

# A SYNDROME RESEMBLING ACUTE POSTERIOR MULTIFOCAL PLACOID PIGMENT EPITHELIOPATHY IN OLDER ADULTS

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## ABSTRACT

*Purpose:* To describe clinical characteristics and visual and anatomic outcomes of a syndrome clinically similar to acute posterior multifocal placoid pigment epitheliopathy (APMPPE) in older patients.

*Methods:* We retrospectively reviewed medical records and photographic studies of consecutive patients over the age of 50 who presented to an academic tertiary care center with acute-onset visual symptoms associated with flat, gray-white lesions at the level of the retinal pigment epithelium reminiscent of APMPPE. Main outcome measures were visual acuity and macular anatomic status at the final follow-up visit.

*Results:* The cohort included 4 men and 2 women with a median age of 72.5 (range, 58-82) years. The disease course was characterized by recurrent episodes in 6 of 11 eyes (55%), with initial or eventual bilaterality in all 5 binocular patients. Five of 6 patients were treated with corticosteroids, and all 6 patients experienced significant short-term improvement in visual acuity. However, 8 of 11 eyes (73%) developed progressive geographic atrophy, and 7 (64%) developed choroidal neovascularization. With a mean ( $\pm$  SD) follow-up time of  $6.6 \pm 5.5$  years, the final visual acuity was 20/200 or worse in 8 of 11 eyes (73%).

*Conclusions:* Although older patients presenting with APMPPE-like lesions are likely to experience visual improvement as acute lesions resolve, progression to geographic atrophy and choroidal neovascular membrane formation is the usual long-term outcome.

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## INTRODUCTION

Acute posterior multifocal placoid pigment epitheliopathy (APMPPE) was initially described by Gass<sup>1</sup> as a syndrome occurring primarily in young adults. The classic description includes rapid resolution of multifocal inflammatory lesions followed by significant improvement in visual acuity. Although most patients enjoy visual acuity outcomes of 20/25 or better,<sup>2</sup> several investigators have suggested that atypical features, such as advanced age, may be associated with a poor visual prognosis.<sup>3-6</sup>

Herein are described the clinical characteristics, disease course, and visual and anatomic outcomes of a syndrome resembling APMPPE in a series of older patients.

## METHODS

We retrospectively reviewed medical records, color fundus photographs, and fluorescein angiograms of consecutive patients over the age of 50 who presented with acute visual loss in one or both eyes associated with flat, gray-white lesions at the level of the retinal pigment epithelium (RPE) reminiscent of APMPPE. The patients were evaluated by one of the authors (M.W.J.) on the vitreoretinal service of a large academic tertiary care center between 1993 and 2006. No patient meeting the inclusion criteria for the study was excluded from analysis. The retrospective records review received an exemption from oversight by the Institutional Review Board at the University of Michigan Medical School.

## REPRESENTATIVE CASE HISTORIES

### Case 1

A 76-year-old man presented with complaints of paracentral metamorphopsia in the right eye for 4 weeks followed by profound loss of central vision in the left eye for 1 week. There were no symptoms of a viral prodrome or neurologic involvement. The medical history was significant for hypertension and coronary artery disease. Visual acuity at presentation was 20/50 OD and 20/300 OS. Anterior segment examination was unremarkable apart from nuclear sclerosis in each eye. Right fundus examination (Figure 1) showed rare cells in the posterior vitreous gel. The optic disc, retinal vessels, and fundus periphery were entirely unremarkable. Several paracentral, flat, geographic lesions with mottled hyperpigmentation and hypopigmentation were seen in the macula at the level of the RPE. Several subtle gray-white patches without pigmentation were evident inferior to the mottled lesions. There was no evidence of macular drusen or exudation. Left fundus examination revealed a subtle, flat, gray-white lesion in the center of the macula with mild pigment mottling in its inferonasal aspect. The fundus periphery was unremarkable in each eye.

Fluorescein angiography (Figure 1) demonstrated early hypofluorescence of both the subacute pigmented lesions in the right eye and the acute gray-white lesions in each eye. In the late phases, there was mild staining of the pigmented lesions in the right eye and minimal staining of the gray-white lesions in each eye. Laboratory workup revealed normal or negative C-reactive protein, erythrocyte sedimentation rate, antinuclear antibodies, C3, prothrombin time, partial thromboplastin time, and fluorescent treponemal antibody absorption (FTA-ABS). A temporal artery biopsy was negative for giant cell arteritis. The patient was treated with intravenous

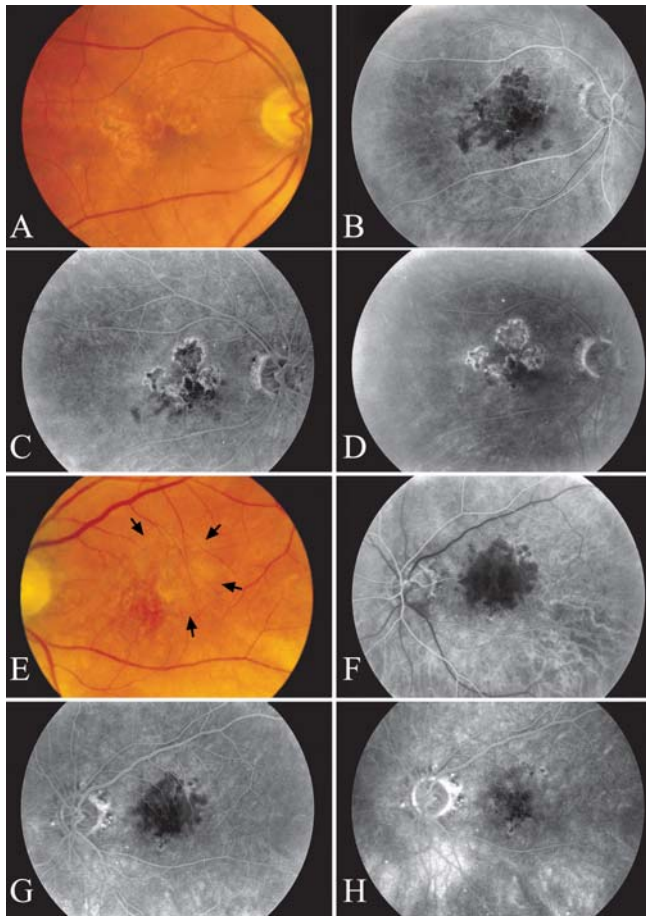
From the Department of Ophthalmology and Visual Sciences, University of Michigan Medical School, Ann Arbor. This study was presented in part at the Association for Research in Vision and Ophthalmology (ARVO) Annual Meeting, Fort Lauderdale, Florida, May 9, 2007.

\*Presenter.

**Bold** type indicates AOS member.

**FIGURE 1**

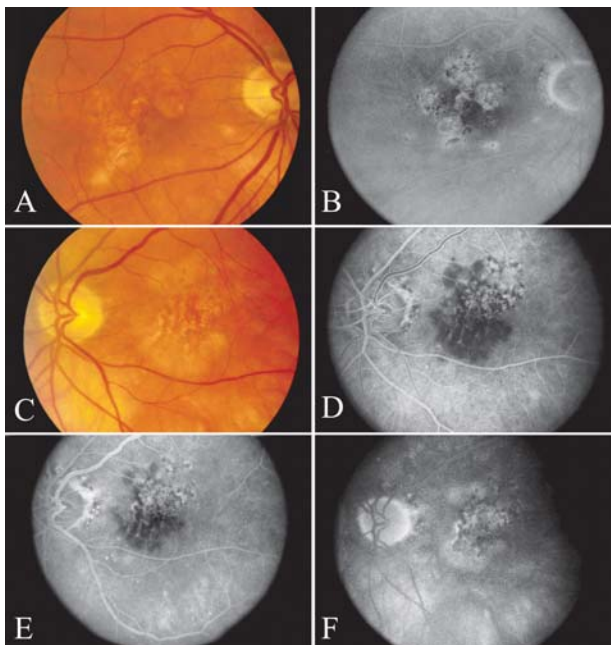
Case 1, initial presentation. A, Fundus photograph of right eye demonstrates flat, geographic lesions with mottled hyperpigmentation and hypopigmentation. Subtle gray-white patches are present in the inferior macula. B, Early-phase fluorescein angiography (FA) of right eye demonstrates hypofluorescence of all lesions. C and D, Mid- and late-phase FAs of right eye demonstrate mild staining of pigmented lesions and minimal staining of the gray-white lesions. E, Fundus photograph of left eye demonstrates a subtle gray-white lesion in the center of the macula (arrows), with mild pigment mottling of its inferonasal aspect. F, Early-phase FA of left eye demonstrates hypofluorescence of macular lesion. G and H, Mid- and late-phase FAs of left eye demonstrate minimal and uneven staining of the lesion.

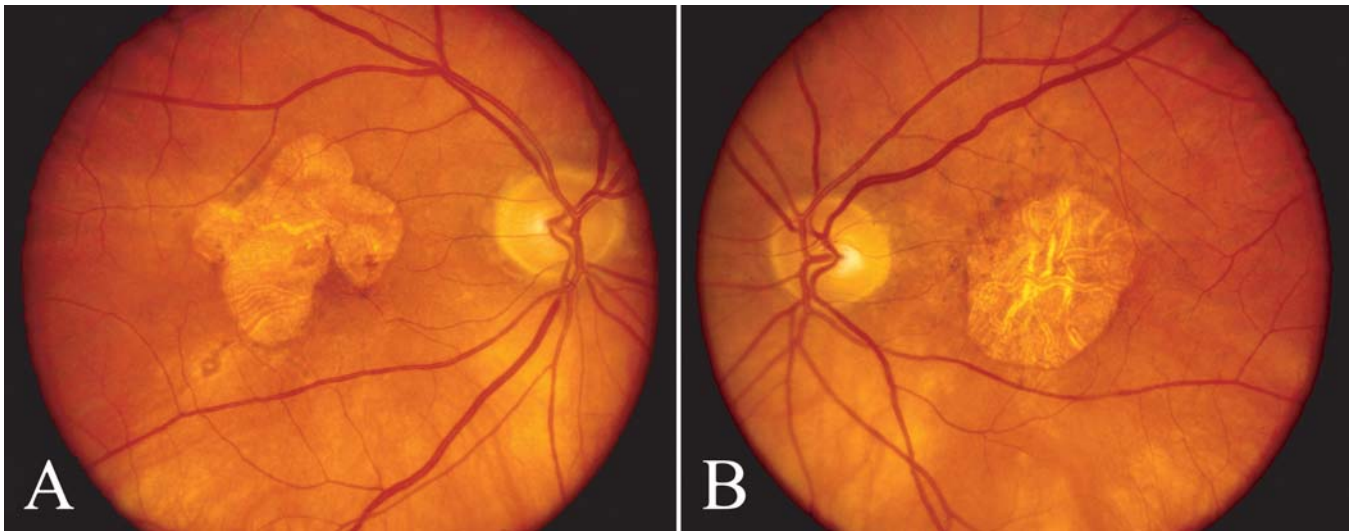


methylprednisolone, 250 mg daily for 3 days, followed by a slow taper of oral prednisone. Following intravenous therapy, the visual acuity improved to 20/30 OD and 20/25 OS. Two months following prednisone taper, the patient developed new lesions in each eye (Figure 2). Prednisone was restarted, the acute lesions resolved into patches of pigment mottling, and the patient elected to continue long-term maintenance therapy with prednisone, 10 mg daily. Over time, the macular pigmented lesions evolved into slowly progressive geographic atrophy (Figure 3). Seven years following initial presentation, the patient developed a subfoveal choroidal neovascular membrane in the right eye. At 10 years and 10 months of follow-up, the visual acuity was 20/200 OU.

**FIGURE 2**

Case 1, 9 months after initial presentation, demonstrating recurrent acute lesions. A, Fundus photograph of right eye demonstrates lightly pigmented old lesions, with acute gray-white lesions in the inferior macula. The acute lesions show minimal late staining on fluorescein angiography (FA) (B). C, Fundus photograph of left eye shows pigment mottling corresponding to the area of previous involvement, as well as flat gray-white acute lesions superiorly and inferiorly. D, Early FA of left eye demonstrates hypofluorescence of acute gray-white patches and mottled fluorescence of chronic lesion. E and F, Mid- and late-phase FAs of left eye show mild late staining of acute and chronic lesions.



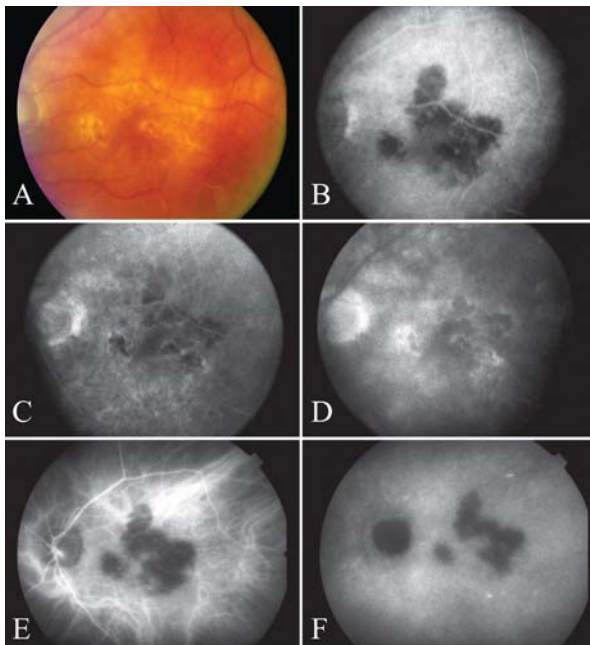


**FIGURE 3**

Case 1, 7 years after presentation. Fundus photographs of right (A) and left (B) eyes demonstrate geographic atrophy involving the retinal pigment epithelium and choriocapillaris.

**Case 4**

An 82-year-old man presented with sudden-onset floaters of 2 weeks duration followed by central and paracentral scotomata in the left eye. There were no symptoms of a viral prodrome or neurologic involvement. The past ocular history was significant for enucleation of the right eye at age 25 secondary to severe trauma sustained at age 15. The past medical history was notable only for atrial fibrillation. The visual acuity was 20/300. Slit-lamp biomicroscopy revealed tiny scattered keratic precipitates, trace cell and flare in the anterior chamber, and 1+ cells in the anterior vitreous, along with small inflammatory precipitates on the detached posterior hyaloid membrane. Left fundus examination (Figure 4) revealed 1-2+ cells in the posterior vitreous gel with inflammatory clumps in the inferior vitreous. There were subtle areas of retinal periarteriolitis along the inferotemporal and inferonasal arcades. In the macula, there were flat geographic lesions consisting of depigmentation and pigment mottling and involving the fovea. There were also 2 subtle gray-white patches without pigmentation at the level of the RPE in the superior and inferior macula. The fundus periphery was unremarkable.



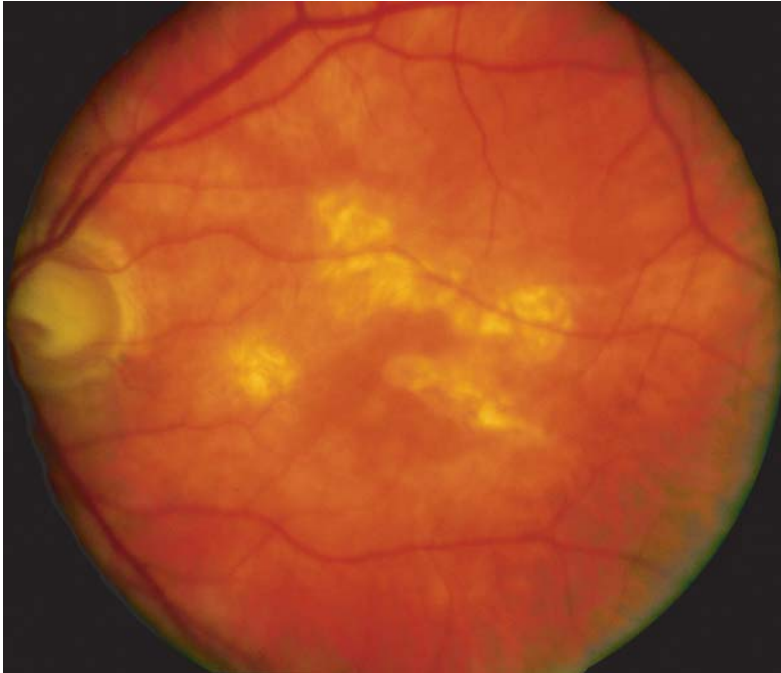
**FIGURE 4**

Case 4, left eye on initial presentation. A, Fundus photograph reveals flat geographic lesions consisting of depigmentation with pigment mottling. Subtle gray-white patches without pigmentation can be seen in superonasal and inferotemporal macular area. Segmental periarteriolitis is present along the inferotemporal arcade artery. B, Early fluorescein angiography (FA) shows hypofluorescence of both the geographic pigmented lesions and the acute gray-white lesions. There is segmental obstruction of flow through the inferotemporal artery. C and D, Mid- and late-phase FAs demonstrate gradual mild staining of the acute lesions as well as the depigmented portions of the subacute lesions. Indocyanine green angiography demonstrates early (E) and persistent late (F) hypofluorescence of the geographic and acute gray-white lesions.

Fluorescein angiography (Figure 4) demonstrated early hypofluorescence of both the geographic pigmented lesions and acute gray-white lesions. In the late phases, there was mild staining of acute lesions and of the depigmented portions of subacute lesions. In the segment of retinal periarteriolitis inferotemporally, there was partial obstruction of blood flow with late staining of the vessel wall. Indocyanine green angiography (Figure 4) demonstrated early and persistent hypofluorescence of both the flat geographic lesions and

acute gray-white lesions. Laboratory investigation revealed a positive antinuclear antibody with titer 1:80 and negative or normal erythrocyte sedimentation rate, FTA-ABS, purified protein derivative with control, chest radiograph, angiotensin-converting enzyme, antineutrophil cytoplasmic antibodies, and anticardiolipin antibodies. Temporal artery biopsy was negative.

The patient was treated with intravenous methylprednisolone, 1 g daily, followed by oral prednisone, 80 mg daily. He returned 2 weeks later reporting subjective improvement. The visual acuity was 20/200, anterior segment inflammation had resolved, there were trace cells in the vitreous gel, and there was no evidence of arteriolitis or acute lesions in the macula. Fluorescein angiography showed less hypofluorescence in early views, and the previously occluded inferotemporal artery showed normal flow throughout its course and no late staining of its wall. Long-term prednisone taper was begun, and the patient's visual acuity gradually improved to 20/70 over the next 2 years (Figure 5). Approximately 1 year after discontinuing prednisone, he presented to a retina specialist in another state with acute vision loss from an acute gray-white lesion in the macular center. Despite re-treatment with prednisone, the final visual acuity 33 months after disease onset was finger counting at 3 feet, and there were extensive patches of geographic atrophy in the macular region.



**FIGURE 5**

Case 4. Left fundus photograph of patient 1 year following initial presentation. There are patches of evolving geographic atrophy in the macular area corresponding to previous acute and subacute lesions.

## RESULTS

The study cohort included 4 men and 2 women with a median age of 72.5 (range, 58 to 82) years. Clinical characteristics are summarized in Table 1. The past ocular histories included nonarteritic anterior ischemic optic neuropathy in 1 patient and enucleation of the fellow eye 57 years prior to presentation in 1 patient. The past medical histories were notable only for systemic arterial hypertension in 2 patients, coronary artery disease in 1 patient, and atrial fibrillation in 1 patient. Two patients reported symptoms of a preceding viral prodrome.

The presenting visual symptoms included central and/or paracentral scotomata in 4 patients, visual blurring in 3, metamorphopsia in 2, and floaters in 1. At onset, the macular lesions were often asymmetric, but initial or subsequent bilaterality was seen in all 5 binocular patients (Table 1). One patient (case 5) presented with acute lesions in the left eye and a history of an APMPE-like episode in the right eye diagnosed by another physician 10 years earlier. None of the patients reported neurologic symptoms.

The acute phase of the disorder was characterized by geographic flat, gray-white lesions at the level of the RPE and inner choroid. The lesions were typically but not universally multifocal and generally measured 0.5 to 2 disc diameters in size. They were clustered in the macular region and did not extend beyond the vascular arcades in any eye. Lesions involving the fovea caused substantial acute loss of visual acuity. Recurrent lesions developed either separate from or contiguous with older lesions. The acute chorioretinal lesions were accompanied by mild vitritis in 3 patients (50%) and by retinal vasculitis in 1 patient (17%). A mild anterior chamber inflammatory reaction was seen in only 1 patient (17%). Two patients had macular drusen and 1 had extramacular drusen.

Fluorescein angiography of the acute lesions showed early hypofluorescence with minimal to mild late staining. Subacute lesions demonstrated early hypofluorescence followed by variable late staining, particularly at the lesion borders. Indocyanine green angiography in 2 patients showed early hypofluorescence of acute lesions that persisted in the late views.

Extensive laboratory evaluations for infectious and noninfectious inflammatory conditions were negative or normal except for a positive antinuclear antibody in 1 patient. Negative or normal laboratory studies included complete blood cell count, prothrombin time, partial thromboplastin time, renal function tests, erythrocyte sedimentation rate, C-reactive protein, angiotensin-converting enzyme, purified protein derivative skin test with control, FTA-ABS, rapid plasma reagin, VDRL test, toxoplasmosis serology, Lyme

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serology, C3-C4 complement, total hemolytic complement (CH50) assay, antineutrophil cytoplasmic antibodies, anticardiolipin antibodies, and chest x-ray. Temporal artery biopsy was negative in the 3 patients tested.

**TABLE 1. DEMOGRAPHIC DATA AND CLINICAL CHARACTERISTICS OF PATIENTS WITH APMPE-LIKE SYNDROME**

NO./AGE/ GENDER	INITIAL VA		POH	PMH	VIRAL PRODROME	DRUSEN	BILATERALITY	VITRITIS	LABORATORY EVALUATION
	OD	OS							
1 / 76 / M	20/50	20/300		CAD, HTN	No	None	Initial	Yes	Negative
2 / 71 / F	20/40	20/300		HTN	No	Macular	Initial	No	Negative
3 / 58 / M	20/80	20/80			Yes	Macular	Initial	Yes	Negative
4 / 82 / M	N/A	20/300	Enucleation OD	A-FIB	No	None	N/A	Yes	ANA +
5 / 63 / F	20/40	20/400			No	Extramacular	Subsequent*	No	Negative
6 / 74 / M	20/15	NLP	nAION OS		Yes	None	Subsequent	No	Negative

A-FIB, atrial fibrillation; ANA, anti-nuclear antibody; APMPE, acute posterior multifocal placoid pigment epitheliopathy; CAD, coronary artery disease; HTN, hypertension; N/A, not applicable; nAION, nonarteritic anterior ischemic optic neuropathy; NLP, no light perception; PMH, past medical history; POH, past ocular history; VA, visual acuity.

\*Patient reported history of APMPE-like episode in right eye 10 years before presenting with acute symptoms in left eye.

Treatment and clinical course data are summarized in Table 2. Acute lesions typically faded over 1 to 2 weeks with or without anti-inflammatory therapy, leaving patches of pigment mottling. These eventually evolved into geographic atrophy of the RPE and choriocapillaris in 8 of the 11 eyes (73%).

**TABLE 2. TREATMENT AND DISEASE COURSE FOR PATIENTS WITH APMPE-LIKE SYNDROME**

NO./AGE/ GENDER	TREATMENT	INITIAL VA IMPROVEMENT*	FOLLOW-UP (MO)	RECURRENCES		CNVM		FINAL VA	
				OD	OS	OD	OS	OD	OS
1 / 76 / M	IV methylprednisolone, prednisone	Yes	130	1	1	Yes	No	20/200	20/200
2 / 71 / F	Prednisone	Yes	114	2	2	Yes	Yes	20/400	20/400
3 / 58 / M	Cyclosporine, mycophenolate mofetil, prednisone	Yes	28	0	0	Yes	Yes	6/200	20/25 <sup>‡</sup>
4 / 82 / M	IV methylprednisolone, prednisone	Yes	33	N/A	1	N/A	No	N/A	CF
5 / 63 / F	None	Yes	3 <sup>‡</sup>	0	0	Yes	No	20/40 <sup>‡</sup>	20/50 <sup>‡</sup>
6 / 74 / M	IV methylprednisolone, prednisone	Yes	165	1	0	Yes	No	20/300	NLP

APMPE, acute posterior multifocal placoid pigment epitheliopathy; CF, counting fingers; CNVM, choroidal neovascular membrane; IV, intravenous; N/A, not applicable; NLP, no light perception; VA, visual acuity.

\*Associated with resolution of acute macular lesions.

<sup>‡</sup>These eyes had macular pigment mottling without frank geographic atrophy.

<sup>‡</sup>Patient reported history of APMPE-like episode in right eye 10 years before presenting with acute symptoms in left eye.

None of the eyes in this series developed postinflammatory subretinal fibrosis or large pigment clumps or plaques. Five of 6 patients were treated with corticosteroids with substantial short-term improvement in visual acuity. The patient receiving no treatment (case 5) had gradual improvement in the acuity of the acutely involved left eye from 20/400 to 20/50 over 3 months of observation. Recurrent episodes were seen in 6 of 11 eyes (55%) and occurred up to 3 years after the initial onset of disease (Table 2). Two of 3 patients re-treated with corticosteroids for recurrence of acute lesions had visual improvement in the short term. One of these patients (case 1) elected long-term maintenance therapy with low-dose prednisone (10 mg daily) and had no further recurrences.

Seven of 11 eyes (64%) eventually developed choroidal neovascularization. With a mean ( $\pm$  SD) follow-up period of  $6.6 \pm 5.5$  years, the final visual acuity was 20/200 or worse in 8 eyes (73%). Severe loss of central vision was attributable to either geographic atrophy or choroidal neovascularization or both. No eyes had recurrent disease that extended outside the macular area.

## DISCUSSION

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Six patients of advanced age who presented with a clinical syndrome resembling APMPE are reported here. These patients developed acute-onset visual symptoms with initial visual acuity ranging from normal to profoundly decreased. Clinical examination in the acute phase revealed flat, usually multifocal, gray-white geographic lesions at the level of the RPE confined to the macular region. Three patients had mild vitritis, 1 of whom also demonstrated segmental areas of retinal perivasculitis. On fluorescein angiography, the acute lesions showed early hypofluorescence with late staining that was minimal to mild, less intense than that seen in typical cases of APMPE. Five of 6 patients were treated with corticosteroid anti-inflammatory regimens with substantial short-term improvement in visual acuity. Since the only patient who did not receive immunosuppressive treatment experienced gradual visual recovery, it is not possible to conclude on the basis of our data that corticosteroid therapy improves the visual outcome of such patients. In each of the cases, the acute lesions faded with or without anti-inflammatory therapy, leaving patches of pigment mottling followed eventually in most eyes by geographic atrophy of the RPE and inner choroid. Infrequent recurrences of active disease within 3 years of onset were seen in over half the eyes in this series. Neither chronic, frequent recurrences nor disease progression outside of the macular area occurred in any of the patients.

Although a subset of eyes retained reading vision over long-term follow-up, severe loss of central vision was the rule, resulting from progression of geographic atrophy and/or the development of choroidal neovascularization. In many eyes, the end-stage macular lesions were indistinguishable from those of advanced age-related macular degeneration (AMD). Even in the acute disease phases, several patients were referred with a misdiagnosis of exudative AMD. In light of its distinct pathogenesis and potential responsiveness to immunosuppression, we believe it is important for the clinician to consider this entity in presumed AMD patients with atypical presentations.

Patients in this study were extensively evaluated for vasculitis and connective tissue diseases, and 3 patients underwent temporal artery biopsies. No association with known systemic disease was identified in the course of these evaluations. Only 2 patients reported symptoms suggestive of a viral prodrome. Although the cause of this syndrome remains unknown, it is possible that it represents idiopathic choroidal vasculitis with lobular ischemic choroidal infarcts. Alternatively, it may represent a choroidal hypersensitivity response to various systemic antigens, a pathogenic mechanism that has been proposed for APMPE.<sup>7</sup> In an older patient with APMPE, the failure to recover and maintain vision in the expected fashion may be related to poor healing of senescent RPE, with subsequent atrophy of the underlying choriocapillaris and overlying photoreceptors. The high incidence of choroidal neovascularization may not be surprising in light of damage to the RPE–Bruch membrane complex combined with the inflammatory and possibly ischemic factors present in these patients.

Other investigators have previously suggested that advanced age is a risk factor for poor visual outcome in patients with APMPE. In a study of 33 eyes of 18 patients with APMPE, Pagliarini and coworkers<sup>5</sup> found at least 1 of the following atypical features in 7 patients with poor (visual acuity worse than 6/24) visual outcomes: age older than 60 years, unilaterality, interval before involvement of the second eye of at least 6 months, recurrence of disease, and leakage from choroidal veins. Similarly, Roberts and Mitchell<sup>6</sup> suggested that advanced age and foveal involvement may be poor prognostic factors. Gass<sup>4</sup> briefly described several patients over 50 years of age with macular drusen and what appeared to be unilateral APMPE progressing to geographic atrophy and resulting in subnormal visual acuity. Damato and colleagues<sup>3</sup> reported that 2 of 3 patients with APMPE resulting in chorioretinal atrophy and vision loss were 50 years or older.

Although we believe the clinical syndrome reported here is most similar to APMPE in an older patient population, the differential diagnosis also includes serpiginous choroiditis, relentless placoid chorioretinitis,<sup>8</sup> syphilitic posterior placoid chorioretinitis,<sup>9</sup> and the recently described entity termed persistent placoid maculopathy.<sup>10</sup> None of the patients described here had serologic evidence for syphilis; furthermore, the multifocal nature and relatively small size of the acute gray-white lesions in our cases are not typical of syphilitic chorioretinitis. Similar to patients with relentless placoid chorioretinitis, our patients exhibited clinical features common to both serpiginous choroiditis and APMPE. However, none of our patients developed lesions outside of the vascular arcades as is characteristic of relentless placoid chorioretinitis.<sup>8</sup>

Serpiginous choroiditis is a rare, chronic, progressive, usually bilateral disease typically affecting healthy young or middle-aged adults.<sup>11</sup> It classically begins in the peripapillary fundus and extends gradually outward in a contiguous pseudopodial or serpentine fashion. In a small minority of patients, serpiginous choroiditis may initially be limited to the macular area.<sup>12,13</sup> Indeed, our patients have several clinical features in common with patients described as having macular serpiginous choroiditis. These include recurrent episodes of active disease and a poor final visual outcome due to atrophic tissue loss or the development of choroidal neovascularization. Although such features have been reported previously in patients with APMPE,<sup>14</sup> we acknowledge the possibility that our patients represent atypical cases of macular serpiginous choroiditis.

However, other clinical characteristics would appear to distinguish our patients from those with serpiginous choroiditis initially confined to the macula.<sup>12,13</sup> For example, none of our patients had peripapillary or extramacular disease in the fellow eye, as is often seen in patients with macular serpiginous choroiditis. Furthermore, our patients typically had multiple round or oval lesions that were sometimes bilaterally active. In contrast, the lesions in patients with macular serpiginous choroiditis are typically pseudopodial or jigsaw in appearance, are usually confluent rather than multifocal, and are generally active in one eye at a time. Approximately half of the eyes in our series had 1 or 2 recurrent episodes, characterized by 1 or more active lesions either separate from or contiguous with older lesions. However, none of our patients exhibited the disease course commonly seen with macular serpiginous choroiditis: frequent, chronic, contiguous recurrences leading over months or years to progressive serpentine extension of chorioretinal scarring to the optic disc or beyond the vascular arcades. Finally, our patients generally had rapid resolution of acute lesions with mild pigment

mottling and substantial initial recovery of vision. Subsequent development of geographic atrophy and choroidal neovascularization led to vision loss in the majority of eyes later in the course. In contrast, patients with macular serpiginous choroiditis usually have sustained vision loss as active lesions progress to a more severe type of chorioretinal scarring characterized by extensive plaques of pigment clumping, marked atrophy of the inner choroid, and subretinal fibrosis.<sup>11-13</sup>

Recently, Golchet and colleagues<sup>10</sup> reported a new clinical entity termed persistent placoid maculopathy. This rare disorder is characterized by single, bilateral, large, symmetric, whitish plaquelike lesions in the macula. The white macular lesions persist, fading slowly over a period of months to years, with angiographic hypofluorescence that often persists for an even longer period. Good visual acuity is generally maintained until late complications such as choroidal neovascularization develop. Eyes do not develop chorioretinal scarring unless related to choroidal neovascularization. We believe that persistent placoid maculopathy is distinct from macular serpiginous choroiditis and from the syndrome described herein.

In summary, an APMPE-like presentation in an older individual carries a guarded visual prognosis. In the short term, resolution of acute lesions is typically associated with visual improvement; however, the subsequent course is usually characterized by a slow progression to geographic atrophy and choroidal neovascular membrane formation, with an overall appearance similar to advanced AMD. Although the initial visual improvement in our patients appeared to correlate with high-dose anti-inflammatory therapy, the benefit of such treatment has not been clearly substantiated. Further research into the pathophysiology and treatment of this syndrome is needed.

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Conformity With Author Information: The University of Michigan Medical School Institutional Review Board determined that this study was exempt from review by the IRB because study data collected from medical records was recorded in such a manner that subjects could not be identified. This retrospective study adhered to the Declaration of Helsinki and all federal laws governing human subjects research.

## REFERENCES

1. Gass JD. Acute posterior multifocal placoid pigment epitheliopathy. *Arch Ophthalmol* 1968;80:177-185.
2. Wolf MD, Alward WL, Folk JC. Long-term visual function in acute posterior multifocal placoid pigment epitheliopathy. *Arch Ophthalmol* 1991;109:800-803.
3. Damato BE, Nanjiani M, Foulds WS. Acute posterior multifocal placoid pigment epitheliopathy. A follow up study. *Trans Ophthalmol Soc U K* 1983;103:517-522.
4. Gass JDM. *Stereoscopic Atlas of Macular Diseases: Diagnosis and Treatment*. 4th ed. St Louis, MO: Mosby; 1997:672-675.
5. Pagliarini S, Piguet B, Ffytche TJ, Bird AC. Foveal involvement and lack of visual recovery in APMPE associated with uncommon features. *Eye* 1995;9:42-47.
6. Roberts TV, Mitchell P. Acute posterior multifocal placoid pigment epitheliopathy: a long-term study. *Aust N Z J Ophthalmol* 1997;25:277-281.
7. Park D, Schatz H, McDonald HR, Johnson RN. Acute multifocal posterior placoid pigment epitheliopathy: a theory of pathogenesis. *Retina* 1995;15:351-352.
8. Jones BE, Jampol LM, Yannuzzi LA, et al. Relentless placoid chorioretinitis: a new entity or an unusual variant of serpiginous chorioretinitis? *Arch Ophthalmol* 2000;118:931-938.
9. Gass JD, Braunstein RA, Chenoweth RG. Acute syphilitic posterior placoid chorioretinitis. *Ophthalmology* 1990;97:1288-1297.
10. Golchet PR, Jampol LM, Wilson D, et al. Persistent placoid maculopathy: a new clinical entity. *Ophthalmology* 2007;114:1530-1540.
11. Lim WK, Buggage RR, Nussenblatt RB. Serpiginous choroiditis. *Surv Ophthalmol* 2005;50:231-244.
12. Mansour AM, Jampol LM, Packo KH, Hrisomalos NF. Macular serpiginous choroiditis. *Retina* 1988;8:125-131.
13. Hardy RA, Schatz H. Macular geographic helicoid choroidopathy. *Arch Ophthalmol* 1987;105:1237-1242.
14. Lyness AL, Bird AC. Recurrences of acute posterior multifocal placoid pigment epitheliopathy. *Am J Ophthalmol* 1984;98:203-207.

## PEER DISCUSSION

DR. THOMAS M. AABERG, SR: The authors present eleven (11) eyes of six (6) patients, with a median age of 72.5 years (range 58-82 years) that otherwise appeared similar to acute posterior multifocal placoid pigment epitheliopathy (APMPPE). The original description of APMPPE by J.D.M.Gass, MD, in 1968<sup>1</sup> was of young patients but it has been reported in older patients and then considered to be a risk factor for lesser final visual acuity.<sup>2,3,4</sup>

APMPPE is one of the entities sometimes grouped as White Dot Syndrome and AZOOR or both. As such it was originally thought beyond concern for recurrence but soon was found to have recurrent possibilities<sup>5</sup>. Indeed, fifty percent (50%) of eyes in this series had recurrent disease or related disorders within 3 years.

My experience with APMPE in young patients, whose Snellen vision usually returns to good levels initially(although relative scotomas persist, is that progressive atrophy of the affected retinal pigment epithelium (RPE) occurs over the following 10-20 years with the scotomas becoming more absolute and resultant decreased acuity. Thus it is not surprising, considering the advanced median age of the authors' patients, that the affected aged RPE would more quickly proceed to geographic, sometimes with accompanying choroidal neovascularization, in a large number (7/11 or 64%) of afflicted eyes. As the authors note, previous reports have found age over 50-60 years is a significant risk factor for poor eventual visual outcome with APMPE. Ophthalmologist must therefore be cautious in their prognostic discussions with patients beyond the fifth decade who present with new-onset APMPE that they are realistic, and not overly optimistic, concerning eventual final visual acuity.

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#### REFERENCES

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1. Gass, J.D.M. Acute posterior multifocal placoid pigment epitheliopathy. *Arch Ophthalmol.* 1968;80:177-185.
2. Wolf MD, Alward WL, Folk JC. Long-term visual function in acute posterior multifocal placoid pigment epitheliopathy. *Arch Ophthalmol.* 1991;109:800-803
3. Damato, B.E., Nanjani, M., Foulds, W.S. Acute posterior multifocal placoid pigment epitheliopathy. A follow-up study. *Trans Ophthalmol Soc UK.* 1983;103:517-522.
4. Gass JDM. Stereoscopic Atlas Of Macular Diseases: Diagnosis and Treatment. 4<sup>th</sup> ed. St. Louis: Mosby, 1997;672-675
5. Lyness AL, Bird AC. Recurrences of acute posterior multifocal placoid pigment epitheliopathy. *Am J Ophthalmol.* 1984;98:203-207.

DR. LEE M. JAMPOL: No conflicts. Dr. Johnson is a very astute observer and has described some new findings in patients thought to resemble APMPE. True recurrences in APMPE are very rare. For the first few weeks and sometimes a month or two, new lesions can occur but once the lesions are actually all healed, a true recurrence is very unusual. Most of the cases in the literature—that have been described as recurrent APMPE, actually are serpiginous, relentless, placoid or some other entity. Dr. Johnson has described in detail two cases. I have only seen his pictures in those two cases. I would be concerned that there is a possibility that this represents the entity that we described at this meeting two years ago as persistent placoid maculopathy. His cases are actually outside the spectrum of findings that we described because our patients had continued hypofluorescence of the choroid for a period of months or years, but what usually happens with the description of a new entity is that you describe cases that resemble each other the most, and then with time additional cases are described that expand the spectrum of disease. I would urge him to look carefully at his pictures to consider that entity as a possibility and he might actually, instead of describing a new variation on APMPE, be describing a wider spectrum of the entity posterior placoid maculopathy. Thank you.

DR. MARK W. JOHNSON: I would like to thank Dr. Aaberg for his very thoughtful discussion of our paper. I agree with him that one of the major factors in this syndrome may be the inability of senescent or aged RPE to recover from an insult that may have been less injurious in a young patient. With respect to Dr. Jampol's comments, I agree that the syndrome we are describing resembles APMPE, but differs in recurrence rate and in visual outcome. It strikes me that a suitable name for this entity might be "macular ampiginous." I did look carefully at our cases after reading the paper on persistent placoid maculopathy, and I believe that our cases are distinct. In persistent placoid maculopathy, the whitish macular lesion and associated hypofluorescence persist over a long period of time, whereas our patients had fading of these changes within several weeks. In addition, persistent placoid maculopathy is characterized by a large single lesion throughout the macula. Although one or two of our patients had smaller single lesions, most patients had lesions that were small and multifocal. Finally, acute lesions in the fovea were always associated with profoundly decreased vision in our patients. In contrast, patients with persistent placoid maculopathy usually retained good vision unless they developed choroidal neovascularization. I believe it is safe to say that the clinical features we describe do not conform precisely to any known entity. However, I think the preponderance of the evidence suggests that this syndrome is a variation on the APMPE theme, with poor visual outcomes likely attributable to age-related factors. Thank you.