An typical case of Acute Posterior Multifocal placoid pigment Epitheliopathy with intraretinal fluid

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Abstract

Acute posterior multifocal placoid pigment epitheliopathy is a rare inflammatory chorioretinopathy, classified as a white dot syndrome. It usually presents in young adults and results in ischemia of the choriocapillaris leading to atrophy of the external retinal layers, including the retinal pigment epithelium. This report describes an atypical case of this disease with the presence of intraretinal fluid.

A 20-year-old male patient presented with complaints of sudden, severe left eye vision loss. He did not report any systemic symptoms, and his medical history was unremarkable. Slit-lamp examination and fundoscopy revealed a normal anterior segment, with yellow placoid lesions on his macula and near periphery. He underwent a spectral-domain optical coherence tomography and fluorescein angiography, which revealed the presence of central intraretinal fluid in his left eye and multiple areas of macular ischemia bilaterally. Treatment was started with oral corticosteroids, and the anatomical changes, including the intraretinal fluid, steadily improved over the following weeks.

Although rare, the presence of subretinal or intraretinal fluid should not decrease the suspicion of the diagnosis of acute posterior multifocal placoid pigment epitheliopathy. The reabsorption of the fluid usually accompanies the improvement of the remaining anatomical changes and the visual function.

Introduction

Acute posterior multifocal placoid pigment epitheliopathy (APMPPE) is a rare inflammatory chorioretinopathy, first described by Gass in 1968. It is classified as a white dot syndrome and has an estimated incidence of 0.15 cases per 100,000 people. The most common presentation is bilateral. It affects men and women equally, often during the 2nd to 4th decades. Its pathophysiology is not clearly understood, and the primarily affected region of the retina is unclear. Initially, it was thought that the disease primarily involved inflammation in the retinal pigment epithelium (RPE), producing the characteristic placoid lesions. Other hypotheses consider ischemia in the choriocapillaris, due to occlusive vasculitis, potentially due to inflammatory or autoimmune processes, resulting in hypoperfusion of the RPE and photoreceptors. The most accepted theory at present refers to a primary affection of the choriocapillaris, leading to secondary injury of the RPE and outer retina, resulting in the atrophy of the choriocapillaris, RPE, and photoreceptors. Approximately 33% of the patients report preceding flu-like symptoms before APMPPE's onset. The disease has also been described as associated with cases of systemic vasculitis, sarcoidosis, ulcerative colitis, thyroiditis, other viral and bacterial infections, and post-vaccination. Genetic associations have been reported involving the HLA-B7 and HLA-DR2 haplotypes.
The diagnosis of APMPPE is established by the clinical presentation, retinoscopy findings, and complementary imaging tests, such as spectral-domain optical coherence tomography (SD-OCT), fundus autofluorescence (FAF), fluorescein angiography (FA) and indocyanine green angiography (ICGA)\textsuperscript{3,5}. The most common ophthalmological complaint is a bilateral, usually asymmetric, rapid onset of blurred vision associated with central or paracentral localized scotomas. Best-corrected visual acuities (BCVAs) may range from 6/10 to count-fingers, and photopsia and metamorphopsia may also develop. Systemic symptoms such as flu-like syndrome and headache may be present concomitantly. The anterior segment evaluation is usually normal, but anterior cell reaction may develop. Mild vitritis is reported in 50\% of the cases. Fundus examination often shows white-yellow placoid lesions at the level of the RPE and choroid\textsuperscript{4}. Papillitis may occur, but cystoid macular edema is uncommon. The most typical acute findings in SD-OCT include hyperreflectivity in the outer retinal layers and the absence of the ellipsoid zone\textsuperscript{14,15}. FA usually exhibits early hypofluorescence corresponding to the placoid lesions, followed by late hyperfluorescent staining. The early hypofluorescence may represent poor perfusion of the choriocapillaris or blockage due to the overlying outer retina and RPE thickening\textsuperscript{16}. ICGA manifests early and late hypofluorescence, due to the poor perfusion of the choriocapillaris.

The natural history of APMPPE is usually self-limited, with partial or complete resolution of the visual symptoms after 4-8 weeks. Most patients achieve a BCVA of 6/12 or better. Foveal involvement confers a worse prognosis\textsuperscript{5}. Other factors which may also lead to a worse prognosis include patients older than 60 years, unilaterality, and an interval of 6 months before the involvement of the second eye\textsuperscript{17}. There is no current consensus regarding the treatment and its impact on the final visual result. Steroids are anecdotally used when the macula is involved. The recurrence of the disease is uncommon and generally predicts a worse prognosis\textsuperscript{3}. All patients with a new diagnosis of APMPPE should receive full neurologic and systemic workup to evaluate for CNS vasculitis and other associated systemic conditions such as autoimmune and infectious diseases.

The purpose of this work is to report a case of this disease with atypical imagiological presentation, diagnosed in a 20-year-old patient.

**Case presentation**

A 20-year-old male patient presented in the emergency department with complaints of severe left eye (OS) vision loss for 4 days. He did not report any other ocular symptoms, such as red eye or pain. He denied trauma or any other precipitating factors. His medical history was unremarkable, and he did not take any medication. There was no history of recent disease or flu-like symptoms. His BCVA was 6/6 and 6/30 on his right and left eyes, respectively. The slit-lamp examination showed a normal anterior segment, with the absence of anterior chamber reaction. Fundoscopy revealed macular yellowish placoid lesions, occupying a large portion of the macula and the near periphery. He underwent a SD-OCT and FA, which showed the presence of central intraretinal fluid dispersed in an atypical pattern, on the OS (Figure 1), and multiple areas of macular ischemia bilaterally, with late central and paracentral diffusion (figure 2). A systemic study with infectious and immunological markers was requested that came out negative. Neurological examination was also unremarkable. After ruling out an infectious cause, an initial dose of 80mg of prednisolone was started.

Three days after the initial presentation, the patient was reevaluated. His OS BCVA had improved to 6/12, the anterior chamber still had no inflammatory reaction, and the fundoscopy appearance was similar. The SD-OCT was repeated, which showed a reduced volume of intraretinal fluid (figure 3). Given the improvement of the clinical picture, treatment was maintained. He was again evaluated 1 week after onset, showing a similar BCVA of 6/12 on his OS, but this time the intraretinal fluid had completely disappeared on the SD-OCT. A progressive weaning of the oral corticosteroid was started, and his BCVA progressively improved during the following weeks. During the last observation, 8 weeks after the initial presentation, the patient had a BCVA of 6/7.5 on his OS. Fundoscopy revealed a marked improvement of the posterior pole lesions, with some regions of cicatrical pigmentary changes (figure 4). SD-OCTs repeated during each examination showed the absence of intraretinal or subretinal fluid, with mild anatomical changes in the outer layers of the retina (Figure 5).

**Discussion**

APMPPE is a rare inflammatory chorioretinopathy of unclear cause, which mainly affects young adults. Although its physiopathology is unclear, recent studies report that ischemia occurring in the choriocapillaris results in hypoperfusion of the RPE and photoreceptors and consequent atrophy of the outer retinal layers\textsuperscript{8}. The case we described consisted of a 20-year-old male patient with initial complaints of sudden unilateral vision loss. Although the subjective complaints were unilateral, imaging studies showed a bilateral, asymmetrical involvement. It was therefore a case with bilateral structural anatomic changes, with unilateral functional manifestations, probably since the pathologic process was more severe on the OS, therefore having a greater functional impact. Those findings were similar to most described cases of APMPPE,
where asymmetric bilateral changes are present. Although many cases are preceded by systemic symptoms like flu-like syndrome, our patient did not have any history of recent systemic disease. Headache or other neurologic manifestations were also not present. In all cases, a full neurological and systemic study must be performed to rule out the existence of complications, namely cerebral vasculitis, which is associated with this disease in some cases. The initial OS BCVA of 6/30 matched the values described in the literature for this disease, which may range from 6/12 to count-fingers. Fundoscopy appearance, consisting of yellowish plaques involving the macula and the periphery were also typical. However, the presence of intraretinal fluid, as evidenced by Figure 1, constitutes a rare finding, scarcely reported throughout the literature. Birnbaum et al. described a small series of cases including some with subretinal (SRF) and intraretinal fluid (IRF) shown in SD-OCT. They hypothesized that a mildly reflective layer forms above the RPE, likely representing inflammatory debris or degenerative material, giving the impression that the fluid is intraretinal, although it is subretinal. They also stated that the quick and substantial recovery of visual acuity supports the presence of SRF, rather than IRF. Nonetheless, even though it is rare, SRF or apparent IRF is a possible finding in APMPPE, and should not decrease the suspicion of the diagnosis. The resolution of fluid usually accompanies the improvement of the visual function and is typically rapid.

Regarding the treatment, the evidence is unclear. Most studies report that structural and functional improvement is usually fast and occurs spontaneously, without any treatment. However, many authors consider treatment with oral corticosteroids when the lesions affect the fovea. When central nervous system vasculitis is present, therapy is mandatory and can be life-saving. A recurrent form of APMPPE may represent a different clinical entity called relentless placoid chorioretinitis, a disease that shares features with APMPPE and serpiginous choroidopathy. It has a high recurrence rate and longer periods of activity. In those cases, immunomodulatory therapy may be necessary. In our case, the patient was promptly treated with oral corticosteroids as soon as an infectious cause was ruled out. The structural changes, namely the presence of intraretinal fluid improved rapidly, within 1 week, while the BCVA steadily, and almost completely improved during the 8 weeks following the onset of the disease. It was not possible to conclude whether the use of corticosteroids had an impact on the improvement of the anatomical and functional outcomes.

**Conclusion**

This report presented a case of APMPPE with atypical imagiological findings, namely the presence of intraretinal fluid. Despite being a rare, scarcely reported finding, in this disease, the presence of foveal subretinal or intraretinal fluid should not lessen the degree of suspicion of this disease. The reabsorption of the fluid is usually spontaneous and fast, accompanying the improvement of the visual function. There is insufficient evidence to conclude that active treatment with corticosteroids influences the rate of improvement of the intraretinal fluid, in this condition.

**References**

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