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CASE REPORT

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Multifocal choroiditis with panuveitis in an 8-year-old boy with long-standing idiopathic acute anterior uveitis

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ABSTRACT

Purpose: To report successful treatment of a rare case of sight-threatening pediatric multifocal choroiditis with panuveitis (MFCPU) and the use of electrophysiology to confirm return of macular function.
Methods: Case report.
Results: An 8-year-old boy with a history of bilateral recurrent non-juvenile idiopathic arthritis acute anterior uveitis (AAU) presented with new-onset blurry vision and floaters in both eyes. Visual acuity had deteriorated to 20/200 right eye and 20/100 left eye. Cells were observed in the anterior chamber and vitreous of both eyes. Ophthalmoscopy showed multiple active small cream-colored chorioretinal lesions and cystoid macular edema (CME) in both eyes in the absence of systemic disease, suggestive of idiopathic MFCPU. Successful rapid visual recovery and resolution of CME confirmed by spectral-domain optical coherence tomography (SD-OCT) was achieved with prompt intensive systemic steroid therapy followed by early introduction of methotrexate. After 9 months, his visual acuities improved to 20/32, and pattern reversal visual evoked potentials and 19 hexagon multifocal electroretinography posttreatment were normal, showing recovery of macular function.
Conclusions: Multifocal choroiditis with panuveitis is rare in children and has not been documented in the presence of previous longstanding recurrent AAU. Onset of floaters in children should alert the clinician to early stages of posterior pole involvement and progression to reduction in vision due to CME requires prompt aggressive steroid therapy monitored by clinical examination, SD-OCT, and electrophysiology, followed by early introduction of immunosuppressive drugs for long-term stability and to avoid steroid-induced adverse effects in children.

Keywords: Corticosteroids, Electrophysiology, Immunosuppression, Multifocal choroiditis and panuveitis, Pediatric, Uveitis

Introduction

Multifocal choroiditis with panuveitis (MFCPU) presents predominantly in young or middle-aged healthy, myopic women (1, 2). Multifocal choroiditis with panuveitis is rare in children, occurring in only 1.1% of patients with pediatric uveitis younger than 18 years (3), and to our knowledge has not been documented in the presence of previous recurrent acute anterior uveitis (AAU). Multifocal choroiditis with panuveitis is characterized by multiple punched-out chorioretinal lesions similar to those seen in presumed ocular histoplasmosis syndrome (POHS) ranging in size from 50 to 350 µm, arranged singly, in clumps or in linear clusters, situated in the posterior pole and/or periphery. However, unlike POHS, vitritis and anterior chamber inflammation are present, associated with negative histoplasmin skin test and chest X-ray (4). Ganzfeld electroretinograms remain nearly normal until there is advanced retinal atrophy and substantial midperipheral field loss, at which time visual loss may be irreversible (5). Pattern reversal visual evoked potentials (PRVEPs) and 19 hexagon multifocal electroretinography (mfERG) represent a means by which localized retinal function may be topographically and objectively evaluated. In this instance, a full protocol mfERG was prohibitive because of the age of the subject and level of cooperation required. We report successful recovery of macular function documented by electrophysiology findings, following timely treatment of sight-threatening sudden-onset MFCPU in a boy with long-standing non-juvenile idiopathic arthritis (JIA) anterior uveitis.

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Case report

An 8-year-old boy was referred by his optometrist with a 5-day history of new-onset blurry vision and floaters in both eyes. There was no pain, eye redness, or discharge. He had been under long-term ophthalmology follow-up since the age of 4 years for bilateral recurrent AAU. Systemic assessment by

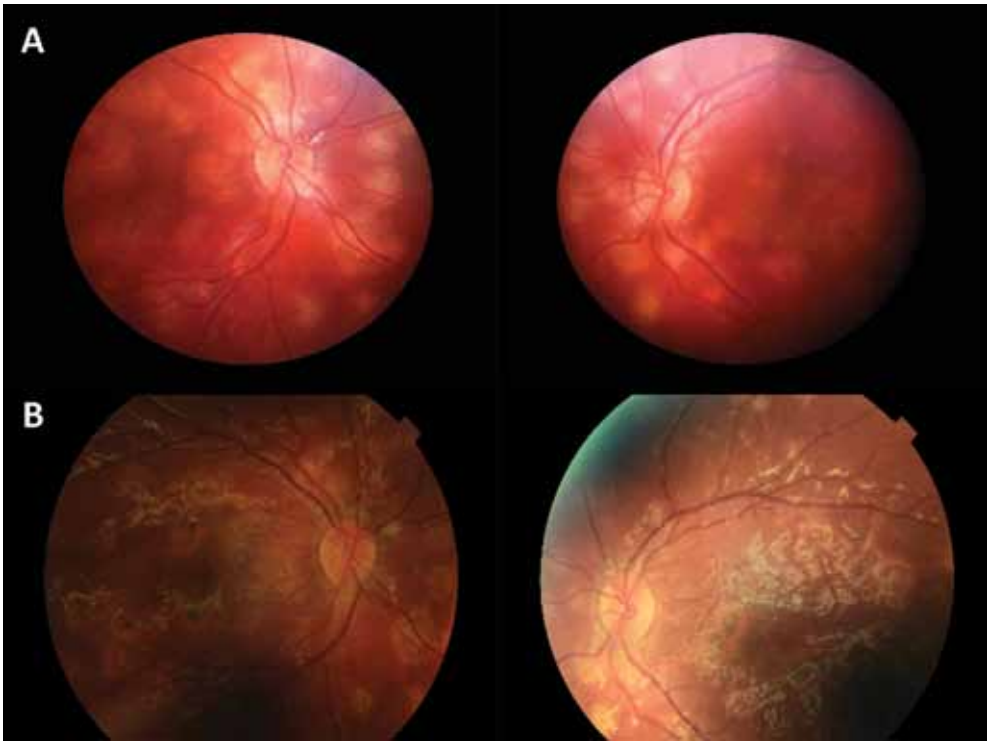

Fig. 1 - (**A**) Color fundus photograph of the right and left eye before treatment shows cystoid macular edema and multiple active deep creamy whitish yellow choroidal lesions in the posterior pole extending to the equator. (**B**) Two weeks posttreatment, cystoid macular edema resolved with multiple inactive, pigmented chorioretinal lesions throughout the fundus.

the rheumatologist at that time could not identify a specific clinical phenotype such as JIA to explain his uveitis. He had 3 episodes of bilateral simultaneous AAU at 1-year intervals while maintaining normal visual acuity with no visible chorioretinal involvement on fundus examination done under mydriasis. The episodes were well-controlled with topical corticosteroids alone.

At presentation, visual acuity had deteriorated to 20/200 right eye and 20/100 left eye. He was moderately hypermetropic. Cells were observed in the anterior chambers, 2+ right eye and 1+ left eye, and grade 2 cells were noted in the vitreous of both eyes. Extensive posterior synechiae were present in his left eye from previous attacks of uveitis. Intraocular pressures were within normal range. Ophthalmoscopy showed multiple active small cream-colored chorioretinal lesions throughout the fundus and cystoid macular edema (CME) in both eyes (Fig. 1A). Laboratory investigations including full blood count, erythrocyte sedimentation rate, C-reactive protein, angiotensin-converting enzyme, and liver and renal profiles were normal. A TORCH screen for toxoplasmosis, rubella, cytomegalovirus, herpes simplex, herpes zoster, and HIV, syphilis serology, and interferon-gamma release assays (QuantiFERON-TB Gold) together with a rheumatology screen were negative. A chest x-ray to exclude tuberculosis and sarcoidosis revealed widening of the upper mediastinum. However, chest computed tomography showed no evidence of significant mediastinal or hilar lymphadenopathy and clear lungs. Systemic assessment revealed no arthritis or any skin rashes. Pattern reversal visual evoked potentials were consistently delayed from each eye and only present to large checks (120'), suggesting poor visual function (Fig. 2A). Multifocal electroretinography recorded with skin electrodes to only 19 hexagons showed markedly reduced amplitudes subfoveally and parafoveally, indicating loss of macular visual function from each eye (Fig. 2B). The patient was diagnosed with severe sight-threatening idiopathic MFCPU.

After consultation with a rheumatologist, the patient was admitted for treatment 5 days after onset with intravenous methylprednisolone, 1 g daily for 3 consecutive days followed by oral prednisolone 60 mg daily for 1 week together with topical prednisolone acetate, 1% 4 times daily to both eyes. At 2 weeks, the inflammation subsided, CME resolved, and the chorioretinal lesions became inactive, punched-out, pigmented, and/or atrophic (Fig. 1B). Spectral-domain optical coherence tomography (SD-OCT) 2 weeks posttreatment confirmed resolved CME together with bilateral sub-retinal pigment epithelium (RPE) lesions (Fig. 3). Pretreatment SD-OCT was not available. The patient's visual acuity improved to 20/40 in both eyes and oral prednisolone was tapered and discontinued in 8 weeks. Three weeks after onset, while on 30 mg of oral prednisolone, subcutaneous methotrexate was introduced as a steroid-sparing immunomodulatory drug at 15 mg per week along with folic acid 5 mg orally once weekly. At 6 months, his visual acuity further improved to 20/32 in both eyes. The PRVEPs were well-maintained down to the smallest check size (7.5') (Fig. 2A), and mfERGs posttreatment were normal (Fig. 2B), showing a significant improvement in macular function. At 9 months, he had no evidence of recurrent inflammation and remains off topical or oral steroids.

Discussion

Multifocal choroiditis with panuveitis is generally a bilateral progressive chronic disorder with recurrent bouts of

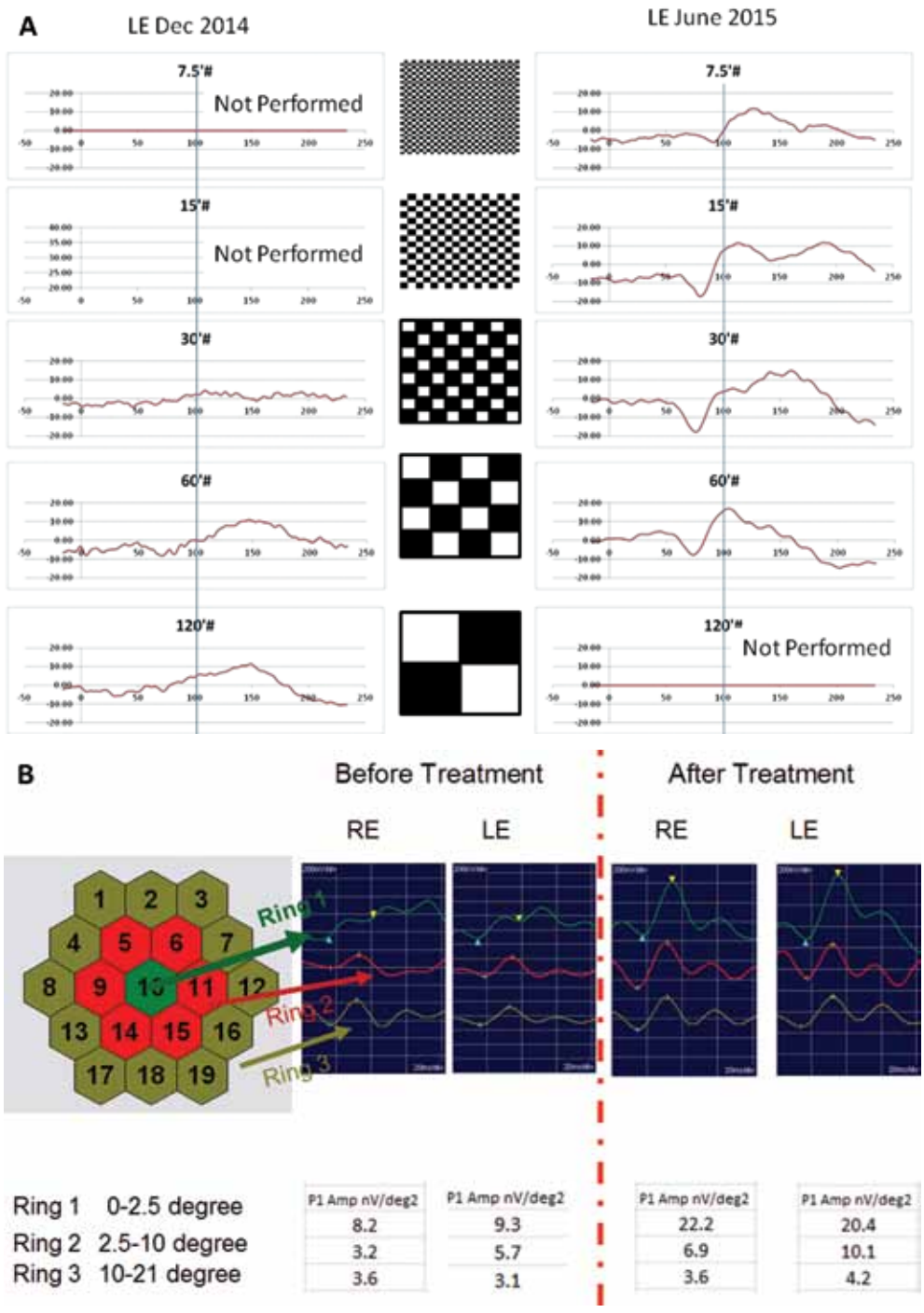

Fig. 2 - (**A**) Pattern reversal visual evoked potentials (PRVEPs) of the left eye before treatment (December 2014) were consistently delayed and only present to large checks (120'), suggesting poor visual function. The PRVEPs 6 months posttreatment (June 2015) were well-maintained down to the smallest check size (7.5'), demonstrating significant recovery of macular function. (**B**) Multifocal electroretinography. Macular responses in rings before treatment showed markedly reduced amplitudes subfoveally and parafoveally. Six months posttreatment, there was significant recovery of the central macula signal.

inflammation and decrease in vision with time (6, 7). Significant permanent visual loss has been reported in more than half of adult cases despite steroid treatment (6) and is usually due to macular involvement, most commonly choroidal neovascularization (CNV) and CME, each occurring in nearly one third of affected eyes (6, 7) or from steroid complications including cataract and glaucoma (4, 7). The incidence of visual loss secondary to pediatric MFCPU has not been documented in the literature due to the rare occurrence of this condition within this age group. Moreover, sudden-onset MFCPU in the presence of previous bilateral non-JIA anterior uveitis has yet to be reported.

During the acute phase, patients with MFCPU characteristically demonstrate severe depression of retinal function on mfERG. In most cases, MFCPU causes significant permanent retinal damage secondary to chorioretinal scarring, which prevents recovery to baseline on mfERG testing (5). In our case, pretreatment mfERG highlighted mainly a central scotoma with abnormal amplitudes and implicit times. Timely treatment improves the visual outcomes and

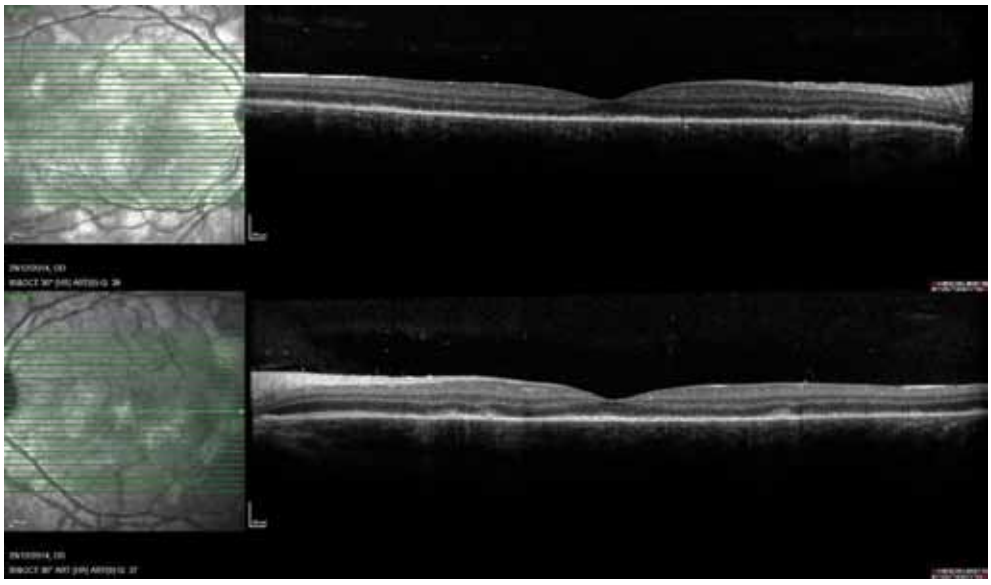

Fig. 3 - Optical coherence tomography (OCT) scan of the right and left eye 2 weeks posttreatment shows cystoid macular edema resolved together with bilateral sub-retinal pigment epithelium lesions. Pretreatment OCT was not available.

reduces complications in children with chronic uveitis (3). Our treatment strategy was to start with intensive systemic and topical steroid therapy in the presence of active sight-threatening inflammation to achieve rapid visual recovery and resolution of CME. The PRVEPs and our reduced protocol mfERG to 19 hexagons with skin electrode are useful to accurately and objectively monitor recovery of macular function in response to treatment in patients with MFCPU, particularly in children. In our case, PRVEPs and mfERG demonstrated significant recovery of the central macula signal posttreatment.

However, MFCPU is generally refractory to long-term steroid therapy, with recurrences and deterioration in vision in addition to a high rate of corticosteroid-induced side effects. Long-term immunomodulatory drug therapy such as methotrexate, used in our patient, is effective and safe in controlling inflammation, and avoids complications caused by chronic administration of corticosteroids (4). Thorne et al (1) reported an 83% reduction in posterior pole complications and 92% reduction in visual loss with the use of immunosuppressive therapy. This is particularly important in pediatric uveitis. We plan to withdraw methotrexate after a quiescent period of 12 months and monitor the controlled uveitis for recurrences.

In conclusion, MFCPU is rare in children and has not been documented in the presence of previous recurrent AAU. Onset of floaters in children should alert the clinician to early stages of posterior pole involvement and progression to reduction in vision due to CME requires prompt intensive steroid therapy as a sight-saving intervention. Early introduction of methotrexate as a steroid-sparing disease-modifying drug controlled the panuveitis. The child had no evidence of recurrent inflammation and did not require long-term systemic or topical steroid therapy, avoiding any steroid-induced adverse effects. Serial monitoring of macular structure and function by clinical examination, SD-OCT, and electrophysiology is recommended as a valuable objective method to evaluate the response to treatment particularly in children, when subjective tests of visual function might not be reliable. It has been shown in this case that a reduced protocol mfERG (19 hexagons) with skin electrode recording can still provide important clues to visual function, even if it is not as precise as corneal electrode recording with many hexagons requiring greater patient cooperation and time.

Disclosures

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Conflict of interest: None of the authors has conflict of interest with this submission.

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