THE **RETINA** PARTNERS

Encino Santa Monica Valencia Thousand Oaks Century City

(877) 3-RETINA

Case of the Month – October 2019

Presented by Christian Sanfilippo, MD

A 31 year-old male presented to clinic complaining of acutely decreased vision in both eyes, and a central blind spot in the left. This began two days prior to presentation, and one day after experiencing a severe and unusual headache. His headache had since resolved, and he denied other neurological symptoms. Visual acuity measured 20/20 -1 and 20/70 in the right and left eyes respectively. Intraocular pressures were normal. His anterior segment examination was unremarkable, with no signs of present or past inflammation. Fundus imaging of the right and left eyes are shown below.

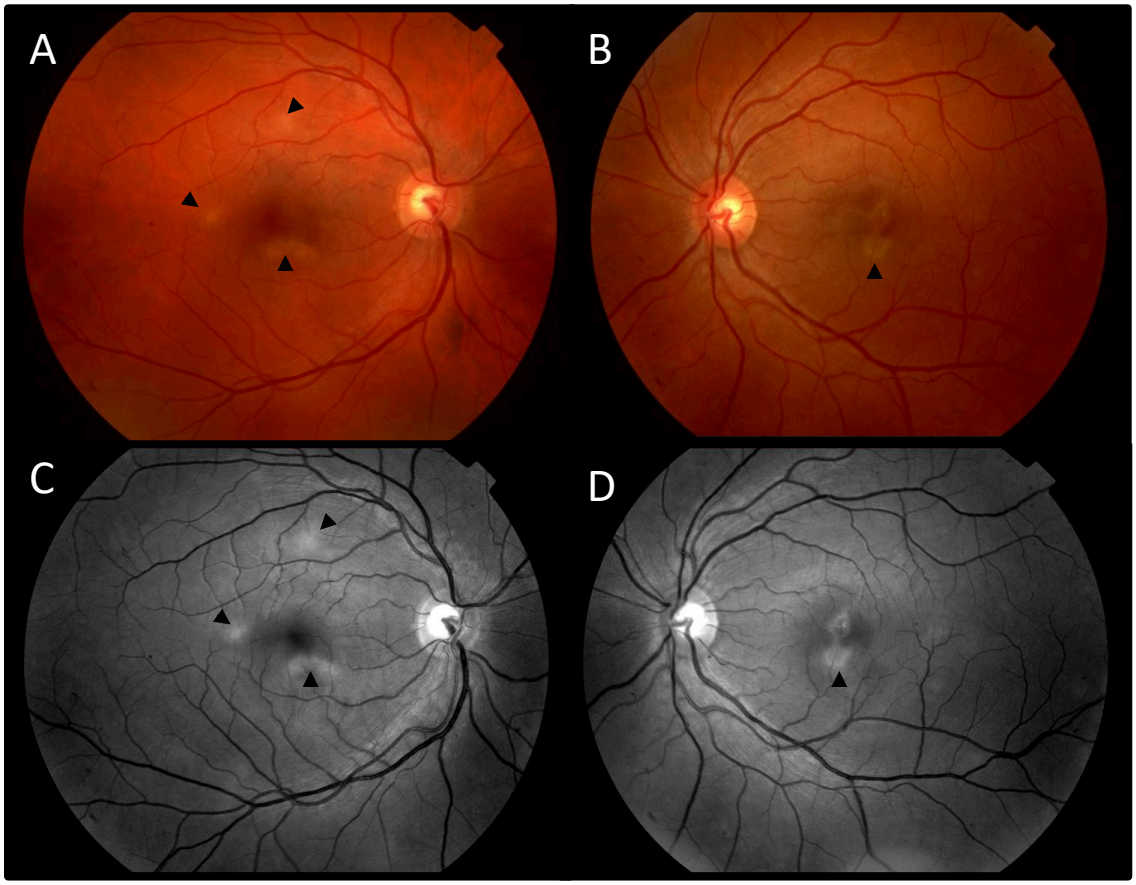

Figure 1: A. Color fundus photo of the right eye shows several, perifoveal, deep yellow lesions. Similar lesions are present in the left eye (arrowheads). These lesions are more prominent on the red-free images **(C and D).**

Additional imaging with SD-OCT and fluorescein angiography was performed and are shown below.

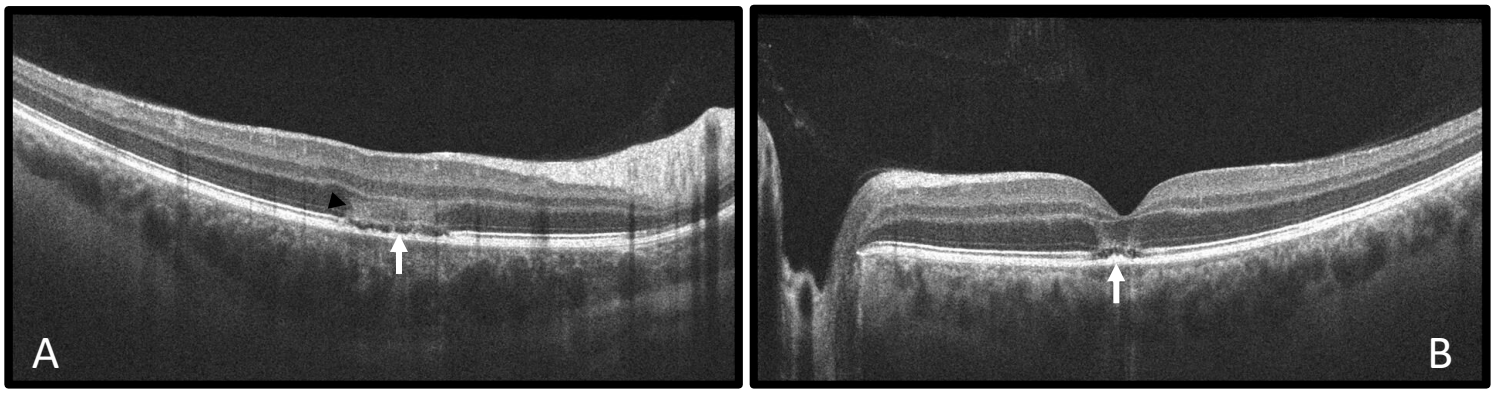

Figure 2: A. SD OCT line scan through the inferior peri-foveal lesions of the right eye shows complete loss of the ellipsoid band, which has been replaced by a thin hypo-reflective sliver (arrow). The overlying outer nuclear layer is diffusely hyper-reflective (arrowhead). **B.** SD-OCT line scan through the subfoveal lesion of the left eye shows a similar appearance with less pronounced outer nuclear hyper-reflectivity.

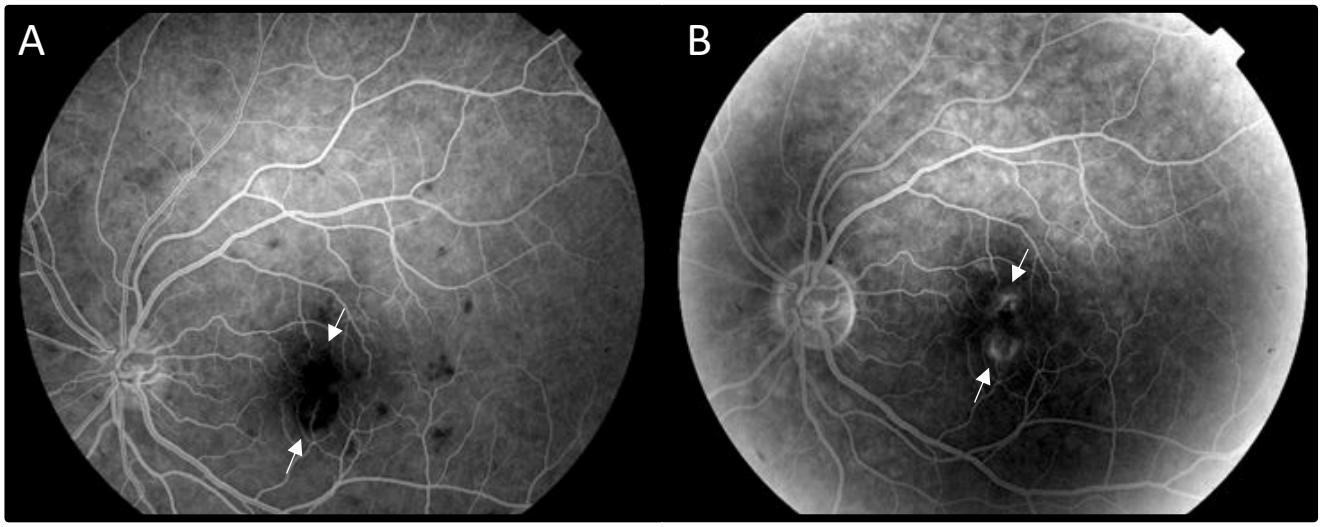

Figure 3: A. Early phase fluorescein angiogram of the left eye demonstrates that the lesions block the choroidal flush (arrows). Note that there are several smaller lesions which are easily seen here, but not noted on the color photos or examination. **B.** Late phase fluorescein angiogram of the left eye shows that the same lesions stain late (arrows). Fluorescein angiogram of the right eye had similar characteristics, but is not shown here.

Differential Diagnosis: Acute macular neuroretinitis (AMN), acute posterior multifocal placoid pigment epitheliopathy (APMPPE), syphilitic posterior uveitis, tuberculosis associated placoid disease, persistent placoid maculopathy, multifocal central serous retinopathy, acute VKH.

Clinical Course:
The patient was diagnosed with acute posterior multifocal posterior pigment epitheliopathy on the basis of examination and imaging features. Blood work including CBC, ESR, CRP, and blood chemistries were normal. Syphilis and tuberculosis were ruled out. He was sent for urgent neurologic evaluation and CT angiography of the brain which ruled out cerebral vasculitis. He was started on oral prednisone at 1 mg/kg. His vision rapidly improved to 20/20 OU and his central scotoma in the left nearly resolved. He was gradually tapered off of systemic steroids over the following 6 weeks. Fundus images and SD-OCT from 3 month follow up are shown below.

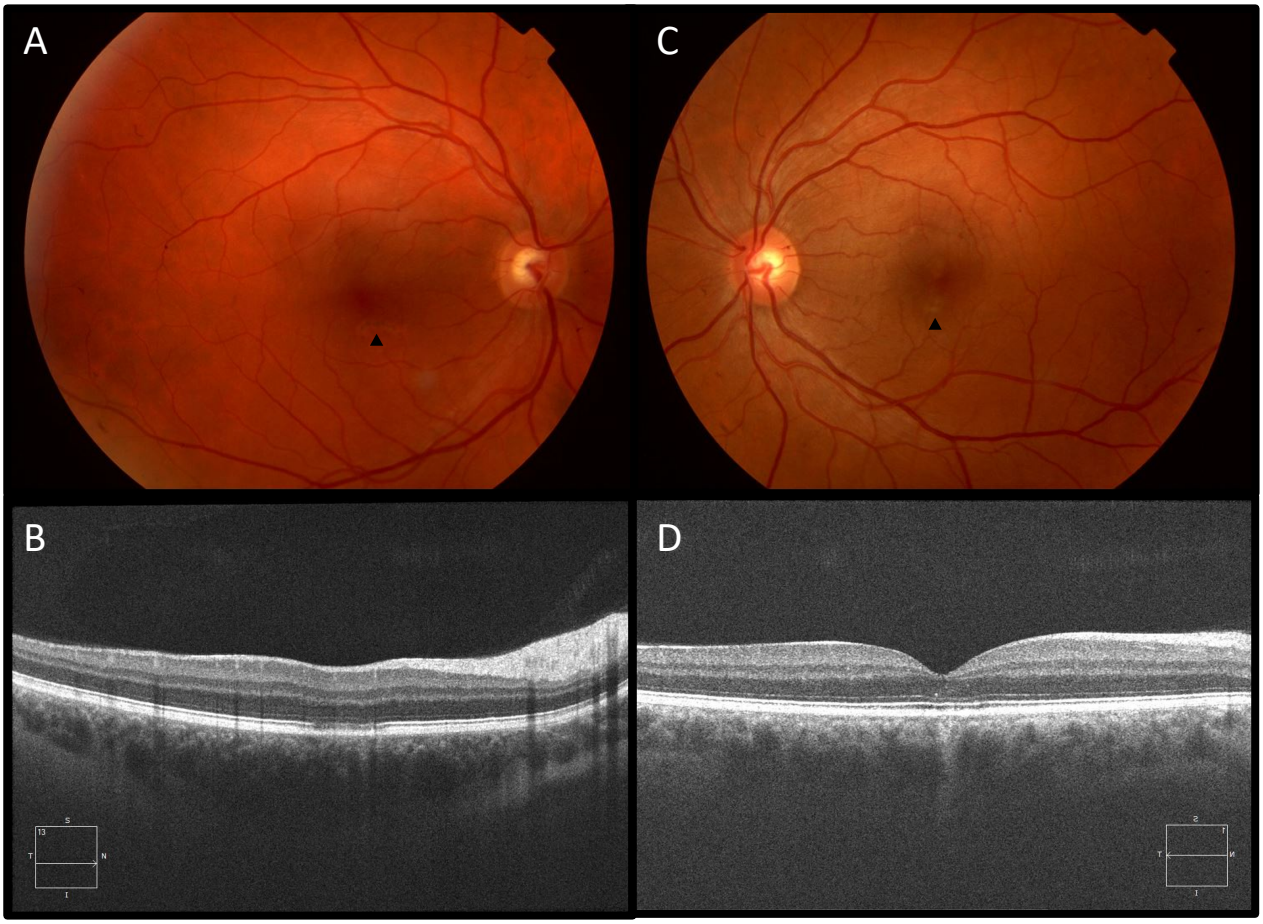

Figure 4: A. Color fundus photograph of the right eye at 3 month follow shows resolution of the yellow placoid lesions. There are subtle RPE clumps inferior to the fovea where the largest lesion was located (arrowhead). **B.** SD-OCT line scan through the lesion shows significant improvement in the outer retinal hyper-reflectivity and early reconstitution of the ellipsoid band. **C.** Color fundus photograph of the left eye also shows resolution of the placoid lesions, which have been replaced by mild RPE mottling (arrowhead). **D.** Follow up SD-OCT imaging through the fovea of the left eye shows a marked improvement in outer-retinal hyper-reflectivity and reconstitution of the ellipsoid.

Discussion:

Acute posterior multifocal placoid pigment epitheliopathy (APMPPE) is an uncommon disease first described by Donald Gass in the late 1960's. It is characterized by multiple small, and typically bilateral yellow plate-like or "placoid" lesions at the level of the RPE and outer-retina. APMPPE typically affects young healthy individuals, between 20 and 50 years old with an equal predilection for either sex.

Clinically, patients present with sudden central vision loss, metamorphopsia and photopsias. Symptoms are typically bilateral, although one eye may be affected first. About 1/3 of affected individuals will complain of a recent flu-like illness, or severe headache immediately preceding the onset of visual symptoms. Presenting visual acuities are dependent upon the exact location, size and number of lesions. Patients with extrafoveal disease (as in our patient's right eye) may maintain 20/20 vision throughout the disease course, while those with foveal involvement may present with markedly reduced acuity. On examination, the eye is typically quiet appearing, perhaps with a very mild amount of vitritis. Most often, the only signs on fundus examination are the placoid lesions which define the illness. Because several diseases can look similar on examination, multimodal imaging with SD-OCT and angiography is essential to secure the diagnosis.

Fluorescein angiography classically shows early hypo-fluorescence of the lesions, followed by late staining. It may also reveal a more extensive number of lesions than noted on examination alone. Similarly, ICG angiography will show early hypo-fluorescence of the lesions which gradually become less distinct and less hypo-fluorescent throughout the course of the study. SD-OCT line scans through the lesions will show hyper-

reflectivity within the outer nuclear layer. This is thought to represent inflammatory changes within the photoreceptor cell bodies. The RPE layer and ellipsoid complex will also be disrupted and irregular. In some cases, intra-retinal fluid collections within the outer retina and subretinal fluid may be seen. As the lesions resolve, the outer-retinal hyper-reflectivity resolves and the ellipsoid band reconstitutes. The RPE band may appear increasingly irregular corresponding to the RPE clumping seen following recovery.

As with many of the white dot syndromes, the pathophysiology of APMPPE is still the subject of debate, but most believe that it is primarily inflammatory in nature, possibly triggered by an antecedent viral infection. But while most authors agree that the disease process is primarily an inflammatory one, there is disagreement on the primary site of inflammation. Donald Gass first postulated that APMPPE was due to a transitory dysfunction of the RPE, with secondary effects on the outer retina. Others have argued that the choriocapillaris is the primary site of the disease, and resultant localized choriocapillaris ischemia causes secondary damage to the overlying RPE and outer retina. Recently studies using OCT angiography have demonstrated decreased flow within the choriocapillaris within the placoid lesions, lending additional support to this hypothesis.

While the diagnosis is a clinical one, there are several systemic diseases which must be ruled out. Syphilis can cause placoid lesions and should be tested for. Tuberculosis should also be ruled out as there are reports of placoid maculopathy in the setting of latent infection. Finally, and perhaps most importantly, cerebral vasculitis and stroke have both been associated with APMPPE. In one reported case, a patient with APMPPE and cerebral vasculitis died after a rapid taper off of systemic steroids. For this reason, it is essential that all patients with APMPPE be evaluated promptly and thoroughly to rule out cerebral vasculitis.

APMPPE, unlike some other related placoid syndromes, is typically self-limited. Even without treatment, the placoid lesions begin to resolve within weeks of the onset of symptoms. As they resolve, RPE hypertrophy develops with variable degrees of lasting outer retinal changes. Fortunately, the prognosis is good for most patients. In those who present without foveal involvement, 88% will experience full recovery of their central vision. The prognosis in patients with foveal involvement is expectedly worse, but even in this population over 50% will recover their central acuity, as our patient did. For this reason, not all retina specialists recommend treatment. However, in cases with reduced acuity and foveal involvement, it may be wise to treat in hopes of limiting the permanent visual changes. Our patient was treated with systemic steroid for 6 weeks, and has recovered 20/20 acuity with minimal persistent subjective visual changes.

Take Home Points

- APMPPE is a rare, likely inflammatory syndrome characterized by bilateral and multifocal macular placoid lesions
- The association with cerebral vasculitis necessitates early neurological evaluation, often with head imaging.
- Characteristic OCT and fluorescein angiogram findings help to secure the diagnosis.
- Prognosis can be good, with or without treatment with systemic steroids.

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