Epidemiological Characterization of Uveitis in Japan: A Systematic Review

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Purpose: Studying the etiologies, behind uveitis, examining anatomical location and exploring how these causes vary across regions in Japan.

Methods: the systemic review conducted following the PRISMA guidelines searching through databases, like PubMed/MEDLINE, Scopus, Central, Web of Science and Google Scholar from January 1990 to January 2024. Our focus was on studies done in Japan. Presented in either English or Japanese providing information, on uveitis causes and affected anatomical areas. We excluded any studies using self-reported data during our selection process.

Results: Out of a total of 831 studies initially considered only 20 met the criteria for inclusion. Sarcoidosis was the most common etiology, followed by Vogt-Koyanagi-Harada (VKH), with Behcet's disease coming next. Most studies showed a greater number of female patients. In Tokyo, sarcoidosis accounts for 8.9% of uveitis cases, making it the most common cause. In contrast, in Hokkaido, while sarcoidosis remains the leading cause of uveitis, it is significantly more prevalent at 19.5%.

Discussion: The findings reveal significant regional variations in the causes of uveitis across Japan, with sarcoidosis playing a major role. These regional differences underscore the importance of considering local factors in the diagnosis and treatment of uveitis. Additionally, the high prevalence of unclassified uveitis cases points to the urgent need for better methods to accurately identify and manage these conditions.

Isolated Ptosis as a Presenting Sign of a Midbrain Cavernous Hemangioma

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Background: Isolated ptosis as a presenting sign of a midbrain lesion is very rare and poses a diagnostic challenge. We describe a case of a healthy woman presenting with an isolated ptosis as a sign of midbrain cavernoma.

Method: A case report

Case History: A 40-year-old healthy female, presented with a 7-day history of blurry vision, weakness and right eyelid ptosis. She reported two short events of transient vertical diplopia. She denied ocular pain or any pain with eye movements, headaches, fever, or any weight changes. Her Ocular examination revealed a slight right upper eyelid ptosis. Visual acuity, ocular motility, pupils and pupillary reactions to light were normal, and slit lamp examination including fundus was normal as well. The eyelid ptosis was mild (1mm). Levator palpebrae function was normal, there was no fatigue and Ice pack test was negative. Her neurologic examination was normal as well.

A head CT-scan revealed an intra-cranial lesion in the right midbrain. Brain MRI revealed a lesion in the right midbrain, sized 1.3x1.7x1.3mm with a developmental venous anomaly and a vasogenic edema proximal to the lesion. Diagnosis of a recent cavernous hemangioma bleeding was made. On follow-up examination a day later, she had bilateral ptosis (more on the right) and rest of the findings remained unchanged.

Discussion: Isolated eyelid ptosis is a very rare presenting sign of 3rd nerve palsy or midbrain lesion. A high level of suspicion is required for accurate diagnosis including appropriate neuroimaging.

Moth-Eaten Retina as the First Manifestation of

Relentless Macular Necrosis Prompting Diagnosis of SSPE

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Background: Subacute sclerosing panencephalitis (SSPE) is a fatally progressive neurodegenerative disorder caused by persistent latent measles wild virion, most commonly affecting children or young adults. Its incidence is extremely low in developed countries. The annual incidence rate varies from one to four per million population in developed countries. We aim to report the case of a healthy young woman who presented with macular necrosis 3 decades after suffering from measles- induced pneumonia. **Methods:** Descriptive case report. **Results :**A 30-year-old healthy woman presented with sudden painless blurred vision of the right eye (RE). Visual acuity (VA) in RE was finger counting and it was 0.8 in LE. Funduscopy revealed RE multifocal macular yellowish lesions and bilateral optic disc edema. OCT showed RE macular“ moth-eaten ”appearance and LE focal peripheral retinal atrophic scar. Fluorescein angiography revealed leakage in pathologic retinal areas. The imaging features prompted a comprehensive workup that revealed positive serological tests for measles in blood and CSF, in addition to positive aqueous PCR .Despite the absence of neurologic manifestations, MRI showed several nonspecific FLAIR hyperintense foci in the supratentorial periventricular and subcortical white matter. Electroencephalogram revealed notable irregularities, specifically characterized by left temporal focal slowing down. CSF oligoclonal bands were positive. The patient was diagnosed with necrotizing retinitis and SSPE. Remdesivir was started in combination with IVIG. Macular necrosis progressed relentlessly. Subsequently, intrathecal interferon-alpha was administered. The patient's family recalled an episode of measles-associated pneumonia at the age of 9 months .**Conclusion**: Moth-eaten retina is a characteristic lesion of SSPE. The ophthalmic symptoms may precede the neurological symptoms by few weeks or sometimes as long as 2 years. The presented case underscores the challenges in diagnosing this rare condition in a country with very high vaccination rate and the uncertainty associated with the use of medical therapies.

Uveitis Associated with PFAPA Syndrome – A Case Series

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Purpose: To present a rare association of uveitis with Periodic Fevers, Aphthous stomatitis, Pharyngitis and Adenitis (PFAPA) syndrome.

Methods: A retrospective case series, in which charts of patients with PFAPA syndrome and uveitis were reviewed. Demographics, systemic and ocular clinical data, including treatment and complications were analyzed.

Results: Five patients (3 females, 2 males) were included in the study. The mean age at the time of uveitis presentation was 5.7 years (range 3.5-8 years). The mean interval from PFAPA diagnosis to the presentation of uveitis was 2 years (range 1-3 years). Two patients developed intermediate uveitis, two had anterior uveitis, of which one also had anterior and posterior scleritis and one patient had panuveitis. The majority of patients had bilateral disease (4 patients, 80%). In 3 patients there was also optic disc edema. All patients had a chronic disease course and an unrevealing workup for other systemic etiologies. All patients required long term systemic treatment with either oral methotrexate, oral steroids, or anti-tumor necrosis factor alpha (TNF-a) agents, in addition to topical steroids.

Conclusions: We hereby report the rare association of uveitis and PFAPA syndrome. Only a single case report of intermediate uveitis associated with PFAPA was previously published. The disease seems to follow a chronic course with mostly bilateral presentation.

A Case of Idiopathic Frosted Branch Angiitis

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A Forty-three-year-old hypertensive man without any ocular history was referred to the ER for scotoma in the left visual field and red-tinted vision. His right eye was unremarkable with VA of 6/6. He had VA of hand motion with RAPD in the left eye. The anterior segment of the left eye was normal and quiet. Fundus examination revealed a swollen optic disc with a normal course of blood vessels without obvious sheathing. He also had sub-macular hemorrhages, macular edema, cotton wool spots, and dot-and-blot hemorrhages with flame-shaped hemorrhages in all quadrants. The patient was referred for anti-VEGF injections with a working diagnosis of central retinal vein occlusion.

Three days later, before he received any injection, he attended the ER again for pain in the left eye and eyelid. Examination showed conjunctival hyperemia and +3 anterior chamber activity. This time, fundoscopy revealed dilated blood vessels with perivascular sheathing, and fluorescein angiography illustrated diffused vasculitis without extensive ischemia. He was admitted for an extensive work-up for uveitis (including CBC, kidney functions, liver functions, CRP, Syphilis, ACE, chest X-ray, HLA B 27, Mantoux, HIV, and AC tap for HSV, VZV, and CMV), but all tests were negative. This led to a diagnosis of idiopathic frosted branch angiitis. The patient received systemic steroids (decreasing doses of oral prednisolone starting with 80 mg daily) and topical steroids (decreasing dose of dexamethasone 0.1% four times daily). This caused a gradual absorption of retinal hemorrhages and macular edema, and an improvement of VA to 6/24.

Subretinal Fibrosis Developing 10 Years After First Presentation with Chronic Ocular Sarcoidosis in A Child

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Abstract

Purpose

To provide a comprehensive overview of the diagnostic and therapeutic journey of a pediatric patient with persistent sarcoid-associated panuveitis over a 10-year period, who ultimately developed bilateral macular subretinal fibrosis and visual loss.

Methods

Retrospective case report

Results

The patient was diagnosed with sarcoidosis after undergoing a transbronchial biopsy. She was followed up because of granulomatous panuveitis, multifocal choroiditis, and papillitis bilaterally. She maintained a stable condition, and visual acuity was 0.3 RE, 0.5 LE. Immunomodulatory therapy included prednisone, methotrexate, and adalimumab. The patient was lost to follow-up for 20 months because of the COVID-19 epidemic. She was represented with active uveitis and was not responding to TNF-α inhibitors (adalimumab and infliximab). Ultimately, the patient's intraocular inflammation was successfully controlled by using intravitreal steroids (Triamcinolone and Fluocinolone acetonide implant). However, the visual outcome was guarded because of bilateral subretinal fibrosis.

Discussion

10% of patients with sarcoidosis-associated uveitis risk blindness in one eye. The index case progressed to sight-robbing bilateral subretinal fibrosis, a rare complication of ocular sarcoidosis despite a combination of conventional and biologic anti-inflammatory therapies. There is a pressing need to develop new treatment agents for refractory non-infectious uveitis.

Granulomatous Anterior Uveitis in a Patient with Persistent Fever and Erythema Nodosum-like Skin Rash

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Purpose: Acute febrile neutrophilic dermatosis (Sweet's syndrome) is a rare dermatological disease characterized by tender, erythematous and edematous papules and nodules located mainly on the face, upper trunk, and extremities. The syndrome has broad spectrum of extracutaneous manifestations including ocular involvement. We aim to describe a rare case of bilateral severe anterior uveitis in an otherwise healthy patient.

Methods: Retrospective case report.

Case Report: A healthy 37-year-old male, presented with fever of 3-day-duration and headache. Systemic work-up revealed elevated CRP. Neurologic assessment including head computed tomography and lumber puncture was un-yielding. Because of persistent fever, worsening headache, new oral thrush, marked elevation of CRP (from 6 to 31mg/dl), he was hospitalized. Extensive infectious and inflammatory workup including bone marrow biopsy was negative. A couple of days later, bilateral granulomatous anterior uveitis was diagnosed concurrent with the appearance of a widespread erythematous papules involving upper trunk, extremities and face. A punch skin biopsy was performed and the histopathological features were suggestive of Sweet's syndrome (SS). Topical and oral corticosteroids were instituted with marked improvement.

Conclusion: Idiopathic SS is a disease of exclusion as 21% of patients have an associated malignancy. It is a multisystemic condition, that may involve the central nervous system, bones, heart, lung, liver, kidneys and intestines. Eye involvement may manifest as blepharitis, conjunctivitis, scleritis and retinal vasculitis. A high index of suspicion is important in patients with widespread red skin papules in order to rule out acute uveitis in such cases.

The Spectrum of Papillophlebitis

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Purpose: Papillophlebitis is a rare condition, manifesting as CRVO in the young adults. We aim to present our experience in managing patients with papillophlebitis.

Methods: Retrospective review of patients' medical files.

Results: Included were seven patients with a mean presenting age of 24.86±4.4 years and mean follow-up of 40.4±50.5 months. No pre-existing systemic illness was reported by any patient. One patient was subsequently diagnosed to have Behçet disease and another patient was diagnosed with homozygous mutation to MTHFR C6771. On presentation, fluorescein angiograms showed diffuse vascular and optic disc leakage. Four patients presented with papillophlebitis-associated CME, for which they were treated with systemic steroids and intravitreal anti-VEGF injections. One patient showed full recovery. In 3 patients, due to the protracted course of papillophlebitis and refractory CME, adalimumab was added. All 3 patients eventually showed complete resolution of CME. Two of them eventually developed extensive peripheral capillary non-perfusion that was treated with panretinal photocoagulation. Three patients did not develop CME: In two patients, papillophlebitis resolved after a short course of prednisone while in the third patient, papillophlebitis resolved spontaneously. Mean±SD presenting log MAR VA was 0.2±0.32 and it was 0.057±0.11 at last follow-up.

Conclusion: To our best knowledge, this is the first description that suggests a role for TNF-α blockers in the management of patients with recalcitrant papillophlebitis and non-responsive CME. Further studies are needed in order to thoroughly investigate the molecular background of papillophlebitis and clinical outcomes associated with this class of medications.

Retinochoroiditis Secondary to Rickettsia typhi Infection: a case report

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Purpose: To report a case of unusual presentation of retinochoroiditis caused by Rickettsia typhi in a patient without prior uveitis.

Methods and Results: We describe a 24-year-old male soldier with no previous eye disease, who was referred to our ophthalmology department due to bilateral retinochoroiditis and vitritis. The patient initially presented with a paracentral scotoma in his right eye persisting for 7 days and scattered dark spots in his left eye for 2 days in June 2023. Preceding these ocular symptoms, he experienced a two-week episode of fever, headaches, night sweats, and rapid weight loss of 10 kilograms. A transient rash covered his body briefly. His mother had a history of recurrent eye inflammation.

Physical examination revealed bilateral keratic precipitates on the lower corneal periphery, 1+ anterior vitreous cells, small retinal lesions and mild optic discs elevation. Fluorescein angiography indicated mild discs hyperfluorescence, and OCT revealed choroidal thickening and retinal changes consistent with retinochoroiditis in both eyes. Laboratory tests were normal except thrombocytosis, elevated ESR, liver enzymes and ACE levels, with positive Rickettsia typhi serology tests.

Rheumatology and infectious disease consultations ruled out autoimmune diseases, confirming Rickettsia typhi infection. Treatment included systemic doxycycline and prednisone, with improvement of visual acuity, ocular symptoms, OCT abnormalities and resolution of inflammation. Prednisone was discontinued, and after two months, additional improvement was seen clinically, with preserved retinal structures on OCT.

Discussion: This study explores retinochoroiditis as a rare ocular presentation of Rickettsia typhi, an unusual infection in the Middle East. Previously reported ocular manifestations include conjunctivitis, vitritis, post infectious optic neuropathy and a few cases of uveitis. Ocular symptoms followed systemic illness, highlighting the need for awareness among clinicians. Diagnosis relies on seroconversion, with fluorescein angiography and OCT aiding in assessment. Empiric doxycycline and systemic corticosteroid therapy is recommended. Ocular symptoms resolved in two months. Awareness of these ocular manifestations is essential for timely diagnosis and management. Further research is needed to fully understand this aspect of murine typhus.

An infection to remember

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Purpose: To report a case of a 39-year-old female who presented with headache, photopsia, and elevated liver enzymes. Ocular examination revealed bilateral asymmetric chorioretinal pathology. Worsening complaints with organ involvement led to extensive workup, revealing the suspected infectious causative agent.
Case presentation: A 39-year-old woman, mildly myopic, 2 months postpartum, with a recent diagnosis of hypertension and worsening headaches and photopsia. Her physical exam, vitals, and blood work were normal during birth and soon thereafter. However, workup upon presentation revealed elevated liver enzymes. Ocular examination was unremarkable except for yellow-white chorioretinal lesions observed on both eyes (LE>RE), manifesting with staining and leakage on fluorescein angiography and surrounded by clinically uninvolved areas of hyper-autofluorescence, expanding in size along follow-up. Empiric treatment with a combination of antibiotics and corticosteroids led us to lean toward a possible infectious etiology. Information derived from a popular medical internet site highlighted a possible causative agent, which was confirmed by serology. Response to direct treatment was curative.
Conclusion: Infectious agents can be proved only by specific clinical suspicion, followed by directed serologic confirmation. However, empiric treatment should be used when clinical deterioration occurs before a diagnosis is established, despite occasional antagonism from infectious disease specialists. This case will be presented with additional primary data from an ongoing multi-center study collecting data from similar patients countrywide.

Acute Bilateral Retinitis following MMRV Vaccine

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Purpose: Several types of vaccines have been linked to the development of uveitic entities, the most recent evidence surrounds the COVID-19 vaccinations. Scarce case reports documented uveitis following the Measles-Mumps-Rubella-Varicella (MMRV) vaccine. We present our 6-year-experience in managing an infant who developed bilateral retinitis after receiving the MMRV vaccine.

Methods: Retrospective case review.

Results: We report the case of a 13-month-old girl who presented to the Hadassah-Hebrew University Medical Center emergency department with an acute and rapid decline in vision, as reported by her parents. Examination revealed bilateral leukocoria caused by bilateral whitish posterior pole lesions. Further history revealed that the otherwise healthy child had received the MMRV vaccine two weeks prior to presentation. Our presentation will detail the case, including imaging, investigations performed, and a discussion of the potential etiologies for the suspected diagnosis.

Discussion: Maintaining a high index of suspicion for unusual presentations is crucial to identify potential associations between recent vaccinations and the onset of atypical uveitis phenotypes.

Persistent Visual Field Defects Despite Excellent Visual Acuity Recovery in Optic Neuritis Associated with Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease

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Purpose: Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is a rare autoimmune demyelinating disorder. In adults, optic neuritis (ON) is the most common clinical manifestation. MOGAD-ON can severely affect visual acuity (VA) and cause visual field (VF) deficits. VA typically improves rapidly with treatment, but little is known about VFs at follow-up. To address this, we analyzed VFs in MOG-ON patients.

Methods: We conducted a multicenter international retrospective review of MOGAD-ON patients. VFs were obtained at presentation and follow-up at least three months later and before the next relapse. VF severity was based on the mean deviation (MD) measurements graded as mild, moderate, or severe. Specific VF deficit patterns and shapes were assessed by a single-blinded neuro-ophthalmologist (as per Optic-Neuritis-Treatment-Trial Group). Time to treatment was also assessed.

Results: 39 eyes of 29 patients were included. The average MD nadir from all eyes was -14.18 (±9.8 dB) and -3.03 (±3.34 dB) at follow-up. At follow-up, 49% of the eyes developed permanent VF deficits with a MD below -2 Db (41% with a recognizable VF deficit pattern) despite recovery to an average VA of 6/6.

Discussion: In contrast to visual acuity, visual fields showed poorer recovery with persistent deficits in MOGAD patients with optic neuritis despite treatment. The mean deviation appeared to be affected by treatment timing, with delays associated with worse severity gradings.