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Sir,

**Acute posterior multifocal placoid pigment epitheliopathy with retinal vasculitis and papillitis**

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Acute posterior multifocal placoid pigment epitheliopathy (APMPPE), defined by Gass in 1968,[1] is characterized by a rapid, but transient, loss of visual acuity associated with acute onset of multifocal discrete yellow-white placoid lesions at the level of the retinal pigment epithelium (RPE) in the posterior pole. Spontaneous resolution over several weeks to months occurs with pigment epithelial alterations but little change in the adjacent retina or choroids. In the acute phase, the fluorescein angiogram characteristically shows early hypofluorescence of the ophthalmoscopically visible lesions followed by late hyperfluorescence. The disorder was presumed to involve primarily the RPE,[1] whereas other investigators proposed that the underlying process in APMPPE is an inflammatory vasculitis affecting the choroidal vessels and that the RPE was secondarily affected.[2–6] This report describes a patient in whom the clinical and fluorescein angiography findings were typical of APMPPE but in whom retinal vasculitis and papillitis were additional features.

### *Case report*

A previously healthy 35-year-old man was referred for ophthalmological examination because of a 7-day history of decreased vision in the right eye. The patient had no personal or family history of eye disease. His medical history was unremarkable and he took no medications. Results of systemic examination were unremarkable. His best-corrected visual acuity at initial examination was counting fingers at 2 feet in the right eye and 20/20 in the left eye. He could not discern any color test plates using the right eye and correctly identified 15 of 15 Ishihara color plates with the left eye. There was a 2+ relative afferent pupillary defect in the right eye. The ocular movements were normal. The anterior segment examination results were within normal limits. There were trace vitreous cells present in the right eye. Ophthalmoscopy disclosed a pigmentary lesion involving the fovea and multiple yellow-white placoid lesions in the right posterior pole, typical of APMPPE. The retinal arteries close to the optic nerve head were surrounded with yellowish infiltration. The optic disc was swollen and hyperemic with blurred margin and peripapillary flame-shaped retinal hemorrhages (Figure 1). No overlying subretinal fluid was seen. The left eye had one chorioretinal scar in the posterior pole and another one in the periphery. Fluorescein angiography of the right eye showed that the placoid lesions were hypofluorescent in the early phases (Figure 2) and hyperfluorescent in the late

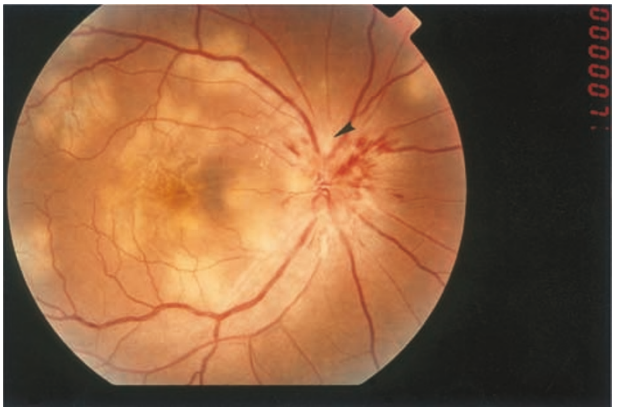

**Figure 1** Acute fundus photograph of the right eye shows placoid lesions at the posterior pole, a central pigmentary lesion, vasculitis (arrowhead) and papillitis with peripapillary flame-shaped hemorrhages.

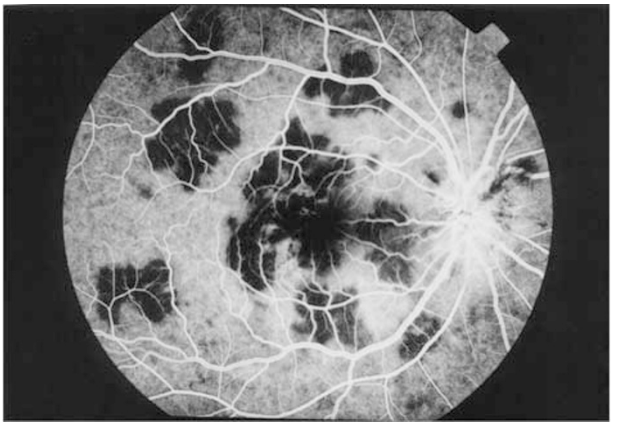

**Figure 2** Early-phase fluorescein angiogram shows areas of hypofluorescence corresponding to the placoid lesions, and optic disc leakage.

stages (Figure 3) of the angiogram. The optic nerve head demonstrated early leakage (Figure 2) and was stained in the later stages (Figure 3) of angiography. Visual field testing of the right eye with a Goldmann perimeter revealed a dense central scotoma. Normal laboratory tests included: chest x-ray, complete blood cell count, erythrocyte sedimentation rate, Venereal Disease Research Laboratory test, fluorescent treponemal antibody absorption test, human immunodeficiency virus (HIV), liver function tests, blood nitrogen urea, electrolytes, antinuclear antibody, anti-DNA antibody, toxoplasma titers, urinalysis, and computed tomographic scan of the brain. The Mantoux test was negative. The patient was treated with oral prednisone 1 mg/kg/day, and cyclosporine A 5 mg/kg/day. Two weeks later, his visual acuity was unchanged and the fundus lesions demonstrated inactive retinal pigment epithelial clumping and atrophy. The patient tapered his course of corticosteroids and cyclosporine A to discontinuation. Ten weeks later, his best-corrected visual acuities were 20/60 in the right eye and 20/20 in the left, the fundus lesions had become irregularly pigmented, and papillitis and vasculitis had resolved (Figure 4).

## Discussion

Several investigators suggested that APMPPE represents a focal choroidal vasculopathy and the RPE changes were a subsequent manifestation.[2–6] Support for primary choroid involvement in APMPPE is based on several lines of evidence. Slow, irregular filling of the early hypofluorescent areas on the fluorescein angiogram has been noted and interpreted as delayed choroidal perfusion.[2] Large choroidal vessels also have been seen occasionally within these hypofluorescent areas, suggesting choriocapillaris loss rather than masking as the cause of the hypofluorescence.[4] Indocyanine green (ICG) angiography studies showed a profound decrease in choroidal blood flow and extensive hypoperfusion of the choriocapillaris,[7–9] providing further evidence that APMPPE is a primary choroidal vasculitis with secondary involvement of the pigment epithelium. Additional support for a vasculitic basis came from the concurrent findings of APMPPE in patients with systemic vasculitis such as cerebral vasculitis,[10] erythema nodosum,[2] acute nephritis,[11] and thyroiditis.[12] This would suggest that APMPPE may result from a primary vasculitis involving the choriocapillaris.

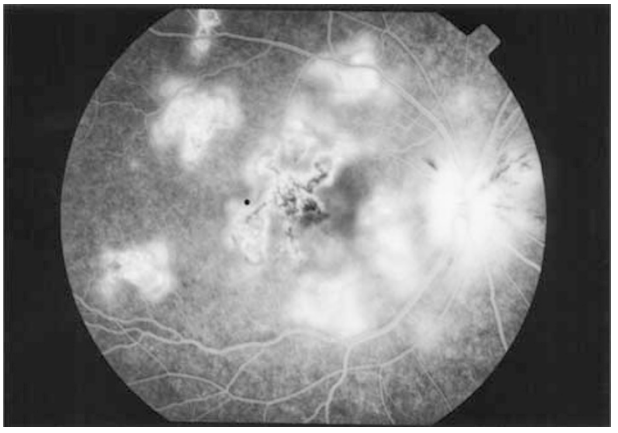

**Figure 3** Late-phase angiogram shows late hyperfluorescence of the placoid lesions, and optic disc staining.

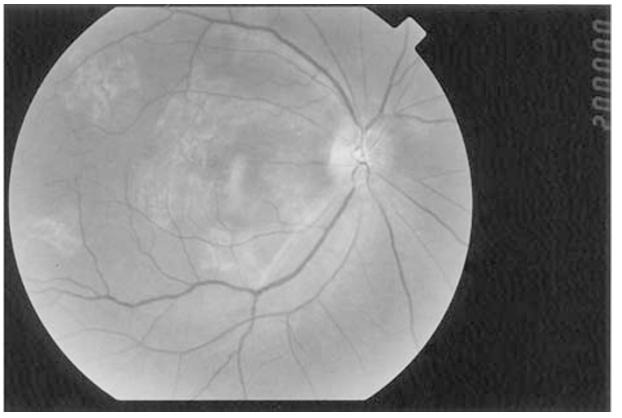

**Figure 4** Ten weeks after presentation, there is resolution of papillitis, vasculitis, and the placoid lesions with hypertrophy and atrophy of the retinal pigment epithelium.

It is proposed that APMPPE is caused by a choroidal delayed type hypersensitivity reaction involving activation of sensitized T lymphocytes to some unknown inciting agent causing choroidal occlusive vasculitis.[13] Acute posterior multifocal placoid pigment epitheliopathy has been reported to be associated with numerous diseases that are consistent with a delayed type hypersensitivity reaction such as sarcoidosis,[14] pulmonary tuberculosis,[15] schistosomiasis,[16] acute group A streptococcal infection,[17] after hepatitis B vaccine,[18] and mumps.[19]

Previous reports of associated corneal stromal infiltrates,[20] episcleritis,[21] iridocyclitis,[21] retinal vasculitis,[22,23] central retinal vein occlusion,[24] and choroidal vasculitis[6] imply a more widespread vascular inflammation throughout the eye. To our knowledge, only three patients have been described in whom APMPPE was associated with papillitis producing an afferent papillary defect in the acute phase.[21,22,25] Our case is the fourth to show such an association. Wolf and associates[26] reported a mother and son who developed optic neuritis and a daughter who developed APMPPE within a 6-month period. The association of HLA antigens B7 and DR2 with

APMPPE has been reported.[27] HLA antigens B7 and DR2 have also been associated with optic neuritis.[28,29] Perhaps in these immunogenetically predisposed individuals, vasculitis in the peripapillary choroid produced papillitis or optic disc vasculitis in APMPPE.

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