Published in final edited form as:

Retina. 2010 May ; 30(5): 810–814. doi:10.1097/IAE.0b013e3181c596f8.

SUBRETINAL FLUID IN ACUTE POSTERIOR MULTIFOCAL PLACOID PIGMENT EPITHELIOPATHY

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Abstract

Purpose—The purpose of this study was to describe the clinical finding of macular subretinal fluid by optical coherence tomography in patients with acute posterior multifocal placoid pigment epitheliopathy.

Methods—Patients with acute posterior multifocal placoid pigment epitheliopathy were identified, and those with macular serous retinal detachment noted clinically and confirmed by optical coherence tomography are described.

Results—Of 8 patients with acute posterior multifocal placoid pigment epitheliopathy evaluated by the uveitis service at the Illinois Eye and Ear Infirmary between 2003 and 2008, 4 eyes of 3 patients presented with macular subretinal fluid. Confirmatory optical coherence tomography was performed in two patients.

Conclusion—Acute posterior multifocal placoid pigment epitheliopathy may present clinically with macular subretinal fluid. This finding can be confirmed and monitored with optical coherence tomography.

Keywords

acute posterior multifocal placoid pigment epitheliopathy; APMPE; foveal detachment; OCT; subretinal fluid; uveitis; white dot syndrome

Acute posterior multifocal placoid pigment epitheliopathy (APMPPE) was first described by Gass¹ as a self-limited inflammatory disorder of the retina and choroid in young, otherwise healthy adults. This idiopathic condition affects men and women equally and is associated with a viral prodrome in over one third of cases.¹ Bilateral involvement is common, and significant visual loss can occur when the macula is involved. Acute posterior multifocal placoid pigment epitheliopathy has been described in association with many common illnesses, including mumps,² adenoviral infection,³ and Lyme disease⁴; administration of vaccines for varicella⁵ and hepatitis B⁶; and in patients with Wegener's granulomatosis.⁷ Vascular inflammation is thought to be a component as evidenced by its association with neurosensory hearing loss⁸ and central retinal vein occlusions.⁹ Patients can present with headache, and some patients develop cerebral vasculitis and ischemia.^{10–13}

Clinical examination of patients with APMPE may reveal mild nongranulomatous anterior chamber inflammation. Retinal findings include creamy yellow, postequatorial subretinal

lesions that vary in size. These lesions typically resolve over several weeks leaving behind areas of retinal pigment epithelial mottling and depigmentation. Fluorescein angiography shows characteristic early blockage and late staining of the subretinal lesions.¹⁴ Most patients regain vision of 20/30, although permanent visual loss is possible.^{15,16} Visual improvement typically follows the resolution of the retinal lesions.¹ Optical coherence tomography (OCT) has been used to evaluate the retinal lesions¹⁷ as well as one case of late cystoid macular edema after APMPE.¹⁸

Methods

We were granted permission from the Institutional Review Board at the University of Illinois to retrospectively review existing medical records of patients seen by the University of Illinois uveitis service with a waiver of informed consent. Patients evaluated by the uveitis service between 2003 and 2008 with a diagnosis of APMPE were identified. The examination details, including best-corrected Snellen visual acuity, slit-lamp examination, and fundus examination, were reviewed. Those patients who had subretinal fluid (SRF) evident both clinically and by OCT are described.

Results

Eight patients were diagnosed with APMPE by the uveitis service of the University of Illinois Eye and Ear Infirmary between 2003 and 2008. Six were men, and the average age was 24.7 years (range, 17–34 years). Fundus lesions were bilateral in seven. Four eyes of three patients had associated SRF clinically. Optical coherence tomography was performed on two patients, which confirmed the presence of SRF.

Case 1

A 26-year-old man was referred for blurred vision of 1-week duration, starting first in the left eye followed a few days later by the right eye. He reported a bout of gastroenteritis and fever 1 week before the onset of blurred vision. Medical history was noncontributory. On examination, best-corrected vision was counting fingers in both eyes. Slit-lamp examination showed [1/2]+ anterior chamber cells in the right eye and 1+ in the left eye. The iris, lens, and vitreous were normal. Dilated fundus examination showed multiple placoid yellow subretinal lesions throughout the posterior pole of both eyes (Figure 1A). The maculae appeared thickened and elevated in both eyes. Fluorescein angiography showed early blockage (Figure 1B) and late staining (Figure 1C) of the lesions. Optical coherence tomography showed fluid beneath the neurosensory retina in the right eye (SRF, Figure 2A) and deep fluid in the left eye (X, Figure 2B). This deep fluid may have been located in the outer nuclear layer and photoreceptor layer or in the subretinal space (Figure 2B).

A diagnosis of APMPE was made. Workup included a negative fluorescent treponemal antibody absorption test. Oral prednisone (60 mg/day) was administered because of the bilateral SRF and poor vision. Subretinal fluid resolved over 1 week (Figure 2, C and D), and prednisone was tapered over 1 month. By 10 weeks, vision improved to 20/30 in the right eye and 20/40 in the left eye with a 1-diopter myopic shift in both eyes and residual retinal pigment epithelial mottling in the fovea of both eyes.

Case 2

A 29-year-old Indian woman presented to a retina service with a central blind spot after an upper respiratory infection. Best-corrected visual acuity was 20/200 in the right eye and 20/20 in the left eye. Slit-lamp examination showed no anterior chamber inflammation, and dilated fundus examination was significant for several white subretinal lesions and a serous

detachment of the macula in the right eye (Figure 3A). The disk was not hyperemic, and SRF did not extend to the optic disk. The left eye had no fundus lesions. Fluorescein angiography showed early hypofluorescence and late leakage of the lesions in the right eye. The presence of SRF was confirmed in the right eye by OCT (Figure 3B). Laboratory examination included negative titers for toxoplasmosis, a negative QuantiFERON Gold (Cellestis, Carnegie, Victoria, Australia) for tuberculosis infection, and a negative fluorescent treponemal antibody absorption test. Magnetic resonance imaging of the brain was performed and was reported as negative for any intracranial lesions or signs of intracranial inflammation. The patient was diagnosed with Harada disease and possible toxoplasmosis and started on sulfadiazine, trimethoprim, leucovorin, and 60 mg/day prednisone. She did not tolerate the medications, took them only for 3 days, and presented to the uveitis service for a second opinion. By this time, there was reduction of SRF and improvement of visual acuity to 20/25. A diagnosis of atypical, unilateral APMPE was made, and no therapy was prescribed. On follow-up at 2 months, the vision was 20/20 in both eyes with resolution of fundus lesions and SRF.

Discussion

Acute posterior multifocal placoid pigment epitheliopathy is an idiopathic, self-limited inflammatory disorder diagnosed based on clinical findings of yellow–white placoid lesions at the level of the pigment epithelium and choroid.¹ Early blockage and late staining of the lesions on fluorescein angiography are characteristic, and patients often show mottling and depigmentation of the retinal pigment epithelium after resolution of the placoid lesions.¹⁴ Subretinal fluid is mentioned as a possible association in the literature. One series of patients with APMPE described 9 of 24 patients who presented clinically with associated serous retinal detachments. All the patients had spontaneous resolution of the SRF (6 days to 2 weeks) with no recurrence in >1 year of follow-up.¹⁹ A second report, which focused on “atypical” cases of APMPE, included three patients with serous retinal detachment confirmed by ultrasonography. All patients improved rapidly while on oral corticosteroids.²⁰

In this series, SRF and intraretinal fluid are shown by OCT. We believe that much of the fluid is in the subretinal space. The mildly reflective layer above the retinal pigment epithelium (deep to X, Figure 2B) likely represents inflammatory debris or degenerative material. The similar but thicker and more hyperreflective areas on the anterior surface of the retinal pigment epithelium (labeled on the OCT images with asterisks [*] in Figure 1 and deltas Δ in Figure 2) correlate with the plaques seen clinically and are likely related to the inflammation. In addition, the rapid and substantial improvement in vision supports the presence of SRF rather than intraretinal fluid, because recovery of vision to within a few lines of 20/20 with a myopic shift is common after resolution of macular SRF. A myopic shift would not be expected if the photoreceptor outer segments remained against the RPE. In our experience, the presence of such large cystoid spaces in the outer retina is associated with schisis or neural disconnection and a less favorable visual outcome.

Although not commonly reported, SRF is a possible finding in APMPE and should not decrease the suspicion of this diagnosis. Resolution of fluid and improvement in vision are typically rapid. In our cases, a short course of oral corticosteroids was prescribed but may not have been necessary for return of good vision.¹⁹ In contrast to Vogt-Koyanagi-Harada disease (VKH), which is commonly associated with foveal detachments, APMPE typically resolves without treatment and does not recur. Furthermore, the detachments of VKH are associated with an inflamed optic nerve and are more pronounced.

Reports of OCT findings in APMPE are limited to patients without foveal detachments. One report describes the fundus lesions as having involvement of the outer plexiform layer

of the retina and the retinal pigment epithelium with sparing of the inner retina. Retinal thickness was not increased in this report.¹⁷ Optical coherence tomography has also been used to follow treatment of cystoid macular edema developing as a late sequela in one patient with APMPE.¹⁷ To our knowledge, this is the first report of foveal detachments in APMPE confirmed by OCT.

We describe three eyes of two patients who presented clinically with APMPE associated with foveal detachments confirmed by OCT. This tool may be helpful in confirming the presence of a foveal detachment and monitoring its resolution over time.

Acknowledgments

Supported by an unrestricted grant from Research to Prevent Blindness, New York, NY (DAG) and, in part, by National Eye Institute Core Grant for Vision Research (P30 EY001792), Bethesda, MD.

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Fig. 1. Color photographs and fluorescein angiography of APMPE associated with SRF: Case 1. **A**, Multiple placoid subretinal lesions are scattered throughout the posterior pole bilaterally. Two of the lesions that correspond to those showed in Figure 2B are labeled with an asterisk (*). Subretinal fluid was noted clinically in both eyes. **B**, Fluorescein angiography showed early blockage of the subretinal lesions. **C**, Late staining of subretinal lesions is also noted.

Fig. 2. Optical coherence tomography showing bilateral sub-foveal detachments in patients with APMPE. **A**, At presentation, the patient had decreased vision associated with SRF in the right eye. **B**, In the left eye, the patient had either intraretinal fluid or SRF (X). The more hyperreflective material at the edge of this space corresponds to the location of the “white dots” (*). **C** and **D**, The fluid had resolved in both eyes by 1 week after presentation.

Fig. 3. Color fundus photograph and OCT of the right eye: Case 2. **A**, The color fundus photograph shows multiple placoid subretinal lesions and SRF in the macula. **B**, Optical coherence tomography of the right eye with SRF and adjacent intraretinal fluid. The subretinal hyperreflective area (Δ) corresponds to the white dot in **A**.