] gain of at least 10 ETDRS letters, or conversion from off-chart to on-chart BCVA) from nadir. For the natural history and idebenone groups, a systematic review of all available individual and aggregate data was performed, resulting in the inclusion of 173 untreated patients (from 5 studies) and 201 idebenone-treated patients (from 6 studies). For the lenadogene nolparvovec group, 174 patients were included from all phase 3 studies: RESCUE, REVERSE, RESTORE and REFLECT. An inverse-variance-weighted method was used to estimate an overall effect and its 95% confidence interval (CI).

Results:
For each meta-analysis, patients were mostly (≥80%) men, aged around 30 years at the time of vision loss. With the random-effects model, the CRR from nadir [95% CI] at eye level was estimated at 19% [9%; 32%], 30% [20%; 41%] and 58% [52%; 63%] in untreated, idebenone-treated and lenadogene nolparvovec-treated patients, respectively. This gradient of recovery was also observed with CRR at the patient level (response in one or both eyes). There was no overlap in CRR 95% CIs when comparing lenadogene nolparvovec versus natural history and idebenone.

Conclusions:
There was a gradient of efficacy of visual recovery with lenadogene nolparvovec intravitreal gene therapy superior to idebenone treatment, and both superior to the natural history of the disease.

References: None provided.

Keywords: Optic neuropathy, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Retina

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Contact Information: None provided.

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Trends and Risk Factors of Tuberculosis Incidence and Optic Neuropathy in a Nationwide Population-based Cohort Study

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Introduction:
This study aimed to investigate the incidence of tuberculosis over time and the incidence and risk factors of optic neuropathy caused by tuberculosis and ethambutol administration using nationwide population-based cohort analysis.

Methods:
The study anaylzed patients diagnosed with tuberculosis from 2002 to 2013 using the Korea National Health Insurance Corporation database. A control group was included that had not been diagnosed with tuberculosis during the same period. Propensity score matching was used to analyze the occurrence of optic neuropathy. The odds ratios associated with optic neuropathy were analyzed, including age, sex, underlying diseases, region of residence, economic level, and ethambutol use.

Results:
The study included 31,175 patients with tuberculosis and 84,522 non-tuberculous patients. The incidence of tuberculosis showed a decreasing trend, while the number of ethambutol prescriptions remained relatively constant. The incidence of optic neuropathy showed a tendency to increase after 2009, although the number of patients remained constant from 2002 to 2009. The ethambutol treatment group had a significantly higher incidence of optic neuropathy, and the risk ratio for optic neuropathy increased significantly with age and daily dose of ethambutol.

Conclusions:
The incidence of tuberculosis in Korea decreased over time, but the incidence of optic neuropathy tended to increase. The risk of optic neuropathy was associated with the occurrence of TB, age, and daily dose of ethambutol. These findings highlight the importance of monitoring patients for optic neuropathy, particularly as they age or receive higher doses of ethambutol.

References: None provided.

Keywords: Neuro-ophth & infectious disease (eg, AIDS, prion), Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Optic neuropathy

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A Comparative Study of LLMs, Human Experts, and Expert-Edited LLMs to Neuro-Ophthalmology Questions

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Introduction:
While large language models (LLMs) are increasingly used in medicine, their effectiveness compared to human experts remains unclear. This study evaluates the quality and empathy of Expert+AI, human experts, and LLM responses in neuro-ophthalmology.

Methods:
This randomized, masked, multicenter cross-sectional study was conducted from June to July 2023. We randomly assigned 21 neuro-ophthalmology questions to 13 experts. Each expert provided an answer and then edited a ChatGPT-4-generated response, timing both tasks. Additionally, five LLMs (ChatGPT-3.5, ChatGPT-4, Claude 2, Bing, Bard) generated responses. Anonymized and randomized responses from Expert+AI, human experts, and LLMs were evaluated by the remaining 12 experts. The main outcome was the mean score for quality and empathy, rated on a 1-5 scale.

Results:
Significant differences existed between response types for both quality and empathy ($p< 0.0001$, $p< 0.0001$). For quality, Expert+AI (4.16 +/- 0.81) performed the best followed by GPT-4 (4.04 +/- 0.92), GPT-3.5 (3.99 +/- 0.87), Claude (3.6 +/- 1.09), Expert (3.56 +/- 1.01), Bard (3.5 +/- 1.15), and Bing (3.04 +/- 1.12). For empathy, Expert+AI (3.63 +/- 0.87) had the highest score followed by GPT-4 (3.6 +/- 0.88), Bard (3.54 +/- 0.89), GPT-3.5 (3.5 +/- 0.83), Bing (3.27 +/- 1.03), Expert (3.26 +/- 1.08), and Claude (3.11 +/- 0.78). For quality ($p< 0.0001$) and empathy ($p=0.002$), Expert+AI performed better than Expert. Time taken for expert-created and expert-edited LLM responses was similar ($p=0.75$).

Conclusions:
Expert-edited LLM responses had the highest expert-determined ratings of quality and empathy warranting further exploration of their potential benefits in clinical settings.

References: None provided.

Keywords: Miscellaneous

Financial Disclosures: Prashant Tailor; Lauren Dalvin; Matthew Starr; Deena Tajfirouz; Kevin Chodnicki; Michael Brodsky; Sasha Mansukhani; Heather Moss: K23 EY 024345 NIH P30 026877 Unrestricted Grant from Research to Prevent Blindness to Stanford Department of Ophthalmology; Kevin Lai; Melissa Ko; Devin Mackay; Marie DiNome; Oana Dumitrascu; Misha Pless; Eric Eggenberger; John Chen

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Analysis of diplopia referrals in a tertiary neuro-ophthalmology center

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Introduction:
To describe referral pattern, morbidity and mortality associated with neuro-ophthalmology consultations for patients referred for the evaluation of diplopia.

Methods:
A retrospective chart review of patients seen by two neuro-ophthalmologists in a tertiary neuro-ophthalmology practice between December 2, 2021 and May 21, 2022 was performed. All patients who were referred for diplopia were included. Our primary outcome was to describe the potential for vision loss, progression of symptoms or systemic morbidity or mortality without a neuro-ophthalmic consult.

Results:
Overall, 196 patients were referred for diplopia. The mean age at presentation was 61.3 ± 17.0 years and 48.5% were women. The most common final diagnosis reached following neuro-ophthalmology consultation were cranial nerve palsies (38.3%), convergence insufficiency and decompensated phoria (22.4%), non-neuro-ophthalmic causes (19.9%), thyroid eye disease (4.5%), myasthenia gravis (3.5%), and multiple sclerosis (3.1%). Overall, 15.3% of patients referred to neuro-ophthalmology for diplopia had potential of morbidity or mortality. Specifically, 1%(2/196) had potential of vision loss due severe papilledema in context of untreated IIH, and 3.0%(6/196) had potential for systemic morbidity or mortality due to brain aneurysms(1.0%), pituitary apoplexy(0.5%), anaplastic glioma(0.5%) and other malignancy(1.0%). In addition, 11.2% (22/196) had potential for progression of symptoms due to thyroid eye disease(4.6%), myasthenia gravis(3.5%), and multiple sclerosis(3.1%). Of the patients who had a pre-referral neuro-imaging study, 30.1% required additional neuroimaging after neuro-ophthalmic consultation.

Conclusions:
While it was previously found that 16% of patients presenting with diplopia in the ED have a life-threatening condition, little is known about the prevalence of systemic and ocular adverse effects specifically in patients with diplopia who receive neuro-ophthalmic consultations. In this study we identified that 15.3% of patients with diplopia had potential for morbidity without neuro-ophthalmology consult. This study emphasizes the importance of urgent neuro-ophthalmologic referral for patients with diplopia to allow for appropriate evaluation and to reduce morbidity and mortality.

References: None provided.

Keywords: Ocular motility, Miscellaneous, Adult strabismus with a focus on diplopia

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Applying the 2022 Optic Neuritis Criteria: Does Optic Nerve T2-Hyperintensity Lead to Misdiagnosis?

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Introduction:
Recent updated diagnostic criteria for optic neuritis include MRI T2-hyperintensity of the optic nerve (ON), with or without associated contrast enhancement, as a paraclinical test.1 However, isolated MRI ON T2-hyperintensity is a nonspecific finding that can be found in any optic neuropathy/severe retinopathy.2 We applied the 2022 optic neuritis diagnostic criteria to patients with non-inflammatory optic neuropathy, acute/subacute vision loss and MRI ON T2-hyperintensity in at least one eye to assess the rate of optic neuritis misdiagnosis using these criteria.

Methods:
Retrospective study of consecutive patients who underwent brain/orbit MRI with/without contrast between 07/01/2019-06/30/2022. Patients with ON T2-hyperintensity in at least one eye were included. Medical record review provided the ON T2-hyperintensity underlying etiology. The 2022 optic neuritis diagnostic criteria were applied to non-inflammatory optic neuropathies with acute/subacute vision loss.

Results:
Of 160 patients included (mean age 55±18 years; 56 % men), 92/160 had compressive optic neuropathy (0/92 fulfilled the criteria); 33/160 had glaucomatous optic neuropathy (33/33 no subacute vision loss; 0/33 fulfilled the criteria); 13/160 had non-arteritic anterior ischemic optic neuropathy (NAION) (3/13 fulfilled the criteria as definite optic neuritis due to T2-hyperintensity/contrast enhancement of the ON head); 12/160 had papilledema-related optic neuropathy (0/12 fulfilled the criteria); 10/160 had hereditary (3), toxic-nutritional (3), radiation-induced (3), traumatic (1) optic neuropathies (1/10 no subacute vision loss; 0/10 fulfilled the criteria).

Conclusions:
The application of the 2022 optic neuritis diagnostic criteria in 160 consecutive patients with non-inflammatory optic neuropathy and ON T2-hyperintensity in at least one eye resulted in a misdiagnosis of optic neuritis in 3 patients, all with acute/subacute NAION. The use of these criteria by neurologists/neuroradiologists without neuro-ophthalmologic evaluation can lead to optic neuritis diagnosis in excess, of particular importance given the proposed inclusion of optic neuritis in the multiple sclerosis criteria.3 Optic neuritis should remain a clinical, not a radiological diagnosis.

References: 1. Petzold A, Fraser CL, Abegg M, Alroughani R, Alshowaeir D, et al. Diagnosis and classification of optic neuritis. Lancet Neurol, 21: 1120–1134, 2022. 2. Labella Álvarez F, Mosleh R, Bouthour W, Saindane AM, Dattilo M, et al. Optic nerve MRI T2-hyperintensity: A nonspecific marker of optic nerve damage. J Neuroophthalmol. (pending publication). 3. Filippi M, Rocca MA, Ciccarelli O, De Stefano N, Evangelou N, Kappos L, et al. MRI criteria for the diagnosis of multiple sclerosis: MAGNIMS consensus guidelines. Lancet Neurol.,15(3):292-303, 2016.

Keywords: Optic neuritis, Neuroimaging

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Contact Information: None provided.

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Assessing Neurology Resident Responsiveness to a Combined Didactic and Simulation-Based Funduscopic Examination Workshop

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Introduction:
The funduscopic examination is an accessible non-invasive diagnostic tool for identifying critical CNS disorders. However, non-ophthalmology trainees often defer this examination because of technical challenges in performing non-dilated ophthalmoscopic evaluations and/or lack of confidence in funduscopic examination skills. This study evaluates the impact of a dedicated funduscopic examination workshop in a series of neuro-ophthalmology workshops.

Methods:
This is a single-center, mixed methods, quantitative-qualitative (convergent parallel design) survey-based study evaluating neurology resident responsiveness to a combined didactic and simulation-based neuro-ophthalmology/funduscopic examination workshop, developed using feedback from a pilot workshop established one year prior. A survey composed of Likert scales (1=strongly agree, 5=strongly disagree) and open-ended questions was administered pre- and post-workshop.

Results:
Nine adult neurology residents (median training-year 3 [range 2-4]) participated in a 1-hour funduscopy workshop and a 1-hour basic neuro-ophthalmology examination workshop the day prior. Using pre-workshop surveys, residents reported an inadequate amount of formal funduscopic training during medical school and residency (median score 4 [range 3-5] and 4 [range 2-4] respectively). They were least confident in identifying retinal vessel abnormalities and disc edema (median score 4 [range 3-5] and 4 [range 2-4] respectively). Post-workshop surveys revealed a significant increase ($p< 0.05$) in confidence in identifying disc edema, retinal vessel abnormalities, and in overall funduscopic examination skills. Residents most appreciated simulation-based learning by practicing a non-dilated examination on fellow residents and on pathology-displaying Kyoto Kagaku Eye Examination Simulators. Residents requested increased workshop frequency, up to twice per quarter.

Conclusions:
A combined didactic and simulation-based funduscopic examination workshop is beneficial in improving resident funduscopic examination confidence, particularly in an iterative educational environment modified yearly based on trainee feedback. The findings can improve neuro-ophthalmology examination skills and highlight learners' desires for simulation-based learning in the medical trainee curriculum. Their utility can continue to be assessed using this study design.

References: None provided.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Challenges Faced In The Diagnosis And Management Of Atypical Optic Neuritis - The Indian Scenario

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Introduction:
Neuromyelitis optica spectrum disorder (NMOSD) and myelin oligodendrocyte glycoprotein antibody disease (MOGAD) has taken the spotlight in optic neuritis in neuro-ophthalmology over the past decade. Studies in India show increased atypical optic neuritis cases, yet data scarcity persists. We aim to determine the etiology, clinico-radiologic profiles, outcomes of atypical optic neuritis in South Indian population and to identify challenges of management in the face of limited serological testing and financial constraints.

Methods:
Retrospective data from July 2022 to July 2023 was analyzed at a tertiary eyecare hospital. Out of 9666 new outpatients to the neuro-ophthalmology clinic, 143 optic neuritis cases (1.5%) were identified. 9 patients with co-existing ocular morbidities or no follow up were excluded. Clinical presentation, demographics, seropositivity for NMOSD and MOGAD, radiological findings and treatment outcomes were studied.

Results:
Though serological testing was advised for all 134 patients, only 91 (68%) tested. Of 91, 34.1% were positive for MOGAD, 6.6% for NMOSD, 1.1% double seropositive, 5.5% demyelination and 48.4% were double seronegative. 59.34% were female. Majority of MOGAD were between 20 to 40 years. Inflammation, tuberculosis, autoimmune, etc. were the other causes. 18 patients had recurrent attacks, of which 8 were MOGAD seropositive, 2 NMOSD seropositive and 3 double seronegative. Neuroimaging was done in all. Majority in MOGAD (14) group had intraocular with intracanalicular involvement and 9 upto pre-chiasmal involvement. Bilaterality was seen in 12 MOGAD and 1 NMOSD. Visual recovery was seen in majority cases after intravenous methyl-prednisolone and 38 patients were started on immunosuppressants by the neurologist.

Conclusions:
In India, despite low rates of serological testing due to financial constraints, the prevalence of MOGAD optic neuritis amongst those tested is high. In this resource poor setting without serological confirmation, clinicians rely heavily on clinical phenotype to guide their management of this condition to prevent recurrence and disease progression.

References: None provided.

Keywords: Optic neuritis

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Characteristics of Hospital-Based Papilledema Screening Consults at a Tertiary Care Center

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Introduction:
Ophthalmology is frequently consulted to evaluate for papilledema in the emergency room and inpatient setting. However, little is known about which patient factors may correlate with the presence of papilledema and these consults strain limited healthcare resources. The purpose of this study is to review the incidence of newly diagnosed papilledema for these consults and identify patient characteristics associated with positive clinical findings.

Methods:
This is a retrospective review of 637 hospital-based papilledema consults at a large tertiary referral center. Patients referred to the hospital with pre-existing papilledema were excluded. Data collection included age, sex, relevant medications, symptoms, obesity, recent weight gain, visual acuity, presence of shunt, presence of optic atrophy, and radiographic signs of intracranial hypertension. To compare patients with versus without papilledema, contingency tables were used for categorical variables and to calculate sensitivity and specificity. A t-test was used for age.

Results:
517 consults were analyzed and papilledema was identified in 11.2% (n = 58). The proportion of patients with visual symptoms (60.3% with vs 39.2% without; $p = 0.00785$), obesity or recent weight gain (44.8% with vs 22.9% without; $p < 0.001$), and radiographic findings suggestive of elevated intracranial pressure (53.4% with vs 16.8% without; $p < 0.001$) was significantly higher for patients with papilledema. Shunted patients were less likely to have papilledema compared to non-shunted patients (31% vs 69%; $p = 0.035$). Patients with papilledema were more likely to be on relevant medications than those without (13.8% on relevant medications vs 1.3% not; $p < 0.001$). Age, sex, and headache were not significantly associated with papilledema.

Conclusions:
This study is the first to identify patient characteristics associated with a positive papilledema evaluation in the hospital setting. This may be useful in increasing the diagnostic yield of papilledema consults and improving utilization of consultant resources.

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Keywords: Miscellaneous, High intracranial pressure/headache, Pseudotumor cerebri

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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Characterizing Eye Pain: An Exploration of Epidemiology, and Healthcare Utilization Patterns

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Introduction:
Eye pain is a challenging condition to diagnose and treat due to a complex interplay of ocular and non-ocular factors contributing to its pathogenesis. The purpose of this study was to characterize patients with eye pain seen in a tertiary care neuro-ophthalmology practice.

Methods:
The research medical repository at our tertiary care institution was used to identify 845 patients, aged 18 and above, with an ICD10 code (H57.1) for eye pain coinciding with an eye institute encounter after January 1, 2021. 232 that also had a neuro-ophthalmology encounter were classified according to the etiology of eye pain (non-ocular, ocular, mixed, or unknown). Their demographics, social history, and details regarding other specialists seen for eye pain were extracted from the EHR.

Results:
Out of 218 patients with known causes of eye pain [mean age 52.93 17 years, 75% female, 42.6% white, 75.2% non-Hispanic] 92 (42.2%) had exclusively ocular causes [59 (64.1%) dry eye], 57 (26.1%) had exclusively non-ocular causes [35 (61.4%) primary headache syndrome, 16 (28.1%) neuropathic pain], and 69 (31.7%) had a mix of ocular and non-ocular causes. Patients with non-ocular or mixed causes were younger (mean age 48.9 vs 58.3, $p< 0.0005$), more likely to be female (76.2% vs. 70.6%, $p= 0.36$) and more likely to also see non-neuro-ophthalmologists for their symptom (77.7% vs. 70.6%, $p=0.23$). There were no differences in race, ethnicity, or smoking status.

Conclusions:
Patients with eye pain seen by a neuro-ophthalmologist were more likely to have a non-ocular cause of pain than exclusively ocular causes and this was associated with seeing more providers. With this study, we obtained a better understanding of the journey of a patient with eye pain which has the potential to improve future diagnosis and treatment outcomes.

References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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Correlation Between Visual Acuity And Automated Visual Field Foveal Threshold Value

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Introduction:
According to prior research there is a positive correlation between foveal threshold value and visual acuity in automated visual field testing (Humphrey). The purpose of our research is to determine if the foveal threshold value obtained during an automated (Octopus) visual field test has a positive correlation with patient visual acuity. Our research specifically focuses on patients with non-glaucomatous optic nerve neuropathy and compares results of patients with healthy eyes. Our hypothesis is that similar to prior studies there will be a positive correlation between visual acuity and foveal threshold value.

Methods:
A retrospective chart review was performed on adult patients diagnosed with optic neuropathy or healthy optic nerves. All patients have undergone an automated visual field test and each patient's foveal threshold value was obtained. All patients' best corrected visual acuity was determined either in their current refractive glasses or with pinhole visual acuity.

Results:
A total of 294 eyes were evaluated and of those 91 were healthy eyes without any optic neuropathy and 203 eyes were diagnosed with a non-glaucomatous optic neuropathy. Analysis of all patients together visual acuity and foveal threshold value correlation coefficient = 0.639, p-value= 4.9x10-35. Healthy eyes only correlation coefficient =0.713, p-value=1.24x10-08. Eyes with non-glaucomatous optic neuropathy correlation coefficient=0.606, p-value=3.4x10-11.

Conclusions:
In conclusion the results of our analysis support our hypothesis that patient visual acuity has a positive correlation with foveal threshold in visual field tests. Although there is a decrease in the amount of positive correlation between eyes with optic neuropathy compared to healthy eyes.

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Keywords: Optic neuropathy, Visual fields

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Development Of An Optometry Rotation For Neurology Residents To Enhance Learning Of Direct Ophthalmoscopy

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Introduction:
Direct ophthalmoscopy (DO) is a critical component in the evaluation of many neurologic conditions. Proficiency in DO has declined for non-ophthalmologists in the last several decades, and numerous educational strategies have been explored in the context of undergraduate medical education. However, there are limited studies on DO training during neurology residency. We propose an innovative, optometry rotation for neurology residents that incorporates deliberate practice and self-regulated learning to enhance DO competency.

Methods:
Nine neurology residents enrolled in a longitudinal, optometry elective. Voluntary subjective pre- and post-questionnaires measuring self-efficacy, volume of practice, and satisfaction were collected. A previously validated instrument was used to objectively assess residents' competency in performing DO. These measures were compared to a control group of 17 neurology residents who did not participate in the optometry elective. Variables were analyzed using an ANOVA test or Wilcoxon signed-rank test.

Results:
The nine residents who participated in the optometry elective demonstrated a significant increase in objective scores for DO performance, from a mean of 13.1 (out of 23 items) pre-rotation to 18.3 post-rotation ($p = 0.0142$). Post-rotation scores trended higher than the control group of residents who did not participate in the optometry rotation (mean 14.2, $p = 0.0617$). Compared to pre-rotation, post-rotation resident confidence trended higher in focusing on the retina (67% vs. 11%, $p=0.0320$), finding the optic disc (83% vs 11%, $p=0.0568$), and finding retinal blood vessels (33% vs 11%, $p=0.0545$). All residents in the control group expressed interest in participating in the optometry rotation.

Conclusions:
Incorporation of an optometry rotation to neurology residency represents an innovative, inter-professional collaboration that provides residents with a unique avenue for learning DO. This curricular model has the potential for expansion to neurology residencies with low sub-specialty exposure in neuro-ophthalmology.

References: Haque R, Abouammoh MA, Sharma S; Validation of the Queen's University Ophthalmoscopy Objective Structured Clinical Examination Checklist to predict direct ophthalmoscopy proficiency. Can J Ophthalmol, 47(6), 484-488, 2012.

Keywords: Retina, Optic neuritis, Visual fields, High intracranial pressure/headache, Miscellaneous

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Grant Support: None.

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Diagnosis of acute retinal artery occlusion in the Emergency Department (ED): Time for change!

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Introduction:
Acute central and branch retinal artery occlusions (CRAO/BRAO) are similar to cerebral ischemic strokes and are associated with risk of recurrent vascular events best prevented by immediate specialized Stroke Center care.1 Visual outcome is poor and acute treatment options are limited by often-delayed diagnosis.2 In the hyper-acute setting (< 4.5hrs), the fundus may appear “normal”, making the diagnosis challenging. Macular OCT demonstrates early inner retinal hyper-reflectivity, aiding the diagnosis of acute CRAO.3 However, OCT is seldom available in the ED, and ophthalmology is rarely on-site to immediately confirm the diagnosis. We evaluated the use of a nonmydriatic ocular fundus camera (NMFP) combined with OCT to facilitate ultra-rapid remote diagnosis and stroke alert for patients with acute visual loss presenting to the ED.

Methods:
Prospective evaluation of all CRAO/BRAO in our ED with a NMFP-OCT [06/06/2023-10/01/2023]. We collected timing of symptom onset, presentation, diagnosis, photographs/interpretation, and NMFP-OCT findings.

Results:
Over 17 weeks, 11 patients were diagnosed with CRAO and 3 with BRAO. Two presented within 4.5hrs, 4 within 4.5-12hrs, 8 >12 hrs. NMFP-OCT occurred within 2hrs-34mins of presentation (30mins-7hrs22mins); remote interpretation occurred within 39 mins of acquisition (0mins-2hrs-33mins); remote diagnosis within 4.5hrs in 2 (2hrs-30mins and 3hrs-55 mins), one receiving intravenous thrombolysis. Of 6 patients with NMFP-OCT within 12hrs, 4 had subtle retinal whitening, but all had OCT inner retinal hyper-reflectivity/edema.

Conclusions:
Implementation of NMFP-OCT in the ED enables remote diagnosis of CRAO/BRAO and facilitates initiation of an Eye Stroke protocol in acute patients.4 OCT complements fundus photography and provides greater diagnostic accuracy in hyperacute cases which may have a near-normal appearing fundus. These positive preliminary results suggest that implementation of NMFP-OCT in the ED changes the approach to acute CRAO and accelerates the diagnosis of acute vision loss, potentially improving patient outcomes. Results of an additional 6 months will be presented at NANOS.

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Keywords: Stroke, Retina, Vascular disorders, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease

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Does AI Democratize or Dilute Knowledge? Comparative Analysis of the Readability of Online Patient Resources and GPT-4-Generated Content for Common Neuro-Ophthalmology Topics

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Introduction:
Patient resource accessibility is crucial within neuro-ophthalmology. Many patients access the American Academy of Ophthalmology (AAO)'s EyeSmart platform for information regarding ophthalmic topics. More recently, generative language models, such as OpenAI's GPT-4 (1), are increasingly being used as patient education tools. We aim to analyze whether AAO resources for neuro-ophthalmology are written at an understandable level, and compare their readability to GPT-4-generated equivalents.

Methods:
28 questions and answers pertinent to neuro-ophthalmology were retrieved from the AAO's EyeSmart platform. These questions were inputted into GPT-4, which was prompted to produce answers that are "patient-focused" and "for the public'' (as EyeSmart is advertised). The readability of AAO- and GPT-4-generated responses were evaluated using WebFx's Readability Tool. Metrics included: Flesch Kincaid Reading Ease (FK-RE), Flesch Kincaid Grade Level (FK-GL), Gunning Fog Score (GFS), SMOG Index (SI), Coleman Liau Index (CLI), and the Automatic Readability Index (ARI). The FK-RE is scored 0-100 based on readability ease; others equate to the grade-level needed for comprehension. Descriptive statistics were performed; comparison was completed using Wilcoxon Rank Sum Tests (WRST; α=0.05).

Results:
Across all six metrics, AAO resources had lower readability (FK-RE: 64.58 [15.08], FK-GL: 8.64 [5.08], GFS: 10.85 [5.43], SI: 7.55 [2.54], CLI: 11.40 [1.35], ARI: 9.15 [6.60]) compared to those written by GPT-4 (FK-RE: 75.38 [5.48], FK-GL: 6.89 [0.95], GFS: 8.88 [1.17], SI: 5.98 [1.05], CLI: 9.99 [1.18], ARI: 7.56 [1.27]). WRST showed statistical significance ($p< 0.02$) for all differences except ARI. On average, AAO resources were written at a tenth-grade level and GPT-4 resources at an eighth-grade level.

Conclusions:
The NIH recommends that health resources be written at no higher than a sixth-grade level (2). Both AAO- and GPT-4-generated resources exceed this recommendation, while GPT-4 significantly surpasses the AAO in readability. Maintaining resource accessibility ensures that the public and patients remain well-informed regarding common neuro-ophthalmic topics.

References: 1. GPT-4. Accessed October 11, 2023. https://chat.openai.com 2. Rooney MK, Santiago G, Perni S, et al. Readability of Patient Education Materials From High-Impact Medical Journals: A 20-Year Analysis. J Patient Exp. 2021;8:2374373521998847. doi:10.1177/2374373521998847

Keywords: Miscellaneous, Adult strabismus with a focus on diplopia, Pseudotumor cerebri, Optic neuritis, Optic neuropathy

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Contact Information: None provided.

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Investigation into Degenerative Foraminal Stenosis as a Potential Etiology for Horner Syndrome

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Introduction:
Part of the oculo-sympathetic pathway passes through C7-T3 neural foramina. However, a possible association of Horner syndrome with neural foraminal narrowing has not been previously explored. We investigated whether presence and/or severity of foraminal stenosis between C7-T3 segments could account for Horner syndrome otherwise deemed to be idiopathic in nature.

Methods:
This retrospective, IRB-approved study included 28 patients with confirmed diagnosis of Horner syndrome, absence of any identifiable cause, and availability of neck CT/CT angiogram obtained within 6 months of the diagnosis. A neuroradiologist masked to the laterality of Horner syndrome reviewed CT scans, documenting presence/ severity of foraminal stenosis at C7-T1, T1-2, and T2-3 levels on a 4-point Likert scale (0:none, 1: mild, 2: moderate, 3: severe). Cumulative foraminal stenosis score was calculated for neural foramina ipsilateral and contralateral to the side of Horner syndrome. Group comparisons for ipsilateral and contralateral foraminal stenosis were done for each segmental level, worst foraminal stenosis, and for cumulative score using t-test for paired data. P value of < 0.05 was considered significant.

Results:
Foraminal stenosis was present ipsilateral to the side of Horner syndrome in 14.3% patients, and on contralateral side in 17.8%. No significant difference in the extent of ipsilateral and contralateral foraminal stenosis was present at C7-T1 ($p= 0.66$), T1-2 ($p=0.32$), or T2-3 ($p= 0.75$) levels. Mean (±S.D.) ipsilateral (0.33 ± 1.0) and contralateral (0.33 ± 1.1) Cumulative Foraminal Stenosis scores were not significantly different ($p=1$). Mean (± S.D.) Maximum Foraminal Stenosis scores ipsilateral (0.22 ± 0.59) and contralateral (0.30 ± 0.81) to the side of Horner syndrome were also comparable ($p=0.54$).

Conclusions:
With low prevalence of foraminal stenosis at C7-T3 segments and with equivalent prevalence and severity of foraminal stenosis ipsilateral and contralateral to the side of Horner syndrome, foraminal stenosis is unlikely to be a common causative mechanism for Horner syndrome.

References: None provided.

Keywords: Neuroimaging, Pupil

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Grant Support: None.

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Is It Real Red?

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Introduction:
When Ganglion Cell-Inner Plexiform Layer (GCIPL) or Retinal Nerve Fiber Layer (RNFL) thickness is below the 1st percentile in Optical Coherence Tomography (OCT), it is indicated in red (red zone). After an episode of optic neuropathy, we observe cases with a red zone on OCT examination. It is commonly believed that the visual function of patients in the red zone may be poor, but in reality, not all of them have poor visual function. Therefore, we investigated the relationship between the GCIPL and RNFL thickness and visual function in patients with red zone in OCT.

Methods:
We examined the clinical characteristics and OCT values of patients with GCIPL or RNFL thickness below the 1st percentile from January 2016 to March 2023 among those under observation for optic neuropathy. Patients with unclear causes of optic neuropathy or thickness changes greater than 2% during the observation period or recurrence were excluded.

Results:
A total of 159 patients with optic neuropathy were included. Patients with optic neuritis (idiopathic, MOGAD, NMOSD), ischemic optic neuropathy, traumatic optic neuropathy, compressive optic neuropathy, toxic optic neuropathy, and Leber's optic neuropathy (LHON) were included. The overall distribution of BCVA in all patients varied from light perception to 25/20. In patients with optic neuropathy, the mean GCIPL and RNFL thickness showed a statistically significant ($p< 0.001$ for both) but subtle correlation with the BCVA. The distribution of BCVA showed significant differences ($p< 0.001$) among underlying etiologies. LHON showed significantly lower BCVA distribution compared to other diseases.

Conclusions:
Patients with GCIPL or RNFL thickness below the 1st percentile measured by OCT exhibited various visual acuity distributions, particularly with significant variations based on the underlying disease. When interpreting OCT results, it is important to consider the possibility of discrepancies with visual acuity and the association differences based on the underlying disease.

References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Optic neuropathy, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease

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Contact Information: None provided.

411
Neuro-Ophthalmic Practice Patterns Around the World

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Introduction:
Neuro-ophthalmic conditions affect many patient populations, yet neuro-ophthalmology is a relatively under-represented subspecialty. Many institutions do not have a neuro-ophthalmologist, limiting opportunities for training and patient care. We aimed to understand neuro-ophthalmology accessibility and practice patterns globally.

Methods:
We distributed a survey to NANOS members through the email listserv, with 18 questions focused on practice environments, type of training available, and limitations to care. 54 responses were submitted voluntarily and anonymously via Google Forms, between March 30th - April 11th, 2023.

Results:
38 neuro-ophthalmologists were from the USA. 2 each were from Canada, Argentina, and Hong Kong. Others were from Columbia, Ecuador, Egypt, France, Lebanon, New Zealand, Pakistan, South Korea, Switzerland, and Thailand. 38 were ophthalmology-trained, 12 neurology-trained, and 4 both. 79.6% worked in an urban environment, 11.1% in a suburban environment, and fewer in a town or mixed setting. 72.2% worked in an academic center, 18.5% in a private practice, and fewer at a private hospital or government-run clinic. 85.2% had trainees in their practice, 83.3% of whom received formal neuro-ophthalmology training. 100% had neuro-imaging within 5 miles, but imaging limitations were cost, insurance, and wait times. 20 physicians noted < 76% of patients followed up appropriately, due to physician distance, taking time off work, insurance, health literacy, and visit cost.

Conclusions:
The most challenging aspects of treating neuro-ophthalmic patients are patient compliance, lack of neuro-ophthalmologists, and insurance. Neuro-ophthalmologists are concentrated in academic centers and urban areas. While there are trainees in these environments, not all receive formal neuro-ophthalmology training. Thus, more trainees need formal training, with possible incentives to work in underserved areas. Additionally, insurance issues, which affect obtaining neuro-imaging and following up as advised, should be addressed by the neuro-ophthalmic community. Efforts should also be made to better patient education, ultimately improving followup and overall care.

References: None provided.

Keywords: Miscellaneous, Neuroimaging

Financial Disclosures: The authors had no disclosures.

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Neuro-Ophthalmology and the EMR: A Quality Improvement Project

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Introduction:

Patients with neurological disease impacting their vision, whether it be acute or chronic, have unique challenges when faced with an unfamiliar environment. During admission for diagnosis and treatment, patients with neuro-ophthalmologic diseases are at higher risk for adverse outcomes during their hospital stay. We created an EMR order set and advocated for implementation of the order sets to increase the comfort and safety of patients admitted with neuro-ophthalmic pathologies.

Methods:

The EMR team of the hospital system was notified of our proposal. An outline was written that contained details to allow creation of an order set addressing issues such as identifying new patients with visual impairment, fall prevention, and food intake. Providers from a variety of specialties and roles met to discuss the proposal. This led to the creation and implementation of an order set by our EMR team. Once the set is ordered, the patient's chart will be flagged with a banner notifying providers of visual impairment. In addition, the order set ensures proper communications to care staff to better assist the patient in navigating their unfamiliar environment.

Results:

Once the order set goes live, all specialties will have access. Surveys will be sent to providers to assess whether the order set improved patient care for patients with visual impairment. There will be a focus on patients admitted to Neurology service with acute to subacute visual impairment due to neurological disorders.

Conclusions:

Through the EMR, providers can improve the hospital experience for patients by identifying care gaps. Order sets specifically addressing visual impairment in patients with neuro-ophthalmic disorders are lacking.

References: None provided.

Keywords: Miscellaneous, Optic neuritis, Stroke, Visual fields, Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Optic Coherence Tomography and Electrophysiological Biomarkers of Optic Neuropathies

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Introduction:
Optic neuropathies have a diverse etiopathogenesis. Their initial clinical presentation is often non-specific, and in addition to essential differentiating methods, optical coherence tomography (OCT) and electrophysiological diagnostics (EP) are used in their differentiation, but also in monitoring.

Methods:
OCT and EP biomarkers of optic neuropathies are presented in 39 patients: 9 within multiple sclerosis (MS), 12 isolated clinical syndrome (ICS), 8 atypical: 2 Devic disease, 2 MOG antibodies positive and 4 within undifferentiated demyelinating disease; 2 had Leber hereditary optic neuropathy (LHON), 2 compressive and 6 non-arteritic anterior ischemic optic neuropathies (NAAION). Changes in retinal ganglion cells were analyzed by OCT (ganglion cell complex -GCC) and pattern reversal and photopic negative responses electroretinography (PERG and PhNRERG), and changes in the retinal nerve fiber layer (RNFL), by OCT images of optic nerve head (ONH), and afferent pathway function by visual evoked potentials (VEP). Their further course was followed by repeated testing.

Results:
The dominant group or individual features are shown. MS and Devic's disease damage retinal ganglion cells to a significant extent, as well as CIS can. In MS, already existing damage can be seen even before clinical manifestations of neuropathy. Atrophic changes develop the fastest in NAAION. In compressive ones, the primary damage depends on the localization of the compression. LHON early shows functional and morphological damage of ganglion cells. The characteristics of OCT biomarkers vary in the acute phase of optic neuritis, depending on the anatomical localization (papillitis, retrobulbar neuritis), but also in LHON. Ganglion cell function and nerve conduction are altered during disease, and may partially recover in some neuropathies.

Conclusions:
EP and OCT examinations are an integral part of optic neuropathies diagnostics. Mentioned biomarkers can be indicative of the possible nature and prognosis of the disease and in therapeutic response monitoring.

References: None provided.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Demeylinating disease, Genetic disease, Miscellaneous

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Contact Information: None provided.

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Optimizing Ophthalmology Patient Education via ChatBot-Generated Materials: Readability Analysis of AI-generated Patient Education Materials and the North American Neuro-Ophthalmology Society Patient Brochures

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Introduction:
The aim of this study is to compare the readability of patient education materials (PEM) of the North American Neuro-Ophthalmology Society (NANOS) to that of PEMs generated by the large language model AI-chat bots ChatGPT and Google Bard.

Methods:
PEMs on 13 common neuro-ophthalmology topics were generated by ChatGPT 3.5 and Google Bard, with and without a 6th grade reading level prompt. The PEMs were analyzed using seven readability metrics: Flesch Reading Ease score, Gunning Fog Index, Flesch-Kincaid Grade Level, Coleman–Liau index, SMOG Index Score, Automated Readability Index, and Linsear Write Readability Score. Each AI-generated PEM was compared with the equivalent NANOS PEM.

Results:
When comparing ChatGPT generated PEMs to NANOS brochures, ChatGPT PEMs consistently had lower readability scores and higher grade level scores, indicating that this material may be the most difficult to comprehend in its unprompted form (Flesch-Reading Ease Score 43.8 vs 49.5; SMOG index 10.4 vs 9.7). On the other hand, Bard generated PEMS were easier to read (at a lower grade level) than NANOS brochures (Linsear-Write Formula 10.6 vs 12.1). Moreover, when prompted to produce PEMs at a 6th grade reading level, both ChatGPT and Bard were able to improve readability scores that were significantly easier to read (Flesch-Reading Ease Score: 69.2, 66.1 respectively).

Conclusions:
This study offers compelling evidence that, when prompted by appropriate prompts, AI chat bots can generate comprehensible PEMs for patients on a variety of NANOS topics. Use of this technology in a clinical setting may offers patients with succinct and readable information on complex topics and can guide patient-oriented decision making. Furthermore, use of AI chat bots in this manner may be clinically beneficial in satellite centers where there is a scarcity of neuro-ophthalmologists by assisting triage of patients for neuro-ophthalmology referrals.

References: None provided.

Keywords: Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Papilledema a "Misnomer" for Optic disc edema: A Single Center Analysis

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Introduction:
Papilledema is the term used to describe optic disc swelling secondary to elevated intracranial pressure (ICP), but many providers use papilledema interchangeably with disc swelling for alternate etiologies that are not associated with elevated ICP. The aim of this study is to assess the knowledge gap across various specialties and evaluate if there is delay in diagnosis due to incorrect labelling.

Methods:
A retrospective chart review of 368 (287 female, 81 male) eligible patient charts over 18 years of age that had a diagnosis of "unspecified papilledema" (ICD-10 H47. 10) using EPIC Slicer Dicer between June 2021 and September 2023 was performed at University of Kentucky. Computerized tomography, magnetic resonance imaging, and lumbar puncture were used to confirm raised ICP.

Results:
Out of 368 patients 42 patients never had any confirmatory tests for elevated ICP for various reasons and were excluded. 151 (46.3%) out of remaining 326 patients labelled as papilledema did not have elevated ICP. We also analyzed data on inaccurate labelling of optic neuropathy as papilledema during the first encounter by various specialties which is as follows: Emergency physicians 27 (17.88%); neurology 22 (15.89%); ophthalmology 21 (13.91%) and other referring providers including primary care 81 (53.65%). In few cases, it took approximately 307 days to reach a final diagnosis from symptom onset.

Conclusions:
Our results suggest that inaccurate labelling of optic dis edema as papilledema prevails among various specialties including ophthalmology. We believe there is potential knowledge gap that must be addressed to prevent unnecessary testing, associated system wide costs and erroneous diagnosis that leads to distress among patients.

References: 1. Minckler D, Lin K. Papilledema: An Inaccurate Term in Our Medical Vocabulary. Ophthalmology [Internet]. 2023; 130(2):137–8. Available from: https://doi.org/10.1016/j.ophtha.2022.12.009 2. Dhoot R, Margolin E. Papilledema. [Updated 2023 Aug 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK538295/

Keywords: Optic neuropathy, Pseudotumor cerebri, High intracranial pressure/headache, Miscellaneous, Demeylinating disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Recruiting Neurologists Into Neuro-Ophthalmology

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Introduction:
The recruitment of neurology residents is vital to the field of neuro-ophthalmology which includes a wide range of background and training experiences. This diversity of perspectives in the evaluation and treatment of complex disease remains a strength of our field. Prior studies have shown the motivations of ophthalmology residents who choose to purse training in neuro-ophthalmology and those who do not. We have constructed 2 separate surveys to gain understanding of trends around these decisions for neurology residents and neurology trained neuro-ophthalmologists.

Methods:
We compiled a list of 180 neurology residency program directors and coordinators through residency explorer and individual program website review. The first survey was sent to reach all neurology programs. The second survey was sent out via NANOS YONO listserv to contact recent neurology trained neuro-ophthalmology fellows.

Results:
34 neurology residents responded to the initial survey, with 97% planning to pursue fellowship. The most common fellowships were stroke (12%), neuromuscular (9%), headache (9%), and multiple sclerosis/neuro-immunology (9%). The majority of residents decided on their subspecialty in their PGY2 year, 42% never considered neuro-ophthalmology as a subspecialty. The main factors that influenced the decision not to pursue neuro-ophthalmology were stronger interest in another field (63%) and lack of exposure to neuro-ophthalmology (50%). Only 58% of neurology residents had a dedicated neuro-ophthalmology rotation. The didactics, clinical exposure and research opportunities were rated as on par or superior to other fields. 46 recently trained neuro-ophthalmology fellows responded to the second survey. Amongst other findings, most notably, 51% of neurology trained neuro-ophthalmologists had exposure during medical school and 32% chose to pursue neuro-ophthalmology in medical school.

Conclusions:
We are still currently in the data collection phase of this project, but preliminary data suggests that exposure to neuro-ophthalmology in medical school may be a driving force for neurology-trained neuro-ophthalmologists.

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Keywords: Miscellaneous

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Referrals to Neuro-ophthalmology for Monocular Diplopia

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Introduction:

Neuro-ophthalmic conditions are complex, and may be urgently vision- and life-threatening, or involve diagnostic dilemmas. Evaluation of these conditions requires a time-intensive diagnostic process and navigating complex work-ups.1-4 However, there is a small number of neuro-ophthalmology providers, which can delay patient access to neuro-ophthalmology consultation and result in patient harm.5-6 Prior studies have focused on how to expand patient access to neuro-ophthalmology, either by telemedicine or interprofessional consultation.7-8 However, the potential impact of neuro-ophthalmology consultation is additionally limited by the quality and appropriateness of referrals.3-5,9-12 Referral to neuro-ophthalmology for monocular diplopia is inappropriate, and may contribute to wait times for patients with neuro-ophthalmic issues.

Methods:

This is a retrospective chart review of consecutive patients referred to our tertiary, academic neuro-ophthalmology clinic for evaluation of diplopia between 9/1/2019 and 9/28/2023. This date range was chosen to correspond with the starting date of one of our attending providers. Data collected will include; demographics, duration of symptoms, time between appointment request and consultation, referring provider specialty, whether final diagnosis was monocular versus binocular diplopia, and in patients with monocular diplopia, reason for monocular diplopia, examination findings documented by referring provider, whether laboratories and neuroimaging were obtained before referral, and whether prism glasses were tried before referral.

Results:

Between 9/1/2019 and 9/28/2023, there were 1234 new patients visits for evaluation of diplopia in our single, tertiary academic neuro-ophthalmology clinic. This is the number of charts we intend to review and analyze. This project has been approved by our Institutional Review Board. We intend to resubmit a more developed abstract before the deadline for producing the syllabus.

Conclusions:

Patients are frequently referred to neuro-ophthalmology for monocular diplopia. Examining patterns of inappropriate referrals to neuro-ophthalmology may also provide an avenue for improving access to neuro-ophthalmology for patients with neuro-ophthalmic issues.

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Keywords: Miscellaneous

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Reliability of the Neuro-ophthalmic Aspects of a Telemedicine Exam in Concussion (Tele-BCPE)

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Introduction:
It is unknown whether concussion patients can be examined reliably using telemedicine; such assessments are especially important for neuro-ophthalmic findings given high symptomatic burden. The Tele-BCPE is a standardized telemedicine concussion exam that includes 7 neuro-ophthalmic elements (optic nerve, ocular motility, smooth pursuits, repetitive saccades, vestibulo-ocular reflex, and two tests of near point of convergence). We determined inter-modality (in-person vs. telemedicine examination) and inter-examiner (two telemedicine examiners) agreement for capturing neuro-ophthalmic manifestations of concussion using the Telemedicine Buffalo Concussion Physical Examination (Tele-BCPE), a 29-item validated instrument for remote evaluation of the neurological manifestations of concussion.

Methods:
Twenty-one patients evaluated within two weeks of suspected concussion participated. Their treating neurologist examined them in-person and via telemedicine. Another neurologist performed a second telemedicine examination. Cohen's kappa measured agreement between elements, scored as present vs. absent, of the two tele-examinations and between the in-person and tele-examinations (inter-modality agreement). Intraclass correlation coefficients were used to determine agreement between total scores of the Tele-BCPE for in-person vs. telemedicine exams and between the two telemedicine exams.

Results:
Among 21 patients enrolled in the study, there was at least moderate agreement (kappa > 0.41) for 3 of 7 neuro-ophthalmic elements between the in-person and telemedicine examinations by a single examiner and at least moderate agreement for 4 of 7 examination subcategories between two different telemedicine examiners. For total scores incorporating only neuro-ophthalmic examination elements, inter-modality agreement (in-person vs. telemedicine, intraclass correlation coefficient [ICC] = 0.78) was excellent (0.75). Inter-rater agreement (for two telemedicine raters, ICC = 0.49) was in the moderate range.

Conclusions:
Standardized neuro-ophthalmic assessments performed by the same examiner are highly reliable, even when performed across modalities of in-person vs. telemedicine. Agreement is at least moderate when two different telemedicine examiners assess the same patients when using standardized examinations such as the Tele-BCPE.

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Keywords: Trauma, Vestibular disorders, Ocular motility, Ocular manifestations of vestibular disorders, Nystagmus

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Segmented retinal analysis in pituitary adenoma with chiasmal compression: A prospective comparative study

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Introduction:
The aim of this study was to determine the alteration in ganglion cell complex and its relationship with retinal nerve fiber layer (RNFL) thickness as measured by spectral-domain optical coherence tomography (OCT) in pituitary adenoma cases and also its correlation with visual field (VF).

Methods:
This is a prospective comparative study wherein detailed neuro-ophthalmic examination including perimetry, RNFL and ganglion cell layer inner plexiform layer (GCL-IPL) thickness were measured preoperatively in the cases of pituitary adenoma with chiasmal compression with visual symptoms and field changes who were planned for neuro-surgical intervention. These parameters were repeated 1 year after the surgery. GCL-IPL, RNFL parameters were compared with controls and were correlated with VF mean deviation (MD). The diagnostic power of GCL-IPL was tested using the receiver operating characteristic (ROC) curve. Healthy age and sex-matched controls without any ocular and systemic abnormality were taken for comparison.

Results:
Twenty-four patients qualified the inclusion criteria. A significant thinning of GCL-IPL ($P = 0.002$) and RNFL ($P = 0.039$) was noticed in the pituitary adenoma group. GCL-IPL ($r = 0.780$ $P < 0.001$) and RNFL ($r = 0.669$, $P < 0.001$) were significantly correlated with the MD. The ROC curve values of GCL-IPL were 0.859 (95% confidence interval 0.744% to 0.973) and of RNFL were 0.731 (95% confidence interval 0.585–0.877). The diagnostic ability of GCL-IPL was more as compared to the RNFL analysis, although it was statistically insignificant ($P = 0.122$

Conclusions:
GCL-IPL measurements on the OCT are a sensitive tool to detect early anterior visual pathway changes in chiasmal compression for pituitary adenoma patients.

References: None provided.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Neuroimaging, Visual fields, Skull base, Miscellaneous

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The evolution of molecular genetic tests and their diagnostic yield for inherited optic neuropathies

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Introduction:
Accurate and timely diagnosis of patients with inherited optic neuropathies remains a clinical challenge for neuro-ophthalmologists. This retrospective study demonstrates the real-world experience and trends in molecular genetic testing over a 9-year period at a specialised clinical genetics service in a tertiary eye hospital.

Methods:
Medical records were reviewed for every patient seen in the neurogenetics clinic between September 2014 - July 2023. Data pertaining to patient demographics, initial diagnosis, reason for referral, pre-referral molecular testing, clinical phenotype, family history, post-referral molecular testing and final molecular diagnosis were collected and analyzed.

Results:
450 unique patients with suspected inherited optic neuropathy were seen. Although 251/450 (56%) came with prior molecular testing, only 153/450 (34%) had a confirmed molecular diagnosis at the time of referral. A final molecular diagnosis was reached in 291/450 (65%) patients. The molecular diagnoses were obtained predominantly using research-based single gene or LHON primary mutation testing in the first 6 years; and using evolving versions of clinical gene panels for optic atrophy in the last 3 years. In 32/450 cases (7%), pathogenic variants in novel candidate genes were found only through further interrogation of whole genome sequencing data; and in 141/450 cases (31%) a final molecular diagnosis was not reached despite extensive testing.

Conclusions:
The genetic tests available to make a confirmed molecular diagnosis in patients with a suspected inherited optic neuropathy have evolved over the years. Our clinic experience suggests that currently available clinical gene panels for optic atrophy have a high diagnostic yield for cases of primary LHON, OPA1 and WFS1-related optic atrophy. However, in cases with a strong genetic phenotype and negative standard testing, performing a robust interrogation of the whole exome or genome allows identification of novel pathogenic variants in genes outside the panel.

References: None provided.

Keywords: Genetic disease, Optic neuropathy

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The Role of Ophthalmology in the Pre-Diagnostic Workup of Suspected Giant Cell Arteritis

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Introduction:
Giant cell arteritis presents with a wide range of symptoms, making it a diagnostic challenge to the myriad of specialists that initially evaluate the patient. Studies have shown that having many subspecialties co-managing an illness can lead to inadequate information sharing and care fragmentation [1,2]. We characterized GCA suspects' healthcare journey and elucidated the role that ophthalmologists play in the pre-diagnostic workup of GCA.

Methods:
A retrospective chart review of patients who underwent temporal artery biopsy for suspected Giant Cell Arteritis (GCA suspects) at a single institution were included in this study and stratified by whether or not they saw an ophthalmologist before their diagnosis was confirmed. Demographics, symptoms, biopsy information, diagnosis, and number of physician specialties contributing to diagnostic evaluation of the patient were extracted from the EHR and compared between patients who saw an ophthalmologist during their GCA workup and those who did not.

Results:
GCA suspects (n=162, median age= 76, 64.8% female, 53% saw an ophthalmologist during pre-diagnostic workup, n= 43 with GCA), saw 1-6 medical subspecialities (mean= 3.3) during their work up. Patients who saw an ophthalmologist were more likely to have ocular symptoms ($p< 0.0005$, chi square) than those who didn't see an ophthalmologist, but were otherwise similar demographically. 24 (29%) patients seen by ophthalmology during work up were diagnosed with GCA, including 16 with positive biopsies, which was a similar proportion to those who did not see ophthalmology.

Conclusions:
Patients who undergo temporal artery biopsy for possible GCA have a complicated journey through the healthcare system. Ophthalmologists, as one of the many specialties that evaluate these patients and see over half of those suspected of GCA, play a crucial role in the diagnosis of GCA.

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Keywords: Vascular disorders

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Visual Outcomes in Patients Treated with Acetazolamide for Papilledema Secondary to Intracranial Mass Effect

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Introduction:
Acetazolamide is routinely used by ophthalmologists to lower intracranial pressure in patients with papilledema, but the literature only supports its use in patients with idiopathic intracranial hypertension. This study will analyze visual outcomes and RNFL thickness after optic disc edema resolution in patients treated with acetazolamide for papilledema caused by intracranial mass effect.

Methods:
This is a retrospective cohort study analyzing visual field mean deviation scores and OCT RNFL thickness values as a function of time between visual symptom onset and initiation of acetazolamide in patients treated for papilledema caused by intracranial mass effect.

Results:
At this time, 23 patients have met inclusion criteria, and the study is ongoing. Preliminary data shows R2 value of -0.5442 with p-value 0.007263 for the correlation between Humphrey visual field mean deviation scores after optic disc edema resolution averaged between both eyes (all negative values) and total number of days from symptom onset to acetazolamide initiation. R2 value for the correlation between final OCT RNFL thickness after optic disc edema resolution averaged between eyes and total number of days from symptom onset to acetazolamide initiation is -0.5687 with a p-value of 0.004631.

Conclusions:
This retrospective cohort study shows a direct correlation between longer delay from symptom onset to acetazolamide initiation and lower performance on visual field testing as well as lower RNFL thickness on OCT, both measured after disc edema resolution. This finding is independent of the effects of time to mass resection, time to drain placement, and time to steroid initiation. This supports the practice of timely initiation of acetazolamide in patients with papilledema secondary to intracranial mass effect. Physicians concerned for papilledema in the setting of an intracranial mass should recommend prompt ophthalmology evaluation and consideration of acetazolamide initiation.

References: None provided.

Keywords: High intracranial pressure/headache, Optic neuropathy, Tumors, Visual fields

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A novel technique for diplopia field test with distant real target and its efficacy

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Introduction:
In most real-life scenarios, visual targets are positioned at a distance. However, conventional diplopia field tests use only near targets. We introduce Head Rotation Diplopia field test (HRDT) for evaluating diplopia in response to distant real-world targets and present efficiency of HDRT compared to conventional Goldmann diplopia field test (GDT).

Methods:
The core concept of the HRDT involves patients rotating their heads while viewing a stationary distant target, with the head rotation recorded. This approach is the converse of the conventional diplopia field test. We enrolled fifteen subjects who have diplopia in a portion of their visual field. Diplopia field testing was conducted using the HRDT fixating on a toy located 6m away (distance HRDT) and the conventional GDT performed twice respectively. Diplopia field testing with HRDT performed fixating near light target that simulate the target of Goldmann perimeter (near HRDT). The primary outcome was the range of single binocular vision in the most constricted meridian (RSBV).

Results:
The RSBV measurement of GDT and near HRDT did not exhibit a statistically significant difference. (p=0.659; Wilcoxon signed rank test). However, a significant difference was observed between the RSBV measurements of the distant HRDT and near HRDT (p=0.011). The repeatability of the distant HRDT was greater than that of GDT (Test-retest correlation: 0.97 on distant HRDT, 0.91 on GDT).

Conclusions:
The results of diplopia field testing when viewing distant real-world targets differed from those obtained using the conventional GDT. We recommend distant HRDT for diplopia field test because it showed reliable performance and better reflects visual experience in the real world. Near HRDT is compatible with GDT for diplopia testing at near fixation.

References: None provided.

Keywords: Adult strabismus with a focus on diplopia, Ocular motility

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An Automated Machine-Learning Approach to Quantify the Relative Afferent Pupil Defect

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Introduction:
Automated pupillometry can provide a fast, objective measurement of afferent visual function, but can be confounded by blinking and relies on constriction amplitude, velocity and latency. This poses limits on identification of clinically significant abnormalities. Machine-learning (ML) analysis of pupillometry waveforms may provide superior performance and uncover hidden connections between pupillary dynamics and disease.

Methods:
We developed a 20-second pupil light reflex (PLR) test using a Neuroptics DP-2000 binocular pupillometer (Neuroptics, Irvine CA) with alternating white light flashes to each eye in escalating intensity. Using data from 230 patients with and without optic neuropathies, we ran several dimension reduction techniques to distill the pupillometry waveform into a small number of variables that represent distinguishing features of the waveform. Machine Learning (ML) classifiers were then applied to determine whether this method could identify patients with right or left optic neuropathies. A separate test set of 65 patients (20 with no afferent problem and 45 with optic nerve or retinal pathology) was reserved for final model validation.

Results:
After dimensionality reduction, the data were distributed along a continuum corresponding to the severity of the RAPD. Our ML classifier (support vector classifier) could identify right and left optic neuropathy cases even better than the standard manual calculation of the RAPD (89% accuracy on cross-validation vs 86% accuracy). Validation of the classifier and direct prediction of the log unit RAPD from the waveforms will be done using this model with the test set.

Conclusions:
ML analysis of light-induced pupil reflex waveforms provides a new, automated approach to detecting and quantifying the RAPD compared to traditional methods. Further refinement of this approach will optimize rapid detection and objective quantification of afferent disease in the clinic and at home, as video-based instrumentation and software to capture and analyze these waveforms becomes widely available.

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Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Pupil, Optic neuritis

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Assessing the Performance of Deep Learning in Classifying Visual Field Patterns Using Humphrey Images

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Introduction:
Recognizing patterns of vision loss is crucial in diagnosing and monitoring a wide array of ocular and neurological diseases. We utilized artificial intelligence algorithms to classify visual field defects (VFDs) using a type of deep neural network called convolutional neural networks (CNNs), which are particularly well-suited for image classification. We classified VFDs into 13 distinct patterns: “Altitudinal field defect”, “Arcuate defect”, “Cecocentral scotoma”, “Central scotoma”, “Blind-spot enlargement”, “Peripheral field constriction”, “Nasal step”, “Homonymous hemianopia”, “Superior quadrantanopia”, “Inferior quadrantanopia”, “Bitemporal hemianopia”, “Nonspecific defect”, and “No defect”.

Methods:
A chart review of 427 patients yielded 561 Humphrey grey-scale images (left and right eye combined), which were labeled from among the 13 patterns based on visual field billing codes. CNN algorithms were trained to associate VF images with their labels by learning features (such as edges or corners) from 449 randomly selected VF images (80% of the dataset). Model predictions were then tested using the remaining 112 images (20%). This process was repeated 5 times using different sets of 449 images to ensure robust results.

Results:
The VGG16 model showed the highest performance with an area under the receiver operating characteristic curve (ROC-AUC) of 0.9 and an area under the precision-recall curve of 0.61. Overall, the models performed better on binocular defects compared with monocular defects, likely due to the additional information provided by both eyes.

Conclusions:
Our study differs from the majority of related studies in that we included binocular homonymous field patterns, labeling was based on clinical chart information, and a broader array of 13 visual field patterns was included. Model performance was likely impacted due to imbalanced data. In addition, the model task was more complex due to the labeling method and the large number of classifications used. Despite this, our study demonstrates promising results and a viable proof-of-concept.

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Keywords: Visual fields, Perimetry, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease

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Automated visual acuity measurement using optokinetic response to stimulation with Gabor patches

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Introduction:
Visual acuity measurement is the most important functional marker for the assessment of the visual function. Current measurement paradigms are time consuming, dependent on patient cooperation and examiner skill and patience. . Alternative testing methods such as visual evoked potentials are prone to artefacts, require a sophisticated setup and long preparation and measurement durations. We present a method to measure visual acuity based on the induction of specific movement patterns of the eye based on visual stimulation using Gabor patches. Combined with eye tracking for the detection and automated analysis algorithms.

Methods:
We present Gabor patches pattern, on a high-resolution PC screen at 4m distance, with spatial size of one period and adjust the period length to match the visual acuity to be tested. We move the patches in a sinusoidal motion and record the resulting eye movements. We process the recorded eye movements to remove saccades and other artifacts and assess how much of the original movement is present. We use Landolt C optotypes as a reference measurement and perform both methods twice.

Results:
We measured 62 eyes of 50 participants (28 female, mean age 41 ± 19 years). We find that the mean visual acuity from the two repetitions of the automated procedure correlates well with the traditional measure using Landolt optotypes (correlation coefficient r = 0.81). Comparison of test-retest performance shows a correlation coefficient of 0.92 for the automated version and a correlation coefficient of 0.95 for the Landolt bases visus measurement.

Conclusions:
The use of optokinetic response as a method to measure visual acuity has been demonstrated in various implementations in the past in experimental conditions. We expand on this existing knowledge in two ways: (1) We show a possibility to implement the testing in an automated procedure. And (2) we tested the acuity level up to 0 LogMAR.

References: None provided.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Higher visual functions

Financial Disclosures: Dominik Bruegger: Dominik Bruegger is CTO of machineMD a medical device startup developing NEOS a device for standardized eye exams used in the diagnosis of brain disorders using a combination of VR and AI. All the results presented in this Abstract were generated before this employment, while employed as PhD student at the University hospital of Berne, Inselspital. No current product, nor a product in active development of machineMD is in relation to this abstract.; Ines Schumacher; Thomas Ferrazzini; Rino Vicini; Mathias Abegg: Mathias Abegg is Medical Director of machineMD a medical device startup developing NEOS a device for standardized eye exams used in the diagnosis of brain disorders using a combination of VR and AI. All the results presented in this Abstract were generated before this employment, while employed as professor at the University Hospital of Berne, Inselspital. No current product, nor a product in active development of machineMD is in relation to this abstract.

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Beyond Retinal Thickness: Textural Changes Precede Retinal Thinning in Acute Non-Arteritic Ischemic Optic Neuropathy (NAION)

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Introduction:
Optical coherence tomography (OCT) can visualize retinal nerve fiber layer (RNFL) and ganglion cell inner plexiform layer (GCIPL) loss in non-arteritic anterior ischemic optic neuropathy (NAION). While thickness maps are used to evaluate structural changes associated with edema and atrophy, RNFL en-face images may provide additional textural information (e.g., showing regionally lower intensity but hyper-reflectivity on vessels) that precedes changes in thickness, as an earlier sign of neuron damage when intervention may improve outcome.

Methods:
OCT scans of 142 NAION patients in the acute stage (≤15 days from onset of vision loss) and 50 days after symptom onset were analyzed. RNFL and GCIPL en-face images and thickness maps were generated from OCT volumes after layer segmentation using a novel deep-learning approach. Mean RNFL and GCIPL en-face pixel intensity and thickness were computed.

Results:
RNFL en-face pixel intensity decreased significantly in the acute NAION stage compared to the fellow eye, but not RNFL or GCIPL thickness. Both RNFL en-face intensity and RNFL/GCIPL thickness all decreased after 50 days from symptom onset; fellow unaffected eyes showed no significant change over time.

Conclusions:
Pixel intensity distribution of the inner retinal layers reveal early NAION damage in the acute stage. Decreased RNFL en-face pixel intensity suggests that early textural change has potential to predict future structural thinning of the inner retina. Texture-based biomarkers based on en-face images show promise for detecting pre-thinning damage in NAION versus thickness measures alone.

References: None provided.

Keywords: Optic neuropathy

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Grant Support: This study was supported, in part, by the Department of Veteran Affairs Center for the Prevention and Treatment of Visual Loss, Rehabilitation Research and Development (RR&D) I50RX003002, RR&D I01RX003797, RR&D I01RX001786, National Institutes of Health (NIH) R01EY031544, R01EY023279, R01EB004640; ISMMS Neuro-Ophthalmology Research Fund; The New York Eye and Ear Infirmary (NYEEI) Foundation, New York, N.Y.; Alfiero & Lucia Palestroni Foundation, Inc. Englewood Cliffs, N.J.

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Developing and Validating a Novel Colour Saturation Threshold Test

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Introduction:
Color vision testing forms an important part of the diagnosis and monitoring of retinal and optic nerve diseases. Further, the symptom of subjective colour desaturation is a well described feature of optic neuritis. Most of the readily available color vision tests are targeted at congenital loss of color vision, assess hue rather than saturation discrimination and are not well graded. In this study, we demonstrate a novel test – the LSS-4 – measuring the colour saturation threshold of perception across multiple hues.

Methods:
30 subjects were recruited with a mix of normal and abnormal ocular health. Testing was conducted with the LSS-4 test comprising a simple detection task within 11 progressively more desaturated pseudoisochromatic plates. 4 hues were tested: mauve, green, red and blue (median wavelengths: 570, 616, 555 and 527nm). Each participant was tested twice using the same equipment on different days. Intraclass correlation coefficient (ICC2,1) was used to assess test-retest reliability.

Results:
Mean test time was 5.18 minutes. ICC2,1 showed high reliability for all hues (mauve 0.93, red 0.95, green 0.87, blue 0.91) as well as the total score (0.96). There was no significant difference in the reliability between hues.

Conclusions:
The LSS-4 is a reliable and easy to perform test that may have utility in clinical neuro-ophthalmological practice. It could complement existing tests of hue discrimination for the diagnosis and monitoring of acquired colour vision deficiencies.

References: None provided.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Optic neuritis, Optic neuropathy, Retina

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Diagnostic Value of Demographic And Clinical Features In ED And Inpatient Consultations For Undiagnosed Papilledema

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Introduction:
True papilledema from increased intracranial pressure (ICP) requires immediate workup and treatment, but the growing number of emergency department (ED) visits for suspected papilledema is burdensome. Our recent study of ED and inpatient consultations for "papilledema" included 153 patients seen over one year; two-thirds of patients with undiagnosed optic disc edema had non-fulminant idiopathic intracranial hypertension (IIH) and one-third had new vision- or life-threatening disease.1,2 Currently, no way exists to identify ocular or neurologic emergencies among patients arriving for emergent evaluation for papilledema. We examined whether demographic and clinical features of ED and hospital patients with undiagnosed papilledema differentiated those with and without IIH.

Methods:
From the cohort of 153 consecutive adult ED and inpatient papilledema consultations at one academic center, a retrospective sub-analysis of 89 with undiagnosed papilledema was performed. Age, sex, BMI, and symptoms of raised ICP were recorded. Patients were excluded if data was missing. The primary outcome included diagnosis of IIH or other causes of papilledema (secondary causes of raised ICP or non-papilledematous optic disc edema). A predictive model was developed with fast-and-frugal trees (FFTs) using default settings in the FFTrees R package version 1.4.0.

Results:
Seventy-six patients were included (median age: 30.5 years (interquartile range: 23.8-36.0); 68 (89%) women; 20 (26%) Black; 56 (74%) with IIH). The fast-and-frugal tree with the highest balanced accuracy (85%) predicted IIH versus another cause based on BMI (>29.7 kg/m2), followed by female sex, lack of symptoms of raised ICP, and age (< 38 years). It had 95% specificity and a sensitivity of 75%.

Conclusions:
In patients presenting to the ED and hospital with undiagnosed papilledema, demographic and clinical features can differentiate the etiology of papilledema. Asymptomatic obese women likely have IIH. Symptomatic obese women likely have IIH if aged < 38 years; if >38 years, an alternate cause is more likely.

References: 1. Ray HJ, Okrent Smolar AL, Dattilo M, Bouthour W, Peragallo J, et al. “Papilledema” Neuro-Ophthalmology Consultations From The Hospital: A Prospective Study. North American Neuro-Ophthalmology Society Annual Meeting. Orlando, FL. March 14, 2023. Poster. 2. Okrent Smolar AL, Ray HJ, Dattilo M, et al. Neuro-Ophthalmology Emergency Department and Inpatient Consultations at a Large Academic Referral Center [published online ahead of print, 2023 Aug 4]. Ophthalmology. 2023;S0161-6420(23)00536-5.

Keywords: High intracranial pressure/headache, Pseudotumor cerebri

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Evidence of an exogenous input to Superior Colliculus (SC) as a source of saccadic inhibition

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Introduction:
Saccadic inhibition refers to the strong temporary decrease in saccadic initiation observed when a visual distractor appears shortly after the onset of a saccadic target. One classical interpretation is that the saccadic inhibition phenomenon results from a competition between the target and the distractor in visuomotor maps within SC (Reingold & Stampe, 2002, 2004). One alternative is that exogenous input to SC suppresses antagonistic oculomotor signals by sending strong inhibitory output to the SC.

Methods:
We used three tasks: oculomotor, auditory, and manual response tasks. In the oculomotor task, the subject must trigger a saccade to a target appearing randomly leftward or rightward. A short duration after the target appearance a structured masked covers the target. In the visuomotor task, the subject uses a computer mouse to move to the target instead of a saccadic task. Finally, in the auditory task, the subject is blindfolded. A stereo sound acts as a fixation followed by a silence gap. Then a sound is played randomly either in the left or the right ear. A short duration after that single-ear sound, a stereo sound is played to both ears, acting like the visual mask. Healthy subjects underwent the three tasks while patients with Parkinson suspicion underwent only the oculomotor task.

Results:
Our results show a decrease in motor initiation following a distractor presentation in all tasks. Furthermore, the depth of the response time distribution appears at a similar delay. Some patients did have their response modulated by the distractor while others where insensitive to it.

Conclusions:
This points to a common source of inhibitory signal acting on SC but that this inhibitory signal is unlikely to be generated at the level of SC. It also shows that the oculomotor task could be a good candidate to help discriminate between patients that have a suspicion of Parkinson.

References: None provided.

Keywords: Ocular motility

Financial Disclosures: Pierre Daye: The device used to record the oculomotor task is neuroClues. I am one of the co-founder of P3Lab, the company that develops neuroClues.; Aude Sangaré; Pierre Pouget: Pierre is one of the co-founders of neuroClues which was used to record the oculomotor tasks in the project.

Grant Support: None

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Feasibility and dynamic range of size-threshold perimetry with the Iowa Head-Mounted Display Perimeter

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Introduction:
The Iowa Head Mounted Open Source Perimeter uses a smartphone in a VR mount, which runs perimetric tests using the Open Perimetry Initiative software. Conventional luminance modulation is hampered by a smartphone's inability to generate low enough contrasts to accurately test normal subjects. Modulating stimulus size instead of luminance leverages the OLED display's excellent spatial resolution, and may reduce variability even in regions with lower sensitivity. An important validation step is to ensure the dynamic range of the test encompasses the continuum from normal to severely damaged.

Methods:
First, frequency of seeing curves were measured using the method of continuous stimuli by modulating stimulus size (6cdm-2 stimulus) in healthy subjects (n=6) and subjects with glaucoma (n=9) in damaged and undamaged locations. Second, healthy subjects and glaucoma subjects performed threshold testing using a ZEST (zippy estimation of sequential testing) procedure with size modulation at several luminance increments. Background luminance for all tests was 10cdm-2.

Results:
Size-thresholds increased as expected with eccentricity in locations with normal sensitivity, and were correlated with luminance-thresholds ($R2 = 0.45$, $p< 0.0001$). Slopes of the FOS curves measured with size-thresholding remained relatively steep in damaged locations. Testing with a bright 10cdm-2 stimulus showed a ceiling effect in central locations in normal subjects, while 1.5 and 3cdm-2 stimuli had floor effects in locations with significant damage. 5cdm-2 was just right, showing no ceiling nor floor effects, and normal thresholds were around a goldmann size II with a 3-log-unit dynamic range.

Conclusions:
Size-threshold testing is a feasible alternative to luminance modulation that avoids issues of poor contrast resolution encountered with 8-bit screens. A stimulus contrast $dL/L=0.5$ (~28dB in standard perimetry) has an adequate dynamic range for normal subjects and those with clinically meaningful visual field loss. Future directions include establishing retest variability, and sensitivity/specificity for detection of disease.

References: Heinzman Z, Linton E, Marín-Franch I, Turpin A, Alawa K, Wijayagunaratne A, Wall M. Validation of the Iowa Head-Mounted Open-Source Perimeter. Transl Vis Sci Technol. 2023 Sep 1;12(9):19. doi: 10.1167/tvst.12.9.19. PMID: 37747414; PMCID: PMC10528495.

Keywords: Perimetry, Visual fields, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease

Financial Disclosures: The authors had no disclosures.

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Contact Information: None provided.

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Heart Rate Variability in Pseudotumor Cerebri Syndrome

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Introduction:
Autonomic system disturbances in patients with intracranial hypertension are well known. Reduced Heart Rate variability (HRV) has been identified and studied extensively in traumatic brain injuries, intracranial mass lesions, and various other neurological conditions resulting in cerebral edema and elevated intracranial pressures. A subset of patients with Pseudotumor Cerebri Syndrome (PTCS) are at an increased risk of permanent vision loss. In this study, we evaluated the prognostic value of ultra-short heart-rate variability (HRV), derived from pre-admission routine ECG, in identifying high-risk patients early in the course of treatment. To our knowledge, this is the first descriptive study analyzing the association between HRV changes in the context of PTCS/IIH.

Methods:
Retrospective analysis was performed on patients admitted with a diagnosis of PTCS to a tertiary hospital over a six-year period. A logistic regression (LR) was used to determine whether HRV parameters obtained from admission ECG correlates with increased intracranial hypertension. A number of HRV indices were calculated, including the standard deviation of normal heart-beat intervals (SDNN) and the root mean square of successive differences (RMSSD).

Results:
170 patients were included based on ICD codes that corresponded to IIH diagnoses. Upon additional medical record review, 105 patients were excluded. Exclusion criteria included patients that did not fulfill IIH diagnostic criteria, had a history of peripheral neuropathy, used antiarrhythmic drugs, had cardiovascular disease, or who did not have an ED ECG on the day of their admission. HRV parameters were compared with published normal 10-second HRV values and corrected for age and gender.

Conclusions:
SDNN, and particularly RMSSD, derived from ultra-short ECG recordings may provide prognostic information regarding patients presenting with intracranial hypertension.

References: Fred Shaffer, Zachary M. Meehan, Christopher L. Zerr. Critical Review of Ultra-Short-Term Heart Rate Variability Norms ResearchFront. Neurosci., 19 November 2020. Lvming Zhang, Shi Qiu, Chunxia Zhao, Peifu Wang, Shengyuan Yu, Department of Neurology, Medical School of Chinese People'sliberation Army, Chinese People's Liberation Army General Hospital, Beijing, China. Department of Neurology, Aerospace Center Hospital, Beijing, China

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Pseudotumor cerebri, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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Grant Support: None.

Contact Information: Pablo Ravenna,

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Improving the Performance of Deep Learning-Based Neuro-Ophthalmologic Disease Classification Through Enhanced Transfer Learning

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Introduction:
Although deep learning (DL) has shown great promise in diagnosing neuro-ophthalmologic conditions, the effectiveness of DL is highly dependent on access to large training datasets. This is problematic for neuro-ophthalmology, as datasets are often small, especially for rare neuro-ophthalmologic conditions. To mitigate this limitation, we investigated the use of RETFound, a foundation model pretrained on 1.6 million retinal images, as an enhanced transfer learning strategy for neuro-ophthalmology DL training. We aimed to compare the performance of RETFound against the popular ImageNet-based transfer learning approach, specifically in classifying optic disc edema (ODE) and optic disc pallor (ODP) across different dataset sizes.

Methods:
Two model architectures were compared: RETFound and an ImageNet-pretrained ResNet-152. From the RFMiD dataset, balanced subsets of 230 fundus images (115 with ODP and 115 without ODP) and 190 images (95 with ODE and 95 without ODE) were curated. To explore how dataset size influenced performance, individual models were trained and tested using ten-fold cross validation with 25%, 50%, 75%, and 100% of the available training data.

Results:
The results revealed that the RETFound model, when trained with just 50% of the data, achieved an AUC (area under the receiver operating curve) of 0.82 ± 0.02 for ODP and 0.97 ± 0.03 for ODE. Importantly, the AUC of the RETFound model, even when trained with only 50% of the available data, was significantly greater ($p < 0.05$) than ResNet-152 trained with 100% of the available data.

Conclusions:
Despite the prevalence of ImageNet-based transfer learning, RETFound demonstrated superior classification performance, even with limited training data. Hence, adopting enhanced transfer learning approaches like RETFound have the potential to greatly improve DL model performance for neuro-ophthalmology tasks. The integration of such methods into clinical practice could significantly improve the diagnosis and treatment of patients with neuro-ophthalmologic conditions, especially for rare conditions with limited data.

References: 1. Leong, Y.-Y., Vasseneix, C., Finkelstein, M. T., Milea, D., Najjar, R. P. Artificial Intelligence Meets Neuro-Ophthalmology. Asia-Pac. J. Ophthalmol., 11, 111, 2022. 2. Zhou, Y. A foundation model for generalizable disease detection from retinal images. Nature, 622, 156–163, 2023. 3. Pachade, S. Retinal Fundus Multi-Disease Image Dataset (RFMiD): A Dataset for Multi-Disease Detection Research. Data, 6, 14, 2021.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Individual Accommodative Variability in Adolescents and Adults with Mild Traumatic Brain Injury as an Objective Index for Evaluating Sensory-Motor Function

Amir Norouzpour [1], Amber Hu [1], Gayathri Srinivasan [1], Jennifer Haensel [1], Sophia Marusic [2], Kristin Slinger [1], Neerali Vyas [2], Joellen Leonen [1], Christabel Ameyaw Baah [1], Erin Jenewein [3], Siva Meiyeppen [3], Mitchell Scheiman [3], Caitlyn Lew [1], Aparna Raghuram [2], Tawna Roberts [1]

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Introduction:
Blurred vision is a common symptom in patients with mild traumatic brain injury (mTBI). Accommodative variability is commonly measured when viewing static targets and has not been reported when viewing a moving target. Here, we present a new methodology to objectively measure the ability to maintain a focused retinal image of a moving target using empirical data obtained from adolescents and adults with mTBI and healthy controls.

Methods:
Participants with a history of recent mTBI and controls viewed a movie on an iPod moving sinusoidally toward and away from them at 0.1 Hz at four accommodative amplitudes (0.25, 0.50, 1.00, and 1.50 diopters (D) relative to a 2.5D reference point) binocularly or monocularly. Accommodative responses were measured using photorefraction (PowerRef 3). Accommodative responses were transformed to the frequency domain using the Fourier transform. Accommodative variability at each accommodative demand was calculated using the variation of the one-cycle Fourier measurements at 0.1 Hz using T2circ statistics. For each participant, the slope of the regression line between the accommodative variabilities and demands was calculated as the accommodative Variability/Demand Ratio (VDR).

Results:
Thirty-two mTBI participants (17+7 years) and 54 controls (19+8 years) were included. The mean time following mTBI was 96 days (ranged 36-183). The binocular VDR of the mTBI and controls were 0.033+0.015 and 0.005+0.013 (P=.16), and the monocular VDR were 0.018+0.015 and 0.016+0.010 (P=.91) respectively. Unlike the controls, the binocular and monocular VDR in the mTBI cases were significantly correlated with age (P=.03 and .016, respectively): the younger, the higher the VDR.

Conclusions:
Our data suggest that adolescents may be more susceptible to the deleterious effects of concussion than adults. The Variability/Demand Ratio may be used as an individual accommodative variability index to quantify the ability to maintain a focused retinal image when viewing moving stimuli.

References: None provided.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Trauma, Higher visual functions

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Introducing the Mobile Integrated Cognitive Kit (MICK) App for Rapid Visual Assessment in a Youth Ice Hockey League for Concussion

Sara Hyman [1], Mason Blacker [1], Marc Balcer [2], Christina Marini [1], Samarah Ahmed [1], Ruby Ross [3], Mitchell Jarmol [1], Scott Grossman [1], Steven Galetta [1], Laura Balcer [1]

[1] NYU Grossman School of Medicine, [2] Model Compilers Inc., San Francisco CA, [3] New York University School of Medicine

Introduction:
This study introduced a new and accessible mobile device which administers vision-based testing for concussion assessment in a youth ice hockey league. The Mobile Integrated Cognitive Kit (MICK) facilitates the testing of rapid picture and number naming using the Mobile Universal Lexicon Evaluation System (MULES) and Staggered Uneven Number test (SUN). Visual pathways involve >50% of the brain's circuits, and are nearly universally involved in concussion. Rapid automatized naming tasks like the MULES and SUN are vision-based performance measures for identifying individuals with concussion. Use of a virtual platform will increase further the accessibility of these measures.

Methods:
Members of a youth hockey league completed tablet-based versions of the MULES and SUN tests using the MICK app during pre-season baseline testing. The app records completion times for two trials of each test at pre-season baseline, and is semi-automated for use.

Results:
Among 71 participants (median age 13 years, range 7-17) median best MULES time for two trials was 51.3 seconds (range 34.0-103.6 seconds). Median best SUN time was 68.5 seconds (range 46.6-203.0 seconds). Learning effects were found between the two trials for the MULES (median improvement 7.3 sec, $p< 0.001$, Wilcoxon signed-rank test) and SUN (median improvement 2.44 sec, $p=0.002$, Wilcoxon signed-rank test). Age was a predictor of best test times, with longer times noted for younger participants on the MULES ($rs=-0.43$, $p< 0.001$, spearman rank correlation) and SUN ($rs=-0.47$, $p< 0.001$). Learning effects did not vary across age groups for the MULES ($rs=0.18$, $p=0.19$) or SUN ($rs=0.24$, $p=0.06$).

Conclusions:
The MULES and SUN tests of rapid automatized naming are feasibly administered by non-physician personnel using the MICK among youth athletes. The MICK will allow for widespread dissemination of the MULES and SUN tests and will add a vision-based performance measure to concussion testing.

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Keywords: Trauma

Financial Disclosures: Sara Hyman; Mason Blacker; Marc Balcer: Marc J. Balcer is chief architect for Model Compilers; Christina Marini; Samarah Ahmed; Ruby Ross; Mitchell Jarmol; Scott Grossman; Steven Galetta; Laura Balcer: Editor in Chief, Journal of Neuro-Ophthalmology

Grant Support: N/A

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436 Quantitative Assessment of Eyelid Dynamics and Variability for Differentiating Causes of Ptosis

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Introduction:
We developed and tested a clinical video-based system for recording and automatically tracking eyelid dynamics and variability to discover features that differentiate causes of ptosis and response to treatment. Currently methods are lacking for use in a clinical setting that automatically tracks the border of the upper and lower eyelids.

Methods:
A four camera video system was developed using 2-megapixel miniature infrared video cameras in surrounding an iPad. Spontaneous and light-induced eyelid and pupil movements were recorded at 57Hz from both eyes simultaneously for 3 minutes. The multicamera system enabled a 3D modeling of the eye and eyelids. Recorded video frames were used to train a model to automatically track the upper and lower borders of the eyelids in each recorded video frame. In this pilot study, we tested patient examples of different causes of ptosis; myasthenia gravis, Horner syndrome, incomplete 3rd nerve palsy as well as normal patients. The dynamics of eyelid closure, eyelid opening, and variability of eyelid fissure, as well as variability of inter-eye fissure asymmetry were quantified.

Results:
In myasthenia, graphs of inter-eye fissure asymmetry revealed small, but significant variations over time, often reversing sign upon eyelid opening following a blink, that were not apparent on viewing of the video (subclinical). Lag of eyelid opening could be observed in Horner syndrome, due to Mueller's muscle involvement.

Conclusions:
Quantitative video-based analysis of eyelid fissure variability and dynamics of eyelid movements in a clinical setting provide a new, accessible foundation for categorizing and differentiating different causes of ptosis and response to treatment.

References: None provided.

Keywords: Higher visual functions, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Ocular motility, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease, Myasthenia

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Quantitative Measurements of Relative Afferent Pupillary Defect in Central and Branch Retinal Artery Occlusion

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Introduction:
Relative afferent pupillary defect (RAPD) is characterized by pupillary dilation upon illuminating the eye during the swinging flashlight test. This sign signifies a deficit in the transmission of light information within the pupillary light reflex from the retina to the rostral midbrain circuitry. Although important, quantification of this sign has not been achieved hitherto. We aim to develop a novel method for the quantification of RAPD using a head-mounted device (HMD).

Methods:
We prospectively recruited 11 consecutive patients with unilateral CRAO (n=7) and BRAO (n=4) from January 2019 to February 2022 at Korea University Medical Center. RAPD was quantified using an HMD device by analyzing the pupillary response metrics of both eyes. The asymmetry of the pupillary contraction between the eyes (i.e. RAPD) was measured by interocular difference (IOD). We compared IOD with the semi-quantified RAPD using the neutral density filter, and parameters of standard automated perimetry and optical coherence tomography.

Results:
IOD showed a negative correlation with the semiquantitative measurements of the RAPD using the neutral density filter ($r=-0.751$, $p = 0.008$). IOD had a positive correlation with the average ganglion cell ($r=0.855$, $p = 0.002$) and retinal nerve fiber layer thickness after 3 months ($r=0.706$, $p = 0.023$). IOD had no correlation with initial or final visual acuity after 3 months ($p = 0.563$), as well as the mean deviation of the Humphrey visual field test ($r = 0.145$, $p = 0.671$).

Conclusions:
Our algorithm allows quantification of the RAPD that correlates with the conventional semi-quantitative measurements. By using this, we can estimate the retinal ganglion cell death after retinal artery occlusion.

References: None provided.

Keywords: Optic neuropathy, Pupil, Vascular disorders

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Recovery of the pupillary response after light adaptation is slowed in patients with retinal disease

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Introduction:
Examination of pupillary response to light may be used to locate disease in the well-known pupillary pathway. Today pupils are used either to determine afferent defects in the optic nerve or efferent deficits. However, also retinal disease may change the pupillary light response. In this pilot study we investigate a novel method that aims to unveil retinal disease by observing pupillary movements after light adaptation.

Methods:
We used a virtual reality headset with integrated eye trackers to measure pupil size and control lighting conditions. We exposed 14 patients with age related macular degeneration and 14 healthy subjects to continuous brightness interrupted by brief dark stimuli. The duration of the dark stimulus increased by 100ms in each subsequent trial. This was repeated at least 50 times. We measured the pupillary response after restoration of brightness. We used a linear mixed model to compare the recovery of the pupillary response between subjects and patients, and we used deep learning models to determine diagnostic accuracy.

Results:
We found that the pupillary response amplitude increases with the duration of the dark stimulus, i.e. the longer the eye is exposed to darkness the bigger is the subsequent pupillary amplitude. This pupillary recovery was significantly slowed by age and by presence of macular degeneration. The accuracy of this test for the diagnosis of AMD was about 78%, with a sensitivity of 66% and a specificity of 75%.

Conclusions:
In a fast and easy to use test with a cheap consumer VR-headset retinal disease was detected better than by chance alone. Modifications to the test protocol may increase the predictive value and allow to apply this technology to more relevant retinal disease. Given that eye- and pupiltrackers are now widely available as consumer devices such test protocols that allow home use may facilitate screening of retinal disease.

References: None provided.

Keywords: Pupil, Retina, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease

Financial Disclosures: Mathias Abegg: Mathias Abegg is Medical Director of machineMD a medical device startup developing NEOS a device for standardized eye exams used in the diagnosis of brain disorders using a combination of VR and AI. All the results presented in this abstract were generated before this employment, while employed as professor at the University Hospital of Berne, Inselspital. No current product, nor a product in active development of machineMD is in relation to this abstract.; Javier Barranco: Javier Barranco, is a paid consultant of machineMD a medical device startup developing NEOS a device for standardized eye exams used in the diagnosis of brain disorders using a combination of VR and AI. All the results presented in this abstract were generated before this employment. He has not received any payment for his work in this study. No current product, nor a product in active development of machineMD is in relation to this abstract.; Thomas Ferrazzini; Dominik Bruegger: Dominik Bruegger is CTO of machineMD a medical device startup developing NEOS a device for standardized eye exams used in the diagnosis of brain disorders using a combination of VR and AI. All the results presented in this Abstract were generated before this employment, while employed as PhD student at the University hospital of Berne, Inselspital. No current product, nor a product in active development of machineMD is in relation to this abstract.

Grant Support: None.

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Virtual Reality Perimeters: A More Comfortable, Engaging and User-Friendly Alternative

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Introduction:
Patients with reduced mobility, short attention span and children are often unable to use table-mounted perimeters, such as the gold standard Humphrey Field Analyzer (HFA). In a neuro-ophthalmology practice, this can dramatically impede care for a significant portion of patients. The purpose of this study was to evaluate user experience when using a Virtual Reality Perimeter (VRP) compared to the HFA in a clinical setting.

Methods:
The study was conducted on glaucoma suspect cases referred to our office for evaluation. Their experience with virtual reality (VR) and perimetry, and their usage of prescription eyewear were noted. 20 otherwise healthy patients were tested on both eyes, on both a validated VRP (Retinalogik – Pico Neo3 Pro Eye) and the HFA. Patients then graded their experience comparing the VRP to the HFA, using a 5-point Likert scale (1=strongly favor HFA, 3=neutral, 5=strongly favor VRP), on 5 different usability measures.

Results:
Mean age was 61.5 (SD=11.28). Participants reported better user experience using the VRP compared to the HFA on all individual measures: learning curve (M=3.90, SD=0.85), comfort (M=4.40, SD=0.75), ability to focus on the task (M=4.10, SD=0.72), engagement (M=4.30, SD=0.66), and general preference (M=4.40, SD=0.66). Not one single answer favored the HFA (all range = 3–5). There was no correlation between age and any individual measure (each $R2(20)<.05$). Subgroup analysis with Mann-Whitney U test showed that new VR users were significantly more positive about their VRP experience compared to more experienced users (each $p<.05$), but no significance was found when looking at prior VF experience and glasses usage.

Conclusions:
VRPs are already establishing themselves as a serious, validated, and cheaper alternative to HFA. This study is the first to demonstrate that, even for patients able to use both devices, the VRP is what they prefer, independent of age or glasses wear.

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Keywords: Perimetry, Visual fields, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease, Stroke, Demeylinating disease

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Grant Support: None.

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18F-Fluorodeoxygluose Positron Emission Tomography in Normal Extraocular Muscles

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Introduction:
PET-CT imaging may provide unique insight into the pathophysiology of extraocular motility in numerous disease processes. There is currently no standardized or widely accepted normal physiologic uptake nomogram for 18F-FDG in extraocular muscles. The present study aims to assess baseline metabolic activity of extraocular muscles on PET-CT in patients with full extraocular motility. Understanding the normal values of FDG uptake of extraocular muscles will allow improved identification of pathological processes through quantitative measures.

Methods:
A retrospective chart review and image analysis study was performed. Patients with normal extraocular motility who had received a PET-CT scan within the past 3 years were included in the study. The maximum standardized uptake value (SUVmax) was calculated for the lateral, medial, superior, and inferior rectus muscles, as well as the cerebellum, for axial and coronal views. These values were analyzed along with the patient's age to create a nomograph of standard age-adjusted values of baseline metabolic uptake in the extraocular muscles.

Results:
Seventy-two patients and 144 eyes with PET-CT scans were analyzed in the study, although total number of extraocular muscles analyzed varied based on quality of PET-CT scans. On axial views, SUV max of the medial rectus muscle was 5.77+/-2.3 and for lateral rectus muscle was 6.48+/-2.3. On coronal views, SUV max of the superior rectus was 4.55+/-1.9 and inferior rectus muscle was 5.61+/-2.7. One-way ANOVA shows significant difference between rectus muscles ($p=0.0002$) suggesting physiologic differences in metabolic uptake. Analysis of SUV max with patient age also showed a significant difference ($p< 0.0001$) suggesting variance in metabolic uptake of extraocular muscles with age.

Conclusions:
There are natural variations in metabolic activity of extraocular muscles and with age. The present study is the first to analyze physiologic metabolic activity of extraocular muscles on PET-CT to establish a baseline value to compare to in future studies.

References: None provided.

Keywords: Neuroimaging, Ocular motility

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Grant Support: None.

Contact Information: None provided.

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Age-related risk of stroke following ocular motor cranial nerve palsy

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Introduction:
Ocular motor cranial nerve palsy (CNP), affecting the third, fourth, or sixth cranial nerves, has been known to be associated with an increased risk of stroke. However, the impact of age on this relationship remains uncertain.

Methods:
In this cohort study, we established a cohort of individuals diagnosed with CNP between 2010 and 2017 who had undergone national health screening within two years of diagnosis. We also included a control group, matched 1:5 for sex and age. Participants were followed until December 31, 2019, and multivariable Cox proportional hazards regression was used to assess the CNP-stroke association, adjusting for various covariates, including lifestyle, health behavior, underlying comorbidities, and Charlson Comorbidity Index score

Results:
Individuals with ocular motor CNP exhibited a increased stroke risk compared to the control group (hazard ratio [HR]: 1.23, 95% confidence interval [95% CI] = 1.08 – 1.39). This association varied significantly by age. Notably, in their 30s, individuals with CNP had a 8.91-fold increased stroke risk (HR: 8.91, 95% CI: 1.63-48.66). The risk remained significantly elevated in their 40s (HR: 2.49, 95% CI: 1.39-4.45), 50s (HR: 1.78, 95% CI: 1.31-2.42), and 60s (HR: 1.32, 95% CI: 1.08-1.62). However, individuals in their 20s, 70s, or 80s did not exhibit a significant increase in stroke incidence.

Conclusions:
This age-stratified cohort study establishes an association between ocular motor CNP and an elevated risk of stroke, with the greatest impact observed in young adults. These findings underscore the importance of considering CNP as a potential risk factor for stroke, especially among individuals in their 30s and 40s, and highlight the need for further research to elucidate underlying mechanisms and potential preventive strategies.

References: None provided.

Keywords: Stroke, Ocular motility, Adult strabismus with a focus on diplopia

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Clinical significance of square-wave jerk in Idiopathic Parkinson's disease

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Introduction:
Square-wave jerks (SWJs) are pairs of small horizontal saccades (typically < 2°) that take the eye away from the target and then return it within 200 ms. They may be common in normal elderly subjects, but a prominent clinical finding in neurodegenerative disorders such as Parkinson's disease. This study aimed to determine the clinical significance of SWJ in idiopathic Parkinson's disease (IPD).

Methods:
We retrospectively recruited 107 patients with IPD in Pusan National University Yangsan Hospital, and compared the frequency, amplitude and shape of SWJs documented by video-oculography between patients with IPD and 48 age- and sex-matched subjects. We also analyzed the correlation between SWJs and clinical scales such as Unified Parkinson's Disease Rating Scale (UPDRS) and Hoehn-Yahr scale.

Results:
A mean frequency of SWJs in IPD was 26.8 per minute, and the amplitude were variable, ranging from 0.2° and 8.0°, which were not significantly different compared to those of control group. Three patients (3 %) had macro-SWJ (> 5°). A staircase SWJ was observed in 49 patients (46%) with high frequency SWJ. Forty-two patients (39%) had SWJ with a dynamic overshoot after each primary saccade, whom they showed higher UPDRS ($p=0.002$, $p< 0.002$) compared to patients without a dynamic overshoot. There was a weak correlation between SWJ frequency and UPDRS ($r=0.274$, $p< 0.01$), but no significant correlations between macro- or staircase SWJ and clinical scales.

Conclusions:
The present study showed that SWJ frequency and SWJ with a dynamic overshoot appear to reflect motor severity in idiopathic Parkinson's disease.

References: None provided.

Keywords: Ocular motility, Nystagmus, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Correlation of Objective Ocular Alignment and Subjective Diplopia After Teprotumumab In Patients with Thyroid Eye Disease (TED)

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Introduction:
Teprotumumab, an insulin-like growth factor one (IGF-1) antagonist improved proptosis and diplopia in patients with thyroid eye disease (TED). Prior clinical trials documented subjective improvement in diplopia in study subjects who received teprotumumab, but have not documented objective measurements of ocular alignment. We sought to objectively measure ocular misalignment in TED patients with diplopia who received teprotumumab.

Methods:
In this retrospective study, we measured ocular misalignment in patients with diplopia due to TED before and after teprotumumab administration. Primary endpoint was improvement in diplopia in prism diopters (PD). Secondary endpoint was to correlate objective improvement with subjective improvement in diplopia.

Results:
Of the 67 patients treated with teprotumumab, 19 had diplopia from TED and 17 were included for analyses. There were 10 females and 7 males (average age 62 years, SD 13). 8 patients had hypertropia (mean 19 PD), 4 had esotropia (mean 21 PD), 2 had exotropia (mean 17 PD), and 3 had combined deviations (mean: 4 PD esodeviation and 21 PD vertical deviation). 41% (7/17) had improvement in their misalignment and 53% (9/17) had improvement in subjective diplopia. Mean improvement in strabismus was 5 (SD 11) PD for hypertropias, 2 (SD 8) PD for esodeviations and 13 (SD 13) PD for exotropias. Gorman score improved from 2.2 (1.0) to 1.5 (SD 1.4). Despite modest improvement in hypertropias objectively, 2/8 had total resolution of subjective diplopia and 5/8 had some improvement (mean Gorman change 0.9, SD 1). Interestingly, subjective diplopia improved in 3/17 patients with worsening/unchanged objective alignment. Change in Gorman score and alignment was poorly correlated (Pearson r = 0.1).

Conclusions:
Teprotumumab objectively improved ocular alignment in 41% and subjective diplopia in 53% of patients. Objective and subjective measures of diplopia are not well correlated and worthy of further inquiry in future studies of teprotumumab for TED.

References: None provided.

Keywords: Graves' disease, Ocular motility, Orbit

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Grant Support: None.

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Diplopia after cataract surgery: retrospective review of orthoptic assessments

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Introduction:
Diplopia after cataract surgery can be an unexpected outcome of technically proficient surgery that can cause patient dissatisfaction. The purpose of this study was to assess etiologies and outcomes of patients referred for orthoptic assessment for diplopia after cataract surgery.

Methods:
A retrospective review was performed for patients seen by orthoptics at two tertiary hospitals between January 1, 2019 and November 30, 2022. Patients were included if the referring history indicated symptoms of diplopia after cataract surgery. Exclusion criteria included: simultaneous cataract with other ocular surgery, age under 18, known preoperative diplopia, or inaccessible operative report. Primary outcomes included: etiology of diplopia and proportion of patients receiving interventions.

Results:
Data collection is ongoing. Fifty-nine patients were included. Mean age at assessment was 74.3 ± 7.0 years, and 48% were female. All patients had cataract surgery under topical anesthesia. Five patients had periocular infiltrative anesthesia for vitrectomy performed either prior to (6.8%) and/or following (3.4%) cataract surgery. Intraoperative complication (posterior capsular rupture) was noted in 1 patient (1.7%). Etiologies of diplopia included decompensated esophoria/exophoria (23.7%), decompensated fourth nerve palsy (10.2%), monocular diplopia (8.5%), convergence insufficiency (8.5%), retinal diplopia (3.4%), periocular anesthetic myotoxicity (3.4%), and sixth nerve palsy (1.7%). The remainder had hypertropia (22.0%) or combined hypertropia with horizontal deviation (18.9%), the etiology of which could not be obviously discerned. Neuroimaging was obtained in 11.9%, none of which revealed explanatory pathology. Interventions included prisms (42.4%), strabismus surgery (10.2%), updated refractive correction (5.1%), and convergence exercises (1.7%). A neuro-ophthalmologist was involved in 22.0% of cases, of which 30.8% was also as the cataract surgeon.

Conclusions:
Many causes account for diplopia after cataract surgery. The most common intervention was prisms, followed by strabismus surgery and updated refractive correction. The majority were evaluated and treated by the referring surgeon and orthoptist, without involvement of a neuro-ophthalmologist.

References: None provided.

Keywords: Ocular motility, Adult strabismus with a focus on diplopia

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Epidemiology and Characteristics of Adult-Onset Nystagmus of the Central Etiologies: A Population-Based Study in Olmsted County, Minnesota

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Introduction:
Nystagmus is one of the most challenging signs in clinical practice, which can cause disability and be from dangerous etiologies. Population-based incidence, types, and etiologies of adult-onset central nystagmus has not been well described in the literature.

Methods:
A population-based study in a single county in the United States was conducted to identify all adult residents (aged ≥18 years) diagnosed with any form of nystagmus or saccadic oscillations between 1972 and 2019. We excluded childhood nystagmus and peripheral causes of nystagmus. Data regarding presenting features, nystagmus description and diagnoses were collected.

Results:
Central nystagmus was diagnosed in 204 cases over the 48-year period, resulting in an annual incidence of 5.95 cases per 100,000 adults. The median age was 56.4 years (range 18.5 to 99.9); 55.4% male. Most patients presented with dizziness/vertigo (73.6%), oscillopsia (68.3%), and nausea/vomiting (64.4%). Ataxia (60.6%), and dysarthria (30.1%) were the most common neurological signs. The most common nystagmus types were gaze-evoked (39.4%), torsional (18.2%), other central vestibular (10.6%), downbeat (7.7%), and upbeat (5.8%). Multiple nystagmus types occurred in 29.4%. About two-fifths of cases showed spontaneous nystagmus in the primary gaze. Fifty-six percent showed improvement or complete resolution at their last visit. Cerebrovascular disease was the leading cause (33.8%), followed by toxic/metabolic causes (18.6%) and demyelinating disease (15.7%). Lesions on neuroimaging could explain the occurrence of nystagmus in 69.5% of cases. The cerebellum and medulla were the most frequently affected sites, with 53.7% having more than 1 lesion site. Stroke and neurodegenerative disease were more common in older patients (≥60), while demyelinating diseases and tumors were common in younger (< 60) patients ($p < 0.05$).

Conclusions:
This is the first population-based study on the incidence and characteristics of adult-onset nystagmus of central origin in North America. Vestibular syndromes and brainstem dysfunction were the most prevalent presentations.

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Keywords: Nystagmus, Ocular motility, Ocular manifestations of vestibular disorders

Financial Disclosures: The authors had no disclosures.

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Etiologic Distribution of Isolated Oculomotor Nerve Palsy: Analysis of 633 Patients and Literature Review

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Introduction:
The etiologic distribution oculomotor nerve palsy has been various among the studies. This study aimed to define the clinical features and underlying etiologies of isolated oculomotor nerve palsy by recruiting patients from all departments in a referral-based university hospital.

Methods:
We reviewed the medical records of 672 patients who had a confirmed diagnosis of isolated oculomotor nerve palsy at all departments of Seoul National University Bundang Hospital, Seongnam, South Korea, from 2003 to 2020. We also compared the proportion of etiology of isolated oculomotor nerve palsy with that of the patients pooled from the previous studies

Results:
The most common etiology was microvascular (n = 168, 26.5%), followed by vascular anomalies (n = 110, 17.4%), neoplastic (n = 86, 13.6%), inflammatory (n = 79, 12.5%), idiopathic (n = 60, 9.5%), and traumatic (n = 53, 8.4%). Neurologists were mainly involved in the management of microvascular and inflammatory oculomotor nerve palsies while ophthalmologists mainly participated in the care of idiopathic, neoplastic, and traumatic palsies. Neurosurgeons mostly took care of oculomotor nerve palsy due to vascular anomalies.

Conclusions:
The proportion of etiologies of isolated oculomotor nerve palsy may differ according to the specialties involved in the management. The results of previous studies on the etiologic distribution of isolated oculomotor nerve palsy should be interpreted with this consideration.

References: None provided.

Keywords: Ocular motility, Ocular manifestations of vestibular disorders

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"Acute Vision Loss" In Patients Presenting To A Large Emergency Department: Impact Of A Hybrid Non-Mydriatic Ocular Fundus Camera With Optical Coherence Tomography

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Introduction:
The chief complaint of "acute vision loss" in the emergency department (ED) may reveal serious ocular and neurologic diagnoses requiring immediate evaluation. However, evaluation of such patients is often delayed and ED stays prolonged because ophthalmologists on-call are typically not on-site, frequently simultaneously covering multiple facilities. We implemented a hybrid nonmydriatic ocular color fundus camera combined with optical coherence tomography (NMFP-OCT) in our large general ED with the goal of facilitating rapid diagnosis of ocular emergencies and avoiding in-person consultations when the examination is normal. We hypothesize that incorporating NMFP-OCT into the workflow of a large general ED, combined with a list of triage questions for "acute vision loss", will facilitate rapid identification of ocular emergencies (e.g., acute central retinal artery occlusion [CRAO]), and reduce length of stay in the ED.

Methods:
Quality improvement project with prospective data collection for all patients undergoing NMFP-OCT in the ED for "acute vision loss". Data collected: demographic information, indications for photographs, timing of photographs, ophthalmology consultations triggered, final diagnoses, lengths of stay, and final outcomes.

Results:
16 weeks after implementation of NMFP-OCT, among 400 patients with NMFP-OCT, 87 patients presented with "acute vision loss" (including 15 CRAO, 11 retinal detachment, 7 vitreous hemorrhage, 5 papilledema, 5 uveitis, 5 optic neuritis). All these patients received in-person ophthalmology consultations confirming the diagnoses after NMFP-OCT showed abnormalities.

Conclusions:
The high prevalence of consultations for "acute vision loss" in our general ED suggests that incorporating NMFP-OCT into the workflow of the ED, combined with a list of triage questions for "acute vision loss", could increase efficiency in the ED by accelerating the diagnosis using remote interpretation of ocular imaging prior to in-person consultation. Further data will be collected and results of the first 9 months (estimated >200 consecutive patients with "acute vision loss") will be presented at the NANOS meeting.

References: None provided.

Keywords: Neuroimaging, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)

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Comparison of Ultrasound Characteristics of Peripapillary Hyperreflective Ovoid Mass-Like Structures (PHOMS) and Optic Nerve Head Drusen in Children

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Introduction:
In children, pseudopapilledema is frequently caused by peripapillary hyperreflective ovoid mass like structures (PHOMS) or optic nerve head drusen (ONHD). While enhanced depth imaging (EDI) OCT can identify both, lack of cooperation especially from younger children often necessitates use of B-scan ultrasound (BSUS). This study investigated whether PHOMS are hyperreflective on BSUS, and if BSUS can differentiate PHOMS from ONHD.

Methods:
Pediatric patients referred by a neuro-ophthalmologist to the diagnostic ultrasound clinic for optic nerve head elevation between March 2019 and May 2021 were eligible. Subjects who underwent BSUS and EDI-OCT and were diagnosed with pseudopapilledema based on exam, imaging findings, stability on follow-up, and in some cases normal CSF opening pressure, were included. ONHD were identified on EDI-OCT as structures above the lamina cribosa with a hyporeflective core and hyperreflective margin prominent superiorly. Hyperreflective horizontal lines (HHL) above the lamina cribosa without ONHD were identified. PHOMS were defined as ovoid, hyperreflective structures above Bruch's membrane external to the optic disc. The BSUS were read by a separate, masked evaluator who graded the reflectivity.

Results:
Ninety-three eyes (47 patients; 61.7% female; mean age = 11.0 years) with pseudopapilledema were included. EDI-OCT mostly demonstrated PHOMS only (63.4%), followed by PHOMS and ONHD (20.4%), and then PHOMS and HHL (16.1%). On BSUS, 86.4% of eyes with only PHOMS demonstrated low or intermediate reflectivity, while 94.7% of eyes with both PHOMS and ONHD demonstrated high reflectivity. In eyes with PHOMS and HHL, 80.0% demonstrated high reflectivity.

Conclusions:
Though PHOMS are hyperreflective on BSUS, ONHD are more highly reflective which may allow clinicians to differentiate the two if EDI-OCT is unavailable. Eyes with PHOMS and HHL have similar characteristics to those with ONHD, supporting current theories that these lines may be early indicators of evolving drusen.

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Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Pediatric neuro-ophthalmology

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Impact of a Non-mydriatic Ocular Fundus Camera at a Quaternary Care Emergency Department

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Introduction:
Ocular funduscopic examinations are rarely performed by non-ophthalmology providers, resulting in diagnostic errors/worse patient outcomes, and of particular concern in emergency departments (ED) where ophthalmologists are not always available. We evaluated the short-term impact of the implementation of a non-mydriatic ocular fundus camera in a busy ED in a metropolitan quaternary care hospital.

Methods:
Quality improvement project with systematic prospective collection of data from patients who had ocular fundus photographs taken in the ED for visual complaints, headaches, neurologic symptoms, “papilledema”, hypertensive crisis. We collected demographic information, indication for fundus photographs, who ordered photographs, timing of photographs, final diagnosis, and whether photographs had an impact on patients’ length of ED stay and final outcomes.

Results:
Over 4 months, 430 patients had photographs (ordered by ED 89.5%, ophthalmology 7.8%, neurology 2.7%). Reasons included visual complaint 32.3%, headache 13.49%, papilledema 14.4%, other neurologic complaints 38.6%, hypertension 0.9%, diabetes 0.2%. Photographs were interpreted remotely, avoiding ophthalmology or neurology in-person consultation in 9.8%. Obtaining photographs took < 5 minutes (60.2% high quality; 75.2% able to exclude emergent findings). Photographs accelerated the management/disposition of patients with acute disorders in 56.7%, including 15 acute central retinal arterial occlusions, 5 giant cell arteritis, 46 papilledema.

Conclusions:
Incorporating a non-mydriatic ocular fundus camera into the ED workflow can be used as a substitute for non-ophthalmology provider funduscopic examinations in most cases, facilitating remote fundus interpretation by ophthalmologists and real-time remote recommendations without seeing patients in person. These positive preliminary results obtained only 4 months after implementation of the camera suggest that this strategy reduces the overall ED stay and accelerates the diagnosis of urgent vision- or life-threatening conditions, resulting in improved patient outcomes. Further data will be collected and results of the first 9 months (estimated >1000 consecutive patients) will be presented at the NANOS meeting.

References: None provided.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Vascular disorders, Optic neuritis

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In Vivo OCT Imaging of Muller and Macrophage-Like Cells in the Retinas of Patients with and without MS and related diseases

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Introduction:
Macrophage-like cells (MLCs) respond to injury and inflammation and have a distinct star-shaped morphology(1,2). Muller cells, associated with Internal Limiting Membrane (ILM) injury, present as hyperreflective dots in the fovea(3-5). Both cell types are visible at the vitreoretinal interface via averaged Optical Coherence Tomography (OCT) scans(6,7). Multiple Sclerosis (MS) and MOGAD (Myelin oligodendrocyte glycoprotein antibody-associated disease) are chronic inflammatory immune diseases and feature ocular manifestations(8,9). The purpose of this study is to compare MLC and Muller cell density in the macula and peripapillary regions of people with and without MS and MOGAD.

Methods:
Using the Optovue device, each eye received 10 volumetric OCT scans using two protocols: 3x3mm centered on the macula and 4.5x4.5mm on the optic nerve head. Flattened slabs, segmented from 0-5 µm above the ILM were created from each OCT volume scans. Image J software was used for processing, as follows. Structural OCT scans were registered and averaged, signal to noise was increased, backgrounds were subtracted with a 5.0-15.0 pixel rolling ball radius and cells identified and counted manually using described morphology. Cell counts for each eye were compared between groups for each image region using generalized estimating equation models accounting for within subject correlation.

Results:
16 subjects (15 MS, 1 MOGAD, age 46.87 ± 15.76 years; 87.5% female) and 5 healthy controls (age 32.5 ± 9.25 years, 100% female), were enrolled. MLC density was similar in both maculae and peripapillary regions of MS and control eyes (MS vs. control: macula: -0.29/mm2, p=0.71; optic nerve: -1.42/mm2, p=0.52). Muller cell density was higher in both maculae and peripapillary regions for MS eyes (MS vs. control: macula: 1.27/mm2, p=0.01; optic nerve: 0.71/mm2 (95% CI: -0.03 to 1.46), p=0.06).

Conclusions:
Muller cell densities were higher in the maculas and optic nerves of individuals with MS and MOGAD compared to those without.

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Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Retina, Neuroimaging

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Methodology of implementation of an ocular fundus camera in the Emergency Department (ED): breaking the barriers

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Introduction:
Studies have shown benefit from using non-mydriatic ocular fundus cameras (NMFC) in non-ophthalmic settings.1,2 Camera cost, reluctance to accept change, and technical difficulties have deterred adoption of NMFCs in most EDs. We describe the necessary steps to successfully implement NMFC in EDs.

Methods:
We analyzed each step of our recent successful implementation of a hybrid (color fundus photography/OCT) table-top NMFC in our large general ED; correlated with Kotter's 8-step model for implementing change.3,4

Results:
Steps occurred over four weeks (2 each for preparation/implementation): 1)Camera choice: based on needs/desired use for ophthalmic emergencies: table-top, non-mydriatic, automatic/user-friendly, color photographs/OCT. 2)Sense of urgency: administration requested NMFC functional within 4 weeks; we reasoned that current practice with attendant risks of misdiagnosis and delayed care warranted the immediate disruptions of implementation. 3)Powerful coalition: formed across departments [Ophthalmology, Neurology, ED, information technology (IT)], and skills [(EVPs (2), department chairs (3), administrators (2), IT (6), attending physicians (5), fellow (1), residents (3), medical students (2)], facilitating rapid implementation. 4)Vision for change: immediate (camera location; electronic medical record connection/image storage) and medium/long-term goals (ED triage/flow changes; photographs obtained by ED personnel before consultations; interpretation/billing) 5)Communicate vision: grand-round videos; lessons learned from patients; faculty/staff meetings; daily communications; weekly IT meetings; weekly emails with updates. 6)Remove obstacles: education of all (flexible hours; hands-on training of 149 personnel; onsite assistance (medical students); written/video tutorials on camera, photograph interpretation; resident education). 7)Generate short term wins: screening photographs/OCT for personnel; shared successful patient stories; abstract submissions (5 within 4 weeks). 8)Build on wins: prospective quality improvement projects with outcome measures. 9)Embed changes into culture: monitoring of camera/outcomes for 18 months (4 hands-on medical students; 1 resident); continued communication with departments; faculty/staff meetings; repeat training.

Conclusions:
Our model for implementation was a team effort contingent upon engaging collaborators (including IT) and ensuring active continuous motivation/engagement and rewards.

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Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), High intracranial pressure/headache, Retina, Stroke

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Novel Ganglion Cell Complex Percentage Loss Patterns Distinguish Eyes Between Multiple Sclerosis and Glaucoma

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Introduction:
Our research aims to establish an objective method for distinguishing between MS and glaucoma by examining the patterns of ganglion cell complex (GCC) defects in macular scans.

Methods:
This was a prospective case-control study. MS diagnoses all met 2017 McDonald criteria, while glaucoma diagnoses met standard clinical criteria, including disc rim thinning or peripapillary nerve fiber bundle defects. Macular scan thicknesses were divided into the nine ETDRS sectors and then converted into percentage loss (% loss) by comparing them to our normative database. Both MS and glaucoma eyes were assigned one of two groups, based on the 2.5th percentile cutoff of the normal reference: eyes with a "significant defect" (SD) and eyes with "no defect" (ND). After grouping, the worse eye from each participant was selected for analysis. We formulated multiple indices based on the pattern of the % loss observed in the macular scans. The diagnostic performance of these indices was evaluated using the area under the receiver operating characteristics curve (AROC).

Results:
Our study enrolled 56 MS subjects (111 eyes) and 91 glaucoma subjects (91 eyes). The SD group comprised 19 MS eyes and 70 glaucoma eyes, while the ND group consisted of 39 MS eyes and 21 glaucoma eyes. Distinct patterns of GCC defects were identified. In MS cases, the defects were observed relatively evenly across the nine ETDRS sectors, whereas glaucoma cases exhibited defects primarily in the outer temporal and inferior sectors. The diagnostic indices yielded a high AROC value of 0.89 (95% CI: 0.82-0.96) in the SD group. In the ND group, the indices also demonstrated a fair AROC value of 0.69 (95%CI: 0.54-0.84).

Conclusions:
Multiple sclerosis and glaucoma exhibit different GCC defect patterns in macular scans. Analyzing the indices derived from the % loss patterns enables accurate differentiation between MS and glaucoma.

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Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Demeylinating disease

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Optic Disc Cupping in NMOSD, MOGAD, and MS and its Relationship with OCT parameters: A multicenter study

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Introduction:
It has been shown that cupping can occur after an episode of optic neuritis (ON). The purpose of this study was to compare cupping in patients after ON from multiple sclerosis (MS), neuromyelitis optica spectrum disorder (NMOSD), or myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) and to investigate the relationship between cupping and retinal nerve fiber layer (RNFL) and ganglion cell complex (GCC) thinning.

Methods:
This was a retrospective cohort involving patients (≥18 years) with ON from 3 institutions. Patients were eligible if they had optical coherence tomography (Cirrus, OCT) performed ≥6 months after a single unilateral ON. The amount of thinning and cupping was estimated from the difference in the OCT parameters between affected and unaffected eyes. Univariable and multivariable regression were used to investigate the relationship between cupping and ON etiology. Pearson correlation was used to investigate the relationship between cupping and RNFL and GCC.

Results:
87 subjects (MS: 35, NMOSD: 26, MOGAD: 26) were included. There was no significant difference in gender and race between the groups, and 74 subjects (85%) were female. Age was significantly different, with a mean ± standard deviation (SD) age of 39.3±9.8, 50.7±18.2, and 36.7±17.0 for MS, NMOSD, and MOGAD, respectively (P=0.002). In the univariate model, cupping was significantly higher in the NMOSD group (P=0.022); however, after adjusting for age, the difference was no longer statistically significant (P=0.073). Cupping was inversely and moderately correlated with GCC thinning (R=-0.46 in MS; R=-0.65 in NMOSD; R=-0.65 in MOGAD). For RNFL thinning, cupping was inversely and moderately correlated in MS and MOGAD (R= -0.66 and -0.70, respectively) and had a weak correlation with cupping in the NMOSD group (R=-0.22).

Conclusions:
Our results demonstrated that cupping after ON is correlated with RNFL and GCC thinning but did not differ in patients with MS, NMOSD, and MOGAD.

References: None provided.

Keywords: Optic neuritis

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Papilledema and Pseudopapilledema Recognition using Artificial Intelligence: A Code-Free Automated Machine Learning Model

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Introduction:
Papilledema is characterized by optic nerve edema secondary to intracranial hypertension. It can sometimes be challenging to differentiate papilledema from pseudopapilledema, which is defined as an abnormal elevation of the optic nerve without edema. Automated Machine Learning (AutoML) allows the production of artificial intelligence algorithms without requiring programming knowledge. The aim of this project is to develop an algorithm using deep learning via Google Image Classification to differentiate between papilledema and pseudopapilledema from optic nerve photos.

Methods:
We used 1368 optic nerve photos from a public database to produce and test the model. This model classifies the photos into three categories: normal, papilledema, and pseudopapilledema. Approximately 80% of the images were used to train the model, and 20% were used for testing. Subsequently, optic nerve images from the web (30) were used for external validation.

Results:
The AutoML model demonstrated excellent discriminating performance, even outperforming bespoke deep learning models handcrafted by experts. The area under the precision-recall curve was 0.981. At the 0.5 confidence threshold cut-off, the overall performance metrics were as follows: precision (97.8%), sensitivity (97.8%), specificity (98.9%), and accuracy (99.0%). Looking at each subgroup specifically, precision varied from 93.5–100.0%, sensitivity varied from 96.6–100.0%, specificity varied from 98.3–100.0% and accuracy varied from 97.8–100.0%. Pseudopapilledema was the most accurately predicted subgroup (with an accuracy of 100.0%).

Conclusions:
A machine learning model produced by an ophthalmology resident without any programming knowledge can accurately distinguish between papilledema and pseudopapilledema. Researchers and clinicians with limited programming knowledge can use these platforms to generate robust algorithms that assist them in their projects and clinical decisions.

References: None provided.

Keywords: High intracranial pressure/headache, Optic neuropathy, Neuroimaging, Pseudotumor cerebri

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Practical Implementation of an Emergency Department Non-Mydriatic Fundus Camera: Pearls and Pitfalls

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Introduction:
The FOTO-ED Study previously demonstrated the feasibility of Emergency Department (ED) fundus photography and the enhanced detection of relevant abnormalities in patients presenting with headache, amongst other indications. Yet, this practice is not widespread - perhaps due to cost, training, feasibility, medical liability concerns. In this observational study, we describe our experience with implementation of an ED fundus photo project.

Methods:
Staff and ED providers underwent education and instruction. Patients presenting (4/2023-8/2023) with headache for whom non-mydriatic fundus photography was ordered were prospectively studied. Photographs were taken by ED technicians, uploaded into the EHR, and sent to a neuro-ophthalmologist to review. All three steps had to be completed for a successful process. Data collected included patient demographics, fundus orders, consults, admission, and impact on clinical practice. As a quality improvement project, this study did not undergo IRB review.

Results:
185 photographs were ordered on 183 unique patients, average of 9.2/week. 110/185 (60.1%) of photographs were successfully uploaded and 75/110 (68%) had finalized results. There was a weakly negative linear relationship in the proportion of photos not marked as completed over the course of the study (R-squared=0.1077). There was no significant difference in proportion of completed photos by weekend vs. weekday or day vs. evening shifts (p=0.4). Of 75 finalized photos, 22 had significant/urgent findings and in 11 cases the photos impacted clinical decision making. 18 patients were admitted; ophthalmology and neurology consults occurred on 19 and 26 patients, respectively. 20 photos were limited by artifact; there was a negative trend over time by month (R-squared=0.6)

Conclusions:
Our findings support the feasibility of ED Fundus photography for headache patients. Future studies will compare this data to ED patients without fundus photography and expand the project's scope beyond headache. We hope this work will inspire other institutions to adopt similar practices.

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Keywords: Optic neuropathy, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Pseudotumor cerebri

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Retinal Microstructural Features Predicting Vision and Survival Outcome in Patients with Glioblastoma

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Introduction:
Glioblastoma is a fatal aggressive primary brain tumor. Though patients experience vision concerns, the visual sequelae are not well studied. This study aims to evaluate the vision and associated survival outcome of glioblastoma patients.

Methods:
We studied neuro-ophthalmic features in a cohort of glioblastoma patients, measuring retinal nerve fiber layer (RNFL) and ganglion cell complex (GCC) thicknesses, and microvascular densities of the radial peripapillary capillaries (RPC), inner/outer retina. We analyzed visual outcome and developed a machine learning algorithm predicting survival outcome. Normal controls were recruited from convenient sampling.

Results:
20 total eligible patients(Male=10, F=10) were enrolled. Average age at diagnosis was 69 years(47-76). Median time from tumor diagnosis and radiation to first eye exam was 3.6 months(0-15) and 1.6 months(0-12), respectively. The average visual acuity by Snellen was 20/25-1 (20/20--20/50-2). Poorer visual fields occurred in occipital tumors with average mean deviation -14.9; and better in frontal tumors with mean deviation -0.23. RNFL was normal in 3/3(100%) patients before, 5/5(100%) during, and 15/16(93%) after radiation. Patients with overall survival (OS)< 15 months had thinner RNFL and GCC than patients with OS>/=15 months ($p< 0.0001$). Similarly, foveal avascular zone(FAZ) was greater in OS< 15 months at times greater than 3 months since diagnosis ($p=0.006$). Eyes ipsilateral to radiation demonstrated no statistical differences in retinal microstructures or VA to contralateral eyes suggesting no radiation spill-over. Machine learning analysis employing a Random Forest algorithm demonstrated separate groups of patients with long and standard survival using retinal microstructural features. A predictive model is being validated.

Conclusions:
Glioblastoma patients sustain visual field impairment that vary between tumor locations. Retinal thinning and FAZ enlargement are observed in patients with OS< 15 months. A machine learning algorithm was established to predict visual and survival outcome. A larger study is warranted to validate the model to improve vision related quality of life.

References: None provided.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Retina, Tumors, Visual fields

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Grant Support: None.

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Retinal Nerve Fiber Layer and its Spatial Pattern in Acute and Chronic Stages of Typical and Atypical Optic Neuritis

Judith Brody [1], Edward Linton [1], Jui-Kai (Ray) Wang [2], Brett Johnson [1], Mark Kupersmith [3], Mona Garvin [4], Riley Filister [1], David Szanto [5], Joseph Branco [6], Randy Kardon [2]

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Introduction:
Causes of optic neuritis (ON) can be difficult to distinguish at presentation before results of serologic testing are known. We applied a novel deep-learning variational autoencoder (VAE) to determine whether OCT thickness maps can distinguish between typical and atypical (MOGAD vs. NMOSD) optic neuritis at presentation and at later time points.

Methods:
A total of 797 OCT scans from 97 healthy subjects and 2036 scans from 147 ON subjects were used to train a VAE model, resulting in 2 variables, d1 and d2, which depict a continuum of spatial patterns of retinal nerve fiber layer (RNFL) in a montage map with axes of d1(x-direction) and d2(y-direction). In the test set, OCT scans of the affected and unaffected eyes (147 MS, 26 MOGAD, and 26 NMOSD subjects) at the acute and chronic stages were identified by their location on the montage map. Average RNFL thickness in the acute and chronic stages were also compared between NMO, MOG, and MS.

Results:
Acute optic neuritis in MOGAD was associated with greater disc edema at presentation [184±81um] than NMO [124±46um (p=0.01)] or MS [99.1±24um (p=< 0.0001)]. NMO cases had lower RNFL thickness [61.2±18um] after 3 months vs MOG [73.4±14um p< 0.0001] or MS [76.6±20.4, p< 0.0001]. Our RNFL VAE map successfully depicted the RNFL spatial patterns in each patient and its change from acute to chronic state in MOGAD, NMO and typical ON.

Conclusions:
The RNFL is an important modality for the assessment of acute and chronic optic neuritis of different causes, and deep learning approaches may improve our ability to classify at presentation and predict outcomes. Ongoing work includes the incorporation of the spatial pattern of the retinal ganglion cell layer, RNFL, visual field, MRI and serologic information into a multi-channel model to diagnose causes of optic neuritis and help predict outcomes for assessment of treatment.

References: None provided.

Keywords: Optic neuritis, Demeylinating disease

Financial Disclosures: Judith Brody; Edward Linton; Jui-Kai (Ray) Wang: This study was supported, in part, by the Department of Veteran Affairs Center for the Prevention and Treatment of Visual Loss, Rehabilitation Research and Development (RR&D) I50RX003002, RR&D I01RX003797; Brett Johnson; Mark Kupersmith: ISMMS Neuro-Ophthalmology Research Fund; NYEEI Foundation; Mona Garvin: This study was supported, in part, by the Department of Veteran Affairs Center for the Prevention and Treatment of Visual Loss, Rehabilitation Research and Development (RR&D) I50RX003002, RR&D I01RX003797.; Riley Filister; David Szanto; Joseph Branco; Randy Kardon: Affiliations: Center for the Prevention and Treatment of Visual Loss, Iowa City VA Health Care System, Iowa City, IA, USA Department of Ophthalmology and Visual Sciences, The University of Iowa, Iowa City, IA, USA This study was supported, in part, by the Department of Veteran Affairs Center for the Prevention and Treatment of Visual Loss, Rehabilitation Research and Development (RR&D) I50RX003002, RR&D I01RX003797, RR&D I01RX001786, National Institutes of Health (NIH) R01EY031544, and NIH R01EY023279. The New York Eye and Ear Infirmary Foundation, New York, N.Y.; Alfiero & Lucia Palestroni Foundation, Inc. Englewood Cliffs, N.J, National Eye Institute (NEI) EY032522. FaceX LLC (Co-Founder)

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Retinal Nerve Fiber Layer Thinning in Pre-Symptomatic Alzheimer's Disease: A Case-Control Study

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Introduction:
Spectral Domain Optical Coherence Tomography (OCT) measurements are proposed to serve as potential biomarkers of Alzheimer's Disease (AD). We aimed to study OCT changes in cognitively intact individuals at risk of developing AD, to test the hypothesis that retinal neurodegenerative changes could detect AD earlier in pathological development, in the stage with no cognitive changes, when targeted therapeutics may be more efficacious.

Methods:
OCT of the optic nerve head and macula was performed in a cohort of consecutive subjects with normal cognition. Subjects were dichotomized based on their amyloid-PET status in amyloid positive (cases, pre-clinical AD) and negative (controls), using a pre-specified SUVR cut-off. We analyzed peri-papillary retinal nerve fiber layer (RNFL), average macular and ganglion cell inner plexiform layer (GCIPL) thickness and compared them between cases and age and gender-matched controls (two-tailed t-test, $p< 0.05$ showed statistical significance).

Results:
We enrolled 15 pre-clinical AD and 33 matched cognitively intact controls. The cases mean (SD) age was 74 years old and 20% were male. The subjects with preclinical AD showed near significantly lower overall RNFL thickness (83.9 vs 97 microns, $p = 0.06$), that showed statistically significant differences in the inferior quadrant (102 vs 127.8 microns, $p = 0.01$). There were no differences in the GCIPL ($p = 0.97$) or the average macular thickness ($p = 0.27$) between the two cohorts.

Conclusions:
Thinner RNFL was noted in subjects with normal cognition and positive amyloid-PET compared to age and gender-matched subjects with negative amyloid PET. Larger prospective studies should further evaluate the potential role of retinal layers thickness as a biomarker of preclinical AD.

References: 1. Porsteinsson, A.P., Isaacson, R.S., Knox, S. et al. Diagnosis of Early Alzheimer's Disease: Clinical Practice in 2021. J Prev Alzheimers Dis 8, 371–386 (2021). https://doi.org/10.14283/jpad.2021.23 2. Victor T.T. Chan, et al. Spectral-Domain OCT Measurements in Alzheimer's Disease: A Systematic Review and Meta-analysis, Ophthalmology, Volume 126, Issue 4, 2019.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Retina

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Grant Support: None.

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Spectral Domain Optical Coherence Tomography Bruch's Membrane Opening Minimum Rim Width as Quantitative Marker Of Optic Atrophy In Optic Disc Drusen

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Introduction:
Optic disc drusen (ODD) are deposits located in the optic nerve head (ONH). Visual field defects seen in ODD patients correspond to peripapillary retinal nerve fiber layer (ppRNFL) thinning seen in optical coherence tomography (OCT). A more recently introduced OCT ONH biomarker is Bruch's Membrane Opening Minimum Rim Width (BMO-MRW) which measures the width of the neuroretinal rim (NRW). This preliminary analysis aims on evaluating the predictive power of BMO-MRW on RNFL loss in ODD.

Methods:
Prospective clinical trial. Patients underwent a full one-day ophthalmological examination including best-corrected visual acuity (BCVA), standard automated visual fields (VF, Humphrey 30-2 SITA fast), echography, as well as OCT ppRNFL and BMO-MRW using the Heidelberg Engineering Spectralis SD-OCT. The existence of optic disc drusen was confirmed by echography and OCT. AUROC was calculated for BMO-MRW as a predictor of ppRNFL disorders which were determined based on the Heidelberg Engineering normative-data based SD-OCT RNFL classification.

Results:
42 eyes of 21 patients with ODD (16 females; 72%, mean age 43.2±18.3 years) and 23 eyes of 12 patients without ODD (4 females; 33.3%; mean age 24.6±1.64 years) were included up until the time of this analysis. Mean ppRNFL was 69.4±20.0 µm, and 94.8±8.7µm ($p< 0.001$), in the ODD, and control group, and mean BMO-MRW was 487.8±71.5µm, and 343±53.4µm ($p< 0.001$), respectively. Mean BCVA was 1.1±0.2 and 1.25±0 Snellen, mean VF mean deviation was -5.58±6.6 dB and -1.18±1.3 dB, respectively ($p< 0.001$). In the ODD group, AUROC for BMO-MRW as a predictor of optic atrophy was 0.2695.

Conclusions:
Our data suggests that in eyes with ODD, BMO-MRW is no valid measure of RNFL loss. Morphological ONH changes caused by ODD significantly increase tomographic NRW delineation, which compromises its diagnostic value. ODD should be ruled out using ophthalmic imaging before applying BMO-MRW measurement.

References: None provided.

Keywords: Optic neuropathy, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)

Financial Disclosures: Christoph Mitsch; Elena Terekhova; Martin Michl; Karl Kircher; Berthold Pemp: Received research support and/or personal compensation from Santhera Pharmaceuticals, Chiesi, and GenSight Biologics

Grant Support: None.

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Unique Signal Related to Vitreous Movement Seen with Real Time Magnetic Resonance Imaging

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Introduction:

This abstract aims to characterize the signal produced by vitreous following eye movement on real-time MRI (rtMRI). rtMRI utilizes a T1-weighted gradient echo sequence and rapid image acquisition to record movement of tissues in vivo. The vitreous body, being 98% water in addition to type II collagen and hyaluronic acid, is normally hypointense to the lens on T1-weighted imaging, but this transient signal is hyperintense (Sebag,PRER). This signal has not been described previously, and in characterizing it we intend to consider its significance and utility.

Methods:

Ten participants with normal neuro-ophthalmic function were enrolled in the non-blinded experimental study. Participants underwent rtMRI of each orbit while moving their eyes between primary, up, and downgaze. Each scan captured 90 frames over 77-seconds. Two periods of oscillation were imaged per eye (Figure 1). There was variation in the rate of eye movements. Angular velocity for each eye movement was estimated and change in signal intensity was recorded. Four measurements were taken per orbit. The association between change in signal intensity and angular velocity of eye rotation was assessed using Spearman's rank correlation coefficient.

Results:

The hyperintense vitreous signal on rtMRI follows rotation of the globe. This signal's whirled appearance begins adjacent to the sclera, decaying toward the center (Figure 2). Figure 3 plots the relationship between vitreous signal intensity and angular velocity of globe rotation. The Spearman coefficient was 0.848.

Conclusions:

This study demonstrates that the signal hyperintensity produced by vitreous in motion is related to the angular velocity of said vitreous, but there are likely many contributing factors such as axial length, age, phakic and posterior vitreous detachment status, and conditions influencing the viscosity or liquefaction of the vitreous. This signature deserves further investigation to aid basic understanding of vitreous biomechanics in addition to shedding light on pathologies related to vitreous traction and liquefaction.

References: 1. Sebag; Vitreous and Vision Degrading Myodesopsia, Progress in Retinal and Eye Research, Volume 79, 2020.

Keywords: Neuroimaging, Orbit, Ocular motility, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: N/A

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Healthcare Utilization for Eye Pain in the United States, 2008-2019

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Introduction:
Eye pain is a common reason for healthcare visits, but nationally representative estimates regarding the frequency of presentations and patterns of care are unknown. Our aim was to describe eye pain visits in the United States occurring in the ambulatory or emergency department (ED) setting.

Methods:
Retrospective, cross-sectional analysis of National Ambulatory Medical Care Survey and National Hospital Ambulatory Medical Care Survey data (2008-2019). Sample data were weighted to estimate ambulatory and emergency department (ED) eye pain visits, patient and provider characteristics, diagnoses, and follow-up care.

Results:
From 2008-2019, there were approximately 4 million (95% CI: 3,523,144, 4,705,344) ambulatory and 1 million (95% CI: 812,590,1,014,934) ED eye pain visits annually. Nearly half of ambulatory visits were for chronic eye pain (1.7 million [95% CI: 1,433,244,1,956,524]). Eye pain was the primary reason for the visit in 47.12% (95% CI: 43.05%,51.18%) of ambulatory and 69.47% (95% CI: 65.80%, 71.13%) of ED eye pain visits. In the ambulatory setting, most (48.18% [95% CI: 42.32%, 54.03%) visits were conducted by ophthalmologists. The most common diagnosis was unspecified conjunctivitis (H109) for acute eye pain and open-angle glaucoma (H401) for chronic eye pain in the ambulatory setting. The most common diagnoses was injury of conjunctiva and corneal abrasion w/o foreign body (S050) for ED setting. Additional follow-up was scheduled in 89.51% (95% CI:86.22%, 96.81%) of visits (acute = 86.89% [95%CI: 82.11%, 91.68%] vs chronic = 93.27% [95% CI: 89.89%, 96.64%]).

Conclusions:
Most eye pain visits take place in the outpatient setting with ophthalmologists and visits for chronic eye pain are common. In nearly half of these visits, eye pain was the primary reason for seeking care, and vision-threatening diagnoses were uncommon. Future studies to define patient outcomes and the association of practice patterns with outcomes should largely be aimed at eye provider practices.

References: None provided.

Keywords: Orbit/ocular pathology, Miscellaneous

Financial Disclosures: Letitia Pirau; Rehbi Abuzaitoun; Yue Pan; Maria Woodward; Lindsey De Lott: NIH grant

Grant Support: None.

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Teprotumumab (Tepezza)-Related Hyperglycemia Is Associated With Baseline Glycemic Status In Thyroid Eye Disease

Tracy Lang [1], Aaron Rael [1], Kristen Park [1], Jessica Chang [1], Sandy Zhang-Nunes [1]

[1] *Keck School of Medicine of USC*

Introduction:
Teprotumumab (Tepezza) is an insulin-like growth factor 1 receptor antagonist that was recently approved for the treatment of Thyroid Eye Disease (TED), a potentially sight-threatening and debilitating orbital inflammatory disease. Despite the relative safety of Teprotumumab, a risk of hyperglycemia was identified. We seek to identify to what extent Teprotumumab causes hyperglycemia in order to clarify current guidelines for monitoring of hyperglycemia as an adverse side effect of Teprotumumab.

Methods:
A retrospective chart review was performed on patients with TED seen at two large academic teaching hospitals from August 2021 to June 2023. We identified 211 patients with TED, of which 42 received Teprotumumab therapy. Demographics, blood glucose (BG) levels, and HbA1c levels were collected. BG levels were averaged across multiple visits.

Results:
The mean age was 58.2±13.08 years. 70% (30/43) were female and 30% (12/42) were male. 21.4% (9/42) were White, 16.7% (7/42) were African American, 19% (8/42) were Asian, and 42.9% (18/42) were other/unreported. For baseline glycemic status, either reported or measured by HbA1c, 84.4% (27/42) were normoglycemic, 16.3% (7/42) had pre-diabetes, and 20.9% (9/42) had diabetes. The mean BG level was 137.1±75.8 mg/dL. Hyperglycemic events (BG≥140 mg/dL or reported) while taking Teprotumumab ($p< 0.0001$) were significantly associated with baseline glycemic status ($p< 0.0001$). Of the 10 patients with reported hyperglycemic events during Teprotumumab therapy, 70% (7/10) had diabetes, 10% (1/10) had pre-diabetes, and 20% (2/10) were non-diabetic.

Conclusions:
This study suggests that baseline glycemic status is significantly associated with hyperglycemic events while taking Teprotumumab. Those with pre-diabetes or diabetes may be at increased risk of hyperglycemia while receiving Teprotumumab therapy. Future studies will be necessary to guide current screening and management of Teprotumumab-related hyperglycemia.

References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: Tracy Lang; Aaron Rael; Kristen Park; Jessica Chang; Sandy Zhang-Nunes: I commit to remain unbiased in our presentation. In fact, our findings report more adverse reactions to teprotumumab, which would not be in the interest of the company for whom I consult for occasionally. Our abstract is unbiased in both its data and its presentation. The data collected for this abstract is drawn from a patient population with thyroid eye disease who were referred for Teprotumumab not only by me, but by multiple other ophthalmologists. While I am involved in clinical trials with Horizon at our institution, none of the patients included in this study were enrolled in the clinical trial. Further, we received no funding or input from Horizon for this study. All data collection and analyses were performed by us. I am an occasional speaker and am a PI of their phase 4 clinical trial, however, my goal is to be truthful in reporting all findings, using rigorous scientific methods which try to eliminate any bias. My relationship with Horizon has not biased this study.

Grant Support: None.

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Teprotumumab thins the retinal nerve fiber layer from a normal baseline in thyroid orbitopathy patients.

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Introduction:
Thyroid eye disease (TED) is an autoimmune disease that causes inflammation of the orbital tissues which can lead to proptosis, diplopia, and blindness. Management strategies include glucocorticoids, radiation, and decompression surgery. Teprotumumab, a monoclonal antibody, works by inhibiting the IGF-1R receptor and has been shown to improve proptosis, and the inflammatory signs and symptoms of TED. Prior to teprotumumab treatment and on subsequent visits, we obtained optical coherence tomography retinal nerve thickness (OCT RNFL) thickness measurements. Interestingly we began observing a reduction of RNFL thickness from a normal baseline over the course of treatment.

Methods:
RNFL thickness measurements of 13 patients who received the full 6-month course of teprotumumab were analyzed using the ZEISS CIRRUS OCT. We continued to monitor RNLF thickness post treatment and have data on 5 of these patients. All patients had normal RNFL thickness measurements at baseline with no evidence of optic nerve dysfunction from either compressive optic neuropathy or elevated intraocular pressure. One patient who had TED but did not receive teprotumumab served as the control.

Results:
On average the OCT RNLF thickness decreased from baseline at 6 months by 6.26 microns compared to control. Interestingly in the 5 patients whose measurements were obtained at least 4 months following treatment, the RNF thickness began increasing and on average was decreased by 4.6 microns. No patient had any clinical decline in their optic nerve function.

Conclusions:
We found a significant decrease in RNFL thickness from an initial normal baseline in our patients treated with teprotumumab for TED while maintaining clinically normal optic nerve function. In addition, the decrease in RNFL thickness began reversing itself following treatment. Because OCT RNFL also measures the non-axonal contents which do not represent neuronal tissues, including Muller cells, perhaps blocking IGF-1R receptors affects these components.

References: None provided.

Keywords: Graves' disease, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)

Financial Disclosures: Mitchell Strominger: Horizon therapeutics speakers board; Gagan Riar

Grant Support: None.

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The Effect Of Teprotumumab On Anti-Thyroid Antibody Positive Versus Antibody Negative Thyroid Eye Disease Patients

Zahir Sheikh [1], Prem Subramanian [1], Anne Lynch [2], Nathan Grove [2], Emily Auer [2]

[1] Sue Anschutz-Rodgers University of Colorado Eye Center, [2] Department of Ophthalmology, University of Colorado School of Medicine

Introduction:
The pathophysiology of thyroid eye disease (TED) is based upon the formation of a complex between the TSH receptor antibody, and the TSH and IGF-1 receptors leading to orbital tissue expansion. We hypothesize that an absence of TSH receptor antibodies results in decreased IGF-1/TSH receptor complexes thus diminishing the effect of teprotumumab, an IGF-1 receptor blocker. In this pilot study we assess the difference in effect of teprotumumab between patients who are Ab+ and Ab-.

Methods:
In this single center, retrospective study we compared the effect of teprotumumab in Ab+ and Ab- TED patients (January 2020 through the present). Clinical response was determined by comparing symptoms and physical exam findings before and after treatment. Logistic and linear regression using generalized estimating equations were used to assess the magnitude of difference in change in findings before and after treatment between Ab+ and Ab- individuals.

Results:
6 Ab+ and 6 Ab- subjects were included. There were similar improvements in symptoms among Ab+ and Ab- group. Following treatment, Ab- individuals appeared to have greater improvement in proptosis [1.2 mm (95%CI: -1.5-3.8, p=0.40) OD and 0.63 mm (95%CI: -1.9-3.2, p=0.63) OS], motility [0.60 (95%CI: -0.10-1.3, p=0.092) OD and 0.56 (95%CI: -0.45-1.6, p=0.28) OS], and strabismus [vertical deviation 8.6 PD (95% CI: -0.45-18, p=0.063), and horizontal deviation 2.8 PD (95% CI: -0.80 to 14, p=0.61)] compared to Ab+ individuals. In the three available muscle biopsies from three Ab- patients, only one revealed evidence of muscle fiber hypertrophy, but all lacked inflammation or deposition.

Conclusions:
Our results suggest that Ab- individuals may show a better response to treatment with teprotumumab than Ab+ individuals. Furthermore, the available muscle biopsy data may suggest differences in pathophysiology between Ab- and Ab+ TED.

References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Graves' disease, Orbit/ocular pathology, Ocular motility, Orbit

Financial Disclosures: Zahir Sheikh; Prem Subramanian: P.S. Subramanian is a consultant for ACELYRIN, GenSight, Horizon (now Amgen), Tourmaline Bio, and Viridian.; Anne Lynch; Nathan Grove; Emily Auer

Grant Support: None.

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THRIVE and THRIVE-2: Phase 3 Trials of VRDN-001 in Thyroid Eye Disease: Next Generation Insulin-like Growth Factor-1 Receptor Blockade

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Introduction:
VRDN-001, a full antagonist antibody to the insulin-like growth factor-1 receptor (IGF-1R), is in development for treatment of thyroid eye disease (TED). Initial results from phase 2 proof-of-concept studies of 2 infusions of VRDN-001 in patients with moderate-to-severe active and chronic TED demonstrated clinically meaningful improvements in TED symptoms at 6 weeks. THRIVE and THRIVE-2 are double-masked, placebo-controlled phase 3 registrational trials to evaluate the safety and efficacy of VRDN-001 for TED.

Methods:
Both THRIVE and THRIVE-2 will investigate 5 infusions of 10 mg/kg VRDN-001 vs placebo administered every 3 weeks in patients with moderate-to-severe TED. THRIVE will enroll adult patients with a clinical activity score (CAS) of ≥3 and onset of signs and symptoms within 15 months of enrollment. THRIVE-2 will enroll patients with any CAS and presence of signs and symptoms >15 months before enrollment. For both studies, the primary efficacy endpoint for regulatory submission will be assessed at 15 weeks (3 weeks after 5th infusion); in the United States, Canada, and China the primary endpoint is proptosis responder rate, defined as ≥2-mm reduction on exophthalmometry, and in Australia, Israel, Turkey, the European Union, and the United Kingdom, it is overall responder rate, defined as proptosis response (≥2-mm reduction) and either ≥2-point reduction (THRIVE) or no worsening (THRIVE-2) in CAS. Secondary and exploratory endpoints include measures of diplopia, CAS, MRI/CT volumetric analyses, and quality of life. Safety and tolerability will be assessed through 52 weeks. Participants in both trials without a proptosis response at week 15 (placebo or active) may roll over into an open-label treatment study to receive VRDN-001.

Results:
None

Conclusions:
Currently enrolling THRIVE and THRIVE-2 studies will assess the efficacy and safety of 5 infusions of VRDN-001, an investigational treatment for TED designed for fewer infusions, lower antibody dose, shorter infusion time, and decreased treatment burden.

References: None provided.

Keywords: Graves' disease, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Orbit/ocular pathology

Financial Disclosures: Barrett Katz: Employee of Viridian Therapeutics; Rochelle Summerfelt: Employee of Viridian Therapeutics; Thomas Ciulla: Employee of Viridian Therapeutics

Grant Support: None.

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Treatment Outcomes Of Primary Optic Nerve Sheath Menigiomas At A Tertiary Cancer Center

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Introduction:
Assessment of the visual outcomes of different treatment modalities and treatment-related outcomes of primary optic nerve sheath meningioma (ONSM).

Methods:
Sixteen patients with confirmed primary optic nerve sheath meningiomas from the MD Anderson Cancer Center database that received treatment from 2010 to 2023 were reviewed to analyze their treatment modalities and outcomes. The primary outcome measure was BCVA post-treatment. Secondary outcomes measures included acute toxicities and chronic toxicities related to treatment

Results:
16 patients, 9 females (56.25%) and 7 males (42.75%) with a mean age of 47.8 years (9-80) were included in the review. Two were treated with surgical debulking only (12.5%), one was treated with conventional radiotherapy (6.25%), seven were treated with proton beam therapy (43.75%), four (25%) received a combination therapy of surgical debulking and radiotherapy/ proton therapy, and two (12.5%) underwent observation only. Eight patients (50.0%) vision remained stable of which two (25.0%) were treated with surgery, two with proton therapy (25.0%), two (25.0%) were observed, one was combination therapy (12.5%) and one was radiotherapy (12.5%). Five (31.3%) had visual improvement of which three (60%) were treated with combination therapy and two (40%) were treated with proton therapy. Three (18.8%) showed worse vision following treatment, all were treated with proton therapy (100%). Three (18.8%) experienced acute toxicity, one (33.3%) from the proton therapy group, one (33.3%) from the surgical only group, and one (33.3%) from the combination group. Ten (62.5%) experienced chronic toxicity, six (60.0%) from the proton treatment group, one (10.0%) from the surgical only group, and three (30.0%) from the combination group.

Conclusions:
The combination group had the greatest number with improved visual acuity. The Proton therapy had the second most patients with visual improvement but also had the greatest number of patients with worsened visual acuity post-treatment and the most patients that experiences chronic toxicities.

References: None provided.

Keywords: Tumors, Orbit/ocular pathology, Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Accommodative Response in Adolescents with Concussion to Static and Moving Targets

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[1] Spencer Center for Vision Research, Byers Eye Institute at Stanford University, [2] Boston Children's Hospital, Harvard Medical School, [3] Pennsylvania College of Optometry, Salus University

Introduction:
Individuals with post-concussion syndrome often report blurred vision when viewing moving targets. We investigated the accommodative response of concussed and control participants viewing static vs moving stimuli under monocular and binocular viewing conditions.

Methods:
Thirty adolescents previously diagnosed with concussion (14.7 ± 2.0 years; mean days since concussion: 95 ± 26 days,) and 31 healthy controls (14.7 ± 2.0 years) participated. Participants viewed a movie on an iPod binocularly and monocularly under randomized dynamic and static viewing conditions. For dynamic, the stimulus moved sinusoidally between 1m and 25cm (3D change) and between 50cm and 33cm (1D change) at a frequency of 0.1Hz. For static, the participant viewed the stimulus at each demand for 15 seconds. Accommodative responses were measured using photorefraction. The difference in the response at the peak and trough for dynamic and the difference in the average response for static was calculated for each change in demand. A three-factor repeated measures analysis of variance (group: concussed, control; viewing condition: monocular, binocular; motion: dynamic, static) was used to analyze the change in accommodative response for each change in accommodative demand.

Results:
There were significant main effects of group, viewing condition, and motion, with changes in response significantly larger in control participants when viewing the stimulus binocularly and dynamically for the change in 3D (group: $F=8.64$, $p=0.01$; viewing condition: $F=44.31$, $p< 0.001$; motion: $F=5.50$, $p=0.02$) and 1D (Group: $F=6.04$, $p=0.02$; viewing condition: $F=17.31$, $p< 0.001$; motion: $F=44.78$, $p< 0.001$) demands.

Conclusions:
On average, individuals with concussion had worse accommodative responses than controls. On average, the greatest accommodative responses were generated when viewing dynamic stimuli binocularly, suggesting vergence enhances the accommodative response. Further work is required to understand the complex interactions between motion and binocularity in adolescents with concussion and how these interactions may impact symptoms when viewing dynamic and static stimuli at near.

References: None provided.

Keywords: Pediatric neuro-ophthalmology

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Adaptive Functioning And Relationship To Visual Behavior In Children With Cerebral Visual Impairment

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Introduction:
Cerebral visual impairment (CVI) is the leading cause of pediatric visual impairment in developed countries and is associated with neurologic conditions that may impair adaptive functioning. However, adaptive behavior in children with CVI has not been systematically studied, and the relationship between visual function and adaptive function (e.g. communication, socialization, and daily living skills) in CVI is unknown(1).

Methods:
We prospectively recruited 49 children with CVI (mean age 4.9 years). Adaptive behavior was evaluated using the Vineland Adaptive Behavior Scale, 3rd edition, (VABS-III) which was completed by the child's caregiver. Visual acuity was assessed by a pediatric neuro-ophthalmologist using the 6-level Visual Behavior Scale (VBS). VBS and VABS-III overall, domain, and subdomain scores were correlated. Multiple regression analysis was used to evaluate the effect of demographic and clinical factors on the relationship between VBS and VABS-III scores.

Results:
In our cohort, mean adaptive behavior scores were below the 1st percentile on all VABS-III domains and subdomains. Visual acuity, as assessed by VBS, was significantly correlated with VABS-III communication ($r=0.31$, $p=0.03$) and socialization ($r=0.31$, $p=0.03$) domain scores. On multivariate analysis, when correcting for age, sex, and neurologic comorbidities, the association between VBS score and VABS-III domain scores was borderline ($p=0.05$ and $p=0.08$).

Conclusions:
Children with CVI have significantly reduced adaptive functioning. Visual behavior correlates with communication and socialization skills, and this effect is partially mediated by neurologic comorbidities. Future longitudinal studies should evaluate whether adaptive functioning increases as visual acuity improves in children with CVI, which may have prognostic implications.

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Analysis of saccadic latency in paediatric pseudotumour cerebri syndrome (PTCS) - A potential novel biomarker and parameter for disease monitoring

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Introduction:
Pediatric PTSC poses an infrequent but potentially significant risk to sight from optic neuropathy. Less is known about the cortical consequences of raised intracranial pressure (ICP) in the pediatric developing brain. Understanding this aspect of the disease is important and could provide useful biomarkers for disease monitoring. Analyzing saccadic latency may provide such an insight. We present a novel portable device allowing capture and analysis of the saccadic latencies of awake children as young as 5 in the outpatient setting.

Methods:
In this prospective pilot study, we used a portable saccadometer device to compare saccadic latency in children at presentation and diagnosis of PTSC (confirmed at subsequent lumbar puncture) aged 5-18 years old vs controls. Testing consisted of a dynamic step task of 200 saccades. Additionally, baseline BCVA, color vision, disc OCT and orthoptics were performed. Any abduction deficit resulted in exclusion.

Results:
9 PTSC patients (7F:2M, mean age 10.0 years) were compared against 9 controls (7F:2M mean age 9.2 years). Mean opening pressure was 35cmH 2 0 (30-40). Baseline mean disc OCT rNFL (PTSC group) was 219um and baseline mean BCVA was 0.06 vs 0.00 (PTSC vs controls respectively). Mean saccadic latency was 258ms (95% CI 242-262ms) vs 190ms (95% CI 175-204ms) $p< 0.0001$ and mean promptness (1/saccadic latency) was 0.0038ms -1 vs 0.0052ms -1 $p< 0.0001$ in the PTSC vs control group respectively.

Conclusions:
In this pilot study, saccadic latency was significantly prolonged in children with PTSC. This association may indicate raised ICP disrupts neural circuits involved in saccadic initiation and may also reflect wider cortical disruption. Saccadic latency may offer a useful novel biomarker, easily obtained in children as young as 5 in the outpatient setting for disease monitoring in pediatric PTSC. This is an IRB approved study with Health Canada Approval of the portable saccadometer.

References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Optic neuropathy, Ocular motility

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Exploring the Etiologies Underlying Pediatric Papilledema at a Tertiary Care Children's Hospital

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Introduction:
Causes of pediatric papilledema include devastating neurologic disorders and idiopathic intracranial hypertension (IIH). Early identification of papilledema can help initiate urgent workup and prevent vision loss. A study of ophthalmology consultations at a large children's hospital found concern for papilledema to be the most common reason for consultation, and they noted a rising incidence of these requests (1). However, the underlying diagnosis in children with true papilledema has only been described in a community outpatient pediatric ophthalmology patient cohort (2). We describe the underlying causes and characteristics of patients diagnosed with papilledema at a tertiary care children's hospital.

Methods:
Retrospective chart review of all patients seen in pediatric ophthalmology consultation or diagnosed with papilledema at a large children's hospital between 01/01/2020-08/18/2023 was performed. Patients with disc edema and intracranial hypertension were identified. Data collected included demographics, opening pressure, encounter location, consulting question, and final diagnosis.

Results:
1736 patients were reviewed during the study period, and 81 patients were found to have papilledema with confirmed or clinically suggested intracranial hypertension [13±1.10 years old; 67.90% female; 49.32% seen as inpatients; 46.58% seen in the ED]. The most common initial consulting questions were papilledema seen by an outside provider (30.00%), evaluating for papilledema (25.71%), blurry vision / vision loss (20.00%), headaches (7.14%), and non-accidental trauma (7.14%). The most common diagnoses associated with papilledema included IIH (51.85%), venous sinus thrombosis (6.17%), subdural hematomas (6.17%), meningitis (4.94%), acute myeloid leukemia (3.70%), and optic neuritis (3.70%). Of the 42 patients with IIH, there were four cases of fulminant IIH (9.52%).

Conclusions:
Pediatric papilledema is associated with a wide range of underlying conditions and requires a comprehensive, multidisciplinary evaluation in an emergency setting. At a tertiary care children's hospital, papilledema is most often caused by IIH.

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Keywords: Pediatric neuro-ophthalmology, High intracranial pressure/headache, Pseudotumor cerebri

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Grant Support: SOUP Award, Emory Eye Center

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Large Language Models' Performance in Generating Patient Education Materials on Pediatric Optic Neuritis

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Introduction:
Artificial intelligence-based large language models (LLM) are capable of generating responses to queries, but their use in generating health information has not been established. This study evaluates the accuracy of ChatGPT and Google Bard responses to parents' frequently asked questions about pediatric optic neuritis.

Methods:
Ten frequently asked questions and responses published on websites of national ophthalmology organizations/hospitals were compiled in this cross-sectional study. The questions were individually entered into ChatGPT and Google Bard chat windows. Three pediatric neuro-ophthalmologists graded responses sentence by sentence as true or false. Descriptive statistics and the Mann-Whitney U test were used to compare the average accuracy both among all questions and per category of question between ChatGPT responses, Google Bard responses, and reference website responses.

Results:
Among all questions, the accuracy of ChatGPT responses (93.9%) was significantly higher (p=0.026) than that of Google Bard responses (85.1%). There was no significant difference between the accuracy of website responses (83.4%) and ChatGPT (p=0.183) or Google Bard (p=0.850) responses. Among all ChatGPT responses, those regarding the prognosis and treatment (n=5) demonstrated the highest accuracy (97.5%) while those regarding diagnosis, signs, and symptoms (n=2) demonstrated the lowest accuracy (85.8%). Among all Google Bard responses, those regarding diagnosis, signs, and symptoms demonstrated the highest accuracy (94.9%), while those regarding the pathophysiology demonstrated the lowest accuracy (75.0%). While 30% of website responses were graded as completely accurate, 20% of ChatGPT responses and no Google Bard responses were graded as completely accurate.

Conclusions:
This is the first study to assess the accuracy of LLMs in generating patient-facing information in neuro-ophthalmology. Although ChatGPT generated more accurate responses than Google Bard, the public should be very cautious when using any online resources for medical information and should rely on board-certified ophthalmologists for medical care. Future studies could investigate the readability and comprehensiveness of LLM-generated information.

References: None provided.

Keywords: Optic neuritis, Pediatric neuro-ophthalmology, Miscellaneous

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OCT Findings In Pediatric MOG Optic Neuritis: A Multicenter Retrospective Cohort Study

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Introduction:
Myelin Oligodendrocyte Glycoprotein Antibody Disease (MOGAD) is a common cause of pediatric optic neuritis. Visual acuity at the onset of optic neuritis is typically worse in pediatric patients compared to adults but with better visual outcomes.1,2 Optical Coherence Tomography (OCT) has been shown to be a sensitive biomarker for optic nerve injury in adult patients with MOGAD-optic neuritis; however, there is a paucity of literature regarding OCT findings in pediatric MOGAD-optic neuritis. We present a retrospective, multi-center study to evaluate the correlation between OCT findings and visual outcomes in pediatric MOGAD optic neuritis patients.

Methods:
We are performing a retrospective chart review examining OCT findings in pediatric patients with MOGAD-related optic neuritis seen at three centers from 2016-2022. We will evaluate initial and final average RNFL and GCL measurements in these patients to evaluate the correlation between OCT metrics and visual acuity outcomes in MOGAD, as well as in a small subset of neuromyelitis optica (NMO).

Results:
Data collection is ongoing, and the preliminary cohort includes 22 MOGAD and 3 NMO patients. In the MOGAD subset, 14 (64%) are female with median age of 10.2 (IQR 8.0-11.7). Median follow-up was 1071 days (IQR 305-1372). In the NMO subset, 2 (67%) are female, and median age is 11.3 years (IQR 7.6-12.9). Median follow-up was 1492 days (IQR 877-1599).

Conclusions:
Further results and discussion will be presented at the conference.

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Keywords: Demeylinating disease, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Pediatric neuro-ophthalmology, Optic neuritis, Miscellaneous

Financial Disclosures: Johanna Yun; Ridhima Guniganti; Erin Lanzo; Shinji Rho; Melley Fesseha; Soe Mar; Andrew Lee; Margaret Reynolds; John Paddock; Cristiano Oliveira; Sachin Kedar: Consultant for Astra-Zeneca; Jason Peragallo; Marc Dinkin; Grace Gombolay; Gregory Van Stavern

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Ophthalmologic Complications in NF1 Patients Treated with MEK Inhibitors

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Introduction:
MEK inhibitors are novel, promising therapies for Neurofibromatosis type 1 (NF1) manifestations including optic gliomas. Due to known potential ophthalmic side effects, such as MEKi associated retinopathy (MEKAR), patients undergoing MEKi treatment receive routine ophthalmology evaluation. Our study scrutinizes the necessity of such routine screening in a largely pediatric population of NF1 patients on MEKi by examining the frequency of ocular adverse events (OAE).

Methods:
We retrospectively reviewed 45 patients with NF1 on MEKi. Inclusion criteria were baseline exam and follow up exam after starting MEKi. A dilated fundus exam, ocular coherence tomography of macula and nerve fiber layer, and Humphrey visual field were obtained at every exam. MEKi type and duration, primary tumor, and clinic course were also noted.

Results:
26 patients were included with average age was 13 years (range 2 to 23) and mean follow up of 413 days. Patients were treated with selumetinib (77%), trametinib (23%), and mirdametinib (4%). Zero patients developed retinopathy at any point during the study. While some patients had preexisting optic neuropathies (27%), no patients developed nerve changes after starting MEKi. Four patients (15%) developed signs of dry eye, and all four were controlled with topical lubrication. There were no OAEs that lead to stopping MEKi treatment.

Conclusions:
MEK inhibitor associated ocular toxicities have been well documented in the literature, thus, the standard of care has been for patients to undergo close ophthalmic follow up while on treatment. Our negative findings suggest the largely pediatric population affected by NF1 may be less prone to ocular toxicity experienced by the largely older oncology patients in literature. While eye examinations are essential in our patients who often have optic gliomas, repeated surveillance for MEKi is likely not indicated and can be safely decreased. Further studies on this topic are needed.

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Keywords: Tumors, Pediatric neuro-ophthalmology, Chemotherapy and radiation injury

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Quality And Agreement Of Papilledema And Pseudopapilledema Classification Among Pediatric Neuro-Ophthalmologists Using Optic Disc Photographs

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Introduction:
Differentiating papilledema from pseudopapilledema is a common pediatric neuro-ophthalmologic dilemma. Serial fundus photographs are frequently used to clarify diagnosis, but the accuracy and inter-rater reliability of neuro-ophthalmologists in interpreting these images are unknown. The purpose of this study was to evaluate the performance of three masked pediatric neuro-ophthalmologists who classified fundus photographs of children with papilledema and pseudopapilledema.

Methods:
Experts graded a multi-center image collection comprising 659 optic disc photographs. Image grading was performed in the same order for each grader and in a fashion blinded to clinical information and grader responses. Papilledema and pseudopapilledema were separately diagnosed for each patient by pediatric neuro-ophthalmologists with all relevant, longitudinal clinical information. Accuracy, sensitivity, and specificity were calculated to determine grading performance; Fleiss' kappa (κ) was calculated to assess inter-rater agreement. A subgroup analysis for papilledema grade (low/high grade = Frisen grades 1-2/3-5) was performed.

Results:
Accuracy, sensitivity, and specificity for detecting papilledema ranged from 58.9-63.9%, 54.3-76.0%, and 56.1-62.6%, respectively. The κ values for the full-dataset, papilledema photos only, and pseudopapilledema photos only were 0.36, 0.40, and 0.28, respectively. The expert-grader ranges of accuracy, sensitivity, and specificity for low- and high-grade papilledema were 53.0-59.0%, 28.0-62.3%, and 56.1-62.6% (low-grade papilledema) and 64.3-67.4%, 84.8-93.8%, and 56.1-62.6% (high-grade papilledema). κ was 0.28 and 0.39 for low- and high-grade papilledema cases, respectively.

Conclusions:
When evaluating fundus photographs, pediatric neuro-ophthalmologists demonstrated moderate accuracy and fair agreement in classifying pediatric papilledema and pseudopapilledema. Accuracy and agreement were lower among experts for low-grade papilledema, reflecting the relative challenge of this diagnosis. These findings suggest the need for objective diagnostic tools, e.g., AI-assisted modalities, when depending solely on fundus photography to determine the likelihood of papilledema.

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Keywords: Pediatric neuro-ophthalmology, High intracranial pressure/headache, Optic neuropathy

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Retinal Nerve Fiber Layer Thickness in Children with Isolated Growth Hormone Deficiency

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Introduction:
Isolated growth hormone deficiency (iGHD) is a condition causing severe short stature due to a lack of growth hormone (GH). GH's impact on the eye, particularly retinal nerve fiber layer (RNFL), is unclear. GH's multifaceted roles in cellular growth, differentiation, and metabolism raise questions about its effects on the RNFL, which is closely linked to retinal ganglion cells and the optic nerve head. This study examines RNFL thickness in pediatric iGHD patients and how recombinant human GH treatment affects it, shedding light on the ocular consequences of GH deficiency and the relationship between GH and RNFL integrity in children.

Methods:
In this study, 24 children with iGHD were compared to 28 healthy children. RNFL thickness was measured using Heidelberg optical coherence tomography, with repeat measurements in the iGHD group after at least 6 months of GH treatment.

Results:
Both groups were sex and age-matched. In the iGHD group, the second RNFL thickness measurements, taken on average at 8 months into treatment, showed no statistically significant difference compared to the control group ($p > 0.05$). Additionally, growth hormone treatment did not significantly alter RNFL thickness in the iGHD group ($p > 0.05$).

Conclusions:
While GH is known to be present in ocular tissues and has been linked to various aspects of retinal function, our study did not find any significant impact of IGHD or GH treatment on RNFL thickness. This aligns with previous research suggesting that GH may not play a substantial role in postnatal retinal development. Our findings also emphasize the intricate regulatory mechanisms involved in ocular development, with other factors likely contributing to visual health. In neuro-ophthalmology, it's vital to avoid automatically associating changes in RNFL thickness with GH deficiency in IGHD patients, underscoring the need to consider a wide range of factors during RNFL assessments.

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Keywords: Pediatric neuro-ophthalmology, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Retina

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The Relationship Between Foveal Sensitivity and Visual Acuity in Pediatric Idiopathic Intracranial Hypertension

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Introduction:
Idiopathic intracranial hypertension (IIH) in children has the potential to cause profound and permanent vision loss. Several factors have been shown to correlate with visual acuity, but none thus far have examined the relationship between foveal sensitivity (reported as foveal threshold by Humphrey visual field testing) and visual acuity in children. Because foveal sensitivity is established early in the course of testing, it may be a more reliable and predictable measure of visual function in children compared to other parameters.

Methods:
A retrospective chart review of visual field and clinical data was conducted. One hundred eyes from 50 pediatric subjects aged younger than 18 years were analyzed for foveal sensitivity and best-corrected visual acuity in each eye. A Spearman's rank correlation coefficient and p-value were calculated to compare the relationship between these two variables.

Results:
A statistically significant negative correlation was found between foveal sensitivity and best-corrected visual acuity ($r_s = -0.31$, $p < 0.01$). As visual acuity improved, foveal sensitivity also improved. This suggests that foveal sensitivity may be a predictor of visual acuity in children with IIH.

Conclusions:
Prior studies demonstrated that foveal sensitivity correlates with visual acuity in healthy and unhealthy eyes, but that the extent of the relationship depends on the underlying disease state of the eye. To date, this is the first study comparing these variables in children with IIH. In addition to serving as a predictor of central visual function, foveal sensitivity may also be useful in cases of nonorganic vision loss.

References: None provided.

Keywords: Pediatric neuro-ophthalmology, High intracranial pressure/headache, Perimetry, Pseudotumor cerebri, Visual fields

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Vergence and accommodation deficits in adolescents with concussion

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Introduction:
To characterize vergence and accommodation deficits in visually symptomatic children and adolescents with concussion compared to age-matched healthy control.

Methods:
A prospective observational study of 33 concussed and 32 controls with best corrected visual acuity of 20/25 in each eye and no history of any ocular diseases participated. The control group had no history of concussion or past known deficits in vergence and accommodation. All subjects had a standard of care eye exam including vergence and accommodation measures and cycloplegic refraction. Vergence measures included near point of convergence (NPC), divergence amplitude (DA), convergence amplitude (CA), vergence facility (VF). Accommodative measures included amplitude of accommodation (AA). Participants were randomized to testing order for vergence or accommodation. Participants who failed individual clinical tests and frequency of vergence and accommodation deficits based on established normative data are reported. Chi-square assessed group differences in vergence and accommodation deficits.

Results:
Among the patients with concussion (mean age 13.3±2.3 years; 76% female; median 107(36-273) days from injury) and the controls (mean age 12.7±2.1 years; 56% female) NPC was failed by 21(64%) to 1(3%); DA by 5(15%) to 0(0%); CA 21(64%) to 1(3%); vergence facility 15(43%) to 3(9%) and AA 25(76%) to 1(3%), respectively. Vergence deficits were more frequent in the concussed (21(64%); 7 convergence insufficiency (CI); 12 convergence deficit (CD); 1 convergence excess (CE) and 1 fusional vergence dysfunction (FVD) than the control group (2 (6%), 1 CI and 1 FVD) (Chi square=23.40; $p< 0.000$). Accommodative insufficiency was more frequent in the concussed (25 (76%) than the control group 1(3%); (Chi square = 35.71, $p< 0.000$).

Conclusions:
Symptomatic concussion patients had high frequency of vergence and accommodation deficits even at 4 months post-injury. Testing for NPC and /or AA are good screening tools to identifying patients with these deficits following concussion.

References: None provided.

Keywords: Pediatric neuro-ophthalmology, Miscellaneous

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Headache Medicine Update [2.0 CME] - Wednesday, March 6th

Moderators: Deborah I. Friedman, MD, MPH & Dane A. Breker, MD

The overlap between headache medicine, neuro-ophthalmology and neuro-otology is broad and almost unescapable in clinical practice. This session covers clinical aspects of headache medicine, such as visual and ophthalmic manifestations of primary disorders, vestibular migraine, cephalgic causes of eye pain, and new migraine treatments.

Upon completion of this session, participants should be able to: (1) Debate whether recurrent painful ophthalmoplegic neuropathy is a form of migraine or secondary disorder, (2) Identify patients with eye pain who should be referred to a headache specialist/ neurologist, (3) Diagnose vestibular migraine, (4) Describe why blurred vision is not a type of migraine aura.

- **Migraine Epidemiology, Diagnosis and Pathophysiology**, *Adriana C Rodriguez Leon, MD*
- **Visual Manifestations of Migraine**, *Kathleen B. Digre, MD*
- **New and Emerging Migraine Treatments**, *Benjamin Frishberg, MD*
- **Eye Pain - When to Refer**, *Stacy V. Smith, MD*
- **Cluster and Trigeminal Autonomic Cephalalgias**, *Deborah I. Friedman, MD, MPH*
- **Recurrent Painful Ophthalmoplegic Neuropathy or Ophthalmoplegic Migraine – Which is it?** *Vivek Lal, MD*

SYMPOSIUM: UPDATE ON HEADACHE MEDICINE

MIGRAINE AND MEDICATION OVERUSE HEADACHES (MOH): EPIDEMIOLOGY, DIAGNOSIS AND PATHOPHYSIOLOGY

Adriana C. Rodriguez Leon, MD, Clinical Assistant Professor Neurology & Neuro-Ophthalmology

University of Iowa Hospitals and Clinics

Iowa, United States

LEARNING OBJECTIVES

1. The attendee will be able to describe migraine disorders, name the different sub-types and know the incidence, prevalence, and demographics
2. The attendee will be able to diagnose the different sub-types of migraines and their pathophysiology
3. The attendee will be able to name and explain the most common treatment approaches to migraine disorders
4. The attendee will be able to identify and explain risk factors associated to migraines including analgesic overuse and medication overuse headaches

CME QUESTIONS

1. A 34-year-old woman presents for headache management. She describes a history of severe throbbing/pulsating headaches, which are primarily right-sided with occasional left-sided occurrence. She has associated nausea and occasional vomiting and reports being significantly sensitive to any light or sound during a headache, causing her to spend the day in bed. Her headaches have been slowly worsening in frequency and she averages at least 18 days of these headaches per month, and this frequency has been present for at least 7 months. She has normal neurologic examination and denies any other associated symptoms. What is the most accurate diagnosis based on her history?

    A. Migraine with typical aura, non-intractable
    B. Chronic migraine, intractable, without aura
    C. Episodic migraine
    D. Chronic migraine, non-intractable, without aura
    E. Migraine with typical aura, intractable

2. A 25-year-old woman with a PMH of Fibromyalgia, IBS, and anxiety, presents to your clinic with a headache. She reports that her headache started in her teenage years without any inciting incident. They are severe, throbbing, and last approximately 5 hours. They are associated with photophobia, phonophobia and osmophobia. She has nausea, but no vomiting. Sometimes her headaches are associated with tearing of both eyes. They are usually unilateral and can be localized to either the left side or the right side. She has paresthesias of her left or right arm that precede headache pain for about 5 minutes. These headaches happen approximately 2 days a month, and she does not take

any medication for it, preferring to sleep in a dark, quiet place instead. For a severe episode, she went to ER, and they provided her with oxygen and a "migraine cocktail". Which relieved her symptoms. Today's physical exam is normal. Assuming a negative workup, what is the most likely diagnosis according to ICHD3?

A. Cluster headache
B. Migraine with typical aura
C. Chronic migraine without aura
D. Migraine with atypical aura
E. Paroxysmal hemicrania

3. A 28-year-old woman with a PMH of Epilepsy and Migraines, presents to the ER with a headache. She reports that her current headache is typical but has been unremitting for 4 days. Her usual headache lasts approximately 4 hours and usually can be aborted with Zolmitriptan nasal spray. However, repeated Zolmitriptan uses have been ineffective for current episode. Her last dose was 3 hours ago. Her seizures are well controlled on Topiramate, and she takes no other medications. Assume all workup is negative, what is the suitable treatment for her headache.

A. Fentanyl patch
B. Dilaudid IV
C. Prochlorperazine IV
D. Valproic acid IC
E. DHE IV

4. A 22-year-old man presented to the ER with a severe headache. This is his third atack in the past 8 weeks. His headaches are bilateral and squeezing in charactaer at the beginning, and then they have some throbbing. They can last 8-12 hours. They are associated with neck pain and nausea. The headache is not made worse by, nor does it preclude routine physical activity. He denies sensitivity to noise but does admit to some light sensitivity. Neurological examination is normal. His headaches appear most consistent with which diagnosis?

A. Migraine without aura
B. Paroxysmal hemicrania
C. Tension-type headache
D. Probable migraine
E. Secondary headache disorder

CME ANSWERS

1. **B**- Chronic migraine, as per ICHD-3, is defined as a recurrent headache disorder, with attacks that last from 4 to 72 hours (about 3 days). Typically, unilateral (although can be bilateral or holocephalic), throbbing in quality, moderate to severe in intensity (7-10/10), aggravated by routine physical activity (walking going up or downstairs), with associated photophobia, phonophobia nausea and/or vomiting. Recurrent headache disorder manifesting in attacks lasting 4-72 hours (about 3 days). Typical characteristics of the headache are unilateral location, pulsating quality,

moderate or severe intensity, aggravation by routine physical activity and association with nausea and/or photophobia and phonophobia.

2. **B**- Migraine with typical aura
3. **C**- Diagnosis of status migrainosus headache that is continuous for >72 hours. AAN guidelines on IV treatment for migraine assigns level B evidence for Prochlorperazine IV. Postsynaptic mesolimbic dopaminergic D1 and D2 receptors, alpha-adrenergic and anticholinergic blocking effect
4. ***D***- *Migraine-like* attacks, that are missing one of the features required to fulfil all criteria for a type or subtype of migraine and not fulfilling criteria for another headache disorder.

KEYWORDS:

1. Migraine
2. Aura
3. Homeostasis
4. Pathophysiology
5. Molecular Mediators

VISUAL MANIFESTATIONS OF MIGRAINE

Kathleen Digre MD, Distinguished Professor Neurology; Professor Ophthalmology
Moran Eye Center
University of Utah, Salt Lake City

LEARNING OBJECTIVES

1. List typical characteristics of a migraine aura; explain why blurriness is NOT an aura
2. Describe 3 visual phenomena which can be aura associated with migraine
3. List 3 important contributors to photophobia associated with migraine

CME QUESTIONS

1. A typical migraine aura will have:

    A. Visual Blurring Only
    B. Both Positive And Negative Phenomena
    C. Will Be Sudden In Onset And Then Disappear Suddenly
    D. Will Have An Element Of Visual Snow

2. Which of the following are types of typical migraine aura

    A. Teichopsias
    B. Visual Snow
    C. Diplopia
    D. Achromatopsia

3. Which of these statement about photophobia is/are true:

    A. Photophobia Is A Psychosomatic Complaint
    B. Photophobia Causes The Most Bothersome Symptom In Migraine
    C. Photophobia Occurs Only In Individuals Who Are Not Blind
    D. Photophobia Is An Illusion Of Brightness

KEYWORDS

1. Migraine Aura
2. Brainstem Aura
3. Photophobia
4. Alice In Wonderland
5. Visual Snow

HIGHLIGHTS

Migraine is common so all neuro-ophthalmologists should be aware that there are many visual manifestations of the disorder. Aura can be followed by a headache or not. Some aura types are

difficult to diagnose, and the International Classification of Headache Disorders (ICHD 3) is very helpful. Download it for free: https://ichd-3.org/

SUMMARY

The visual system occupies in some way or another at least 50-60% of the brain and is very vulnerable to conditions like migraine. Migraine is a brain disorder affecting almost 20% of all women and 10% of all men—so it is common. Ophthalmologists and neurologists are going to see individuals with migraine every day in clinic whether they recognize it or not! Estimates are that 28-49% of all neurologists have migraine (Yeh, et al). Once at one of our NANOS meetings (2005) Peter Goadsby asked the audience how many have had a migraine—and up shot over 50% of hands! So, we have it too. Migraine and aura are related to patients we see every day as neuro-ophthalmologists whether we like it or not! Furthermore, migraine is associated with reduced visual quality of life, and therefore, we MUST care about this! While chronic migraine is the worst, even episodic migraine has reduced visual quality of life. (Hanson et al).

Patients tell us that there must be something wrong with my eyes! The first job of a neuro-ophthalmologist is to determine whether the patient has aura and sometimes this is very hard to do. "I lost vision in my right eye and I have headaches"—unless a careful history is done, you don't know what the cause of the visual loss is. To detect an aura, you must really get the patient to tell you about the disturbance. **Aura IS NOT JUST BLURRING**—which can accompany migraine! An aura is a discrete neurological event that starts small and gradually builds. There are positive and negative features to an aura. See the video https://www.youtube.com/watch?v=AVYjbthGk2s. While the patient in the video may first experience blurring centrally in this video, he develops a bright light with colored edges going off to the right side of his visual field over 5-60 minutes and it is followed by a headache. Patients will swear that the visual loss occurred in one eye! If you have ever had a migraine aura, you know what the patient means—It looks like one eye but if you carefully examine the vision during the aura by reading text and covering up the disturbed eye, the patient will realize that the vision in the opposite eye is also not normal. If you or the patient are unsure, send them home with an Amsler grid to view the aura with each eye individually when it occurs. There are many types of aura that we need to understand.

Typical migraine aura by International Classification of Headache Disorders (third edition) (ICHD-3) gives us our criteria for diagnosing aura. While MOST auras are visual, it is helpful to know what other neurological symptoms can be aura too. We need to expunge the term "Ocular Migraine" from our vocabulary! Most patients and providers use that term when they mean migraine with aura and rarely with retinal migraine! We also do not use the terms: classical migraine, ophthalmic migraine. Visual aura is the most frequent and seen over 90% of all auras. Typical auras do not have motor, retinal or brainstem symptoms**. See Table 1: ICHD3 criteria of Migraine with aura.** You can download the ICHD-3 for free on your computer, tablet or phone!! See: https://ichd-3.org/ It is GREAT reading, you will never know there are so many headache disorders—one for every kind of headache!!! Typical aura is usually teichopsias, or zig-zag line, with a shimmering edge that progresses to the right or left—corresponding with possible spreading depression (NOT change in blood flow) to the occipital lobe.

Table 1: ICHD 3 criteria for Migraine with aura (from ICHD-3) see reference

Description: Recurrent attacks, LASTING MINUTES, of unilateral fully reversible visual, sensory or central nervous system symptoms that usually develop GRADUALLY and are associated by headache and associated migraine symptoms.

Diagnostic criteria:

A. At least 2 attacks fulfilling criteria B and C
B. One or MORE of the following full reversible aura symptoms:

1. Visual
2. Sensory
3. Speech and/or language
4. Motor (*these are atypical and think about hemiplegic migraine*)
5. Brainstem (*see discussion of this aura; it is rare*)
6. Retinal (*rare and atypical; see discussion)*

C. At least 3 of the following 6 characteristics:

1. At Least One Aura Symptom Spreads GRADUALLY Over 5 Minutes
2. Two Or More Aura Symptoms Occur In Succession
3. Each Individual Aura Symptom Lasts 5-60 Minutes
4. At Least One Aura Symptom Is Unilateral
5. At Least One Aura Symptom Is Positive
6. The Aura Is Accompanied Or Followed Within 60 Minutes By Headache

D. NOT better accounted for by another ICHD-3 diagnosis

How individuals describe their aura is so variable, and sometimes this can be confusing. There are many common descriptions of elementary visual phenomena—that are seen with aura—but **remember these have to comply with the criteria above**—slowly develop, last 5 minutes to an hour and be followed by a headache! See table 2.

Table 2: Descriptions from patients of common visual phenomena of visual migraine aura (see Viana et al) :
Zig-zag or jagged lines (24-81%)
Flickering light (12-91%)
Scotoma (23-77%)
Flashes of bright light (16-38%)
Heat waves or water (8-24%)
Black dots (3-17%)
White spots (7-24)
Colored dots/spots (3-19%)
Curved lines (4-18%)
Tunnel vision (4-28%)
Corona phenomena (2-18%)

Typical aura can be seen without headache; we call this **Typical Aura without Headache.** In fact, as individuals age, they may lose the headache and only have the aura. These can be tricky, and we need to be sure there are no other problems following the aura. There is a list of disorders associated with migraine aura that should be at least considered. See table 3: List of other causes of Aura without headache.

Table 3: Other causes of Aura without Headache to consider when atypical or frequent (see Pederson et al)

Transient ischemic attacks (but these are usually sudden in onset, almost always NEGATIVE phenomena [LOSS of vision])
Tumors
Seizures (usually stereotypic, last seconds are more complicated: pinwheels, circles, balls, multi-colored, rapid and brief seconds or 1-3 minutes and in the same field all of the time
Reversible cerebrovascular constriction syndromes (RCVS)
Amyloid angiopathy
Arteriovenous malformation
Dissection (carotid or vertebral-basilar artery)
Autoimmune disease (systemic lupus, anti-phospholipid antibody syndrome)
Eclampsia/severe pre-eclampsia

Importantly, aura without headache can occur while individuals age as well, and we call this "Late-onset migraine aura" or LOMA. (Shah et al) These also can be tricky and it is important to distinguish aura from transient ischemic attacks and amyloid angiopathy. (See Table 3) Distinguishing features between aura and TIA are important! See Table 4.

Table 4: How to tell a Migraine aura form a transient ischemic attack (See also Vongvaivanich K et al)

	Migraine Aura	**Transient Ischemic Attacks**
Visual	Mostly POSITIVE (bright light)	Usually negative (LOSS of vision)
	Can involve both visual fields; usually not side locked	Involves unilateral visual field each time
	SLOW moving across the field	Static and abrupt onset
	Average 15-60 minutes	3-10 minutes (can be longer)
Sensory	Gradually builds up	Abrupt onset
	Positive paresthesias (tingling)	Negative feeling (numbness)
	Hand and face (cheiro-oral)	Usually unilateral
	Often sequential: visual to sensory to speech	Everything starts at once
	Lasts 20-30 minute and no more than 1 hour	Variable can be shorter 5-10 minutes; can be longer

Some auras are more visually complex. For example, there can be visual distortions of body image—like macrosomatognosia, microsomatognosia (where the body feels to big or small for the environment), sometimes called Alice in Wonderland syndrome. Lewis Carol's (Charles Lutwidge Dodgson) character Alice undergoes body changes after drinking several potions and becomes—too big, then too small for her environment. These phenomena have been reported in migraine and after infectious diseases and autoimmune disease (Lanska, Lanska). Migraine is the most common cause of Alice in Wonderland syndrome and these visual perceptions, to be a migraine aura, would be followed by a headache most of the time.

Another unusual aura that has been reported is achromatopsia—where the scenery becomes monochrome without color—in some case reports, other disorders of higher cortical function such as prosopagnosia occur and of course a headache may follow or not. (Lawden, Cleland)

Migraine aura can also be prolonged—that is MORE than 1 hour or persistent—even present for more than 1 week—Persistent Aura has to be evaluated with an MR scan to be sure that a stroke has not occurred. Persistent aura without infarction is difficult to treat! Some of the typical treatments do not work. People have tried valproate, furosemide, verapamil lamotrigine, gabapentin, topiramate, acetazolamide, magnesium. (Robertson, Digre)

The other confusing part of aura for neuro-ophthalmologists is the term "Retinal Migraine" See Table 5.

Table 5: ICHD3-Retinal migraine criteria

Description: Repeated attacks of MONOCULR disturbances, including scintillations, scotomas, or blindness associated with migraine headache.

Diagnostic criteria:

A. Attacks fulfilling criteria for Migraine with aura (see table 1) and criterion B

B. Aura Characterized by both of the following

1. Fully reversible, monocular, positive and/or negative visual phenomena (e.g. scintillations, scotomata, or blindness) confirmed during an attack by either or both of the following:
    a. clinical visual field examination
    b. patient's drawing of a monocular field defect (made after clear instructions)
2. At least 2 of the following:
    a. spreading gradually over 5 minutes
    b. symptoms lasting 5-60 minutes
    c. accompanied or followed within 60 minutes by a headache.

C. NOT better accounted for by another ICHD-3 diagnosis and other causes of amaurosis fugax have been excluded.

To diagnose retinal migraine which is exceedingly rare, you need a lot of proof! You need to CONFIM by a clinical visual field during the attack OR get a drawing after clear instructions. Patients have a very hard time telling if it is definitely in one eye. Many reported cases have called vasospasm of the central retinal artery, retinal migraine, and we don't think it would fit these criteria or go along with our current

understanding of migraine itself. (Chong et al) While spreading depression in the retina has been shown in chicks and amphibians, it has not been convincingly demonstrated in humans. This is a disorder that needs more study and consideration.

Another migraine aura type that neuro-ophthalmologists need to know about is migraine with brainstem aura. This aura used to be called Basilar artery migraine, basilar migraine, or Bickerstaff migraine. We have gotten away from the term basilar artery migraine since this is NOT caused by basilar artery spasm or compression and does NOT represent a vascular event. While not common, understanding this migraine may be helpful. (Yamani et al) See Table 6—Migraine with Brainstem aura ICHD 3 criteria

Table 6: Migraine with brainstem aura by ICHD 3 criteria

Description: Migraine with aura symptoms clearly originating from the brainstem but no motor weakness
Diagnostic Criteria:

A. Attacks fulfilling criteria for Migraine with aura (see table 1)

B. Aura with both of the following;

1. At least TWO of the following fully reversible brainstem symptoms:
   A. dysarthria
   B. vertigo
   C. tinnitus
   D. hypacusis
   E. diplopia
   F. ataxia not attributable to sensory deficit
   G. decreased level of consciousness (Glasgow Coma Scale of less than 13)

2. NO motor or retinal symptoms

While neuro-ophthalmologists may not want to make this diagnosis, be aware, that changes in consciousness can occur in migraine and also diplopia may be a migraine symptom in this disorder.

There are many elementary visual phenomena that get confused with aura! We see them all, so we need to be aware of what is NOT aura. Individuals with migraine have “sensitive” brains and all sorts of visual noise that is NOT aura—but sometimes it is tricky to determine its source. Grant Liu brought this to our attention many years ago in his article about persistent positive phenomena that are just seen in individuals with migraine. (Liu et al). See table 8 for a partial list of many of these phenomena and their other sources.

Visual Snow is an important disorder that needs to be separated from visual aura! (Schankin et al). These individuals have pixelated or sometimes called analog television static vision that can be seen in adolescence/childhood and also can be induced by different stimuli. The visual snow syndrome has many other features. The ICHD-3 has put the criteria in the Appendix section and these criteria are

helpful for neuro-ophthalmologists to know since most individuals are referred for aura or other unknown visual complaints. (See Table 7 for criteria for Visual Snow.)

Table 7: ICHD 3 Criteria for Visual Snow

Diagnostic criteria:

A. Dynamic, continuous, tiny dots across the entire visual field, persisting for >3 months

B. Additional visual symptoms of at least two of the following four types:
   1. Palinopsia
   2. Enhanced entoptic phenomena
   3. Photophobia
   4. Impaired night vision (nyctalopia)

C. Symptoms are not consistent with typical migraine visual aura

D. Symptoms are not better accounted for by another disorder

There are non-visual accompaniments to visual snow like tinnitus. Migraine is over represented in individuals with visual snow—up to 58% of Visual snow patients have migraine. (Robertson and Digre)

Visual snow can be precipitated by other conditions including: traumatic brain injury, new medications, hormonal changes, infection (including COVID), hallucinogenic drugs (HPPD), idiopathic intracranial hypertension, stroke, demyelinating disease, neoplasm of the central nervous system, epilepsy, and degenerative disorders like Creutzfeld-Jakob disease or posterior cortical atrophy. In addition, eye conditions can mimic snow like chorioidopathies and retinopathies. So a careful history and evaluation is warranted. (See Robertson, Digre). Remember all that flickers is not snow! The cause of visual snow is not completely known, but functional MR and FDG PET have given us information that it indeed is a brain disorder and may be related to connectivity pathways in the brain. And that the brain is either hyperexcitable, or lacking inhibitory signals and others propose a thalamocortical dysrhythmia. (Bou Ghannum, Pelak; Robertson, Digre).

Table 8: Flashes and flickering and visual phenomena that are NOT necessarily aura of migraine! (adapted in part from Robertson and Digre 2023)

Complaint	Causes	Other thoughts
Temporal flickering/flashing	Vitreal detachment, chorioretinal disease, optic disc drusen	Migraine can do this, but remember the criteria—gradual over 5-60 minutes
Photopsias with eye movement	Normal entopic phenomena, traction of the vitreous, optic neuritis, thyroid eye disease	
Shimmering light in the periphery or scotoma	Papilledema, medications (like clomiphene), retinitis pigmentosa; paraneoplastic, autoimmune, Arteriovenous malformation	Can be migraine but gradual and progressive over 5-60 minutes
Generalized photopsias	Medications (digitalis, quetiapine, voriconazole, paclitaxel), chorioretinal disease (infectious, autoimmune, paraneoplastic, toxic metabolic)	

Halos	Medications (chloroquine, digitalis amiodarone, hydroxychloroquine), glaucoma, keratitis, cataracts or lens	
Dysphotopsia	Cataract with lens replacement	Usually transient after cataract surgery
Circular light in primary colors	Occipital lobe epilepsy	May require getting an EEG
Metamorphopsia	Medication (topiramate); papilledema; retinal disorders; IIH	
Macrosomatognosia	Thinking your body is too big for your surrounding	Part of Alice in Wonderland; can be migraine, seizure
Micosomatognosia	Thinking your body is too small for your surrounding	Part of Alice in Wonderland; can be migraine, seizure
Macropsia	Things look too big	Part of Alice in Wonderland; can be migraine, seizure
Micropsia	Things look too small	Part of Alice in Wonderland; can be migraine, seizure
Teleopsia	Thing look too far away	Part of Alice in Wonderland; can be migraine, seizure
Pelopsia	Things look too close	Part of Alice in Wonderland; can be migraine, seizure
OTHER VISUAL PHENOMENA		
Visual Snow	Distinct from migraine; 40-60% of individuals will have migraine	NOT a migraine Aura See Schankin et al; see discussion
Stripe-induced discomfort	Prominent in individuals with migraine	Marcus et al
Strobe light or flickering lights making migraine worse	Very common symptom of migraine; may not always be aura	
Palinopsia	Seeing objects again; or a trailing image. This can be related to migraine or even brought on by other drugs and disorders	Nice review: Gersztenkorn D, Lee AG.)
Floaters	Seen frequently in myopes. Some individuals are deeply bothered. NOT an aura	
Blue Field Phenomena	Seeing ones own blood cells on a blue back ground or sky.	
Self light of the eye	Instead of blackness, some can see waves of color –luminous clouds. Not everyone sees this, but prominent in visual snow	

There is another REALLY important reason for providers and patients to pay attention to aura. Vascular disease is more prevalent in individuals with aura! Several studies have shown that Migraine Aura is associated with cardiovascular disease compared to migraine without aura. Smoking and estrogen containing contraceptives can increase this risk. So any patient with migraine with aura should be sure to have their risk factors addressed by primary care provider. (Oie et al; Ibrahami et al)

What are the OTHER Visual phenomena that accompany migraine?

The most bothersome symptom of migraine is PHOTOPHOBIA!!! (Munjal et al) In fact, almost all of the patients in the MAST study said photophobia was their most bothersome symptom, beating out nausea (28%), and phonophobia (22%). Photophobia also affects the visual quality of life. (Redfern et al) Recent studies have shown that photophobia affects disability and reduced work productivity! It is affecting our economy and people's ability to work. (Leibovit-Reiben et al). We do know that you don't need vision to have photophobia; in fact, visually blind individuals can have even severe photophobia by way of the melanopsin or the intrinsically photosensitive ganglion cells (Noseda et al).

As neuro-ophthalmologists we know there are MANY causes of photophobia and an organized approach to the diagnosis is absolutely required. See list of common causes of photophobia (Table 9) In a review of patients who presented to our clinic with the chief complaint of photophobia the most common conditions were dry eye, migraine, traumatic brain injury, and others. (Buchanan et al). Many children and adults left without a diagnosis, making this important that we give a diagnosis to this symptom, just as we would any other symptom in ophthalmology.

Table 9: Common Causes of Photophobia (adapted in part from Digre, Brennan; Katz, Digre)

Eye and Anterior Segment causes
- Dry Eye
- Corneal Neuropathy
- Iritis and ocular inflammation
- Blepharitis

Poster Segment
- Uveitis, vitritis
- Retinal causes: albinism, achromatopsia, retinitis pigmentosa, rod-cone dystrophy
- Optic nerve: optic neuritis, papilledema, Idiopathic intracranial hypertension

Brain causes
- Meningitis and any meningeal irritation e.g., eintracranial hypotension
- Subarachnoid hemorrhage
- Pituitary apoplexy; hypophysitis, pituitary tumors
- Pre-eclampsia/Eclampsia

Important Brain causes
- Migraine
- Blepharospasm
- Traumatic brain injury
- Cyclic vomiting syndrome
- Progressive Supranuclear Palsy—differentiates form Parkinsons Disease!

Psychiatric Conditions
- Agoraphobia

Depression
Attention Deficit Disorder

Other

Measles, Rabies
Inflammatory Bowel Disease
Chediak-Higashi Syndrome
Trisomy 18
Ichthyosis follicularis with alopecia and photophobia (IFAP)
Fibromyalgia

Drugs: Barbiturates, benzodiazepine, methylphenidate, opioids and others

In order to make the correct diagnosis, PLEASE use an organized approach to photophobia.

Many causes of photophobia so use the steps outlined in Table 10. See table 10.

Table 10: An organized approach to the symptom of photophobia

Step 1: Take a history and do a neurological examination! Is there anything in the history or neurological examination that suggests a central etiology or is a RED FLAG for secondary disorder? Ask about head trauma too. If so, MR imaging and look for a central cause. (Check the medication list too!) If not,

Step 2: Slit Lamp examination for any anterior segment cause: iritis, inflammation—if so treat this, if not

Step 3: add a drop of proparacaine and does the pain and photophobia go away? Do a Schirmer's test for dry eye. If the photophobia goes away and/or the Schirmer's is low, treat dry eye and corneal neuropathy if not

Step 4: careful retinal examination looking for a retinal cause, if so, treat this, if not

Step 5: look for excessive blinking—this is tricky since blepharospasm will often have spontaneous blinking, but if you shine a light in the eye and you develop REFLEXIVE blinking, you may have blepharospasm a major cause of photophobia! If so, treat blepharospasm, if not

Step 6: is there a migraine history? (headache, photophobia and nausea?) if so treat this, if not—start all over—what did you miss?

Please see several comprehensive reviews about photophobia—this is a neuro-ophthalmic symptom that we all must be able to diagnose and treat! (Katz, Digre; Digre, Brennan). While these patients may have increased depression and anxiety (Llop et al) it is part of the disease in some, and depression and anxiety can be treated as well.

If the photophobia is related to migraine, then there are many treatments that individuals can undergo with great relief. See our discussion of treatments in migraine. Photophobia due to blepharospasm can be improved with onabotulinum toxin. Aggressively treat dry eyes when it is accompanying migraine, head injury since they often share a pathophysiology. (Diel et al)

CME ANSWERS

1. B
2. A
3. B

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VESTIBULAR MIGRAINE

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LEARNING OBJECTIVES

1. Learn the diagnostic criteria for vestibular migraine
2. Learn the variety of symptoms that may occur in vestibular migraine
3. Learn the different treatments for vestibular migraine

CME QUESTIONS

1. What are the migraine symptoms that are used in the Barany Society-International Headache Society consensus criteria for vestibular migraine?
2. Which phase of the migraine attack do vestibular symptoms occur?
3. Can treatments used for migraine headache also work for vestibular migraine?

KEYWORDS

1. Vertigo
2. Dizziness
3. Vestibular migraine

HIGHLIGHTS

Migraine is the second most disabling chronic disorder in the world. Approximately 55% of migraine patients experience vestibular symptoms at one time or another. Many people with vestibular migraine experience no accompanying headache; vestibular symptoms being the most debilitating symptom. Vestibular migraine must be addressed via a holistic, multidisciplinary approach that combines medical management, lifestyle changes, and rehabilitation therapies.

SUMMARY

Approximately 55% of migraine patients experience vertigo or dizziness at one time or another. Vestibular testing in people with migraine often reveals non-specific findings, like positional nystagmus, saccadic pursuit, and abnormalities of vestibular evoked myogenic potentials. Furthermore, patients with migraine also have a higher risk of multiple vestibular conditions, including benign paroxysmal positional vertigo (BPPV), persistent postural perceptual dizziness (PPPD), Meniere's disease, and mal de debarquement syndrome (MDDS) [Beh, 2019].

The mere presence of vestibular symptoms in a patient with migraine does not make the diagnosis of vestibular migraine. According to the Barany Society and International Headache Society, the consensus diagnostic criteria for diagnosing vestibular migraine are: (1) at least five episodes of vestibular symptoms of moderate to severe intensity, lasting between 5 minutes to 72 hours; (2) with at least half of these episodes accompanied by at least one migraine symptom, which include (a) headache (with at least two features: unilateral, throbbing, moderate/severe intensity, aggravated by routine physical

activity), (b) photophobia and phonophobia, or (c) visual aura; (3) current or previous history of migraine with or without aura; (4) not better accounted for by another diagnosis [Lempert, 2012].

Patients with vestibular migraine often describe a wide variety of vestibular symptoms, including spontaneous and triggered vertigo/dizziness [Beh, 2019]. The reported incidence of headache in vestibular migraine varies widely. Even it present, headache is often less debilitating than the vestibular symptoms [Beh, 2019]. More commonly, photophobia and phonophobia are more frequently encountered [Beh, 2019]. Visual aura is reported by a subset of patients [Beh, 2019]. Although not part of the diagnostic criteria, many other symptoms may occur in vestibular migraine, including neck pain, osmophobia, neuropsychiatric symptoms (e.g., word-finding difficulties, trouble thinking, anxiety, depression), autonomic symptoms (e.g., diaphoresis, dry mouth, tearing, nasal congestion, diarrhea), and visual disturbances (e.g., visual snow, blurred vision) [Beh, 2019].

While vestibular migraine is a clinical diagnosis, patients often and should undergo a battery of tests to exclude other conditions. A brain MRI is essential in all patients presenting with vestibular symptoms for the first time. For those in whom MRI is contraindicated, a head CT should be performed. Angiographic imaging (either CT or MRI) of the head and neck can be ordered in the right clinical setting or if there is a concern for a cerebrovascular event (stroke). Basic vestibular tests (video-nystagmography, bithermal caloric testing, and video head impulse testing) and pure tone audiometry should be performed on all patients. Ancillary audiovestibular testing (e.g. vestibular evoked myogenic potentials, rotary chair, electrocochleography, auditory brainstem responses, computerized dynamic posturography) can be considered in the right clinical setting.

The best approach to vestibular migraine treatment is a holistic, multidisciplinary plan that encompasses non-pharmacologic nutraceuticals, medications, lifestyle changes, vestibular rehabilitation therapy, and addressing comorbidities. Non-pharmacologic nutraceuticals are often safe and well-tolerated. Potentially beneficial supplements include riboflavin, magnesium, and cozenzyme-Q10. Lifestyle modifications in vestibular migraine should include regular exercise, stress management, consistent meals, and proper sleep hygiene. Trigger avoidance includes restricting one's intake of caffeine, alcohol, monosodium glutamate (MSG), and high-processed foods.

Preventive treatments for vestibular migraine should be considered in those with frequent or severe attacks that interfere with a patient's ability to function. These include classic migraine prophylactics like antidepressants, anti-epileptic medications, beta-blockers, and calcium-channel blockers. There is emerging evidence that neuromodulation, onabotulinumtoxin and calcitonin gene-related peptide antagonists may also be beneficial in vestibular migraine. Rescue treatments can be used for vestibular migraine attacks. There are a variety of rescue treatments that can be deployed as monotherapy or in combination. These include triptans, non-steroidal anti-inflammatory drugs, antiemetics, antihistamines, and benzodiazepines. Neuromodulation and calcitonin gene-related peptide antagonists may also be effective in some patients.

Vestibular migraine patients often experience comorbid conditions that interfere with their quality of life. Cervical disorders like cervical spondylosis, cervical facet syndromes or muscle spasms that cause pain and reduce range of motion. Addressing these issues via joint mobilization, stretching and cervical/scapula strengthening exercises will help restore normal cervical motion. Mood disorders like anxiety, panic, and depression are also very common in those with vestibular migraine. If treatment with the patient's primary care physician and/or neurologist does not adequately address their mood

disorder, the patient should be referred to a psychiatrist. In patients with significant tinnitus, tinnitus retraining therapy, hearing aids, or white noise generators may help [Beh, 2019].

CME ANSWERS

1. Headache, photophobia and phonophobia, or visual aura
2. All phases (prodrome, aura, attack, postdrome)
3. Yes

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UPDATING YOUR MIGRAINE THERAPEUTIC TOOLBOX

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LEARNING OBJECTIVES

1. Recognize calcitonin gene related peptide (CGRP) therapeutic options for migraine prevention
2. Recognize calcitonin gene related peptide (CGRP) therapeutic options for acute migraine therapy
3. Identify new neuro-modulatory nonpharmacologic migraine therapies

CME QUESTIONS

1. Which of the following migraine therapies is administered intravenously
   A. galcanezumab
   B. zevagepant
   C. lasmiditan
   D. eptinezumab

2. Which of the following migraine therapies is administered every other day for migraine prevention?
   A. zevagepant
   B. rimegepant
   C. ubrogepant
   D. atogepant

3. Which one of the following nonpharmacologic therapies have not been FDA approved for the treatment of migraine
   A. transcranial magnetic stimulation
   B. supraorbital nerve stimulation
   C. remote electrical neuromodulation
   D. photo-therapeutic trigeminal stimulation

KEYWORDS

1. CGRP
2. Migraine therapy
3. Neuromodulation
4. Gepants

HIGHLIGHTS

Therapy for migraine dates back literally thousands of you years when trephination was used to release the evil spirits from the skull. The use of ergotamine for my brain therapy with first report in 1925, and then promoted by Drs. Graham and Wolff in the late 1930's. Dihydroergotamine (DHE) came a decade later and is still used today as one of the acute treatments for migraine (1). Triptans were later approved for acute treatment of migraine in 1993 with the introduction of subcutaneous sumatriptan (2). Six more

triptans were released over the next 9 years and became the standard of care for acute migraine therapy, and today remain the most widely prescribed acute migraine medications. Other than reformulations of approved migraine medications and combining therapies by adding a nonsteroidal anti-inflammatory to a triptan, no new medication or new mechanisms of action became available for either acute or preventive treatment of migraine. As far as preventive therapies, oral agents for migraine prevention including topiramate, divalproate sodium, propranolol, and amitriptyline had been used for decades with modest effect and moderate tolerability issues. For years nothing more was made available for migraine therapy until onabotulinum was approved for migraine prevention in 2010 (3)
A sea change occurred in May 2018 when erenumab, the first calcitonin gene related peptide monoclonal antibody (CGRP Mab) was approved (4). While erenumab is a Mab that binds to the CGRP receptor, the next three CGRP Mabs to come to market; eptinezumab, fremanezumab, and galcanezumab all bind the ligand CGRP molecule rendering it inactive. The CGRP Mabs are all parenteral and are subcutaneously administered by the patient with an autoinjector. They are all given every 4 weeks, although Fremanezumab may be given every 3 months with a triple dose. The exception is eptinezumab which is given as IV infusion every 3 months (5). This class of drugs has been a game changer due to their excellent tolerability and safety profile. For the most part there are no significant contraindications. Erenumab has a warning about the potential for serious constipation, and increases in blood pressure have also been reported. These drugs are not indicated for women who are pregnant or trying to become pregnant. As CGRP is a ubiquitous signalling protein throughout the human body, it still on clear as to the long-term effects of blocking this antibody.
As far as efficacy, greater than 50% of patients in the clinical studies have a greater than 50% improvement in migraine days a month, and improvement and greater than 75% reduction is noted in a significant number of patients. These highly significant improvements in patient's migraine frequency and associated with excellent tolerability has led to the increasing use of these medications for migraine prevention (6). The major hurdle has been insurance coverage. The American Headache Society's Consensus Statement on *integrating new migraine treatments into the clinical practice* from 3/2021 has suggested using preventive therapy when migraines significantly interfere with patient's daily routine despite acute treatment, those with 6 or more headache days a month, and those with contraindications to or failure of acute therapy (7). Using evidence-based guidelines they suggest a trial of CGRP monoclonal antibodies in those patients at least 18 years of age who have tried and failed 2 or more oral agents and have at least moderate disability. This has been rather controversial as the newer therapies have major advantages over the older therapies, the major hurdle being cost.

Given the significant role CGRP plays in migraine pathophysiology, work has been done on oral agents that act as antagonists at the CGRP receptor. This class is referred to as the Gepants and have been under study for over 15 years but due to liver issues requiring reformulation and further clinical studies, it took more than another decade before the second generation gepants were approved. Subsequently, ubrogepant was approved in 12/19 and rimegepant in 2/20 for the acute treatment of migraine (8). Very recently a new gepant which is given by nasal spray, zavegepant was approved for treatment of migraine in 7/23 (9). This class of medications has no vasoconstrictive effects and therefore is safe to use in patients with cardiovascular and cerebrovascular disease where triptans are contraindicated. Unfortunately, while safe and tolerable, efficacy is no better than currently available therapies, and costs are high. Another major advantage of this class of drugs is the absence of medication overuse headache. While triptans and over-the-counter medications such as acetaminophen and nonsteroidal anti-inflammatories when used more than 10 to 12 days a month may promote an increase in headache frequency referred to his medication overuse headache, there is no evidence that the gepant class of therapies induce medication overuse headache and have been used to help patients transition off of their offending medications.

In open-label clinical studies of rimegepant patients were allowed to use it as needed up to daily, it became clear that this medication may work preventively (10). Subsequent studies proved that alternate day treatment with the standard 75 mg dose substantially reduced migraine frequency and it was subsequently approved for not only for acute treatment of migraine, but also for preventive treatment of migraine.
Atogepant, a longer acting gepant was approved for migraine prevention providing data similar to the Mabs as far as reduction in migraine days per month using a daily oral pill with an excellent safety profile (11). Tolerability issues include nausea, constipation, and fatigue all of which occurred at a rate of 6% of patients on the high 60mg dose in the Phase III clinical trial.

Lasmiditan, another new small molecule for acute migraine treatment of migraine was introduced in October 2019. Lasmiditan acts on the serotonin 1f receptor while triptans are active on the serotonin 1b and 1d receptors. They are not associated with vasoconstriction and are not contraindicated in cerebrovascular and cardiovascular disease. This class is referred to as the ditans, but lasmiditan is the only one currently available. They have higher efficacy than the gepants but may cause sedation and dizziness and have an 8-hour driving warning after use as well as having a Class 5 Controlled substance designation due to the possibility of abuse. Despite their efficacy, use is mostly limited to headache specialists due to the side effect issues (12,13,14).

An ongoing unmet need for the treatment of migraine has been nonpharmacologic therapy. Neuro-modulatory devices have been used for chronic pain issues for some time, but over the last decade multiple devices have been approved by the FDA to treat migraine. These include the following devices:

- E-TNS – an external trigeminal nerve stimulator (Cefaly)
- nVNS – a noninvasive vagal nerve stimulator (Gammacore)
- sTMS– a single-pulse transcranial magnetic stimulator (sTMS mini)
- REN – a remote electrical neuromodulator (Nerivio)

These devices have had moderate success in treating both acute migraine, as well as for migraine prevention. (15,16) Major hurdles have been reimbursement as insurance usually does not cover devices.

SUMMARY

We will discuss new therapeutic agents for both acute treatment of migraine and preventive treatment of migraine as well the role of neuromodulation devices that may be helpful for your patients with migraine.

CME ANSWERS

1. **D**
2. **B**
3. **D**

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EYE PAIN: WHEN TO REFER TO HEADACHE MEDICINE?

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LEARNING OBJECTIVES

1. Recognize the signs and symptoms of headache disorders that may present to the ophthalmology setting.
2. Review the differential diagnosis for pain in and around the orbit.
3. Discuss treatment options for disorders causing eye pain.

CME QUESTIONS

1. Which of the following is *most* concerning for an orbital lesion, versus a primary headache syndrome?
    a. Anisocoria
    b. Conjunctival injection
    c. Unilateral ptosis
    d. Relative afferent pupillary defect
2. Patients commonly present with eye pain for all of the following disorders except:
    a. Migraine
    b. Occipital neuralgia
    c. Trigeminal neuralgia
    d. Primary stabbing headache
3. Which of the following would be safe and effective for continuous use in eye pain management (i.e. pain prevention)?
    a. Gabapentin
    b. Sumatriptan
    c. Lidocaine nasal spray
    d. Ibuprofen

KEYWORDS

1. Headache
2. Neuropathic Pain
3. Orbital Inflammation
4. Dry Eye Syndrome
5. Photophobia

HIGHLIGHTS

- "Eye pain" is a common presenting complaint in ophthalmology and neurology clinics.[1] While a comprehensive ophthalmic exam can identify the cause in most cases, there remain many cases in which no clear etiology for the pain is evident on clinical exam. It is crucial to obtain a thorough

history to understand the patient's experience and guide the rest of the evaluation, diagnosis, and treatment.

- A normal ophthalmological exam excludes many of the secondary causes of pain such as corneal pathology, glaucoma, ocular inflammation, ischemia, and mass lesions.
- The International Classification of Headache Disorders 3rd edition provides detailed information on Primary Headache Disorders, Secondary Headache Disorders, and Neuropathies and Facial Pain Syndromes that may present with the chief complaint of eye pain.[2]
- Target the treatment towards the presenting phenotype. There are many symptomatic, pharmacological, and procedure options in managing pain.

SUMMARY

Background

Defining pain is a highly subjective and variable concept for patients. For the intents of this review, we will consider eye pain any unpleasant sensation on the surface, within, behind, or around the globe. The pain may be directly related to a globe or orbit process, or referred from other cranial regions. The ophthalmic branch (V1) of the trigeminal nerve innervates the orbit structures, as well as parts of the intracranial dura, cavernous sinus, carotid artery, and nasal cavity and sinuses. Even cervical disorders can cause eye pain due to the close proximity of trigeminal nucleus caudalis and C2 sensory neurons in the upper cervical cord.[1,3]

Pain conditions are commonly divided into primary and secondary disorders. The primary headache disorders do not have another causative condition and the diagnosis is based chiefly on the history. If physical signs occur, these are fully reversible between attacks. Secondary headache syndromes have an underlying etiology such as a mass, trauma, or inflammation. Exam abnormalities typically are persistent and localizing to the lesion in the case of a secondary disorder.

History

The diagnosis of most primary pain syndromes is made clinically based upon a thorough history. Elucidating the quality, location, and timing features helps build the differential diagnosis. Common descriptors of eye pain "quality" include throbbing/pulsating, aching, stabbing, pressure, burning, or foreign body sensation. The location of pain can be unilateral or bilateral. Unilateral pain that never occurs on the opposite side is distinct from pain that may occur on each side at different times. "Side-locked" pain is much more concerning for a structural lesion than pain that moves to different locations within and between attacks, but is also seen in some primary headache disorders. Diagnosis is further aided if the patient can precisely localize the pain (e.g. superficially, retrobulbar, periorbital, or within the globe) and if it radiates to another part of the head or face. Many aspects of the timing also differentiate headache syndromes, including time of onset, time to peak pain, duration of each attack, and frequency of attacks. Pertinent positive and negative symptoms that may occur with the pain should also be considered. Examples include photophobia, change in pain with eye movement, nausea, and autonomic features such as ipsilateral tearing, rhinorrhea, nasal congestion, and/or aural fullness.

Physical Exam

In many cases, patients with pain complaints have an unremarkable physical examination. This is especially true in patients presenting to tertiary care after multiple prior evaluations. However, it is important to rule out signs of a secondary process before focusing care on pain management. Certain primary pain disorders also cause objective autonomic findings that could further support their diagnosis. In the case of episodic complaints, it is helpful to have the patient video or take a picture

when the signs are present. External features of proptosis, periorbital edema, tenderness to palpation of the periorbital region, and extraocular movement abnormalities may indicate an orbital or cavernous sinus process. Evaluate the pupils for anisocoria, pupil reactivity, and relative afferent pupillary defect. While some primary headache syndromes may cause mydriasis or myosis, a relative afferent pupillary defect should immediately raise concern for a structural lesion. Notable anterior segment findings may include ptosis, lid retraction, keratopathy, cell and flare, and conjunctival abnormalities. Assess the posterior segment for optic disc edema, venous engorgement, and other fundus abnormalities. Spontaneous venous pulsations are a normal finding, but can also be a sign of low intracranial pressure. They may be absent with elevated intracranial pressure.[4, 5]

Differential Diagnosis

Dry eye syndrome is one of the leading causes of eye pain in both ophthalmology and neurology clinics,[1] causing a form of neuropathic pain (neuropathic corneal pain).[6] The pain may radiate to other areas in the trigeminal distribution including the orbit and face, and commonly has associated photophobia.[7] Other ophthalmic disorders that may present with eye pain are conjunctivitis, keratitis/keratopathy, herpes virus, hordeolum/chalazion, cellulitis, ectropion, entropion, acute angle closure glaucoma, uveitis, iritis, scleritis, thyroid eye disease, myositis, ischemic optic neuropathy, optic neuritis, and microvascular ischemia of a cranial nerve. Intracranial causes include carotid-cavernous fistula, Tolosa-Hunt syndrome, cerebral aneurysm, neoplasm, and intracranial pressure disorders.[1,4,5,8] Paratrigeminal oculosympathic syndrome consists of a constant unilateral pain in the V1 distribution with an ipsilateral Horner syndrome and is due to a middle cranial fossa or carotid artery lesion.[2] Disease of the sinus cavities surrounding the orbit can also cause eye pain.

Primary headache disorders that may present with eye pain include migraine, trigeminal autonomic cephalalgias (TACs; i.e. cluster headache, paroxysmal hemicrania, hemicrania continua, short-lasting unilateral neuralgiform headache attacks), and primary stabbing headache. Migraine and TACs are discussed in detail elsewhere in this session. Primary stabbing headache is head pain occurring as single stab or series of stabbing pains, each lasting up to a few seconds. They have an irregular frequency and do not have associated autonomic symptoms. Although 70% of cases experience pain outside of the trigeminal region, a common presentation to the ophthalmology setting is for the complaint of “ice pick” like pain in the eye. This headache syndrome is more common in people with a comorbid migraine diagnosis.[2]

Trochlear headache may occur as a primary headache disorder or secondary to inflammation of the trochlea and/or superior oblique muscle sheath.[2,9] The pain localizes to the ipsilateral periorbital region. It is associated with tenderness to palpation of the trochlea and aggravated by the eye movements. Neuropathic pain from both the trigeminal nerves and occipital nerves can present with eye pain. Trigeminal neuralgia is severe electric, shooting, and/or stabbing pain following one of the trigeminal dermatomes. Mild tactile stimuli such as touch or wind on the face may provoke pain attacks. Patients more commonly complain of “facial pain” in this disorder, but involvement of the ophthalmic branch could cause eye pain. Imaging may show neurovascular compression (classical trigeminal neuralgia), but others will have no identifiable cause (idiopathic trigeminal neuralgia).[2] Occipital neuralgia also causes shooting and/or stabbing pain, but over the C2 dermatome. Due to interneuronal connections of the trigeminal nuclei in the cervical cord, the pain from occipital neuralgia may radiate into the ipsilateral periorbital region and lead to the complaint of eye pain. Patients have allodynia and dysesthesia when palpated in the occipital region.[2,3,9]

Additional Evaluation

Further work up after clinic-based evaluation is guided by the differential diagnosis and how the testing could impact treatment options. Imaging is generally low yield in patients with migraine and a normal neurological exam, and may identify incidental anomalies that then cause the patient additional distress (e.g. nonspecific white matter lesions, Chiari malformation). Patients with "red flag" symptoms and/or exam abnormalities merit additional testing, as do those whose history and physical cannot reasonably exclude intraorbital or intracranial pathology. Of note, a commonly used mnemonic called the SNNOOP10 lists "painful eye with autonomic features" as an indication for additional imaging. Contrast enhanced magnetic resonance imaging (MRI) of the brain and orbits can help identify mass lesions and areas of inflammation. Fat suppression allows for better visualization of the orbit structures. Computed tomography and B-scan ultrasonography can also provide good images of the orbital structures.[11] Serum laboratory testing for inflammatory antibodies, sedimentation rate, and C-reactive protein can also be completed if there is concern for an autoimmune process.

Management

In the case of secondary pain syndromes, it is imperative to recognize and treat the underlying disorder. Pain management therapies can be used in conjunction to improve the patient's quality of life. Selection of an agent depends on the pain phenotype and patient preferences. Dry eye and photophobia are both common causes of eye pain as well as frequent comorbidities in migraine patients. Many patients will benefit from low-risk, symptomatic therapies such as preservative-free artificial tears, FL-41 filters, and selenium supplementation. Selenium as an antioxidant has been studied for use in thyroid eye disease, dry eye disease, and peripheral pain management.[12-14] Pharmacological therapies include antiepileptic agents and antidepressants with data for prevention of headache and neuropathic pain. Gabapentin showed benefit for eye pain due to dry eye disease and neuropathic ocular pain in a small, nonrandomized open label study.[15] Calcitonin gene related peptide plays a role in trigeminally mediated headache syndromes and multiple agents are now available for both headache prevention and treatment of acute pain attacks. Other acute treatment options include non-steroidal anti-inflammatory drugs (oral or ophthalmic), triptans, and lidocaine nasal spray. Procedures to mitigate pain include nerve blocks of occipital and trigeminal nerve branches, sphenopalatine ganglion (SPG) block, trochlear injections, and onabotulinum toxin A injections. Greater occipital nerve blocks may provide relief for pain in both the occipital and periorbital region in migraine and cluster headache, as well as occipital neuralgia.[9] The injected agent is a local anesthetic (e.g. lidocaine, bupivacaine, ropivacaine), with or without a steroid. Many patients achieve a good response to the local anesthetic alone, while avoiding the increased risk of injection site complications such as tissue necrosis and hair loss due to steroids. In the case of trochleitis, adding a steroid to the injection can help with the local inflammation.

CME ANSWERS

1. **D**
2. **C**
3. **A**

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CLUSTER HEADACHES AND THE TRIGEMINAL AUTONOMIC CEPHALALGIAS (TACS): WHAT THE NEURO-OPHTHALMOLOGIST NEEDS TO KNOW

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LEARNING OBJECTIVES

1. Name the neuro-ophthalmic manifestations of the TACs
2. Distinguish the trigeminal autonomic symptoms of the TACs from those of migraine
3. Describe the symptoms common to both migraine and cluster headache

CME QUESTIONS

1. A 43-year-old woman relates a 2-year history of very severe right-sided headaches. It feels like she is being stabbed in the right eye with pain in the right temple, jaw and retro-orbital area. The pain peaks in intensity within 3 minutes and is accompanied by ipsilateral tearing, rhinorrhea and ptosis, with photophobia, phonophobia, nausea and vomiting. The episodes last 45-60 minutes and occur 1-3 times daily, sometimes awakening her from sleep. Her interitcal neuro-ophthalmic and neurologic exams and brain MRI with contrast are normal. What is the likely diagnosis:

   A. "Crash" migraine
   B. Chronic cluster headache
   C. Chronic paroxysmal hemicrania
   D. Chronic migraine without aura
   E. Cluster-migraine

2. A 78-year-old man describes episodes of left-sided eye pain associated with ipsilateral tearing and redness which started about 3 months ago. The pain is severe, lasts 1-2 minutes and may occur up to 25 times daily. Brain MRI and MRA are normal. What is the first-line treatment?

   A. Lamotrigine
   B. Carbamazepine
   C. Indomethacin
   D. Noninvasive vagus nerve stimulation
   E. Topiramate

3. Which of the following structures is the postulated "generator" (the first area activated during an attack) of cluster headache?

   A. Trigeminal nucleus caudalis
   B. Periaqueductal gray
   C. Posterior hypothalamus
   D. Sphenopalatine ganglion
   E. Superior salivatory nucleus

KEYWORDS

1. Cluster headache
2. Paroxysmal hemicrania
3. Short-lasting unilateral neuralgiform headache with autonomic features (SUNCT, SUNA)
4. Hemicrania continua
5. Indomethacin

HIGHLIGHTS

- With a combination of orbital/periorbital pain and neuro-ophthalmic features, such as Horner syndrome, ptosis, conjunctival injection, lacrimation, eyelid edema and miosis, the trigeminal autonomic cephalalgias (TACs) are the most interesting of the primary headache disorders for our specialty! Plus, patients with a TAC just might show up in your office.
- TACs include cluster headache, paroxysmal hemicrania, the short-lasting unilateral neuralgiform headache attacks (SUNCT and SUNA) and hemicrania continua
- Paroxysmal hemicrania and hemicrania continua are diagnosed in part by their response to indomethacin
- The TACS are primarily clinically distinguished from each other by the attack duration and frequency. However, there is some overlap between them, as well as with migraine and other secondary headache disorders.
- The longer the name (spelled out), the shorter and more frequent the headache, and vice versa
- This review contains the diagnostic criteria, helpful hints for taking the history and tables of cluster headache treatments (Tables 1-3) and features to help distinguish the TACS (Table 4)
- In contrast to migraine, all patients with a TAC should undergo MR imaging and additional evaluations as clinically indicated

CLUSTER HEADACHE

EPIDEMIOLOGY

Cluster headache is the “prototype” and the most common of the TACs. It is one of the most painful conditions known to humans, to the point where is sometimes to referred to a “suicide headache”. In fact, it a patient ever tells you that they think about killing themselves during their headache attack, chances are that they have cluster headache. Cluster headache is much less common than migraine, affecting 0.1% of the population.[1] It generally starts between ages 20 and 40 years but has been reported to begin throughout the lifespan. Although it is more prevalent in males, and commonly thought of as a headache occurring in “middle aged, male smokers”, it affects females as well.

The ratio of males to females has decreased since the 1960s, likely related to heightened awareness of misdiagnosis in women although some ascribed it to a rise in female smokers. It is currently estimated at 2.5:1.[2] One study showed a bimodal peak of onset in patients with chronic cluster headache, peaking in the second and sixth decades compared to men, peaking in the third and fifth decades. In patients with onset at $\leq$ 15 years and $\geq$50 years, the male-to-female ratio was reversed.[3] Females with cluster headache may have a prior history of migraine and are often misdiagnosed as migraine on the basis of their sex alone.

Misdiagnosis is common, and the mean diagnostic delay is 6 years.[4] The most common misdiagnoses are migraine, sinusitis and dental disease.[5] Cluster headache is associated with a high burden on quality of life and economic effect for healthcare.

DIAGNOSIS AND CLINICAL FEATURES

The International Classification of Headache Disorders (3rd edition) diagnostic criteria (ICHD-3) for cluster headache are:[6]

A	At least 5 attacks fulfilling criteria B-D	
B	Severe or very severe unilateral orbital, supraorbital and/or temporal pain lasting 15-180 minutes (when untreated	
C	Either or both of the following	
	1	At least one of the following symptoms or signs, ipsilateral to the headache:
		a. conjunctival injection and/or lacrimation
		b. nasal congestion and/or rhinorrhea
		c. eyelid edema
		d. forehead and facial sweating
		e. miosis and/or ptosis
	2	A sense of restlessness or agitation
D	Occurring with a frequency between one every other day and eight per day	
E	Not better accounted for by another ICHD-3 diagnosis	

Cluster headache is further categorized as either episodic or chronic. Episodic cluster headache is diagnosed when there are two cluster periods ("bouts") lasting from 7 days to one year and separated by pain-free remission periods of at least 3 months.[6] Typical cluster periods last between 2 weeks and 3 months. Chronic cluster headache attacks last at least a year without remission, or with a remission period lasting less than 3 months. Eighty percent of cluster headache patients have episodic cluster headache [7]; however, their greatest fear is knowing that they can potentially transition to chronic cluster headache over time. Transition from one subtype to another occurs in about 15% of patients.[8] Not only is chronic cluster headache more disabling, it is more difficult to treat.

In addition to the manifestations required for diagnosis in the ICHD-3, patients may experience facial flushing or pallor, facial edema and aural fullness during attacks. Ipsilateral pain may also be present in the oral cavity (leading to unnecessary dental extractions), jaw, head, neck and shoulder. The majority of patients also have "migrainous" features, such as photophobia, phonophobia, nausea and vomiting and some even experience typical migraine aura.[8] The migraine-like symptoms often lead to misdiagnosis – keep in mind that *if the patient meets the diagnostic criteria for cluster headache but have additional autonomic or migraine symptoms, they have cluster headache* and should be treated as such. The trigeminal autonomic symptoms, such as nasal congestion, rhinorrhea and tearing may erroneously lead to a diagnosis of sinus disease. Although people with migraine may also have trigeminal autonomic symptoms, such as lacrimation, they tend to be bilateral and less severe than in cluster headache. Additionally, the duration of cluster headache is shorter than migraine and attacks are more frequent and are associated with restlessness and agitation – people with cluster headache may scream and cry. People with migraine prefer being motionless in a dark, quiet room. People with cluster headache often can't be

still – they pace, rock back and forth or impose self-injurious behaviors (cutting, hitting their head against the wall, rubbing the skin, pressing on the eye).[8] Even if they lie down during an attack, they toss and turn, unable to get comfortable.

While the ICHD-3 criteria allow for up to 8 attacks per day, most patients have 2-4 attacks daily. The average duration is 45-90 minutes.[7]

The attacks tend to have a very abrupt onset, peaking in intensity within minutes. The pain is severe to very severe in intensity, described as excruciating, boring, a hot poker, dagger, knife or burning thorn.[8] It is not throbbing. The pain is typically side-locked (always occurs on the same side of the head) during a cluster period, more commonly right-sided). Most patients always have their cluster attacks on the same side of the head but the pain may change sides in fewer than 20% of patients.[2] Some patients experience premonitory symptoms minutes to hours before the pain starts, such as mild aching or discomfort in the same location as the headache pain, tearing, nasal congestion, trouble concentrating and mood changes.[9] These symptoms, or "shadows", may also precede a cluster period. While most patients are pain-free in between attacks, some have persistent, milder pain. Thus, it is important to ask the patient how long the *severe* pain lasts.

Cluster headache also has the unique features of circadian and circannual periodicity. About 80% of cluster headache patients can predict the time of day their attacks will occur.[7] The most common time between 0200-0300, and they may begin during any phase of sleep. The fear of nocturnal attacks leads to sleep avoidance and sleep deprivation. Circannual periodicity is reported by 2/3 of episodic and 1/3 of chronic cluster headache patients.[8] Spring and fall are the most common times for bout onset, related to daylight hours and possibly other environmental factors.

Attack triggers include vasodilators such as nitroglycerin (used to trigger attacks for research purposes), alcohol (the most common trigger) and PDE-5 inhibitors.[8] Other common triggers include a change in sleep pattern, (travel to a different time zone, daylight savings time, shift work), stress or relaxation, low testosterone, high altitude, bright sun, strong odors and weather changes. Note that triggers only provoke attacks during a cluster period.[7]

PATHOPHYSIOLOGY

Based on clinical features, functional neuroimaging and molecular changes, the key systems involved in cluster headache are the hypothalamus, trigeminovascular system and autonomic nervous system. The ipsilateral posterior hypothalamus is activated at the beginning of an attack.[8] The hypothalamus has direct connections with the other two aforementioned systems and its involvement explains many features of cluster headaches, such as the circadian and circannual periodicity (suprachiasmatic nucleus), restlessness and agitation and some of the premonitory symptoms. The trigeminovascular system, most importantly V1 but including the upper cervical nerves, includes dermatomes of the head and neck, which explains why many patients feel the pain beyond the eye area. Given the therapeutic response to non-invasive vagus nerve stimulation in cluster headaches and other TACs, the vagus nerve is likely involved in some way, yet to be elucidated.

The cranial autonomic system involvement includes parasympathetic hyperactivity (lacrimation, conjunctival injection) and sympathetic inactivity (Horner syndrome) with a circuit extending from the superior salivatory nucleus to the sphenopalatine ganglion, lacrimal gland and other glands in the face and the paraventricular nucleus of the hypothalamus.[7,8,10] Low frequency stimulation of the

sphenopalatine ganglion induces attacks and high frequency stimulation inhibits attacks of cluster headache.

At the molecular level, several signaling molecules in the autonomic nervous system (also active in migraine) are calcitonin gene-related peptide (CGRP), pituitary adenylate cyclase activating polypeptide (PACAP-38) and vasoactive intestinal peptide (VIP).[8] Infusions of these peptides trigger cluster headache attacks in people with cluster headache.[11]

GENETICS

Both autosomal dominant and autosomal recessive patterns of inheritance are described, with a rate of positive family history of 6.4%-8.2%.[8] No specific gene has been identified and, similar to migraine, cluster headache may arise from a combination of genetic and environmental factors, including second-hand smoke exposure in childhood. [12, 13]

CO-EXISTING CONDITIONS

The most common co-morbidities of cluster headache are smoking, sleep apnea, anxiety and depression.[14] A multicenter study (n=175) showed that suicidality rates during an attack were: passive (64.2%), active (35.8%O, suicidal planning (5.8%) and suicide attempt (2.3%).[15] Those rates decreased to less than 5% each interictally. Smoking cessation does not affect cluster headache. Low testosterone levels may be present in both men and women with cluster headache.

DIFFERENTIAL DIAGNOSIS

Cluster headache and paroxysmal hemicrania may be difficult to distinguish because of overlapping attack duration; when in doubt, a trial of indomethacin is indicated.[7] Patients with cluster headache and interictal pain may be misdiagnosed with hemicrania continua, another indomethacin-responsive headache. Migraine, acute angle glaucoma, giant cell arteritis and Tolosa-Hunt syndrome may present similarly to cluster headache but are usually distinguished based on the history and examination.

EVALUATION

As secondary causes for cluster headache uncommonly exist (pituitary adenoma/prolactinoma, meningioma, arteriovenous malformation) an MRI of the brain with contrast with special attention to the pituitary and cavernous sinus is recommended for all patients with cluster headache - and all TACs - even if the neuro-ophthalmic and neurologic exams are normal. [7,8] Screening for sleep apnea and testosterone levels is recommended.

TREATMENT

For patients who are starting a cluster headache period, symptomatic, transitional, and preventive treatment are started simultaneously. Excellent reviews of general and refractory cluster headache treatment are found in references. The following Tables are adapted from various sources [8, 16-19].

TABLE 1. ACUTE TREATMENT OPTIONS
Non-oral routes of administration are preferred due to more rapid onset of action.

Medication	Dose	Comments

Oxygen	6-15 L/min with nonrebreather mask	
Sumatriptan	6 mg SC or 20 mg NS	
Zolmitriptan	5-10 mg NS	
Non-invasive vagus nerve stimulation	Three 2-minute stimulations	
Lidocaine	1 ml of 10% solution IN	
Octreotide	100 µg SC	May cause headache, including cluster headache
Dihydroergotamine	4mg NS	Likely effective in reducing severity, not well studied

SC=subcutaneous, NS=nasal spray, IN=intranasal

TABLE 2. TRANSITIONAL TREATMENT OPTIONS

Medication	**Dose**	**Comments**
Prednisone	Not defined	60-100 mg daily X 5 days, titrate by 10-20 mg every 3 days until finished. Headaches may recur as lower doses are reached.
Occipital nerve blocks with steroid	Not defined	
Ergotamine tartrate		Short-term prevention, not well studied, side effects

TABLE 3. PREVENTIVE TREATMENT OPTIONS

Medication	**Dose**	**Comments**
Verapamil	180 mg TID	May cause severe constipation, heart block at high doses
Galcanezumab	300 mg SC monthly	FDA approved for episodic CH, anecdotal reports of effectiveness in chronic CH
Melatonin	10 mg PO HS	Take 2 hours before bedtime. Some advocate offering melatonin to all cluster patients
Non-invasive vagus nerve stimulation	Three 2-minue stimulations BID	
Lithium	600-1500 mg daily with serum levels 0.6-0.8.	Considered a 3rd line treatment and requires slow dose titration. Renal, hepatic and thyroid monitoring required. May cause blurred vision, tremor, diarrhea, slurred speech, weakness, facial involuntary movements
Civamide (not available in US; similar to capsaicin)	100 µl of 0.025% each nostril daily	May cause nasal burning, lacrimation, rhinorrhea
Gabapentin	Not defined	800-3600 mg daily. Low level of evidence, maya be helpful as

		adjunctive treatment. May cause sedation, confusion, constipation
Topiramate	Not defined	50-400 mg daily. Low level of evidence. May cause paresthesia, cognitive impairment, weight loss, kidney stones
Baclofen	Not defined	5-10 mg PO TID. Low level of evidence
Sodium valproate	Not defined	600-2000 mg daily. May cause nausea, tremor, weight gain, alopecia
Sphenopalatine ganglion stimulation		Effective for chronic CH in RCT but currently unavailable
Posterior Hypothalamic DBS		Effective but recommended as a last resort because of risk

CH=cluster headache, RCT = randomized clinical trial, DBS=deep brain stimulation

Other treatments with less evidence include onabotulinumtoxinA, clomiphene citrate which may help in refractory chronic cluster headache, gamma knife surgery, caffeine, LSD and psilocybin.[16] The latter two are illegal but retrospective surveys and case reports indicate that non-hallucinogenic doses of bromo-LSD may abort attacks and extend remission periods.[20, 21] Anecdotally, while the medications are illegal in the U.S., cluster headache patients are able to obtain the seeds for psilocybin mushroom plants across state lines and cultivate them at home. A preliminary trial of microdose psilocybin in episodic and chronic cluster patients vs placebo pulse-dosed every 5 days found no statistical difference between groups in efficacy and side effects.[22] However, the effect was greater in patients with chronic cluster headache and the medication was well tolerated. Further trials are planned. In general, patients with cluster headache are significantly more likely to use illicit drugs during their lifetime than the general population.[23]

PROGNOSIS

Data regarding prognosis are sparse. Approximately 13% of patients who initially have episodic cluster headache develop chronic cluster headache and 33% of those with initial chronic cluster headache shift to the episodic form.[2] Cluster headache seems to remit with age with less frequent bouts and longer periods of remission between bouts.[24]

THE PAROXYSMAL HEMICRANIAS

The paroxysmal hemicranias were initially described by Sjaastad and Dale in 1974.[25] They are less common than cluster headache with a prevalence of 0.5 per 1000 or less. [7, 26] However, they are important to know about because of their clinical overlap with cluster headache. Additionally, they are one of the “indomethacin responsive” primary headache disorders, so misdiagnosing them as cluster headache could lead to a rabbit hole of ineffective treatment trials.

The ICHD-3 criteria for diagnosis are:[6]

A	At least 20 attacks fulfilling criteria B-D	
B	Severe unilateral orbital, supraorbital and/or temporal pain lasting 2-30 minutes	
C	Either or both of the following	
	1	At least one of the following symptoms or signs, ipsilateral to the headache:
		a. conjunctival injection and/or lacrimation
		b. nasal congestion and/or rhinorrhea
		c. eyelid edema
		d. forehead and facial sweating
		e. miosis and/or ptosis
	2	A sense of restlessness or agitation
D	Occurring with a frequency of > 5 per day	
E	Prevented absolutely by therapeutic doses of indomethacin	
F	Not better accounted for by another ICHD-3 diagnosis	

As in cluster headache, there are episodic and chronic forms. Episodic paroxysmal hemicrania consists of at least 2 bouts, lasting from 7 days to one year (untreated) and separated by pain-free remission periods of at least 3 months. Chronic paroxysmal hemicrania occurs without a remission period, or remissions lasting < 3 months, for at least one year.[6]

Both sexes are equally affected with a mean range of onset in the 30s.[7, 26] Pediatric onset is described [27, 28], as well as onset into the 8th decade. The most common locations of pain are orbital, retro-orbital, temple, and frontal, vertex, occipital, cheek.[29] The oral cavity, ear, shoulder and upper limb may be involved. The pain is typically described as sharp, stabbing, throbbing, boring, claw-like or dental. It is strictly unilateral in 90% of cases with no side predilection. Less commonly, the attacks are bilateral. Autonomic and migraine-like features occur with rates similar to cluster headache, with lacrimation being most common.[26] About 1/3 of patients have interictal pain, half have circadian attacks and circannual attacks are rare.[29] Most patients have restlessness and agitation and about one quarter exhibit verbally aggressive behavior during attacks. Triggers are similar to those of cluster headache and interictal pain sometimes occurs. Nocturnal awakening is possible.

The main factors distinguishing the paroxysmal hemicranias from cluster headache are their duration and frequency. The average attack duration is 17-26 minutes (range 10 seconds to 4 hours) and the attacks tend to be more frequent than cluster headache, ranging from 2-50 times daily in one large study, mean 11 times daily. Additionally, the attacks may be precipitated by neck movement, coughing, sneezing and bending down, which are atypical for cluster headache. Motion sensitivity, which is unusual in cluster headache, may be present and various types of aura have been reported.[29] Unlike cluster headache, most people have a chronic pattern from onset.[29]

PATHOPHYSIOLOGY

The pathophysiology is similar to cluster headache although functional imaging reveals activation of the posterior hypothalamus contralateral to the pain.[7]

TREATMENT

When in doubt about cluster headache vs. paroxysmal hemicrania, give an indomethacin trial first. Although that sounds simple, it is not always easy.

First, indomethacin is a “tough drug” to take. It is not well tolerated, particularly regarding GI side effects.[28] The tolerability problem can preclude trying an adequate dose, which can range from 150 mg to 300 mg daily. There are several published dosing regimens but I try to use the lowest effective dose (with gastroprotective prophylaxis) so I typically start with 25 mg BID or TID with a meal. If tolerated but ineffective after3-7 days, the dose is gradually increased.[26] Once effectiveness lasts at least 2 weeks, incremental downward titration may be initiated to find the lowest effective dosage. [26]

What happens if the patient doesn’t tolerate indomethacin? Assuming that it didn’t cause an ulcer, other selective COX-2 inhibitors such as celecoxib can be tried. But if other NSAIDs are out of the question, things get tricky. Other medications with reported benefit include topiramate, verapamil, flunarizine, melatonin (which has a chemical structure similar to indomethacin), noninvasive vagus nerve stimulation and local nerve blocks.[30, 31]

Second, some individuals do not meet the ICHD-3 criteria because (1) the respond to indomethacin but do not fulfil the other criteria; (2) their headache phenotype is consistent with paroxysmal hemicrania but that do not have a complete response to indomethacin, although it works better than other therapies; (3) their headache phenotype is consistent but there is no response to indomethacin; (4) they are unable to tolerate indomethacin to see if works.[29]

DIFFERENTIAL DIAGNOSIS

The major differential diagnosis is cluster headache and the short lasting unilateral neuralgiform headaches. Secondary causes are rare and not well established, including head trauma, PDE-5 inhibitors and various brain mass lesions (pituitary adenomas, demyelinating lesions, metastatic leiomysarcoma to the eye, gangliocytoma of the sella), of which the response to surgical removal is inconsistent regarding resolution of the headache.[29, 30, 32]

HEMICRANIA CONTINUA

Hemicrania is an easy diagnosis to miss. It was initially described by Medina and Diamond in 1991 and a cluster headache variant and described as an indomethacin-responsive headache in 1984.[33, 34]. Hemicrania continua accounts for about 1% of patients with unilateral or daily headaches with age at onset between 30-50 years and a definite female preponderance.[26, 33] The typical pattern is unremitting from onset.

The ICHD-3 diagnostic criteria are:[6]

A	Unilateral headache fulfilling criteria B-D	
B	Present for >3 months with exacerbations of moderate or greater severity	
C	Either or both of the following	
	1	At least one of the following symptoms or signs, ipsilateral to the headache:
		a. conjunctival injection and/or lacrimation
		b. nasal congestion and/or rhinorrhea
		c. eyelid edema
		d. forehead and facial sweating
		e. miosis and/or ptosis

	2	A sense of restlessness or agitation, or aggravation of pain by movement
D	Responds absolutely to therapeutic doses of indomethacin	
E	Not better accounted for by another ICHD-3 diagnosis	

The phenotype is just what the name implies: a unilateral, side-locked headache that is constantly present albeit with intermittent exacerbations that have a migraine phenotype. The diagnostic error occurs because many patients fail to spontaneously report the constant background pain. For this reason, it is very important to ask patients with strictly side-locked unilateral headaches (that may sound like migraine) *whether they are ever completely headache free*.

The continuous pain may be completely hemicranial or only involve certain parts of the head: frontal, periorbital or temporal involvement may bring patients to an eye care specialist. The pain may be dull, sharp, throbbing, aching or stabbing and some patients describe unilateral ocular foreign body sensation or itching.[29] Many times, the constant pain is so mild that people ignore it.

The autonomic features are not as prominent as with other TACs, lacrimation being most common.[7] Triggers are similar to migraine (stress, alcohol, skipping meals, poor sleep). The exacerbations may last between seconds and weeks although they most commonly last 2 days.

DIFFERENTIAL DIAGNOSIS

The main differential diagnoses are migraine and cluster headache (with interictal pain). Unlike hemicrania continua, which is side-locked, migraine usually changes sides or is bilateral and is characterized by pain-free periods. Hemicrania continua always responds to indomethacin.

There are many causes of unilateral side-locked headache to consider such as dental pain, temporomandibular disorder, giant cell arteritis and chronic sinus disease. A similar phenotype has been reported in postsurgical and posttraumatic cases, carotid dissection, cortical venous sinus thrombosis, metastatic cancer to the brain, nasopharyngeal carcinoma and orbital inflammatory disease.[26]

EVALUATION

MRI with dedicated cavernous sinus and pituitary views followed by evaluations for other secondary causes per clinical suspicion.

TREATMENT

The first line treatment is indomethacin with second-line treatments as per paroxysmal hemicrania. In addition to medications occipital nerve blocks, onabotulinumtoxinA (migraine protocol) and noninvasive vagus nerve stimulation have reported benefit.[31] Radiofrequency of the sphenopalatine ganglion and occipital nerve stimulation may be helpful for refractory patients.

SHORT-LASTING UNILATERAL NEURAGIFORM HEADACHE ATTACKS (SUNHA)

This group of TACs comes in two varieties: short-lasting unilateral neuralgiform headaches with conjunctival injection and tearing (SUNCT) and short-lasting unilateral neuralgiform headaches with cranial autonomic symptoms (SUNA). By definition, SUNA has either conjunctival injection or tearing, or

neither. Their prevalence is between 1-100 per 100,000, with SUNCT being 5 times more common than SUNA.[35] Typical age at onset is 40-70 years and both types are more common in men.

The ICHD-3 diagnostic criteria are:[6]

A	At least 20 attacks fulfilling criteria B-D	
B	Moderate or severe unilateral head pain with orbital, supraorbital, temporal and/or other trigeminal distribution, lasting 1-600 seconds and occurring as single stabs, series of stabs or in a saw-tooth pattern	
C	Either or both of the following	
	1	At least one of the following cranial autonomic symptoms or signs, ipsilateral to the pain:
		a. conjunctival injection and/or lacrimation
		b. nasal congestion and/or rhinorrhea
		c. eyelid edema
		d. forehead and facial sweating
		e. miosis and/or ptosis
	2	A sense of restlessness or agitation
D	Occurring with a frequency of at least once per day	
E	Not better accounted for by another ICHD-3 diagnosis	

Episodic and chronic forms exist, corresponding to those defined for cluster headache.[6]

The pain is variously described as burning, stabbing or electric and usually occurs in the ophthalmic nerve distribution.[35] It is not as severe as cluster headache and also much briefer. The sawtooth pattern is a period of elevated pain punctuated by stabs. Similar to cluster headache, episodic patients usually have 1-2 bouts per year lasting weeks to months. Attacks usually last seconds with mean attack frequency of 30 per day (up to 100 or more may occur). There may be mild interictal pain.

DIFFERENTIAL DIAGNOSIS

SUNCT and SUNA are often misdiagnosed as trigeminal neuralgia as they have many common features. All are brief, can be stabbing or electric, and have cutaneous triggers, such as touching the face, brushing the teeth, wind and chewing.[36] Trigeminal neuralgia does not have cranial autonomic features and most commonly affects V_2 and V_3. SUNCT and SUNA affect V_1. SUNCT and do not have a refractory period after trigger zone excitation while trigeminal neuralgia does.[7]

Other differential diagnoses include primary stabbing headache (which does not have cranial autonomic symptoms), cluster headache, paroxysmal hemicrania, herpes zoster and dental issues. Secondary causes include pituitary tumors, posterior fossa tumors and, rarely, vascular malformations and trigeminal nerve compression by the superior cerebellar artery.

EVALUATION

MRI with dedicated cavernous sinus and pituitary views, followed by MRA head if treatment is unsuccessful.[26,35]

TREATMENT

Initial treatment is lamotrigine 100-200 mg daily.[7] Lamotrigine is always initiated gradually because of the risk of Stevens-Johnson syndrome and other allergic reactions. There is also a rare risk of hemophagocytic lymphohistiocytosis.[35] The most effective treatment is inpatient intravenous lidocaine by continuous infusion of 1-3.5 mg/kg/hour for up to a week, which may provide relief for several months. Continuous telemetric monitoring is required.[35, 37]

Other medications that may be effective are topiramate, duloxetine, oxcarbazepine, carbamazepine, pregabalin, greater occipital nerve blocks and oral steroids. Microvascular decompression and occipital nerve stimulation are reserved for refractory cases.[35]

SUMMARY

The TACs are unusual and fascinating headaches! When successfully treated, you can literally give someone their life back! They have similar features but can usually be distinguished by a careful history. Remember to ask about pain-free days (hemicrania continua vs migraine), duration of severe pain (cluster headache vs hemicrania continua or paroxysmal hemicrania) and, when in doubt, try indomethacin. Brain MRI should be performed in all patients with a suspected TAC.

TABLE 4. COMPARING THE TACs:

	Cluster Headache	Paroxysmal Hemicrania	SUNCT/SUNA	Hemicrania Continua
ICHD Criteria (mean, from literature)				
Duration (mean)	150-180 min (45-90)	2-30 min (17-26)	1-600 sec (seconds)	>3 months
Frequency (mean)	1-8 per day (2-4)	>5 per day (11)	At least 1 per day (30)	Constant with flares
Autonomic features	Yes	Yes	Yes	Not as prominent
Restlessness/agitation	Yes	Yes		Yes
Response to indomethacin		100%		100%
Epidemiology				
Male:Female	2.5:1	Equal	1.5:1	1:2
Episodic:Chronic	90:10	35:65	10:90	15:85
Triggers				
Alcohol Neck movements Cutaneous	Yes	Yes Yes	 Yes Yes	Yes

Table modified from Burish and Rozen [26]

CME ANSWERS

1. B
2. A
3. C

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RECURRENT PAINFUL OPHTHALMOPLEGIC NEUROPATHY OR OPHTHALMOPLEGIC MIGRAINE – WHICH IS IT?

VIVEK LAL, MD, DM Neurology, FIAN, FRCP Edin, Director, PGIMER, Chandigarh, Prof and Head Department of Neurologym Postgraduate Institute of Medical Education and Research Chandigarh, India

LEARNING OBJECTIVES

1. Whether ophthalmoplegia with headache is directly attributable to migraine (ophthalmoplegic migraine [OM]) or is due to an inflammatory neuropathy (recurrent painful ophthalmoplegic neuropathy [RPON]).
2. What is the pathway of ophthalmoplegia in patients with headache and what is its relation with migraine (chronic/ episodic/ migraine with and without aura)
3. Highlighting clinical profile, natural course, prognosis and management of headache and ophthalmoplegia in children and adults

CME QUESTIONS

1. Who is credited with first describing Ophthalmoplegic migraine

A. William Gowers
B. Thomas Willis
C. Ramon y Cajal
D. Jean Martin Charcot

2. Which is the major neuropeptide associated with migraine

A. Substance P
B. Calcitonin gene related peptide
C. Vasoactive Intestinal Peptide
D. Nitrous oxide

3. Which nerve is most commonly involved in ophthalmoplegic migraine in children

A. Oculomotor nerve
B. Trochlear nerve
C. Abducens nerve
D. Optic nerve

KEYWORDS

1. Ophthalmoplegia
2. Migraine
3. Oculomotor and Abducens Cranial Nerves
4. Calcitonin gene related peptide

CME ANSWERS

1. **D**
2. **B**
3. **A**

Surgical Challenges in Neuro-Ophthalmology [1.5 CME] - Wednesday, March 6th

Moderators: Ore-ofe Oluwaseun Adesina, MD & Courtney E. Francis, MD

A case-based discussion of surgical challenges in neuro-ophthalmology for thyroid eye disease, chronic progressive external ophthalmoplegia and paralytic cranial neuropathies.

Upon completion of this session, participants should be able to: (1) Recognize when surgical vs other interventions can or should be applied to the management of selected neuro-ophthalmic conditions, (2) Compare and contrast surgical options for patients with neuro-ophthalmic diagnoses amenable to surgical intervention, including type of surgery, timing of surgery, and expectations from surgical outcomes, (3) Identify gaps in understanding of surgical interventions for neuro-ophthalmic conditions and utilize the skills gained to apply to patient care.

- **TED: Strabismus – When and How to Operate**, Madhura A Tamhankar, MD
- **TED: Orbitopathy – When to Decompress or Not**, Prem S. Subramanian, MD, PhD
- **CPEO: Strabismus Management**, Nicholas J. Volpe, MD
- **CPEO: Goals and Surgical Approaches to Eyelid Surgery**, Anne Kao, MD
- **Paralytic Cranial Neuropathy from Brainstem Stroke** – Strabismus Management, Lauren C. Ditta, MD
- **Paralytic Cranial Neuropathy from Brainstem Stroke** – Lid Management, Roger E. Turbin, MD

TED: STRABISMUS – WHEN AND HOW TO OPERATE

Madhura A. Tamhankar MD
Scheie Eye Institute, University of Pennsylvania
Philadephia, Pennsylvania

LEARNING OBJECTIVES

At the end of the symposium the attendee will be able to:

1. Describe the evaluation of patient with diplopia from thyroid eye disease.
2. Explain the approach to managing diplopia in thyroid eye disease including optical, medical, and surgical treatments.
3. Know about the surgical challenges including preferred type of extraocular muscle surgery, timing of surgery and challenges of operating on restricted muscles.

CME QUESTIONS

1. A 43-year-old male presents with thyroid eye disease causing proptosis, diplopia, and clinical activity score of 7. He has received intravenous steroids and is currently on oral prednisone 45 mg daily. His previous treatments have included thyroidectomy, orbital radiation and cellcept with little benefit. He desires surgical correction. He will likely benefit by

    A. Orbital decompression followed by strabismus and eyelid surgery.
    B. Teprotumumab to treat thyroid eye disease.
    C. Another course of intravenous steroids.
    D. Close monitoring till his eye disease becomes stable.

2. The frequency of involvement of extraocular eye muscles in thyroid eye disease is as follows:

    A. obliques> medial rectus> superior rectus > inferior rectus> lateral rectus
    B. medial rectus> superior rectus> inferior rectus> lateral rectus> obliques
    C. inferior rectus> medial rectus> superior rectus>lateral rectus> obliques
    D. superior rectus> medial rectus> inferior rectus> lateral rectus> obliques

3. A 67-year-old patient has thyroid eye disease with left hypertropia of 20 PD in primary gaze, increasing in upgaze to 30 PD of LHT and decreasing in downgaze to 12 PD of LHT. There is elevation deficit of the right eye with enlargement of the right inferior rectus muscle on MRI. The optimal surgical approach would be to do a

    A. Right superior rectus resection.
    B. Left superior rectus recession.
    C. Left inferior rectus resection.
    D. Right inferior rectus recession.

KEYWORDS

1. Thyroid eye disease
2. Restrictive strabismus
3. Diplopia
4. Teprotumumab
5. Strabismus surgery

HIGHLIGHTS

1. Thyroid eye disease
2. Restrictive strabismus
3. Strabismus surgery

SUMMARY

Introduction

Restrictive strabismus with diplopia occurs in 30-50% of patients in thyroid eye disease (TED) due to a decrease in muscle fiber elasticity caused by the direct infiltration of inflammatory cells, related to cytokines and eventually fibrosis of the extra ocular muscle[1]. Impairment of motility occurs significantly more often in smokers and older patients[2]. Several extraocular muscles may be affected although single unilateral muscle involvement can also occur. Hypertropia with restricted elevation due to inferior rectus involvement and esotropia with restricted abduction from medial rectus involvement are the most common types of restrictive strabismus in TED[3]. The lateral rectus and the oblique muscles are the least affected. Early in the process most patients typically adopt a chin-up posture due to a tight inferior rectus muscle. New onset diplopia can also occur after orbital decompression because of changes in muscle pads and orbital anatomy. Esotropia is most common after medial orbital wall decompression due to displacement of the medial recti muscles in the ethmoid sinus.

Management of diplopia in TED

During the active and progressive phase of TED, medical treatment and orbital radiotherapy may improve diplopia minimizing expansion of orbital tissues and limiting restriction of ocular motility and strabismus.

Optical treatment of patients with diplopia due to thyroid eye disease includes giving prism glasses, ground in or temporary. Smaller degrees of ocular misalignment (<10PD) are well suited for prisms while with larger misalignment or both vertical and horizontal diplopia patients may not be optimally satisfied with prism prescriptions. It is also important realize that with incomitant deviations the prisms may not relieve diplopia in all directions of gaze.

Medical treatment for improvement of diplopia in acute stages of TED involves use of corticosteroids and newly approved insulin like growth factor 1 antagonist Teprotumumab which was found to be effective in relieving double vision in clinical trials[4,5].

While many protocols for corticosteroid administration exist, weekly infusions of steroids either 250 mg or 500 mg for 4-12 weeks has been proposed by European group of Graves' ophthalmopathy in their consensus statement in 2008[6].

The effect of teprotumumab in improving diplopia in TED was studied in the phase 2 and phase 3 clinical trials. In the teprotumumab phase 2 and phase 3 (OPTIC) clinical studies conducted in patients with recent onset TED (≤ 9 months and clinical activity score (CAS) ≥4 as well as open label extension study optic X conducted in non-responders from OPTIC which included placebo and re-treated patients with a mean (SD) TED duration 12.3 months (2.5) and mean CAS of 3.6 (1.7), patients presenting with diplopia were evaluated from baseline to study week 24 with off treatment evaluations at weeks 28 up to week 72.
At week 24 in the phase 2 and phase 3 studies, 53% of patients in the teprotumumab group had Gorman diplopia score of 0 compared to 25% of patients in the placebo group (P<0.01).
In the optic X at week 24, 56.5% of patients receiving their first course of teprotumumab had a diplopia score of 0. In the phase 4 clinical trial conducted in patients with longer duration TED (2 to < 10 years) and CAS < 1 there was a trend towards diplopia improvement (not significant).

Medical treatment can have variable efficacy in improving double vision in TED and some patients may continue to have persistent disabling double vision requiring surgical intervention.

While the CAS is the system most widely used to distinguish between active and inactive phases of TED there are a subset of patients that demonstrate rapidly worsening extraocular muscle dysfunction in the absence of elevated CAS[7]. In one study 44% of patients with TED and double vision had a CAS <3[7]. Another study found that there was no difference in age, sex, duration of ocular symptoms or smoking status between the group that had high CAS and double vision versus the group that had low CAS double vision[6]. It is important to realize that there are limitations in the modified CAS scoring system and differences in Graves' orbitopathy subtype. The scoring does not reflect ocular muscle involvement and CAS may not be as sensitive as previously reported[6].

Surgical Management of diplopia due to TED

In chronic inactive stages of thyroid orbitopathy, orbital decompression should be considered if the patient has significant proptosis. The occurrence of double vision after orbital decompression can occur in 3.8-64% patients in TED[8]. Risk factors associated with development of diplopia following orbital decompression include older age at surgery, elevated CAS, proptosis, presence of preoperative compressive optic neuropathy and imaging findings of enlarged cross-sectional areas of each rectus muscle to the overall orbital area[8]. Regarding surgical factors, postoperative diplopia was more common among those undergoing medial wall decompression, bilateral orbital surgery whereas endoscopic medial wall decompression was found to be relatively protective[9].

Preoperative counseling is essential to prepare patients for the potential of new onset postoperative diplopia following orbital decompression surgery.

Surgery for strabismus in thyroid eye disease should be carried out in the inactive phase of the disease and once orbital decompression has been performed if felt necessary.

Preoperative measurement of deviation and ductions in TED

Extraocular motility should be assessed in all positions of gaze noting the direction of maximum deviation. Incomplete ocular ductions indicate more restriction of the extraocular muscle. Ocular misalignment is measured in both primary and reading positions with alternating prism cover test as well as in all other cardinal directions of gaze. Preoperative fusion capacity in the field of binocular single vision or with the use of prisms provide valuable information for dosing muscle surgery. Note should be made of presence of compensatory head posture.

Principles of strabismus surgery in TED

The overriding principal in treating restrictive strabismus in TED is to relieve the restriction which is usually achieved by a muscle recession. Those with esotropia respond well to medial rectus recession surgery. In those with inferior rectus restriction and resulting vertical diplopia, weakening the tight inferior rectus will help to improve the primary position deviation but may induce a double vision in downgaze which can then be alleviated by doing a recession of the contralateral inferior rectus muscle or a Faden operation (posterior fixation suture).

The choice between adjustable versus non-adjustable is surgeon dependent. There are no published randomized controlled trials comparing adjustable and nonadjustable sutures. Some authors do not recommend adjustable sutures due to a risk of postoperative late muscle slippage while others do[10]. Lueder et al demonstrated long-term symptomatic relief of diplopia in patients treated with adjustable sutures[11]. Some authors suggest mildly under correcting the recession especially when performed with the adjustable suture technique[12].

Surgical challenges

Surgery is generally carried out with the patient under general anesthesia .At surgery the affected extraocular muscles are usually tight and fibrotic. Gaining access to the muscles can be challenging. Following decompression, muscles maybe incarcerated in bone. Due to severe muscle tightness exposure can be difficult. It may be difficult to place a strabismus hook under the muscle. Forced ductions are generally positive. A Wright hook placed underneath the muscle insertion may be helpful and safer. Some authors advocate fixing the recessed muscle in the "relaxed muscle position"; this is where the muscle lies at surgery with the eye centrally placed[13]. There is controversy over the use of adjustable sutures when recessing the inferior rectus muscle. Several authors have described late over-correction using this technique[14]. However, a recent study found no significant difference between fixed recession and adjustable sutures[12]. Some surgeons use nonabsorbable sutures to reduce the risk of late over-correction, but these sutures have a higher risk of infection and a tendency to erode through the conjunctiva. Recession of inferior rectus muscle results in between 3-4 PD of effect per mm of surgery[12]. Recession of the vertical muscle carries the risk of exacerbating lid retraction as there are fibrous connections between the superior rectus and the levator complex in the upper lid and the inferior rectus and the lower lid retractors. At the time of strabismus surgery, it is advisable to divide these fibers as far posteriorly as possible. Several authors advice aiming to under correct vertical deviation to allow for a late over-correction[12]. The aim should be to achieve single vision with both eyes in about 10° of downgaze. This facilitates reading and walking down steps well requiring only a minimal chin-up head position for distance vision.
The reported strabismus surgery success rate is anywhere between 43-100%[15] and reoperation rate of between 17 and 45%[16]. Rectus muscle resection is generally not advocated because of concerns of worsening muscle restriction. However, in certain cases of strabismus with large angle deviation causing

intractable diplopia more extensive surgery may be required and resections may be an option in those circumstances.

Usually over-correction can develop and increase slowly in the weeks or months following surgery and may be seen after recession of the inferior rectus muscle. Delayed scarring, fibrosis of the ipsilateral antagonist, progression of thyroid orbitopathy and scarring of the Lockwood ligament has been proposed as possible etiologies[17].

Outcome criteria for successful extraocular muscle surgery in thyroid eye disease include achievement of binocular single vision in primary and downgaze, improvement in head posture which in turn improves quality of life including restoring ability to drive, walk or read[18]. Success rate of strabismus surgery varies between 55-100%and may be less in those that have had prior orbital decompression although these patients have more challenging thyroid eye disease phenotype[19]. Patient expectations in the perioperative phase must be carefully managed. It is usually possible to achieve single vision in the primary position without the aid of prisms by one operation, but the patient may have to get used to moving their head to have single vision in other directions where double vision may still remain. Sometimes more than one operation may be necessary to achieve a satisfactory outcome. Fortunately, many patients develop a large fusion range which helps reduce the diplopia. Patients may need to be warned that their proptosis and lid retraction may become more noticeable after strabismus surgery.

Finally, botulinum toxin injection has also been tried in patients with diplopia due to thyroid eye disease with variable success. In one study 22 consecutive patients with thyroid eye disease received botulinum toxin injections and a 3rd of these patients were able to avoid surgery, 27% improved after the injection there was no change in alignment in 23% and alignment got worse in 18% although the authors suggested that the alignment could have worsened even more since the injections were given in the active phase of the disease[20].

CME ANSWERS

1. **B**
2. **C**
3. **D**

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TED: ORBITOPATHY – WHEN TO DECOMPRESS OR NOT

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LEARNING OBJECTIVES

1. The attendee will be able to recognize surgical indications for orbital decompression in TED.
2. The attendee will be able to distinguish patients who may benefit from medical vs surgical decompression.
3. The attendee will identify the relative risks of changes in strabismus after medical and surgical orbital decompression.

CME QUESTIONS

1. Which of the following signs or symptoms is least likely to improve with surgical orbital decompression?

    A. Corneal exposure
    B. Eyelid fat herniation
    C. Orbital pain
    D. Periocular redness
2. Which orbital decompression technique is most likely to result in new onset diplopia?

    A. Combined medial and lateral
    B. Deep lateral wall
    C. Floor/medial wall
    D. Intraconal fat resection
3. Teprotumumab treatment after prior surgical orbital decompression may result in which complication?

    A. Cheek numbness
    B. Enophthalmos
    C. Optic neuropathy
    D. Rebound chemosis

KEYWORDS

1. Thyroid decompression
2. Diplopia
3. Surgical risk

HIGHLIGHTS

1. When to decompress: acute versus chronic/longstanding disease

Patients with recent onset thyroid eye disease (TED) may present with rapidly progressive proptosis, periocular swelling, and ocular surface inflammatory signs. Signs and symptoms of orbital congestion may result both from the inflammatory mediators of TED (interleukins, other cytokines) and from increased turgor from water absorption/retention that comes from glycosaminoglycan deposition. In this acute phase, swelling and tissue expansion may cause eyelid retraction and lagophthalmos in addition to diplopia. Pain often occurs as well. If severe enough, swelling may cause vision-threatening corneal exposure and/or compressive optic neuropathy. Urgent orbital decompression is needed in these cases, and surgical decompression is otherwise deferred until later in the disease course.

Patients with more chronic or longer duration disease, characterized by lesser signs of orbital inflammation, also may benefit from decompression to reduce proptosis and lagophthalmos. Chronic orbital pressure/pain often responds to orbital decompression as well. Venous congestion may produce chronic redness and swelling that may be difficult to distinguish from inflammatory signs, and decompression often relieves this disease manifestation.

2. Medical vs surgical decompression

Until recently, medical interventions (including orbital radiotherapy as well as oral or infused drugs) were given to reduce inflammatory signs and symptoms with low expectation that treatment would reverse proptosis. Some patients would experience improvement in proptosis if there was significant orbital edema that remitted after medical therapy with corticosteroids; however, clinical practice has been to perform later surgical decompression when proptosis is stable. With the use of biologic agents, both broader spectrum drugs such as rituximab and tocilizumab as well as teprotumumab, a targeted therapy against the IGF-1 receptor, we have observed proptosis reduction and can achieve a medical decompression of the orbit that may obviate the need for surgical therapy. Initial results with teprotumumab were observed in patients with more acute disease manifestations, and subsequent data have shown that proptosis may improve in patients with longer-duration disease when teprotumumab is used. Clinical decision making will be influenced by the amount of proptosis reduction desired, patient expectations for immediate vs delayed improvement, and potential side effects and risks of each approach.

3. How strabismus is affected by orbital decompression

Patients with diplopia and strabismus before surgical decompression rarely experience diplopia resolution from the procedure. Clinical observation also suggests that patients with constant diplopia before teprotumumab treatment are less likely to have resolution of double vision than are patients with inconstant symptoms. Surgical decompression can cause new strabismus and diplopia that is often transient but may not resolve even after several weeks. Preservation of the inferomedial orbital strut lessens the likelihood of diplopia after surgery; removal of fat alone likely carries the lowest risk of new strabismus onset after surgery as reported in the literature.

SUMMARY

Surgical orbital decompression remains an important tool to be used in the care of patients with TED. It may be indicated when patients have acute, inflammatory symptoms and signs and there is compressive optic neuropathy; both proptosis reduction and relief of orbital congestion are reasons to perform a decompression in the setting of a more quiescent disease state.

CME ANSWERS

1. **D**
2. **C**
3. **B**

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STRABISMUS MANAGEMENT IN CHRONIC PROGRESSIVE OPHTHALMOPLEGIA

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LEARNING OBJECTIVES

1. The attendee will be able to know the differential diagnosis of chromic progressive external ophthalmoplegia
2. The attendee will be able to describe pre operative considerations and planning of surgery in patients with chronic progressive ophthalmoplegia
3. The attendee will be able to explain the realistic expectations of strabismus surgery in patients with chronic progressive ophthalmoplegia.

CME QUESTIONS

1. Common symptoms of strabismus in patients with CPEO include all of the following except:

    A. Double vision
    B. Psychosocial concerns about eye misalignment
    C. Abnormal head posture
    D. Oscillopsia
    E. Reduced peripheral vision

2. The least common deviation in patients with CPEO is:

    A. Esotropia
    B. Hypertropia
    C. Exotropia
    D. Exotropia and hypertropia
    E. Orthotropia

3. Strabismus surgery in patients with CPEO:

    A. Rarely requires reoperation
    B. Should not include the use of adjustable sutures
    C. Is often best accomplished by a combination of recessions and resections
    D. Can restore normal eye movements
    E. Should be done after ptosis is corrected

KEYWORDS

1. Ophthalmoplegia
2. Strabismus surgery
3. Kearns-Sayre syndrome
4. Mitochondrial DNA
5. Diplopia

HIGHLIGHTS

Chronic Progressive External Ophthalmoplegia (CPEO) is an umbrella diagnosis encompassing a heterogenous group of patients that develop progressive limitation of eye movements and ptosis. CPEO generally results from defects of the mitochondrial respiratory chain and has an estimated prevalence of 1 in 5000 births. Approximately 65 mitochondrial DNA point variants leading to pathogenic mutations have been recorded,[1] although CPEO is sporadic in approximately 50% of cases. There is an association with other neurologic abnormalities such as pharyngeal weakness and there are also other ophthalmic findings in some patients such as optic atrophy and a pigmentary retinal degeneration (Kearns-Sayre syndrome).[1] Although the condition was recognized in the 19th century, the earliest report of strabismus surgery in these patients was in 1963 by Stanworth.[2]

The condition develops insidiously and patients generally do not become symptomatic of their strabismus since the eyes develop impaired eye movements together and slowly become fixed in a central and aligned position. Symptoms are typically well compensated and despite significant "misalignment" there may be minimal complaints of disabling double vision.[3] In addition to developing a form of "suppression", asymmetric ptosis also can often prevent them from being aware of their double vision. The differential diagnosis is limited and includes myasthenia gravis, progressive supranuclear palsy, Miller Fisher Syndrome, orbital fibrosis and orbital inflammation.

CPEO patients present for strabismus surgery with very limited eye movements and generally because of double vision (most common), psychosocial issues or abnormal head posture/turn.[4] The vast majority of patients present with exotropia for unknown reasons. In three studies examining strabismus in CPEO, large angle exotropia is the most common deviation, (91% of patients with exotropia) with hypertropia, orthotropia and small esotropia making up the other 10% of patients.[4,5,7] Some patients have exotropia with hypertropia, and patients often develop a compensatory head position to use their eye in an exotropic position. Similarly, a chin up posture is often present since upgaze is often most impaired initially and downgaze is relatively spared.[6] In the largest surgical series,[4] during an 18 year period, only 28 patients presented to a large tertiary referral center with strabismus surgery recommended in only 12 of the patients.

While assessing CPEO patients with strabismus, it can be difficult to do cover testing because of impaired refixation movements and therefore estimating deviations based on prism light reflex or elimination of diplopia with prisms are generally the preferred methods for assessing strabismus. It is important to discuss with the patient that in the setting of large angle strabismus, they may be in fact ignoring an image and if strabismus surgery results in images close to each other, without establishing fusion, they could find double vision more intrusive. The potential for binocularity should be assessed based on responses to prism correction. Cyclotropias are rare and therefore generally if one can achieve fusion and realignment of the eyes with prism, the same can also be achieved with horizontal and vertical rectus muscle strabismus surgery. MRI or CT of the orbit to assess for muscle atrophy of thinning is generally not necessary but can be an important corroborating finding and rule out other abnormalities. Forced ductions should be attempted in office (especially if esotropic) as restriction can develop in some cases,[4] and it is important to address this during surgery.

Surgical management after assessment must first include careful informed consent. Achieving a normal head posture and/or fusion in the primary position is the best possible outcome. Extending the field of single binocular vision beyond the primary position is unlikely in eyes that do not move. Additional risks

of general anaesthesia from associated cardiac abnormalities should be considered and planned for if present. Finally, the presumed increased risk of torn muscle ("pulled in two (PIT)") should be discussed given the tendency of these atrophic muscles to be friable with increased prevalence of PIT in CPEO patients.[8]

Because the most common deviation is a large exotropia (50-70 PD) surgery often requires both lateral rectus weakening and medial rectus strengthening on both eyes (maximal surgery). Careful assessment of intraoperative forced ductions informs the decision and reasonable benefit from lateral rectus recession can be anticipated since the lateral rectus can be tight/fibrotic with chronic exotropia.[5] In the end it is the "tethering effect" of medial rectus resection that works best for exotropia and can be performed with an adjustable suture on one or both muscles to avoid the rare overcorrection.[4] Generally under corrections and recurrence of exotropia are more common because the muscles are non-functional,[4] but successful long terms results after several years have been reported.[7] Transposition procedures can also be employed, in which eye muscles or portions thereof can be transposed to improved function or at least create a tethering effect. For instance, the superior and inferior rectus (or just their nasal halves) can be moved to the insertion of the medial rectus to create an adducting force and reduce exotropia.[9] Wallace reported that small vertical strabismus may need not be addressed when correcting large angle horizontal strabismus in patients without diplopia.[5]

There are a small subset of patients with esotropia who, in my experience, often have a restrictive component to their strabismus secondary to medial rectus contracture (?fibrosis) or perhaps "early presenters" of CPEO. Hypertropias can occur and the basic approach is to weaken muscles in the direction of the deviation and strengthen the antagonist muscles to achieve the best possible alignment. The strabismus surgeon is wise to consider chronic progressive external ophthalmoplegia variants in patients who present atypically without an obvious diagnosis of CPEO, but subsequently recur/progress. An example is two young adult patients (not aged related esotropia or highly myopic patients) I have managed who were initially thought to have a simple decompensated intermittent esotropia. They had MR recessions and developed an early recurrence of esotropia with the insidious development of abduction deficits and were ultimately diagnosed with CPEO.
The use of botulinum toxin has been described in CPEO. This may seem counterintuitive given the already weak/fibrotic muscles, and indeed had little to no effect on 7 patients in the Tinley series, however, it was useful in post operative patients with recurrent or residual deviations after maximal surgery.[4]

SUMMARY

In the end, surgical decision making is based on the characteristics of CPEO muscles using standard muscle weakening and tightening procedures. Excellent results which improve patients 'quality of life can be achieved. If the CPEO patient is bothered by either abnormal head position, psychosocial issues and or double vision, strabismus surgery should be offered. By this time most patients often have very limited eye movements and depending on the angle of strabismus both recessions and resections in both the horizontal and vertical plane can be used to re-establish the eyes in a more central and normal position. In the most common setting of large exotropia, bilateral large lateral rectus recessions combined with medial rectus resections on adjustable suture is the most commonly reported successful procedure. Extra care should be taken to avoid tearing an extraocular muscle (PIT syndrome). The possibility of more intrusive double vision needs to be considered and abnormal head positions can almost always be eliminated by paying attention to the dominant eye and the patient's preference. Strabismus surgery is always done prior to ptosis surgery since operating on both horizontal and vertical

muscles can alter the position of the eyelid in relation to the eye.

CME ANSWERS

1. D
2. A
3. C

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CPEO: GOALS AND SURGICAL APPROACHES TO EYELID SURGERY

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LEARNING OBJECTIVES

1. The attendee will be able to explain how surgical considerations in patients with myogenic ptosis differ from those in patients with aponeurotic ptosis.
2. The attendee will be able to list the different surgical approaches to treat myogenic ptosis.
3. The attendee will be able to list the risks to surgical intervention in a patient with myogenic ptosis.

CME QUESTIONS

1. A 20-year-old woman was recently diagnosed with Kearns-Sayre Syndrome. She is referred for evaluation of ptosis, since she is unhappy with the droopy appearance of her eyelids. She does not endorse any difficulty with her vision and denies, specifically, that she has difficulty reading or driving. On examination her measurements are as follows (right eye/left eye): palpebral fissure 7mm/7mm, margin-reflex distance (MRD1) 2mm/2mm, levator function 11mm/11mm. The best treatment option for her is:

    A. Mullers muscle conjunctival resection
    B. Levator advancement
    C. Frontalis sling
    D. Frontalis advancement
    E. Defer any surgical intervention at this time

2. Which surgical approach is used to treat myogenic ptosis?

    A. Frontalis sling
    B. External levator advancement
    C. Frontalis advancement
    D. A and B
    E. All of the above

3. Which of the following is an expected risk of surgery to correct myogenic ptosis?

    A. Retinal detachment
    B. Lagophthalmos
    C. Recurrent ptosis
    D. B and C
    E. All of the above

KEYWORDS

1. Ptosis
2. Surgery

3. Levator
4. Frontalis
5. Lagophthalmos

HIGHLIGHTS

There are three muscles that elevate the eyelid: levator palpebrae superioris, Mullers muscle, and, to a much lesser degree, the frontalis muscle in the forehead. Ptosis of the eyelid can be congenital or acquired. Congenital blepharoptosis is most commonly due to dysgenesis of the levator palpebrae superioris, but may sometimes be neurogenic, such as in congenital third nerve palsy or Horner's syndrome. The most common type of acquired blepharoptosis is aponeurotic, which involves dehiscence of the levator aponeurosis from its point of attachment at the tarsus and is often age-related. Other causes of acquired ptosis include: myogenic, as seen in chronic progressive external ophthalmoplegia and associated syndromes, oculopharyngeal muscular dystrophy, myotonic dystrophy, and myasthenia gravis; neurogenic, as seen in third nerve palsy and Horner's syndrome; traumatic; and mechanical, which is due to a mass weighing down the lid.

Important components in the evaluation of blepharoptosis include: measurement of the palpebral fissure (PF), or the distance between the upper and lower eyelid; assessment of levator function (LF), which involves measuring the excursion of the levator palpebrae superioris muscle; measurement of margin reflex distance 1 (MRD1), which is the distance from the pupil to the upper eyelid; measurement of lagophthalmos, or the degree to which the eyelids cannot shut completely; assessment of orbicularis oculi tone and frontalis function.

The goals of surgery to treat myogenic ptosis are different than those to treat aponeurotic ptosis. It is important to allow time for an extended discussion with the patient about the nature of the disease and the expectations of surgical intervention. The aim is to clear the visual axis without complete resolution of ptosis. The discussion should address the increased risk of problems such as lagophthalmos, exposure keratopathy, and recurrent blepharoptosis. Surgical approaches to the repair of myogenic blepharoptosis include external levator advancement, frontalis sling, and frontalis advancement. Patients with good levator function may respond well to levator advancement surgery, while patients with poor levator function will need a frontalis sling or advancement procedure. However, while the degree of levator excursion is an important consideration in the selection of the surgical procedure to treat myogenic blepharoptosis, there is no clear consensus on what value serves as the cutoff for choosing one surgical approach over another. Other considerations in the selection of the surgical approach include: the age of the patient, since the causes of myogenic ptosis are often progressive diseases; whether the frontalis muscle is involved in the myopathy; whether there is lower eyelid retraction; and the risk of postoperative lagophthalmos.

SUMMARY

Surgeries to treat myogenic blepharoptosis include external levator advancement, frontalis sling, and frontalis advancement. The goals of treatment for myogenic blepharoptosis are different than those in aponeurotic blepharoptosis and it is important to set patient expectations accordingly. Patients with myogenic ptosis are at increased risk of post-operative lagophthalmos and exposure keratopathy, which may lead to corneal ulceration. Patients with myogenic ptosis are also likely to need repeat surgeries, particularly if the underlying etiology is a progressive disease. Levator function is an important consideration when selecting the surgical approach.

CME ANSWERS

1. **E**
2. **E**
3. **D**

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PARALYTIC CRANIAL NEUROPATHY FROM BRAINSTEM STROKE – STRABISMUS MANAGEMENT

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LEARNING OBJECTIVES

1. The attendee will be able to recognize the unique challenges ocular motor cranial neuropathies create for the patient and the strabismus surgeon.
2. The attendee will acquire management strategies for use of chemodenervation in the treatment of CN III and CN VI nerve palsies.
3. The attendee will be able to identify advanced strabismus surgical procedures for the treatment of CN III and VI nerve palsies, including transposition procedures.

CME QUESTIONS

1. Botulinum toxin can be beneficial in the management of CN III and VI nerve palsies during both the acute and chronic phases of treatment.

    A. True
    B. False

2. In a complete CN III palsy, what action of the superior oblique muscle may contribute to the outward position of the eye?

    A. Primary
    B. Secondary
    C. Tertiary
    D. Quaternary

3. When considering treatment options for a CN VI palsy, which of the following clinical findings helps guide management?

    A. Lateral rectus muscle function
    B. Prior strabismus surgery
    C. Onset of diplopia
    D. Primary angle of deviation
    E. All the above

KEYWORDS

1. Cranial nerve palsy
2. Botulinum toxin
3. Transposition procedure
4. CN III palsy
5. CN VI palsy

HIGHLIGHTS

- Paralytic cranial neuropathies (e.g., CN III, CN VI) affecting the extraocular muscles greatly impact patient quality of life, causing incomitant strabismus, intractable diplopia, and creating challenges for both conservative and surgical management.
- Understanding the etiology of paralytic cranial neuropathies facilitates the development of management strategies, which are often divided into acute and chronic phases of treatment.
- Treatment of paralytic cranial neuropathies should focus on reducing symptoms of diplopia, expanding the range single binocular vision, and improving cosmesis. In children, attempts to gain binocularity is particularly important to reduce the risk of amblyopia, while awaiting return to function.
- Conservative treatment strategies for diplopia caused by paralytic cranial neuropathies include partial occlusion, prisms, and chemodenervation; however, for cranial nerve palsies that have a long-term poor prognosis of recovery, surgical intervention is often necessary.
- Thoughtful consideration of the patient's disease process and patient expectations of care, as well as setting realistic goals of treatment are critical for optimization of management and for obtaining "successful" outcomes.
- For patients with paralytic cranial neuropathies who are co-managed by other subspecialties, a multi-disciplinary care conference may help to further elucidate appropriate management strategies during the acute and chronic phases of a patient's care.

SUMMARY

Management of oculomotor (cranial nerve III) palsies is particularly complicated since multiple extraocular muscles (levator palpebrae superioris, superior rectus, medial rectus, inferior rectus, and inferior oblique muscles), each with its own functionalities, may be affected. Oftentimes, patients experience intractable diplopia as well as undesirable cosmesis, particularly in the setting of a complete CN III palsy, where the eye is fixed in abduction, infraduction, and intorsion, and with eyelid ptosis. In a complete CN III palsy, the goal of surgery is to improve alignment in primary position. In this situation, counseling the patient that there may be limited rotation of the eye, persistent diplopia outside the primary position of gaze, and potential for a minimal range of single binocular vision even after surgery is critically important. With a partial CN III palsy, it may be possible to restore a functional field of binocular single vision in addition to improving primary position alignment—but this is dependent on the involved muscles, the degree of residual muscle function, and the tone of the paretic muscles' antagonists.[1]

In addition to conservative strategies, chemodenervation with Botulinum toxin A (BTX) during the acute phase while waiting for definitive surgery, may play an important role. BTX injection of the lateral rectus muscle may help to eliminate the horizontal deviation (especially if there is residual medial rectus function) and reduce long-term contracture of the lateral rectus (the antagonist of the weakened medial rectus muscle).[2]

BTX can also be injected into tight vertical recti; however, injection of a superior rectus muscle should be done carefully, as toxin injected into the levator-superior rectus complex may cause or worsen concomitant ptosis. While BTX can be used in the chronic phase of the cranial nerve palsy, it may be less predictable, and a higher dose of toxin may be needed to achieve a desired effect. Finally, BTX can be a useful adjunct to any strabismus surgery, especially to augment the effect of surgery or when multiple

recti muscles are being considered to reduce the risk of anterior segment ischemia. In this scenario, patients should be made aware of the potential benefit, risk, and long-term outcomes of the treatment.

Many surgical techniques have been reported to improve ocular alignment of CN III palsies. Prior to proceeding with any surgical procedure, it is reasonable to delay surgery for a period (at least 6 months) to monitor for recovery and to confirm stable alignment.[3] When assessing ocular alignment and extraocular motility, evaluating the diagnostic positions of gaze to identify the muscles involved, (including potential for multiple cranial nerve palsies), as well as the degree of residual muscle function is important. Additionally, the effect of contracted paretic muscle antagonists--which can be assessed by force generation or force duction testing in the office and/or intraoperatively—may call for an altered surgical plan. If aberrant regeneration occurs during the recovery period, appropriate diagnostic investigations should be pursued and considered for the surgical planning.

The most challenging aspect of a complete CN III palsy is correcting the large angle exotropia, which invariably recurs. A supramaximal recession and resection of the lateral rectus (14-16mm) and medial rectus (8-14mm) respectively [4,5] will give immediate improvement in cosmesis but will gradually weaken over time. To provide resistance to progressive abduction forces (note the tertiary action of the superior oblique muscle is abduction), several techniques have been described, which manipulate the globe position through either direct fixation or utilize remaining functional muscles for adduction tone.[6-15]

For partial CN III palsies, where the vertical recti may have residual or full function, transposition procedures may be advantageous. However, risk of full tendon transposition procedures includes anterior segment ischemia—especially when operating on multiple vertical recti. Vessel sparing procedures, plications, or chemodenervation may need consideration in select situations.[16]

The abducens nerve (CN VI) is the most frequently involved cranial nerve in ocular motor nerve palsies.[17] In adults over >50 years, most isolated CN VI palsies, are often related to microvascular risk factors (e.g., diabetes mellitus, hypertension hyperlipidemia). In younger adults and children, the etiology may be more ambiguous, with a higher incidence of trauma, infectious and inflammatory processes, as well as intracranial mass lesions. Depending on etiology, probabilities of spontaneous recovery or the possibility of recurrence may vary.[18] Because of this, patients should be managed closely in the months after the acute onset, with consideration of delaying definitive surgical procedures for at least 6 months following onset.

During the acute phase, interventions should aim to reduce symptoms of diplopia, create a meaningful area of single binocular vision, and prevent secondary contracture of the antagonistic medial rectus muscle. A trial of BTX can may be particularly helpful if the patient has limited to no range of single binocular vision, and it may reduce the risk of chronic contracture of the medial rectus muscle. There is some evidence to suggest that the injection of BTX during the acute phase of treatment of a unilateral CN VI palsy may improve recovery and reduce the need for future surgery. Therefore, early chemodenervation with BTX may prevent contracture of the antagonist medial rectus muscle, promoting binocularity, and hasten the recovery of normal ocular alignment.[19,20] While, optimal timing of injection is debatable, with good counseling in an appropriate patient, the procedure can be performed soon after onset of diplopia symptoms.[21,22]

Once in the chronic phase of a CN VI palsy, the likelihood of spontaneous improvement is much less likely. The definitive surgical procedure should be based upon residual muscle function and the limitation of abduction. This can be assessed with force generation of the lateral rectus muscle, saccadic

velocity as well as intraoperative force duction testing. For a partial sixth nerve palsy with residual lateral rectus function, a recession-resection of the horizontal recti may be of benefit. Deviations > 40Δ may require additional surgery on the contralateral eye (medial rectus recession). Adjustable sutures can also be of benefit.

When there is limited to no abduction function in a complete CN VI palsy, a transposition procedure is often needed. This procedure may improve abduction, expand the range of single binocular visual field, and eliminate an acquired face turn. There are many modifications of transposition techniques, with varying levels of surgical risk—namely under and overcorrections, and newly induced vertical and torsional strabismus.[23,24] These procedures can also be augmented with BTX. [25] Finally, the risk of anterior segment ischemia should be considered, especially when additional surgery on the medial rectus may need to be performed. In these scenarios, staged, ciliary sparing strabismus surgery should be considered.

CME ANSWERS

1. A
2. C
3. E

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PARALYTIC CRANIAL NEUROPATHY FROM BRAINSTEM STROKE – LID MANAGEMENT

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LEARNING OBJECTIVES

1. The attendee will recognize characteristics of facial nerve palsy grading systems, strengths and weaknesses.
2. The attendee will identify high risk characteristics in VII nerve induced lagophthalmos that warrant interventional strategies to protect vision.
3. The attendee will recognize medical and surgical strategies to mitigate ocular surface complications.

CME QUESTIONS

1. Which of the following statements are true:

    A. Implantation of upper eyelid load with both gold and platinum weights has been shown to improve paralytic lagophthalmos.
    B. The relative density of 99.9% gold at 21.5 g/cm^3 versus platinum at 97% purity and 19.3 g/cm^3 leads to gold eyelid weights being 10% smaller and therefore thinner than the platinum counterparts.
    C. The higher density of gold is responsible for greater total number of implanted gold rather than platinum weights.

2. Upper eyelid loading with gold or platinum weights, and lower eyelid resuspension are both considered permanent and irreversible “end of the line procedures” and should not be considered as initial treatment for flaccid paralysis of any cause.

    A. True
    B. False

3. Treatment options for synkinesis after facial palsy include which of the following:

    A. Targeted chemo-denervation into the normal side to neutralize hyperkinetic movements
    B. Targeted chemo-denervation into the normal side to balance contralateral prosopoplegia
    C. Targeted chemo-denervation into the synkinetic side to neutralize aberrant synkinetic and spasmic movement
    D. Retraining of synkinetic facial musculature with physical therapy
    E. All of the above

KEYWORDS

1. Gold/platinum eyelid loading
2. Chemodenervation
3. Synkinesis

4. Corneal neurotization

CME ANSWERS

1. A
2. B
3. E

HIGHLIGHTS

Treatment of paralytic lagophthalmos may prevent permanent visual disability as well as untoward cosmetic deformity and requires a multifaceted approach. The physician tackling lagophthalmos and its complications should have knowledge of a variety of short, intermediate and long term medical and surgical therapies. Timing and selection of treatments are directed at the underlying etiology, and expected duration of lagophthalmos. Ocular disease such as trigeminal dysfunction affecting corneal sensation and underlying ocular tear film dysfunction may force earlier and more aggressive interventions. Panel discussants will review a clinical scenario highlighting therapeutic techniques and provide an introduction to corneal neurotization as a method to regenerate corneal sensation.

SUMMARY

The assessment and management of facial nerve motor weakness leading to paralytic lagophthalmos overlaps multiple subspecialities as well as other ancillary services such as audiometry and physical therapy. Acute Bell's Palsy is the commonest cause of facial nerve dysfunction with an incidence of 11.5-53.3 adult cases per 100,000 and a lifetime prevalence of 1 in 60. Although approximately 70% are reported to realize complete recovery, half of those who incompletely recover will suffer mild and half moderate to severe sequelae including ophthalmic complications. [1-2] Complete recovery may be achieved in 90% with appropriate early medical pharmacologic management with oral prednisolone with or without a course of acyclovir or valacyclovir, which may reduce the necessity for surgical intervention.[3,4]

While residual orbicularis oculi function (innervated by the zygomatic branch of the facial nerve) is an important determinant of susceptibility to ocular complications from incomplete closure of the eyelids, other factors remain important[5-7]. These include static and dynamic features, regional effects of the major facial nerve branches, symmetry, and secondary findings such as synkinetic motor movement as well as other factors such as corneal sensation (trigeminal sensory function), Bell's phenomenon, corneal surface wetting, and secondary eyelid contracture that affect the likelihood of developing ophthalmic complications. A validated grading system was recently designed to address ophthalmic complications [8,9] (Table 1) and authors have begun to assess and report the system's predictive capability to determine the need for medical versus surgical ophthalmic management[10].

Initial decisions regarding surgical management of paralytic lagophthalmos are strongly influenced by patient conditions/functional status, the underlying etiology, expected recovery course, and the aforementioned factors. A variety of surgical options exist, and it is reasonable to consider an approach based on the immediate threat to the ocular surface, the cosmetic expectations of the patient, as well as short term, intermediate, and long-term outcomes of the different procedures.

The immediate protection of the ocular surface in patients failing conservative measures (taping regimens, temporary external eyelid loads, continuous wear soft bandage contact lens, ocular lubrication, moisture chambers, temporary/ permanent punctal plugging techniques) can be surgically

addressed in the short term (days to weeks) by temporary sutured lateral, medial or complete tarsorrhaphies. Bolsters can be employed to promote surgical durability and prevent “cheese-wiring” of temporary sutures. In the longer term (months to years) more permanent tarsorrhaphy procedures can be employed and typically induce more stable closure by promoting transposition of upper and lower eyelid tissues. Short and long term tarsorrhaphy techniques remain quick, available, and ultimately reversible, but limited with respect to cosmetic result.[11] Intermediate eyelid closure options (weeks to months) for patients with etiologies with expected longer duration lagophthalmos have been described utilizing chemo denervation (typically botulinum toxin A) of the levator palpebrae superioris to induce a chemical tarsorrhaphy which may be repeated.[12]

Eyelid loading techniques provide mechanical passive eyelid closure, and are commonly performed, readily available and surgically reversible. They are most commonly performed by surgical implantation of gold and more recently platinum eyelid weights ranging from 0.6 to 1.8 grams under regional eyelid anaesthesia. Heavier weights up to 2.8 grams are also available, typically by special order.. Effectiveness is greatest when the patient maintains an upright or elevated position to influence the passive weighting. Surgical modifications may limit implant extrusion, the increasing visibility of the underlying weight from thinning of overlying tissues, and secondary induced astigmatism affecting visual acuity[13]. Techniques using injectable fillers have been described and may be reversed by selecting short acting fillers or dissolution with hyaluronidase[14]. Care and proper technique must be exercised to avoid intravascular injection, over filling, tissue necrosis or arterial embolism. Dynamic eyelid closure may be achieved by implantation of an eyelid “spring” that is typically fixed to the superior orbital rim and upper eyelid tarsus; the spring expands constitutively closing the upper eyelid until mechanically elevated by the levator superioris. This latter technique is a technically challenging and extensive procedure, and much less commonly employed due to a high complication rate and revision rate from spring migration and extrusion[11].

Flaccid paralysis of the brow and midface may significantly affect eyelid function and influence flaccid lower eyelid malposition, surface wetting, lacrimal pumping, and cosmesis. Underlying tissue tone, canthal laxity as well as severity of muscular weakness affect the severity of prosopoplegia, ectropion and eyelid retraction. Surgical interventions that improve suspension and function are an important consideration in the short, intermediate, and long term and include medial and lateral canthoplasty, eyelid tightening procedures, brow and midface suborbicularis oculi fat lifting procedures (SOOF Lift)[15], weakening of unopposed eyelid retractors, placement of lower eyelid spacers at the level of the lower eyelid retractor musculature, and correction of anterior lamellar deficiency due to tissue contraction from long term flaccid paralysis. More detailed discussion of the many techniques is beyond the scope of this abstract.

Treatment with chemodenervation may promote symmetry by balancing hyperkinetic action of nonparalyzed muscles acting against flaccid paralysis, controlling ipsilateral synkinetic aberrant contraction and syndromes of aberrant regeneration such as gustatory, olfactory, and masticatory lacrimation (Bogorad syndrome).[16-17]

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Table 1 Mahotra, Personal communication 10/18/23

Cornea		Static **Asymmetry**		**Dynamic** Function		**Synkinesis**	
No staining	0	● No brow ptosis ● No ectropion ● No upper or lower eyelid retraction	0	● No blink lagophthalmos	0	Absent	0
PEE < 5	1	● Mild brow ptosis ● Medial ectropion ● Upper eyelid at limbus ● Mild lower eyelid retraction ≤2mm inferior scleral show ● LMBD >5mm shorter than contralateral side	1	● Lagophthalmos on blink< 5mm ● Brow elevation reduced but present	1	● Mild eye closure when smiling/speaking/eating ● Gustatory epiphora: not bothersome	1
PEE ≤ ½ cornea	2	● Severe brow ptosis ● Significant ectropion ● Superior scleral show ● >2mm inferior scleral show ● LMBD ≤20mm	2	● Lagophthalmos on blink≥5mm ● Lagophthalmos on gentle closure≤5mm ● Brow elevation-none or twitch	2	● Significant eye closure when smiling/speaking/eating ● Gustatory epiphora: bothersome	2
PEE >½ cornea or epithelial defect	3			● Lagophthalmos on gentle closure> 5mm ● Lagophthalmos on forced closure >2mm	3		
● Absent corneal sensation ● Absent/ reduced Bell's phenomenon ● *Schirmer's ≤ 5mm ● Affected eye is the only eye	a						

PEE=Punctate epithelial erosion, LMBD=Upper lid-margin to brow distance (mm).
*Schirmer's test with anaesthetic and if lower eyelid is apposed to the globe

Publication Symposium [2.0 CME] - Thursday, March 7th

Moderators: Victoria S. Pelak, MD & Laura J. Balcer, MD, MSCE

Publishing in the field of Neuro-ophthalmology is critical to our field and to the career of a neuro-ophthalmologist, but it can be fraught with challenges that demand knowledge and skills to overcome. This symposium will provide a practical overview and solutions to present-day publication challenges, including the use of AI writing tools, responding to reviewer critiques, publishing data from clinical trials, and the pros and cons of case report publishing. We will hear from a seasoned editor on the skills necessary to be an astute reviewer and editor, as well as a report on the current state of the JNO. Please bring your questions and ideas!

Upon completion of this session, participants should be able to: (1) Describe the pros and cons of clinical case report publishing, (2) Implement one important characteristic of a good reviewer while serving as a reviewer for a manuscript, (3) Understand the limits and pitfalls of using AI writing tools, (4) Respond to reviewer critiques appropriately.

- **Using AI Writing Tools in Your Scientific Writing Process/Ethics and Plagiarism**, Tim Requarth, PhD
- **Author "Predicaments" in Publishing**, Valerie Biousse, MD
- **The Pros and Cons of Case Report Publishing**, Edward A. Margolin, MD, FRCSC & Mays A. El-Dairi, MD
- **Lessons Learned from Clinical Trials Publishing**, Mike Wall, MD
- **What Makes a Good Reviewer/Editor?** Lanning B. Kline, MD

Using AI tools in your scientific writing process

Tim Requarth, PhD
Vilcek Institute of Graduate Biomedical Sciences, NYU Grossman School of Medicine
New York, NY

LEARNING OBJECTIVES

1. Describe the pros and cons of using AI writing tools with regards to accuracy, originality, and efficiency
2. Identify opportunities within the drafting and revising phases of writing that can be optimized by AI tools
3. Develop strategies for crafting prompts that enhance the accuracy and relevance of AI-generated content

CME QUESTIONS

1. When integrating AI tools into the drafting phase of writing, which approach is likely to be most beneficial to the accuracy and readability of the final product?
   A. Relying solely on AI-generated text without further user input
   B. Using AI to create an extensive outline that the writer passively accepts without critical evaluation.
   C. Using AI to provide a basic structure that is then expanded upon manually
   D. Allowing AI to autonomously conduct all research and synthesis of information

2. Which use of an AI writing tool best maintains the originality of your scientific writing?
   A. Generating complete sections of content to be used as-is
   B. Modifying existing texts from similar research papers
   C. Directly copying and pasting AI-generated content without citation
   D. Using AI as a writing coach to overcome writing roadblocks

3. What is a key consideration when crafting prompts for AI-generated content to ensure relevance and accuracy?
   A. Keeping prompts as vague as possible
   B. Providing detailed context and specific instructions in the prompts
   C. Using complex, technical jargon to impress the AI
   D. Limiting the prompt to one-word inputs for simplicity

KEYWORDS

1. Writing
2. Artificial Intelligence
3. ChatGPT
4. Publication

HIGHLIGHTS

- Researchers must skilfully juggle the roles of both scientist and writer, often under significant pressure and tight deadlines
- The workshop aims to unveil the capabilities of AI writing tools like ChatGPT, examining how they can enhance the scientific writing process
- Participants will learn how to leverage AI for generating ideas, drafting documents, and editing content while upholding the scientific integrity of their work

SUMMARY

As a researcher, you're a professional writer. You write grants to fund your research and papers to share your findings with the world. You work under deadline — and under pressure. But, that doesn't mean writing comes easy to you. In this workshop, you'll explore the power and pitfalls of using AI writing tools such as ChatGPT. These powerful tools can generate and critique ideas, draft sophisticated text from scratch, and refine human writing. You'll discuss AI-based strategies to streamline your writing process without compromising the integrity of your work.

CME ANSWERS

1. C
2. D
3. B

PREDICAMENTS IN PUBLISHING (AUTHOR POINT OF VIEW)

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LEARNING OBJECTIVES

1. The attendee will be able to explain what constitutes co-authorship as opposed to acknowledgements.
2. The attendee will be able to list effective strategies for navigating and addressing reviewers' comments.
3. The attendee will be able to know all steps required for successful publication

CME QUESTIONS

1. Indicate who should qualify as co-author of a scientific article:

   A. The person designing the study and providing funding
   B. The person providing administrative assistance for formatting references or tables
   C. The lab director or chair of the department
   D. The clinical coordinator who consented patients in the clinical trial

2. When revising a scientific article:

   A. It is essential to carefully answer all questions from the reviewers
   B. You should accept all reviewers' comments and change your manuscript accordingly
   C. You should systematically involve all co-authors in the revision process
   D. You should do the revision as soon as possible in order to resubmit the article promptly to increase your chances of acceptance

3. After an article is accepted:

   A. You are done and no further work will be necessary!
   B. You may receive more requests for revision from the editor in chief
   C. You should delegate reviewing the proofs of the article to the junior writer
   D. You should always respond to letters to the editor criticizing your work even when you think the comments are not fair

KEYWORDS

1. Research
2. Publication
3. Impact factor

HIGHLIGHTS

- Publishing article is rewarding and should be fun!
- Understanding of each step and basic rules is essential to a successful outcome.
- The reviewing process is tedious and often stressful and time-consuming. However, it is important to keep in mind that the ultimate goal is to make the article better.

SUMMARY

Scientific publications are essential for researchers and clinicians in academic centers. Who should be included as co-authors is an important decision which should be made before the article is finalized. How to ensure that an article is eventually published is always challenging and time consuming. We have all experienced the challenges and setbacks of difficult reviewers. These critiques can be both an emotional and intellectual hurdle to overcome, particularly after dedicating so much work. Careful response and attention to detail as well as persistence are the key to success. This presentation will address common questions such as why publish and how can I be an author?; my paper was rejected! Now what?; mastering reviewers' feedback: A revision is requested! How to respond to reviewers?; my paper is accepted! Now what?; someone did not like my paper and sent an aggressive letter to the editor! Now what?

CME ANSWERS

1. A
2. A,D
3. B,D

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(CONS) - THE PROS AND CONS OF CASE REPORT PUBLISHING

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LEARNING OBJECTIVES

1. Case reports are level 4 evidence.
2. Case reports are prone to bias.
3. We can't generalize case reports.

CME QUESTIONS

1. Case reports are high level evidence (true/false)
   A. True
   B. False

2. New interventions described in a case report are generalizable (true/flase)
   A. True
   B. False

3. Case reports are free of bias (true/flase)
   A. True
   B. False

KEYWORDS

1. Case reports
2. retrospective fallacy
3. level 4 evidence

HIGHLIGHTS

Case reports are level 4 evidence and are prone to bias

SUMMARY

Case reports may be useful to gather information about expected manifestations of certain rare disorders but one must keep in mind the high likelihood of bias, the lack of generatability and the inability to prove a true cause to effect relationship. This is specifically important to keep in mind in case reports describing new interventions.

CME ANSWERS

1. B
2. B
3. B

LESSONS LEARNED FROM CLINICAL TRIAL PUBLISHING

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LEARNING OBJECTIVES

1. Understand how to plan a clinical trial to maximize publications
2. Know how to choose the most appropriate type of variables to measure
3. Understand the importance of reading centers

CME QUESTIONS

1. Articles should be planned when developing the study protocol.
   A. True
   B. False

2. When choosing outcome variables, which of the following variables enables the most statistical power
   A. Nominal
   B. Ordinal
   C. Discrete
   D. Continuous

3. Which of the following are important in optimizing clinic trial publications
   A. Choosing an experienced reading center
   B. Carefully selecting writing committees
   C. Working with the editors of the journal you submit to
   D. Taking care planning for publications when developing case report forms
   E. All of the above.

KEYWORDS

1. clinical trials
2. statistical variables
3. publications
4. reading centers
5. case report forms

HIGHLIGHTS

This talk will review the lessons learned by our study team to maximize publications from the Idiopathic Intracranial Hypertension Treatment Trial. Our study started in 2009 and there are still recently started articles in progress. In all, 32 articles have been published to date. There are a variety of strategies we used to optimize publishing our data from protocol development to selecting the right variables to measure to choosing the right reading centers to selecting the appropriate journals for our work.

While the primary outcome may be the reason to do the trial, if you structure the data collection thoughtfully, much more will be learned. It is important to spend extra time with case report form

development, planning the possible future publications at that time. This includes collecting historical data, exam and laboratory findings including saving blood and CSF samples for later studies like genetics and metabolomics.

When choosing variables, continuous variables allow more statistical power than nominal, ordinal or discrete variables. For example, instead of rating visual field results as better, worse or the same at six months, use mean deviation as a continuous variable that allows much more powerful statistical modelling.

Once data is collected, writing committees should be chosen. Choose team members you can count on to deliver. Give reasonable deadlines and make it known up front that if steady progress is not made, the lead author will be replaced. And don't hesitate to reassign authorship if someone is not delivering. In addition, have monthly or bi-monthly videoconferences to keep everyone accountable and monitor progress.

Be sure not to dilute your messages by spreading the findings across too many articles; this has been called slicing and dicing. And don't publish the same findings multiple times.

Be sure and choose your reading centers carefully; that is, the reading center should have an excellent track record. A good reading center will be vigilant in providing you with clean and valid data. This cannot be overemphasized.
Of course, it is very important to choose the right journal. We were fortunate to have the editors of JAMA work with us and they really wanted to assist us. They helped us a great deal to come up with the best manuscript.

SUMMARY

In order to optimize clinical trial publications, first plan potential articles when you develop the Protocol. After data has been collected, choose writing committees for each article and crack the whip! Be sure not to slice and dice the data. And choose your reading centers with care. Lastly select the appropriate journals where you will submit the articles and work with the editors of the journal as they want to assist you.

CME ANSWERS

1. A
2. D
3. E

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WHAT MAKES A GOOD EDITOR/REVIEWER

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LEARNING OBJECTIVES

1.Become familiar with the role of the Editorial Board of a peer-reviewed medical journal
2.Describe the pro's and con's of an open-access publication
3.Examine the process by which an individual is selected to review a manuscript

CME QUESTIONS

1. Criteria for selecting a member of the Editorial Board include:

A. Having served on other editorial boards.
B. Awarded extramural grant funding.
C. Established a record of academic excellence.
D. Being a close friend of the Editor-in-Chief.

2. Concerns when publishing a manuscript in an open access journal include:

A. Whether your manuscript will be indexed in a bibliographic database.
B. Your article will be freely available on the internet.
C. The image quality will be of poor quality.
D. The public will benefit from greater output of scientific knowledge.

3. The process of selecting a reviewer for a manuscript requires:

A. Expertise in the subject matter.
B. Membership in honorary medical societies.
C. Timely response in completing review of a submission.
D. Being a faculty member in an academic department.

KEYWORDS

1. Editor-in-Chief
2. Peer-reviewed medical journal
3. Open-access journal

HIGHLIGHTS

The Editor-in-Chief requires a multitude of skills and interactions with many stakeholders including authors, readers, reviewers, and publishers. The publishing landscape is currently in flux, in part caused by the effects of artificial intelligence, social media and open-access journals.

SUMMARY

The role of the Editor-in-Chief (EIC) of a peer-reviewed medical journal while thought to be straightforward is actually quite nuanced. To begin with, the individual should have a recognized academic record and be respected in his/her field of expertise. The ability to multi-task and have strong organizational skills is essential. In selecting the Editorial Board, one must look for qualities of excellence in scholarship, timely in responsiveness and a willingness to do "the work". Organizationally, the flow of manuscripts must move efficiently and reviewers must be engaged in the process, promptly submitting their reviews. Simultaneously, the EIC must interface with the publisher to make certain that the quality of every issue of the journal is produced with appropriate and consistent layout, design and tone. Here is where attention to detail is critical.

The EIC must be aware of and deal with a number of challenges in medical publishing including the impact of open-access, artificial intelligence and social media. Finally, the EIC must use his/her "EQ" (emotional intelligence) in overseeing the journal. Interpersonal communication, remaining flexible, and the ability to accept criticism are high on the list of job requirements. To be an effective EIC, recall what President Harry S. Truman opined: "It's amazing what you can accomplish when you do not care who gets the credit".

CME ANSWERS

1. **C**
2. **A,C**
3. **A,C**

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Using AI tools in your scientific writing process

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LEARNING OBJECTIVES

1. Describe the pros and cons of using AI writing tools with regards to accuracy, originality, and efficiency
2. Identify opportunities within the drafting and revising phases of writing that can be optimized by AI tools
3. Develop strategies for crafting prompts that enhance the accuracy and relevance of AI-generated content

CME QUESTIONS

1. When integrating AI tools into the drafting phase of writing, which approach is likely to be most beneficial to the accuracy and readability of the final product?
   A. Relying solely on AI-generated text without further user input
   B. Using AI to create an extensive outline that the writer passively accepts without critical evaluation.
   C. Using AI to provide a basic structure that is then expanded upon manually
   D. Allowing AI to autonomously conduct all research and synthesis of information

2. Which use of an AI writing tool best maintains the originality of your scientific writing?
   A. Generating complete sections of content to be used as-is
   B. Modifying existing texts from similar research papers
   C. Directly copying and pasting AI-generated content without citation
   D. Using AI as a writing coach to overcome writing roadblocks

3. What is a key consideration when crafting prompts for AI-generated content to ensure relevance and accuracy?
   A. Keeping prompts as vague as possible
   B. Providing detailed context and specific instructions in the prompts
   C. Using complex, technical jargon to impress the AI
   D. Limiting the prompt to one-word inputs for simplicity

KEYWORDS

1. Writing
2. Artificial Intelligence
3. ChatGPT
4. Publication

HIGHLIGHTS

Pediatric Neuro-Ophthalmology Symposium - Pediatric Brain Tumors:

In Childhood and Beyond [2.0 CME] - Thursday, March 7th

Moderators: Shannon Beres, MD & Melinda Chang, MD

Brain tumors in children are different from adults in presentation, treatment, and outcomes. In this session, we will discuss the differential diagnosis of brain tumors by location in children. We will also present data on neuro-ophthalmic outcomes and

complications of treatment in children with brain tumors. Finally, we will discuss considerations for driving in pediatric brain tumor survivors.

Upon completion of this session, participants should be able to: (1) Formulate a differential diagnosis for supratentorial, infratentorial, and suprasellar tumor presenting in children. (2) Identify appropriate intervals for monitoring of ophthalmic complications of cancer treatment in children. (3) Describe strategies for assessing driving safety in survivors of childhood brain tumors with neuro-ophthalmic complications.

- What is this Mass? Supratentorial and Infratentorial Brain tumors in Children vs. Adults, Jason Peragallo, MD
- What is this Mass? Deep Dive into Suprasellar Tumors: Ryan Gise, MD
- Is It Iatrogenic? Monitoring of Ophthalmic Complications: Radiation, MEK inhibitors, and Chemotherapy, Marc Dinkin, MD
- What to Expect? Neuro-Ophthalmic Outcomes in Pediatric Brain Tumor Survivors, Allison Liu, MD, PhD
- Will My Child Be Able to Drive? Navigating the DMV and Driving Safety with Driving Aides for Brain Tumor Survivors, Deepta Ghate, MD

WHAT IS THIS MASS? SUPRATENTORIAL AND INFRATENTORIAL BRAIN TUMORS IN CHILDREN VS. ADULTS

Jason Peragallo, MD
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LEARNING OBJECTIVES

1. The attendee will be able to describe differences between presentations of supratentorial and infratentorial brain tumors in children and adults.
2. The attendee will be able to name the most common supratentorial and infratentorial brain tumors in children and adults.
3. The attendee will be able to describe the differences in behavior and outcomes of common pediatric and adult brain tumors.

CME QUESTIONS

1. What is the most common non-suprasellar central nervous system tumor location in children ages 0-19 years?

   A. optic nerve
   B. temporal lobe
   C. brainstem
   D. cerebellum
   E. pineal gland

2. What type of cancer (malignant or non-malignant) has the highest incidence in childhood (age 0-19)?

   A. brain and other central nervous system
   B. epithelial neoplasms and melanomas
   C. leukemia
   D. lymphoma
   E. soft tissue sarcomas

4. Juvenile pilocytic astrocytomas in children have the worst survival in which age range?

   A. <1 year
   B. 1-4 years
   C. 5-9 years
   D. 10-14 years
   E. 15-19 years

KEYWORDS

1. Pediatric neuro-oncology
2. Brain tumor epidemiology
3. Brain tumor genomic profiling

4. Supratentorial pediatric brain tumors
5. Infratentorial pediatric brain tumors

HIGHLIGHTS

Pediatric brain tumors remain the most frequent cause of cancer death in childhood. Presentation, clinical characteristics, treatment, and prognosis are all dependent upon tumor type and location. Similar histology for pediatric brain tumors may present in adult patients, but may behave differently. Recent advances in the understanding of molecular alterations and gene expression in these tumors are leading to novel targeted molecular treatments.

SUMMARY

An estimated 5,620 brain tumors are expected to be newly diagnosed in children and adolescents (ages 0-19 years) living in the United States in the year 2023.[1] For the years 2014-2018 an average of 539 children and adolescents died each year from malignant brain tumors (0.66/100,000 population).[1] Overall five-year relative survival rates for children and adolescents with malignant or non-malignant brain and central nervous system (CNS) tumors is 83.9%.[1] In 2022 an estimated 40,594 children and adolescents were living with brain and CNS tumors, which is a similar number to those living with leukemia (40,738).[1] Incidence of brain and CNS tumors in children (0-19 years) is estimated to be 6.23 per 100,000 per year.[1]

New cases numbers of pediatric leukemia, lymphoma, other malignant epithelial neoplasms, soft tissue and other extraosseous sarcomas are 4,043, 2496, 1,984, and 1,001 per year, respectively.[1] Overall the most common locations for CNS tumors in the pediatric age group are pituitary gland and craniopharyngeal duct, cerebellum, other brain, brainstem, and cranial nerves (17.7%, 14.3%, 11.5%, 10%, 7.3%, respectively).[1]

The broad category of gliomas, glioneuronal tumors, and neuronal tumors as defined by the World Health Organization (WHO) consists of a total of 41 tumor subtypes, defined by such characteristics as histopathology, patient age, tumor location, and genetic modifiers.[2] Gliomas are the pediatric brain tumor with the highest average annual incidence.[1] Gliomas in childhood tend to have low-grade histopathology, with the most prevalent subtype being pilocytic astrocytoma representing an estimated 8,264 cases.[1] When considering the low-grade glioma type tumors (WHO I and II) as a whole, pilocytic astrocytomas (WHO Grade I) represent 65% of low grade cases in children, while diffuse astrocytomas (WHO Grade II) represent 80% of low grade tumors in adults.[3] Malignant transformation in children is rare (2.9-6.7%) and is much more common in adult low grade cases (up to 86%).[3] Pediatric low grade gliomas commonly have a driver mutation, including KIAA1549-BRAF (35%), BRAFV600E (17%) and NF1 (17%).[3] Underlying mutations influence progression-free survival and available treatment modalities as novel targeted chemotherapeutic agents target tumors with specific mutations. Higher grade gliomas of the brainstem (such as diffuse intrinsic pontine gliomas [DIPG]) account for 10-20% of all CNS tumors in the 0-19 year age group, with the highest incidence in ages 1-9 years.[4] DIPGs commonly have mutations in the *H3F3A* or *HIST13B* genes allowing a continued progenitor/self-renewing phenotype.[4] Median survival for pediatric high grade gliomas is 15 months.[4]

Pilocytic astrocytomas are the most common histologic brain tumor group in children between ages 5-14, and the second most common in children between 0-4 years old.[5,] The age adjusted incidence rates for pilocytic astrocytomas are 0.71-0.96/100,000 for ages 0-19 years, and 0.10-0.16/100,000 for ages

≥20 years.[6] Histology of pilocytic astrocytomas is considered benign (WHO Grade I). Five-year survival rates for patients with pilocytic astrocytomas aged 0-19 years are 96.8%.[1] In comparison to the pediatric age group (ages 0-19 years), pilocytic astrocytoma specific deaths in the adult population are higher, with a hazard ratio of 2.67 for those 20-39 years, 5.34 for those 40-59 years, and 12.89 for those 60+ years old.[6] Diagnosis at under 1 year of age is also associated with poor survival.[5] Pilocytic astrocytomas in pediatric aged patients most commonly involve the cerebellum (36%), in contrast to adults in whom the supratentorial region is most commonly involved.[5] Infratentorial pilocytic astrocytomas may originate from the oligodendrocyte cell lineage.[7] Cerebellar location is associated with higher survival rates (10-year survival rate >99%) in comparison to other locations.[5] A non-cerebellar midline location is associated with higher risk of pilocytic astrocytoma related death (relative risk 1.58), while cerebellar location had a lower risk (relative risk 0.50).[6] It is possible better survival for tumors in the cerebellar region could be related to easier gross total resection.[5]

Oligodendrogliomas are rare tumors in the pediatric population with an average of 13 cases per year diagnosed in those under 14 years of age, in comparison to those ≥15 years with an average of 1096 cases per year.[8] Survival for children with oligodendrogliomas is better than adults, with a 5-year survival rate of 85% in children and 67% for adults.[9] *IDH1* mutation, a common finding in adult oligodendrogliomas with better prognosis, occurs less frequently in children.[9] Extracortical location in both pediatric and adult patients have poorer prognosis.[9]

Glioblastoma (WHO Grade IV) is the third most common CNS tumor, and is the most common malignant CNS neoplasm, accounting for 14.2% of all tumors (among the total population) and 50.1% of all malignant tumors.[8] Glioblastoma can occur at any age, but is more common among older adults and less common among children. Glioblastoma accounted for 2.7% of all CNS tumors in the 0-19 year age range.[8] Overall survival is generally poor, with an average of 6.9% 5-year survival rate. However, children aged 0-14 years had better 5-year survival rates of 20.6%.[8,10] *MGMT* methylation is associated with improved survival in gliomas in general. This alteration, commonly found in glioblastoma, may improve sensitivity to alkylating chemotherapeutic agents such as temozolamide.[8,11] DNA mismatch repair genes are frequently altered in glioblastoma cases, and the genes involved can be different in pediatric versus adult cases.[12] One study identified that pediatric patients have a higher number of alterations in these mismatch repair genes, which might make their tumors better targets for immune checkpoint inhibitor therapy.[12]

Ependymal tumors are classified into 9 subtypes dependent upon location and molecular features.[2,10] These subtypes have distinct age predilections and clinical behavior.[10] Posterior fossa ependymomas may potentially originate from the cerebellar astroglial cell lineage.[7] Ependymomas decrease in incidence with increasing age.[13] Tumor location is age dependent, with posterior fossa ependymomas most frequent among the very young, supratentorial ependymomas most frequent among adolescents, and spinal cord ependymomas most frequent among adults.[10,13] Ependymomas comprise 5.3% of all CNS tumors in children, and 1.6% of all tumors among all ages.[8,10] 5-year survival rates for children (0-14 years) with ependymal tumors is 80.4%, for adolescents and young adults (15-39 years) is 94.7%, and for adults ≥40 years is 91%.[8] Molecular changes in tumor tissue differ in pediatric ependymomas versus adult ependymomas, with 4.1B deletions and loss of 4.1R expression more common in children.[14] Recurrent disease appears to be more common in pediatric patients.[15]

Medulloblastomas are classified as embryonal tumors, and are often classified by their molecular characteristics.[2] The most common molecularly defined subtypes of medulloblastoma in children are non-WNT/non-SHH (median age of diagnosis of 7 years), followed by SHH-activated and *TP53* activated

(median age of diagnosis of 4.5 years), and WNT-activated (median age of diagnosis of 9 years).[1] SHH-activated and *TP53*-mutant subtype is rare in children.[1] The most common medulloblastoma in adults is the SHH-activated TP53 wild-type classification.[8] SHH and Group 3/4 medulloblastomas (subgroups not defined by molecular expression but by clinico-biologic characteristics, with large cell/anaplastic features and *MYC* amplification [Group 3] or isochromosome 17q [Group 4]) originate from granule cell and unipolar brush cell lineages.[7,16] The majority of medulloblastoma cases occur in the pediatric age range, with 61.8% occurring in children 1-14 years of age.[17] Adult cases account for 27.7% of all medulloblastomas.[17] Five-year survival rates are similar for children (72.6%) and adolescents/adults (77.5%).[10] WNT-activated tumors have the best survival rate in children of approximately 90%.[18] Atypical teratoid/rhabdoid tumors (ATRT) are classified as embryonal type tumors.[2] Children with ATRT have a worse prognosis than other embryonal tumors, with 5-year survival rates of 33%.[10]

Tumors of the pineal region (primary pineal parenchymal) are relatively uncommon, with an average of 43 cases per year diagnosed in patients 19 years and younger.[1] Five year relative survivial is worst for those 14 years and younger (68.5%) and best for adolescents and young adults (80.9%).[8]

Germ cell tumors are comprised of yolk sac tumors, teratomas, germinomas, embryonal carcinomas, choriocarcinoma, and mixed germ cell tumors.[2,19] Germ cell tumors account for 0.5-3.2% of intracranial tumors in adults and 11.8% of intracranial neoplasms in children.[19] Children with germ cell tumors present most commonly in a bimodal distribution in the early teens or under 3 years of age.[10] Germ cell tumors are relatively uncommon after age 40, representing about 6% of all cases.[8] Incidence rates for germ cell tumors are 3-fold higher in males than females.[20] The overall relative survival rate at 5 years is 89%, and is relatively similar among adults and children.[8] Two-thirds of germ cell tumors are germinomas, which are highly sensitive to radiotherapy with an over 90% 5-year survival rate after radiotherapy alone.[20] However, non-germinomatous germ cell tumors have much poorer 5-year survival rates of 15-20% if treated only with radiotherapy, with combined treatment with chemotherapy improving survival rates to 76% in adults and 93% in children.[20]

Meningiomas are the most common CNS tumor histology overall (39.7%), and the most common non-malignant histology (55.4%).[8,10] Non-malignant meningiomas account for only 1.6% of all CNS tumors in children 14 years or younger, but account for 44.6% of all CNS tumors in adults ≥40 years.[10] Meningiomas have the highest incidence in those 65 years and older.[8] Of the 33.686 meningiomas diagnosed annually, 62 are in children under the age of 14.[10] Non-malignant meningiomas occur 2.3 times more frequently in women than in men.[8] Relative 5-year survival rates for non-malignant meningiomas is 96.8% for children 14 years and younger, and 87.5% for those 40 years and older.[8]

Choroid plexus tumors occur with decreasing frequency with age.[1] An average of 86 cases are diagnosed per year, representing 1.6% of all pediatric brain tumors, at a median age of 2 years.[8]

Novel treatments, including monoclonal antibodies, chimeric antigen receptors, oncolytic viruses, and vaccine-based therapies are being proposed and evaluated in clinical trials for treatment of many CNS tumors.[21,22] Collaborative treatment networks are an essential component of these clinical trials given the often relatively small numbers of patients with the specific molecular expressions targeted by these therapies.

CME ANSWERS

1. D

2. A
3. A

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What is this Mass? Deep Dive into Suprasellar Tumors

Ryan Gise MD, FAAP

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Boston Children's Hospital/Harvard Medical School

*Boston, MA***LEARNING OBJECTIVES**

1. The attendee will be able to describe the differential diagnosis of suprasellar tumors

2. The attendee will be able describe common the neuro-ophthalmologic sequelae suprasellar tumors

3. The attendee will know the utility and availability of ancillary ophthalmic testing in the prediction of visual outcomes.

CME QUESTIONS

1. Which of the following statements is true about adamantinomatous craniopharyngiomas?

   A. They are almost all malignant with a high rate of metastasis to the visual system causing visual loss.
   B. They are benign and pose little risk to the visual system.
   C. They are mostly malignant but the risk to the visual system is related to local mass effect.
   D. They are mostly benign with only a small risk of malignant transformation in childhood but pose a risk to vision related to local invasion and mass effect

2. Approximately 16% of arachnoid cysts are suprasellar in location. How do these differ from other types of arachnoid cyst?

   A. Unlike other types of arachnoid cyst they are benign and do not generally cause symptoms or require treatment.
   B. They never cause hydrocephalus.
   C. They frequently cause hydrocephalus and most commonly present with ventriculomegaly and macrocrania.
   D. They arise from non-arachnoid origins

3. Which of the following is the most common type of pituitary neuroendocrine tumor/adenoma.

   A. Corticotropin (ACTH)-releasing adenoma
   B. Prolactinoma
   C. Growth Hormone Releasing Adenoma
   D. None of the above, most commonly these tumors are endocrine inactive.

KEYWORDS

1. Suprasellar Mass
2. Visual Field Defects
3. Optic Atrophy

4. Craniopharyngioma

HIGHLIGHTS

Sellar and Suprasellar Tumors are a diverse group of malignant and benign lesions that cause significant visual morbidity because of their location. A high index of suspicion and a multidisciplinary team including neuro-ophthalmology, neuro-oncology and neurosurgery is needed as different lesion types have drastically different treatments. Optical Coherence Tomography – both Retinal Nerve Fiber Layer and Ganglion Cell Layers, provide neuro-ophthalmologists with a tool to aid in the assessment of visually threatening lesions and can allow for earlier detection prior to visual symptoms. Children as young as 2-3 years can sit (or stand) for optical coherence tomography and often can do this well before they are able to complete formal visual field assessment.

SUMMARY:

Solid tumors of the central nervous system (CNS) are the most frequently identified brain tumor in the pediatric population and comprise nearly 27% of pediatric cancers. (1) Tumors of the sellar and suprasellar region make up around 10% of CNS tumors. (1) The sellar and suprasellar region of the brain sits directly under the optic chiasm making pathology of this area extremely threatening to vision. The differential diagnosis of neoplastic disorders that occur in the sellar and suprasellar region of the brain is broad. (2)

A. Craniopharyngioma

Craniopharyngiomas are cystic and calcified tumors that develop in the sellar and suprasellar region. They divided into two separate types – Adamantinomatous and Papillary. (3) Craniopharyngiomas that occur in childhood are almost all Adamantinomatous (ACP) subtype. ACP most often have an intrasellar and suprasellar component (approximately 50-75%) followed by suprasellar component only (20-40%) depending on the study. Most (>90%) have a suprasellar component at least. (4) Pediatric patients with this type of tumor may present with increased intracranial pressure secondary to obstructive hydrocephalus, endocrinopathies that manifest in ways such as short stature and/or delayed puberty, and visual impairment. One meta-analysis found that 50.3% (1041/2071) of children in its included studies had some degree of visual impairment. (5) In terms of treatment, the modality of choice is complete resection if possible. A portion of ACP (up to 27%) have firm adherence to the hypothalamus making this not achievable. (1) Some argue for subtotal resection followed by adjuvant radiation. (6) ACP may also demonstrate with local invasion of surrounding structures including the visual pathway and hypothalamus. Papillary craniopharyngiomas are much less common and are not typically seen in pediatric patients.

B. Pituitary adenoma/pituitary neuroendocrine tumor

Pituitary adenoma is the classic name for this cohort of tumors; however, in the most recent WHO classification, there has been a transition a new nomenclature: pituitary neuroendocrine tumors (PitNET). This is more much more descriptive and accurate. These tumors had been labelled as adenomas because they rarely metastasized. The term adenoma is not entirely accurate as it denotes a benign disease course that is not true of all of these processes. (1,3) These tumors are most often sporadic but can be associated with inherited syndromes such as Multiple Endocrine Neoplasia Type 1. They do not generally present until adolescence and occur more often in girls. There is no gender predilection in prepubertal patients. (1)

The clinical presentation of each of these types of tumors is partially dependent on the hormone that is being oversecreted. Additionally, the presentation will differ depending on the size of the lesion as well as the age and gender of the patients. Given the location, the generalized symptoms of visual field loss and headache are risks for any of these different lesions. Treatment also varies - though over 90% of lesions requiring surgery are either adrenocotricotropic hormone (ACTH) or prolactin secreting. This is a marked difference from the adult population. (7) Pituitary apoplexy is rare in children.

Prolactin secreting lesions (prolactinomas) will most often present after puberty with amenorrhea and/or galactorrhea in girls and gynecomastia or signs of decreased hair production in boys. First line treatment is with dopamine agonists such as Cabergoline. These agents have been shown to shrink these lesions and preserve vision. They even have been shown in some cases to reverse vision loss rapidly. (8,9) Tumors of this type do not typically respond well to surgical resection and/or radiation and recur. (3)

PitNETs that secrete ACTH typically present with growth failure or rapid weight gain. These are preferentially treated with transphenoidal resection and radiation is utilized in recalcitrant cases. (3) On the other hand, those that secrete Somatotropin are more common in boys and these children present with either acromegaly or gigantism depending on their degree of development and whether their growth plates have fused. These are usually treated with a combination of therapies including transphenoidal resection, medical therapy with somatostatin analogues and radiation. Medical therapy can lead to growth hormone level normalization as well as decreased size of the lesion and improvement in visual function. (1,3,10) Gonadotropin secreting PitNETs are more rare in childhood and are usually follicle stimulating (FSH) secreting though may instead produce lutenizining hormone (LH). These most commonly present with precocious puberty in children. Tumors that are either non-functioning or those that secrete thyrotropin are not typically diagnosed in childhood. (1,3)

C. Langerhans cell histiocytosis

Langerhans cell histiocytosis (LCH) and juvenile xanthogranuloma (JXG) are histocytic lesions that can present in the sellar and supersellar region and thus cause a threat to vision. LCH derives from the clonal proliferation of Langerhans-type cells. It can present in the central nervous system (CNS) without any other systemic involvement and the most common intracranial location for it to occur is the hypothalmic-pituitary axis which is between 25% and 50% of cases. In these cases, Diabetes Insipidus may be the only presenting sign or symptom of the disease. The pituitary gland may also become involved in a subset (10%) of patients. LCH is very sensitive to chemotherapy with an excellent cure rate. (1) JXG is rare in this location is extremely rare.

D. Germ Cell Tumors

Germ cell tumors (GCT) account for around 3-4% of all pediatric brain tumors and are subdivided into germinomas and nongerminomatous. Only a small subset of GCT are found outside of the gonads and when they are it is secondary to the migration that starts with primordial germ cells through the course of embryogenesis. As a result, they are commonly found in the suprasellar and pineal regions when in the CNS. (1) Children and adolescents are the most common demographic that is affected and the highest incidence is between 10 and 14 years of age. When these tumors are suprasellar in location there is no sex prediliction though the pineal region is more common affected in boys. (11)

Suprasellar GCTs typically present with visual impairment, hypothlamic-pituitary failure and diabetes insipidus. (1) In terms of diagnosis, oncoproteins in the serum and the CSF are evaluated. Beta-human chorionic gonadotropin (B-HCG) is not found with pure germinomas while nongerminatous GCT have the potential to secrete both a-fetoprotein (AFP) and B-HCG. Differentiating between these two types of

GCT becomes crucial for treatment as germinomas tend to be extremely sensitive to both radiation and chemotherapy while most nongerminomatous GCT are sensitive but less so. Germinomas tend to have good outcomes while nongerminomatous GCT including immature teratomas, choriocarcinomas, embryonal carcinomas and intracranial yolk sac tumors have very poor outcomes. (12)

E. Hypothalamic and optic pathway glioma

Hypothalamic and optic pathway gliomas (OPG) make up 25-30% of all suprasellar tumors in children and 4% of all intracranial ones. (1) These tumors are described as OPGs because they arise from the tissue of the visual pathway and hypothalamus and most often involve both. Most of these tumors are diagnosed before the age of 5 and there is no difference in incidence between boys and girls. (13) Patients with Neurofibramatosus type 1 (NF-1) are at high risk of developing OPGs (15% incidence) and are screened regularly to ensure that there is no evidence of vision loss. Those that are not associated with NF-1 are sporadic and tend to demonstrate a more aggressive clinical course. These lesions are benign but can cause significant morbidity secondary to their location. Treatment is most often initiated in order to preserve vision. (1)

F. Other Lesions

Atypical Teratoid/Rhabdoid Tumors (AT/RT) are high grade, malignant neoplasms that contain some component of Rhabdoid cells. AT/RT commonly affect younger children (less than 3 years) and suprasellar locations are very rare. The overall prognosis is poor. (1) CNS Lymphoma can also present in the suprasellar location and should be suspected when there is rapidly increasing mass size on imaging. Arachnoid cysts are a non-neoplastic entity that can also occur in this area; they rarely cause morbidity but due to this location can be associated with either hydrocephalus or vision loss.

The Role of the Neuro-ophthalmologist

Given the location of suprasellar lesions, the neuro-ophthalmologist plays a crucial role in the protection and preservation of vision in these patients. This is done in several ways. First and foremost is the physical examination and monitoring of afferent visual function. Visual acuity can be tested in all ages starting with fixing and following behavior at 2-3 months of age and then with Teller acuity cards once their visual behavior allows. As they reach age 2-3 years, most are able to match LEA symbols and letters. Teller cards can continue to be used as needed for nonverbal and developmentally delayed patients. It is important to realize that Teller cards can overestimate visual function in all patients and a difference between two eyes on Teller cards is often smaller than what it would be if the patient were able to read Snellen letters.

A. Kinetic and automated perimetry

In addition to the physical exam, kinetic and automated perimetry can be used to monitor the peripheral vision in patients who are able to sit for this type of testing. Kinetic is easier for the children. Visual field loss is one of the major morbidities associated with sellar and suprasellar tumors with incidence being between 38% and 72% of patients requiring surgical intervention. (14-16). Damage to afferent visual function can manifest as loss of visual acuity or damage to peripheral vision. Visual field defects most commonly present as bitemporal but depending on the location of the compression they may present as other types of loss including junctional scotomas from compression of the optic nerve as it enters the chiasm or homonymous hemianopia from compression of the retrochiasmal optic tract. (14)

B. Optical Coherence Tomography

Optical coherence tomography is now a widely available technology that allows for rapid assessment of the structural integrity of the visual pathway while the patient is in the office. It is noninvasive, relatively inexpensive and most importantly can be performed on most pediatric patients. (17-18) While there are no definitive normative databases, there are publications that demonstrate norms in the pediatric population may not be significantly different from adults, especially in the older age groups. (18) Both OCT Retinal Nerve Fiber Layer and Ganglion Cell Layer or Complex (depending on the machine that is used) can be obtained in children.

As in adults, it has been demonstrated in pediatric craniopharyngioma patients that visual field and visual acuity loss is correlated with lower RNFL values. (19) In adults it has also been demonstrated that the Ganglion Cell Complex may be even more accurate than RNFL in determining chiasmal compression in patients. It may even identify those who have yet to clinically display visual field loss. (20-21) The Ganglion Cell Complex has been shown to be able to differentiate between children with optic pathway gliomas who have vision loss and those that do not. (22) OCT RNFL and GCL/GCC both provide surrogate markers that require less participation and put forward more accurate results given that there is less user cooperation required.

Suprasellar lesions in the pediatric population are a diverse group of benign and malignant processes. The main area of overlap in symptoms is vision loss and headaches. Other symptoms depend greatly on the tumor, if it secretes any hormones, and its location within the suprasellar region. Neuro-ophthalmologists play a crucial role in the care of these patients as they monitor visual function through visual acuity testing and perimetry. OCT RNFL and GCC/GCL are evolving ocular imaging modalities that have been shown in adults and children to be sensitive markers for visual dysfunction caused by suprasellar tumors. They offer a non-invasive testing option that requires less cooperation and attention from the patient than perimetry. Adult studies have demonstrated that the GCC may detect structural damage prior to detectable vison loss on perimetry. With all of these tools available, neuro-ophthalmologists have the ability to accurately and effectively monitor the vision in these patients and aid our neurosurgical and neuro-oncologic colleagues in their care.

CME ANSWERS

1. D

2. C

3. B

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Is this Iatrogenic? Monitoring of Ophthalmic Complications: Radiation, MEK inhibitors, and Chemotherapy

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LEARNING OBJECTIVES

After participating in this session, the learner will be able to:

1. Describe the clinical and radiological presentation of radiation optic neuropathy in children, distinguish it from neoplastic optic neuropathy and outline proposed treatment options.
2. Outline the most common visual complications of MEK (mitogen-activated protein kinase kinase) inhibitors in children.
3. Recognize various neuro-ophthalmic complications of other chemotherapeutic agents such as intracranial hypertension related to high dose cytarabine (HIDAC).

OUTLINE

I. INTRODUCTION

This lecture will review some of the potential neuro-ophthalmic complications of various anti-cancer therapies in children. Through a case-based approach, we will discuss the risks of radiation therapy including radiation optic neuropathy and ocular neuromyotonia, retinopathies related to the mitogen-activated protein kinase kinase (MEK) inhibitors and the cytarabine induced intracranial hypertension syndrome. Theoretical mechanisms will be discussed as will the diagnostic challenge of differentiating cancer-associated symptoms from those that are iatrogenic.

II. COMPLICAITONS OF IONIZING RADIATION

Radiation Optic Neuropathy (RON)

Ionizing radiation that includes the optic nerve within the field can result in a delayed but severe optic neuropathy, with associated vision loss. The mean onset is 18 months after radiation therapy but typically does not occur prior to 6 months. Vision loss includes loss of visual acuity, color vision and neurogenic visual field loss, accompanied by a relative afferent pupillary defect when asymmetric. Bilateral involvement may occur, in which case, it is typically serial. The onset is usually acute, but in some cases, a slower, progressive loss of vision can occur. In cases of retrobulbar radiation therapy as might be used for intracranial tumors, funduscopy is typically normal at first, although pallor and retinal nerve fiber layer will ensue within months. However, following direct radiation to the eye, such as occurs with proton beam irradiation of peripapillary melanomas[1] or with palladium-103 slotted plaque brachytherapy[2], disc edema may occur (radiation papillopathy), with or without radiation retinopathy. In intracranial cases, MRI demonstrates enhancement of the affected optic nerve in most patients, typically within the field of the radiation beam, which lasts a mean of 6 months.[3]

The risk of RON increases with higher doses of radiation. In on meta-analysis, 4.5% of patients treated with cumulative doses >50 Gy experienced RON while the incidence was 1.7% in those receiving <50 Gy.

Limited evidence supports the use of hyperbaric oxygen therapy for RON, including a case series in which 2/4 showed improvement after treatment, although they were both given corticosteroids as well.[4] Based on the efficacy of intravenous bevacizumab to treat intracranial radiation necrosis, the vascular endothelial growth factor inhibitor has been used to treat RON as well, While small case series support its use for intraocular radiation papillopathy,[5] only a single case report demonstrated significant improvement in retrobulbar RON after intravenous treatment.[6] In 458 children (875 eyes), Bates and colleagues found that the rate of RON was 1% if they were treated with 52.7 Gy to 0.1 cm3 of the optic nerve or chiasm but increased to approximately 5% when 56 Gy was used.[7] A recent model based on a meta-analysis estimated a 50% risk of pediatric RON if 64 Gy was used.[8]

Ocular Neuromyotonia

Ocular neuromyotonia (ONM) refers to a hyperexcitation of a cranial nerve involved in ocular motility resulting in paroxysmal contraction and transient strabismus, often after prolonged eccentric gaze. Often occurring as a rare, delayed complication of radiation therapy, ONM has only rarely been described in children, the largest case series including five children.[9] However, its occurrence in adults years after childhood intracranial radiation, is more common. Presentation in children may differ from that of adults in that they are more likely to have blurry vision or a head tilt rather than diplopia, and spontaneous resolution may occur more frequently. Treatment consists of membrane stabilizing agents such as gabapentin or carbamazepine.

Secondary Intracranial Malignancies

The British Childhood Cancer Survivor Study studied the rate of secondary intracranial malignancies (SIM), which refer to cancers that arise after treatment of a primary cancer, in children under 15 from 1940-1991.[10] Among 17,980 patients surviving at least 5 years from diagnosis of a childhood cancer, there were 137 meningiomas, 73 gliomas, and 37 other tumors of the central nervous system. The relative risk of developing a meningioma in tissue radiated with ≥40 Gy was 479 as compared with unexposed tissue and the risk of developing a glioma or primary neuroectodermal tumor (PNET) was 4.

III. COMPLICATIONS OF MEK-INHIBITORS

Complex extracellular signaling pathways that lead to the transcription of genes involved in cell growth and proliferation involve molecules called mitogen-activated protein kinase kinases (MEK), which act by phosphorylating target molecules. Various molecules in the pathway, such as BRAF, can become constitutively activated due to mutations, promoting uncontrolled cell proliferation and cancer. "MEK inhibitors" act by inhibiting one of the molecules in the cascade such as MEK or BRAF. In adults, they are used to treat BRAF-mutated melanoma, and are being evaluated for KRAS/BRAF mutated colorectal cancer. But in children their primary use is for pediatric neurofibromas, low grade gliomas (LGG) or high-grade gliomas and for rare tumors such as gangliogliomas and diffuse leptomeningeal glioneural tumors (DLGNT). Numerous ocular complications have been described in adults, including central serous chorioretinopathy (CSCR), uveitis, retinal veins occlusion, retinal edema and rarely, optic neuropathy.[11]

Ocular complications appear relatively rare in children. Among 32 children treated with dabrafenib for BRAF V600–mutant LGG, there were no ocular complications, for example.[12] In a retrospective multi-center study of pediatric LGG in Germany, there were no ocular complications reported among 18 patients treated with the MEK inhibitor trametinib[13] although in a separate study of 10 children treated

with the drug for LGG, 1 child had a pigment epithelial detachment and two children developed intracranial hemorrhage, one with devastating neurological consequences. Results of a study using Cobimetanib in 56 patients (54 of whom were younger than 18) with previously treated solid tumors revealed 2 cases of chorioretinopathy and 3 retinal detachments.[14] Among 56 children treated with Selumetinib for low grade gliomas, there were no reported ocular complications[15] and among 74 treated for inoperable plexiform neurofibromas, there was only one asymptomatic CSCR.[16] Avery and colleagues reported on the separation of the ellipsoid zone from the retinal pigment epithelium and presence of a new hyper-reflective band between them in two children approximately 6 months after treatment with Selumetinib for optic pathway gliomas.[17] In both cases, the OCT observed changes reversed with cessation of therapy and in one case was safely resumed. The mechanism for MEK-inhibitor retinopathy remains unclear but may be related to the role of the mitogen-activated protein kinase signaling pathway in maintaining the blood retinal barrier and RPE integrity.[18] In summary, retinal complications from MEK-inhibitors in children are relatively rare and typically result in subtle visual effects. However, given the danger of losing any vision in these children, many of whom already have vision threatening optic pathway tumors, careful ophthalmological monitoring, including with OCT, is recommended.

IV. HIGH DOSE CYTARABINE INDUCED INTRACRANIAL HYPERTENSION

Discovered in the Caribbean sponge *Cryptotethia crypta*, cytosine arabinoside is a molecule consisting of the DNA base cytosine bonded to the sugar arabinose. It is similar enough to cytidine (cytosine bonded to ribose) that it can interpolate into DNA, but the aberrant sugar leads to damage and halts DNA replication. Also known as ARA-C, it has been used as a mainstay chemotherapy for ALL, AML and non-Hodgkin's lymphoma. To decrease cellular resistance to ARA-C a high dose regimen (HIDAC) is used.[19] The first case of a pseudotumor cerebri (PTC) like syndrome reported in association with HIDAC was in a 29-year-old woman, 10 days after the third cycle.[20] This was followed by pediatric reports, including in an 11-year-old boy receiving an intermediate dose.[21] In another child, elevated CSF pressures persisted for months despite acetazolamide.[22] In one teenager receiving liposomal intrathecal cytarabine in addition to systemic administration, progressive visual loss required placement of a ventriculoperitoneal shunt. Rakez and colleagues' case of papilledema on HIDAC with concurrent COVID-19 infection highlight the diagnostic challenges when papilledema is found in a child treated with HIDAC, since secondary intracranial hypertension related to infection need to be considered. In Miller and colleagues' case of HIDAC induced PTC, the tumor being treated was a Langerhans cell histiocytosis at the right orbital apex, which was already threatening vision. The mechanism of HIDAC induced PTC is unknown but may result from local phosphorous depletion which in turn disrupts the ATPase-dependent choroidal secretion of CSF Although HIDAC induced PTC is likely a rare complication, given the potential for serious visual loss from papilledema, it is reasonable to monitor children on HIDAC with funduscopy, especially those too young to communicate the presence of visual symptoms or headaches.

CME QUESTIONS:

1. Level I evidence for improvement in radiation optic neuropathy in children exists for which of the following treatments:

    A. Intravenous bevacizumab
    B. Corticosteroids
    C. Hyperbaric oxygen

D. Pentoxifylline
E. None of the above

2. The following are all well described complications of MEK (mitogen-activated protein kinase kinase) inhibitors in children except:

A. Central serous chorioretinopathy
B. Retinal vein occlusion
C. Pigment epithelial detachments
D. Retinal artery occlusion
E. Intraretinal edema

3. A 12-year-old being treated for acute myeloid leukemia with dexamethasone, high dose cytarabine and all trans retinoic acid (ATRA) develops bilateral papilledema and headaches. Important considerations in the differential diagnosis for the disc edema include all of the following except:

A. Infectious meningitis
B. All trans-retinoic acid induced pseudotumor cerebri
C. Pseudotumor cerebri caused by high dose corticosteroids.
D. Cytarabine induced pseudotumor cerebri.
E. Leptomeningeal involvement by the leukemia.

CME ANSWERS

1. E
2. D
3. C

KEYWORDS:

1. Pediatric oncology
2. Radiation optic neuropathy
3. MEK inhibitors
4. BRAF inhibitors
5. Immunotherapy

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WHAT TO EXPECT? NEURO-OPHTHALMIC OUTCOMES IN PEDIATRIC BRAIN TUMOR SURVIVORS

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LEARNING OBJECTIVES

1. Visual sequelae in children with primary brain tumors can be as high as 90% while only 10-15% has visual complaints.
2. The most common visual sequelae are strabismus and visual acuity impairment.
3. Serial neuro-ophthalmic exams are recommended for all children with brain tumors.

CME QUESTIONS

1. What is the approximate percentage of children with primary brain tumors who may experience visual sequelae, even if only a small percentage of them have visual complaints?

A. 5-10%
B. 20-25%
C. 45-50%
D. 90-95%

2. Which of the following are the most common visual sequelae in children with primary brain tumors, as mentioned in the learning objectives?

A. Visual field defects and color blindness
B. Nystagmus and cataracts
C. Strabismus and visual acuity impairment
D. Hearing loss and balance problems

3. According to the learning objectives, what is the recommended course of action for all children with brain tumors concerning their eye health?

A. Annual pediatrician check-ups
B. Serial neuro-ophthalmic exams
C. Immediate eye surgery
D. No need for regular eye examinations

KEYWORDS

1. Visual sequelae
2. Children
3. Primary brain tumors
4. Strabismus
5. Neuro-Ophthalmic exams

HIGHLIGHTS

Visual sequelae in pediatric primary brain tumors are a critical concern, with as many as 90% of affected children experiencing such issues, even if only 10-15% report visual complaints. The most common sequelae include strabismus and visual acuity impairment. Detecting these problems early is paramount, and serial neuro-ophthalmic exams are strongly recommended for all children with brain tumors. These exams enable healthcare providers to monitor changes in vision and make timely interventions to mitigate potential long-term visual impairments. Understanding the prevalence and nature of these visual sequelae is vital for healthcare professionals to provide comprehensive care to pediatric brain tumor patients.

SUMMARY

Visual sequelae in pediatric primary brain tumors are a critical concern, with as many as 90% of affected children experiencing such issues, even if only 10-15% report visual complaints. The most common sequelae include strabismus and visual acuity impairment. Detecting these problems early is paramount, and serial neuro-ophthalmic exams are strongly recommended for all children with brain tumors. These exams enable healthcare providers to monitor changes in vision and make timely interventions to mitigate potential long-term visual impairments. Understanding the prevalence and nature of these visual sequelae is vital for healthcare professionals to provide comprehensive care to pediatric brain tumor patients.

CME ANSWERS

1. D
2. C
3. B

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WILL MY CHILD BE ABLE TO DRIVE? NAVIGATING THE DMV AND DRIVING SAFETY WITH DRIVING AIDES FOR BRAIN TUMOR SURVIVORS

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LEARNING OBJECTIVES

1. Review the diverse medical criteria for vision requirements for driving license eligibility in the United States
2. List common driving errors in individuals with common patterns of vision loss from brain tumors
3. Evaluate the efficacy and applicability of driving aides for brain tumor survivors with visual defects

CME QUESTIONS

1. Which of the following is an incorrect statement regarding driving in the USA

   A. 87% of all adults over driving age were licensed drivers in the USA in 2019
   B. 45% of Americans have no access to public transport
   C. There were 6 million police reported motor vehicle crashes including 39,508 fatal crashes in 2021
   D. Uniform criteria for visual assessment have been established by the federal government for driver license issuance.

2. Based on available literature, which of the following group of patients may not have an increased risk for MVA compared to normal sighted drivers:

   A. Patient with complete homonymous hemianopia from ischemic stroke
   B. Patient with homonymous quadrantanopia from brain tumor
   C. Patient with sudden severe monocular vision loss (20/800 affected eye)
   D. Patient with long standing monocular vision loss (20/800 affected eye)

3. Which of the following statements is true regarding driving

   A. Cessation of driving in the adult population has no impact on the quality of life
   B. Cessation of driving in the adult population is associated with increased mortality risk
   C. A patient with severe vision loss (not meeting driver license criteria) can be allowed to drive in an automated vehicle capable of complete on-road driving control
   D. Driver assistance technologies such as rear-view cameras and lane departure warnings do not reduce risk for MVC

KEYWORDS

1. Brain tumor
2. Vision loss
3. Visual field loss
4. Driver license

5. Driving aids

HIGHLIGHTS

Driving is an activity of daily living with important implications for quality of life, healthcare utilization and mortality. Driving ability is based on a complex interplay between visual input, cognitive decision making and physical ability. It is important for ophthalmologists to be aware of the decision-making processes that govern driving performance, the medical conditions that put a driver at risk and possible compensatory techniques that may mitigate this risk. States in the United States have varying visual function criteria for driving license eligibility. Predicting driving safety is a challenging and complex topic and may require driving evaluation by a driving rehabilitation specialist.

SUMMARY

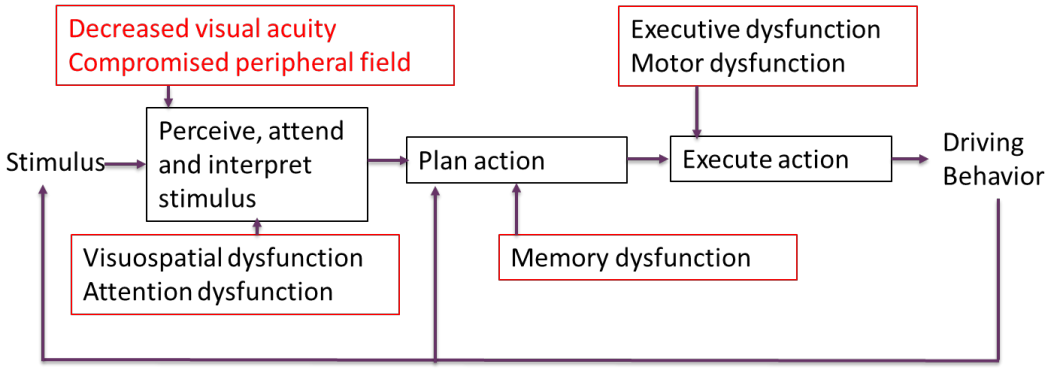
Driving is an activity of daily living with important implications for quality of life, healthcare utilization and mortality:
Driving is considered the most complex activity of daily living in the United States (USA). According to the US Department of Transportation (2019 data), there were 229 million licensed drivers in the USA which represents 87% of all adults over driving age[1]. Driving ability is critical to everyday functioning in many geographic locations in the USA. According to the American Public Transportation Association, 45% of Americans have no access to public transport[2]. The National Highway Traffic Safety Administration reports 6 million police reported motor vehicle crashes in 2021 of which 39,508 were fatal and 1.7 million caused bodily injury[3]. On the other hand, driving cessation has been associated with not only a reduction in quality of life but also with impaired healthcare utilization and worryingly increased mortality[4–6]. It is important for ophthalmologists to be aware of the decision-making processes that govern driving performance, the medical conditions that put a driver at risk and possible compensatory techniques that may mitigate this risk.

Driving ability is based on a complex interplay between visual input, cognitive decision making and physical ability[7]. The interaction between the various factors that impact driving errors has mostly been studied in the elderly adult population, but the results can be extrapolated to brain tumor survivors who often have impairments in vision (visual acuity, visual field loss), impairments in visual processing ability (executive function, visual search, processing speed) and cognitive ability (memory, executive function) all of which impact driving performance.

Figure 1 describes a theoretical framework of information processing pathway in vision and driving (modified from Anderson et al[7]. Stimulus perception is governed by visual input and mediated by pathways of attention and visuospatial processing. This stimulus must be then attended to, and an action must be planned. This pathway can be impacted by impairments of memory and executive function. Finally, each driver monitors their own behaviour continuously and modifies it using the same pathways.

Figure 1: Information processing model for understanding driving error in brain tumor survivors.

Modified from: Anderson DE, Ghate DA, Rizzo M. Vision, attention, and driving. Handb Clin Neurol. 2021



Vision criteria for driving license eligibility vary by jurisdiction in the United States

Every state in the USA has different visual function criteria for driving license eligibility[8]. The minimal visual acuity requirement varies from 20/40 to 20/100 in the better seeing eye. For an unrestricted license, criteria are stricter ranging from 20/40-20/60 visual acuity in the better seeing eye. The visual field requirement is even more varied. Several states do not have a minimum visual field requirement; for others the requirements vary from 20 degrees of visual field to 140 degrees of horizontal field. The stimulus size or the technique for visual field assessment have not been specified.

Driving safety with vision loss:

Brain tumor survivors have a variety of ophthalmic sequalae. There is a difference between being "legal" and "safe" to drive. The next section will look at driving performance in subsets of individuals who would be considered legal to drive with neuro-ophthalmic manifestations shared by childhood brain tumor survivors. It is also important to recognize that driving research encompasses a wide range of methodologies ranging from driving simulators (some with low fidelity, others with higher fidelity that better simulate the experience on-road driving) to instrumented vehicles and driving evaluations with driving rehabilitation specialists.

The next section will review driving studies in glaucoma to illustrate the impact of peripheral visual loss on driving. Our previous work has shown that individuals with glaucoma (peripheral vision loss with intact central vision) see their field loss as blur or missing objects in the region of their scotomas[9]. We have also demonstrated that subjects with glaucoma are impaired at divided attention tasks in a driving simulator[10] and glaucomatous field loss impairs visual information processing in the superior (traffic lights) and lateral (roadside signs) driving environment[11]. This naturally leads to impaired driving performance. Individuals with glaucoma have a 3-5 times higher risk of motor vehicle crashes (MVC)[12] and 10 times higher risk of at-fault MVC in comparison to age matched controls[13] and a greater risk of receiving failing driving safety rating (52% vs 21%) [14]in on-road tests. Interestingly, tasks of cognition, visual processing speed, executive function have been shown to have an independent and significant impact on driving performance in subjects with vision loss from glaucoma[14,15].

Most states prohibit driving licenses to patients with complete homonymous defects. But partial homonymous defects may be allowed to drive in many states[8]. In a study from Alabama over 8 years, 50% drivers with hemianopia (2.7 RR) and 28% of quadrantanopic drivers (2.3 RR) reported an at-fault MVC (RR compared to drivers with normal visual fields). With on-road tests, drivers with hemianopic defects exhibited a wide range of driving performance with particular challenges in lane maintenance and steering and braking[16]. Individuals with hemianopic defects as compared to normally sighted

controls demonstrated impairment in cognitive tasks, visual processing tasks and tasks of attention and visual function, all factors that independently influence driving performance[17].

It is important to note that any degree of central vision loss impacts driving performance. In an on road study, patients with macular degeneration with at least 20/40 vision demonstrated a higher number of critical driving errors and problems in lane keeping, and gap selection errors and traffic light errors[18].

And lastly, binocular vision status may also affect driving performances. Deprivation studies[19,20] show that sudden monocular vision loss significantly impacts driving performance. However, drivers with long term monocular status (compared to binocular drivers) demonstrated no difference in highway driving measures of visual search, lane keeping, clearance judgment, gap judgment, hazard detection, and information recognition in an on-road test[21]. Young individuals with amblyopia or unilateral vision impairment in USA (compared to typically sighted peers) were less likely to acquire a license (66-69% vs 81%) but once licensed, drivers with amblyopia or unilateral vision impairment did not demonstrate any increase in MVC rates[22].

Driving aides and augmented reality cues for brain tumor survivors:
Automated vehicles capable of complete on-road driving control have been proposed to improve vehicle safety by removing human error as a factor in MVCs. As of 2023- all the commercially available vehicles in the USA fall within the level 2 category[23] defined by the Society of Automated Engineers : the driver has to remain fully engaged and attentive even as the vehicle provides continuous assistance with both acceleration/braking and steering. Even a level 3 (conditional automation) vehicle in which the driver must be available to take over driving tasks is not commercially available in the United States. This is likely due to concerns for legal responsibility for MVCs and moral concerns about decision making amongst other complex factors.

Driver assistance technologies such as rear-view cameras and lane departure warnings are standard in most new cars in the USA. These technologies are new and have not been specifically evaluated in the visually impaired population. In a large metanalysis of 324 studies[24] evaluating the impact of advanced vehicle technologies, the authors commented on the varying populations, the varying study methodologies and testing environments in these research studies. Overall studies demonstrated that the assistance technologies and augmented reality cues appear to have a positive impact on MVC prevention and likely also on driver safety.

Answering the query “can I drive”: Brain tumor survivors may have a whole range of vision, cognition, motor or sensory impairments which may impact driving. The American Geriatrics Society has published the Clinician’s Guide to Assessing and Counselling Older Drivers[25] which can be used as a template to understand driving assessment for individuals with disabilities. Driver screening may be done by a health care professional (e.g., physician, social worker,
neuropsychologist). A clinical instrumental activities of daily living evaluation can be done by an occupational therapy practitioner or other health professional degree with expertise in IADL. A driving rehabilitation evaluation may be necessary by a certified driver rehabilitation specialist or an occupational therapist with specialty certification in driving and community mobility. Vehicle adaptation may be needed for physical disabilities. If driving cessation is recommended, the physician must follow each state’s reporting requirements to the department of motor vehicles.

CME ANSWERS

1. D
2. D
3. B

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