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Acute posterior multifocal placoid pigment epitheliopathy associated with CN III palsy

Shani Pillar [a,b,*], Raz Gepstein [a,b], Orly Gal-Or [b,c], Michal Kramer [b,c]

[a] Department of Ophthalmology, Meir Medical Center, Kfar Saba, Israel
[b] Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel
[c] Department of Ophthalmology, Rabin Medical Center, Petah Tikva, Israel

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ABSTRACT

Purpose: To report a case of acute posterior multifocal placoid pigment epitheliopathy (APMPPE) associated with cranial nerve (CN) III palsy.

Observations: A 20-year-old woman developed bilateral anterior uveitis, which resolved with topical steroids. Three weeks later she exhibited posterior pole lesions in both eyes, corresponding with a diagnosis of APMPPE, as confirmed by multimodal imaging. Two days later the patient presented with right CN III palsy. The patient was started on oral prednisone, which was gradually tapered off. Signs and symptoms improved rapidly, with complete resolution within two months.

Conclusion and importance: Though rare, APMPPE may present with neurological involvement, as in this previously unreported association with CN III palsy. Unlike uncomplicated APMPPE cases, in patients with neurological manifestations systemic therapy is advocated.

1. Introduction

Acute posterior multifocal placoid pigment epitheliopathy (APMPPE) is a rare inflammatory chorioretinal disorder, typically affecting both eyes of young healthy adults, causing visual blurring or scotomas.[1] The pathogenesis is thought to involve small choroidal arterioles, leading to the characteristic presentation of multiple yellow creamy placoid lesions in the macula at the level of the RPE. Visual prognosis is generally good, with signs and symptoms usually resolving within weeks.[2,3] Thus, indications for treatment are controversial. Concurrence of central nervous system (CNS) involvement may be as common as 61% of APMPPE patients, when including mild involvement, such as headaches.[4,5] Rarely, cerebral vasculitis, and even death may occur.[5–7] Here, we present a novel association of APMPPE and isolated CN III palsy in a 20-year-old woman.

1.1. Case report

A 20-year-old woman, with no relevant medical or ocular history, presented with redness and pain with ocular movements of her left eye (LE) for one week. At that time, uncorrected visual acuity (VA) was 20/20 in both eyes, and eye exam was positive only for LE congestion of conjunctival vessels. Five days later she experienced increased pain and decreased vision in her LE to 20/40. There were trace cells in the anterior chamber of both eyes (BE), while fundus examination was normal. The decreased VA seemed excessive in the clinical setting, but the exam's reliability was compromised by patient's self-reported pain. Working diagnosis at the time was of a first episode of bilateral anterior uveitis of inflammatory etiology, and the patient was treated with topical corticosteroids (CS) in both eyes. One week later LE VA was significantly improved (20/25) and treatment was later tapered down upon further improvement of signs and symptoms.

Three weeks later the patient's complaints had resolved, VA returned to normal (20/20) in BE, and anterior chambers were quiet, but fundus exam revealed multiple creamy yellow plaques at the level of the RPE in both posterior poles (Fig. 1A). LE exam was also positive for mild vitritis with +o.5 haze and a mildly swollen optic disc. Ocular imaging, including fluorescein angiography (FA), ocular coherence tomography (OCT), fundus autofluorescence (FAF), and OCT angiography, all demonstrated RPE and outer-retinal lesions corresponding with a diagnosis of APMPPE (Fig. 1B–D). Of note, the patient reported no recent viral illness or vaccination. Review of systems was normal, with the patient denying any neurological system when questioned.

Two days after being diagnosed with APMPPE (5 weeks after initial

* Corresponding author. Department of Ophthalmology Meir Medical Center, 59 Tchernichovsky St. Kfar Saba, 4428164, Israel.
E-mail address: shanigo@gmail.com (S. Pillar).

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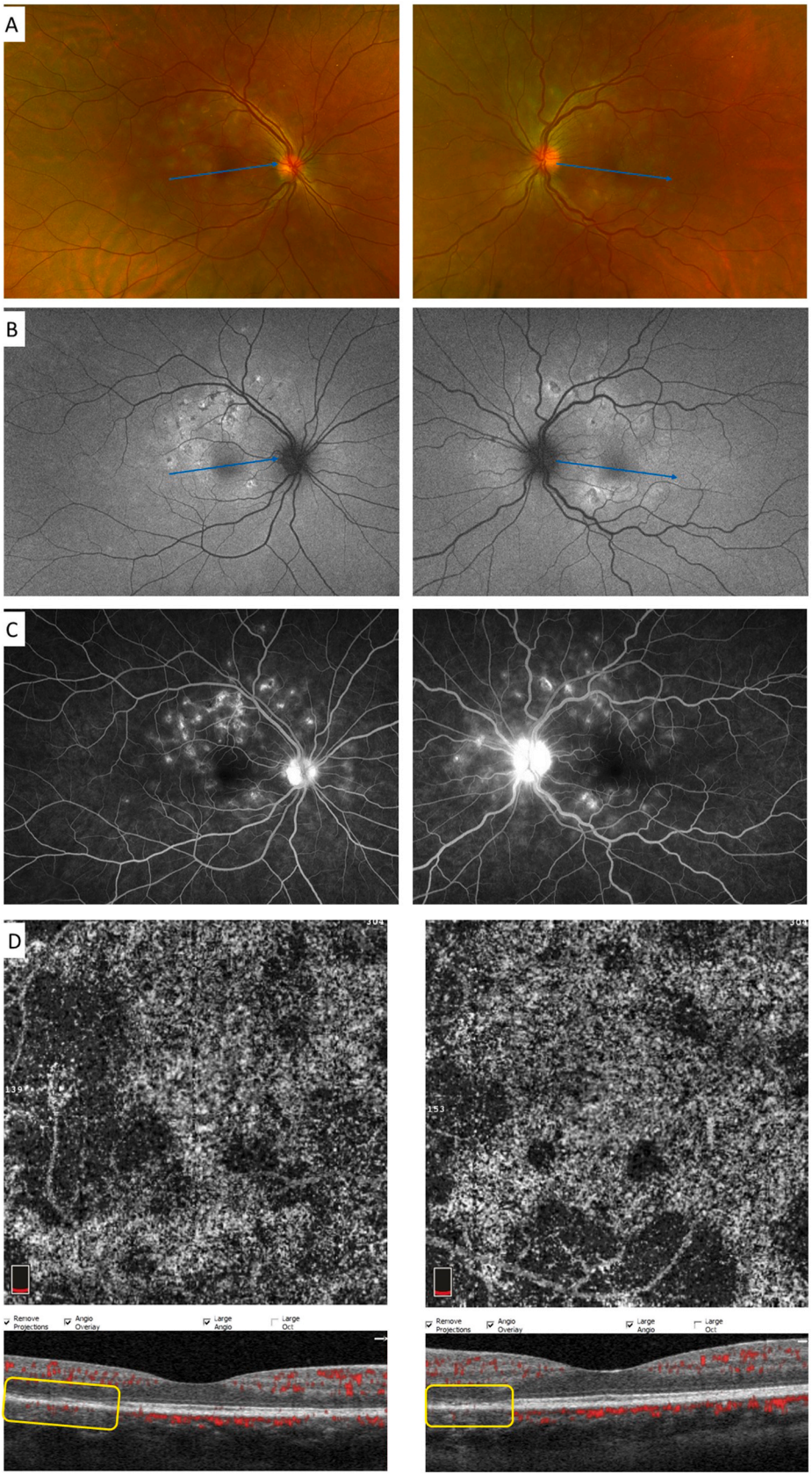

Fig. 1. Multimodal imaging findings in the acute phase of disease.

onset of ocular symptoms), the patient returned with right upper eyelid ptosis and diplopia. BE had VA of 20/20, normal color vision, and full visual fields on confrontation. Pupils were asymmetric, right larger than left, but there was no relative afferent pupillary defect. Extraocular movements revealed limitations in elevation, depression, and adduction in the right eye, corresponding to right CN III palsy. Fundus findings were unchanged. Magnetic resonance imaging (MRI), computed tomography-angiography and lumbar puncture were non-revealing. The patient was started on oral prednisone at 60 mg once daily. Signs of CN III palsy improved rapidly and CS dosage was gradually tapered over the course of 10 weeks. Neurologic and ocular signs had resolved in a follow-up clinic visit 7 weeks after the diagnosis of APMPPE (Fig. 2).

2. Discussion

APMPPE is a rare entity causing occlusive vasculitis of choroidal vessels. The age of onset is between 20 and 40 years with no gender predilection.[1,4,8] Since flu-like symptoms precede the onset of the disease in 40–50% of cases, a viral etiology has been postulated.[9,10] An association to certain HLA haplotypes (HLA-DR2, HLA-B7) has been previously reported,[11] but an exact etiology of AMPPE remains unclear. Diagnosis is usually made clinically, but characteristic imaging such as early hypofluorescence and late hyperfluorescnce of lesions on FA may be supportive. In recent years, OCTA imaging is gaining significance as a diagnostic tool, as well as aiding in uncovering the disease's pathophysiologic mechanisms.[2,3,12]

In an extensive literature review, Algahtani et al. found 56 well-documented cases of APMPPE-associated neurological complications, reported between January 2000 and December 2, 015.[6] Brownlee et al. identified five patients with neurological complications of AMPPE seen at Auckland Hospital between 2008 and 2013, and summarised cases in the literature between 1976 and 2013.[7] Published complications most

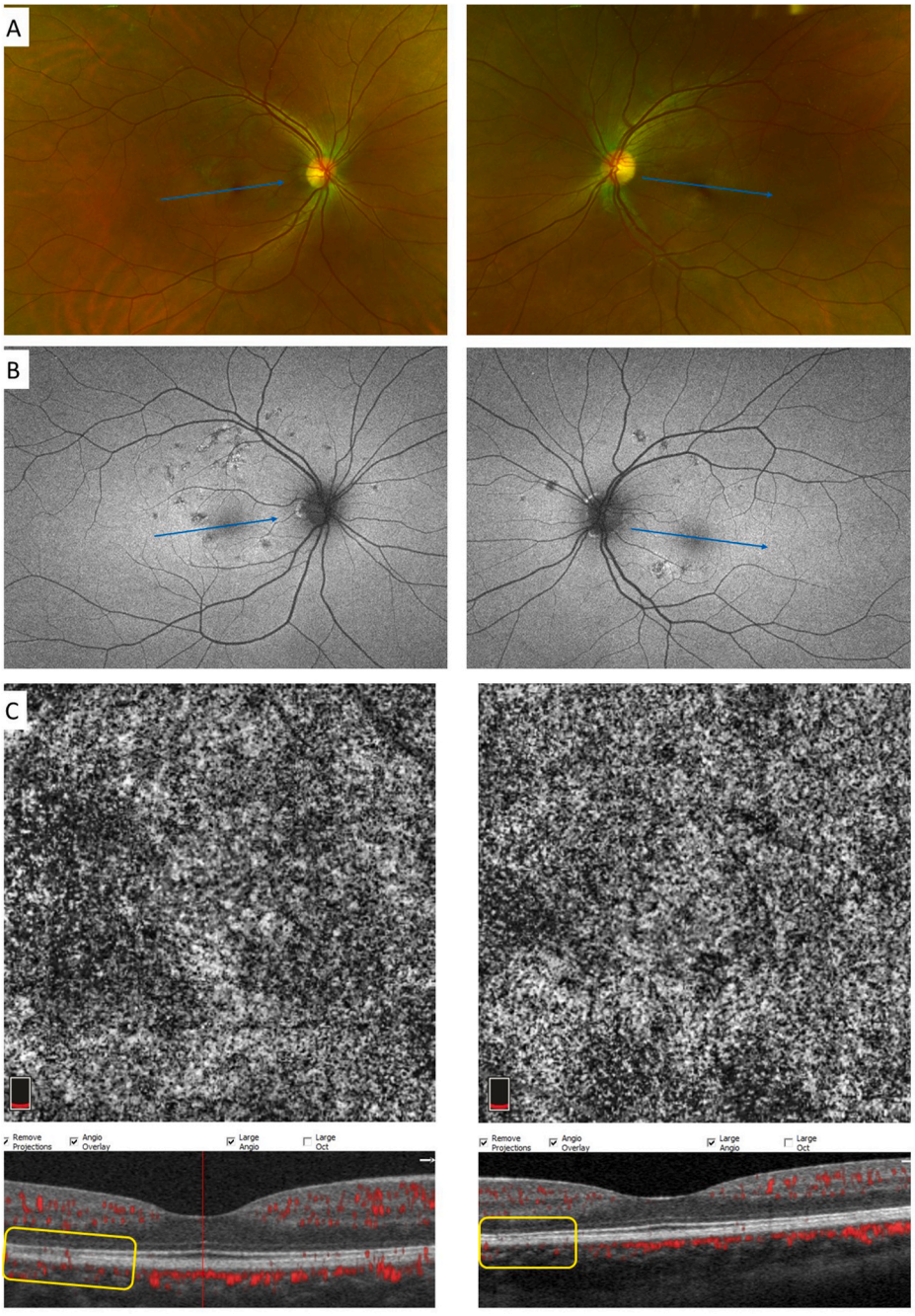

Fig. 2. Multimodal imaging (MMI) findings at last follow up. MMI of the right and left eyes at last follow up visit, 4 months after APMPPE presentation. A, Ultrawidefield Fundus photographs demonstrating very few remaining placoid lesions of the posterior poles. B, Ultrawidefield Fundus autofluorescence showing remaining lesions, which have lessened in number, and are now predominantly hypoautofluorescent. C, Optical coherence tomography angiography illustrating improved flow signal of the choriocapilaries at the area of the lesions, with restoration of outer retinal anatomy and some mild irregularity seen at the level of the RPE.

commonly include cerebral vasculitis and stroke, but have also been known to include headaches, meningoencephalitis, viral meningitis, seizures, peripheral neuropathy, CN VI palsy, transient hearing loss, cavernous sinus thrombosis, hypoesthesia & paresthesia.[6,7] CNS complications were observed to occur twice as often in men, and may occur simultaneously with ocular symptoms or months later,[6,7,13] with two thirds of ischemic events occurring within 4 weeks of visual symptom onset.[7] Most of the neurological complications resolve completely, but prognosis may vary, as 18–25% of patients sustain long-term disability, and 11–13% of CNS complications result in death.[6,7]

Our report is, to our knowledge, the first to reveal an association between APMPPE and CN III palsy. Acquired CN III palsies may be caused by vascular ischemia, trauma, neoplasm, hemorrhage, or they may be idiopathic. Most commonly, the basilar portion is affected, in the setting of diabetes mellitus or aneurysm.[14] Cerebral vasculitis is not considered one of the typical causes of CN III palsy,[14] though isolated cranial nerve palsies are described in the other forms of cerebral vasculitis, such as Churg–Strauss angiitis and granulomatosis with polyangiitis.[15]

The potential severity of the prognosis of neurological complications in APMPPE necessitates a high level of suspicion from the treating ophthalmologist, possibly suggesting a need for a neurological evaluation to be performed for all APMPPE patients. MRI and cerebrospinal fluid (CSF) examination must be considered as well, however, caution is needed when relying on such tests for prognostication. 5 of 23 (22%) patients with cerebrovascular complications of AMPPE were reported to have normal initial MRI results, and one patient later developed multifocal brain involvement and consequently died.[7] Cerebrospinal fluid (CSF) pleocytosis was detected in the majority, but not all, of APMPPE patients with CNS involvement who were sampled,[7,16] and yet pathological CSF results in APMPPE patients without major neurological complications have also been described.[17,18] In some reports neurologic complaints constituted the initial presentation of APMPPE patients, and so neurologists must also be vigilant for any visual complaints communicated by patients.

There is no general consensus regarding treatment of APMPPE. Since the prognosis is generally favorable, most patients with APMPPE are not treated. Though efficacy has yet to be substantiated in literature, systemic CS are often prescribed for extensive disease, or one that involves the fovea.[19,20] In patients with a neurological manifestation, however, aggressive management is strongly advocated. For cerebral vasculitis, Weinstein et al. suggested CS treatment for 4 months, for stroke risk reduction.[21] Others favored steroids for 2–3 months, followed by azathioprine for long-term immunosuppression.[6,22,23] "Escalation of care'' to immunomodulatory medications such as azathioprine, cyclophosphamide, or mitoxantrone, has been described in previous case reports when patients deteriorate on CS alone.[24]

In this case of APMPPE associated with CN III palsy, immunomodulatory medications were not deemed appropriate in light of the rapid recovery after initiation of oral CS. The paucity of published cases of APMPPE with CNS involvement in the literature doesn't allow for well-constructed systematic reviews. Thus, protocols regarding neurological investigations or treatment indications have yet to be established. Based on this present case as well as previously published cases, CS therapy, with potential escalation of care to immunomodulatory treatment in severe cases, appears to benefit clinical outcomes.

Patient consent

This report does not contain any personal information that could lead to the identification of the patient.

Declaration of competing interest

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A, Ultrawidefield Fundus photographs demonstrating multiple placoid subretinal lesions scattered throughout the posterior pole bilaterally. B, Ultrawidefield Fundus autofluorescence showing hyperautofluorescent active lesion and some hypoautofluorescent areas. C, Late phase fluorescein angiography showing multiple hyperfluorescent foci of late staining. D, Choriocapillaris slab of the Optical coherence tomography angiography presents distinct areas of decreased flow signal, seen as dark areas, on the enface view, and decreased flow signal (yellow boxes) on the B-scan view with flow overlay, corresponding to the location and orientation of the blue arrows in A and B. The B scan view also demonstrates areas of outer retinal hyperreflectivity in areas of ellipsoid zone and RPE discontinuity, corresponding to the location of the lesions.

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