Multimodal Imaging in Persistent Placoid Maculopathy

Mohamed G. Gendy, MD; Amani A. Fawzi, MD; Robert T. Wendel, MD; Dante J. Pieramici, MD; Joel A. Miller, MD; Lee M. Jampol, MD

IMPORTANCE Persistent placoid maculopathy (PPM) is a rare clinical entity with features that superficially resemble acute posterior multifocal placoid pigment epitheliopathy (APMPPE) and macular serpiginous choroidopathy. It is important to differentiate PPM from APMPPE because both conditions may appear similar at presentation.

OBJECTIVE To investigate the short-term and long-term retinal changes in patients with PPM using spectral domain optical coherence tomography (SD-OCT), indocyanine green angiography (ICG-A), fluorescein angiography (FA), and fundus autofluorescence (FAF).

DESIGN, SETTING, AND PARTICIPANTS We performed a retrospective medical record review in 5 patients diagnosed as having PPM at tertiary retinal practices.

MAIN OUTCOMES AND MEASURES Findings on SD-OCT, FA, digital FAF, and ICG-A images.

RESULTS Patients presented within 2 weeks of subjective symptoms. Mean best-corrected visual acuity was 20/144 (range, 20/25-20/400). At presentation, all but 1 patient had bilateral macular lesions. Four eyes developed extramacular lesions during follow-up. On SD-OCT, the acute placoid lesions revealed hyperreflectivity of the outer nuclear layer; disruption of the external limiting membrane, ellipsoid layer, and interdigitation zone; and, in some patients, hyporeflective spaces at the level of absent outer segments. On follow-up, lesions revealed either partial or complete restoration of the outer retinal architecture or they progressed to atrophy. On FA, all placoid lesions were hypofluorescent in early frames and hyperfluorescent in late frames. In the acute stage, ICG-A revealed sharply delineated dense hypofluorescent lesions, which persisted on late frames in all patients. Hypofluorescent lesions faded completely or partially after resolution of the placoid lesions on SD-OCT and clinical examination. Variability was seen on the FAF patterns; most lesions were hyperautofluorescent, except in 1 patient, in whom they were hypoautofluorescent. Bilateral choroidal neovascularization developed in only 1 patient. The mean follow-up was 28 weeks (range, 2-92 weeks). On the final follow-up visit, mean best-corrected visual acuity was 20/125 (range, 20/25-20/400).

CONCLUSIONS AND RELEVANCE On SD-OCT, acute retinal changes in PPM involve the outer nuclear layer, external limiting membrane, ellipsoid layer, and interdigitation zone. The retinal pigment epithelium and choroid are involved in severely affected patients. The variable extent of retinal pigment epithelium involvement was reflected in variable FAF findings. We discuss clinical features that differentiate this entity from other white spots, including acute placoid multifocal pigment epitheliopathy. Additional long-term imaging studies are needed to further clarify the exact location and pathogenesis of this rare disease.
Persistent placoid maculopathy (PPM) is a rare clinical entity first described by Golchet et al in a series of 6 patients with clinical features that superficially resembled acute posterior multifocal placoid pigment epitheliopathy (APMPPE) and macular serpiginous choroidopathy. It is typically a bilateral disease that primarily involves the macula and has a good prognosis unless choroidal neovascularization (CNV) or atrophy develop.1,2 On fluorescein angiography (FA), placoid lesions in PPM are hypofluorescent in early frames and hyperfluorescent in late frames,1,2 whereas on indocyanine green angiography (ICG-A), they exhibited hypofluorescence in early and late frames.1,2 It is important to differentiate this entity from APMPPE because both conditions may appear similar at presentation. Compared with APMPPE, in which lesions start to pigment and begin to resolve within days to a few weeks, in PPM, the white placoid lesions and angiographic findings are symmetric and may persist for up to 3 months.1,2

We present a case series of 5 patients with PPM to report the imaging characteristics of PPM on spectral domain optical coherence tomography (SD-OCT) and the correlations with ICG-A, FA, and fundus autofluorescence (FAF). The use of SD-OCT is helpful in evaluating the outer retinal architecture, which aided in determining the location of the placoid lesions in PPM. The registration feature of Spectralis HRA+OCT (Heidelberg Engineering) has facilitated the point-to-point correlation of B-scans between different visits and long-term follow-up of lesion evolution. We also sought to analyze retinal pigment epithelium (RPE) involvement in this disorder by evaluating FAF, an imaging tool that has been recently used in various inflammatory and degenerative diseases.3–5

Methods

A retrospective medical record review was performed on 5 patients diagnosed as having PPM after Northwestern University Institutional Review Board approval was obtained. Informed consent was waived for the purpose of this retrospective study. Patients presented within 1 to 2 weeks of initial symptoms in at least one eye. Patients were included in the study if the diagnosis of PPM was made based on imaging and clinical features. Records were reviewed at initial presentation and during follow-up. Data collected included patient age and sex, medical history, best-corrected visual acuity (BCVA), slitlamp biomicroscopy and funduscopic examination findings, and history of therapy. The SD-OCT, FA, digital FAF, and ICG-A images were reviewed and analyzed for each patient. The SD-OCT images of patients 2, 3, and 4 were obtained using Spectralis HRA+OCT. The registration feature of Spectralis HRA+OCT facilitated point-to-point correlation of B-scans obtained at different visits. Cirrus OCT (Carl Zeiss Meditec Inc) was used in patients 1 and 5. The ability of Cirrus OCT to obtain C-scans or C-slabs through the z-axis was used to reveal unique views of the placoid lesion in the outer nuclear layer (ONL) and the underlying choroid. Digital FAF images were obtained using Spectralis HRA+OCT. Both FA and ICG-A were performed with a confocal laser scanning ophthalmoscope (Heidelberg Retinal Angiograph; Heidelberg Engineering).

Results

Five patients (10 eyes) diagnosed as having PPM were included in this series. The demographic characteristics and ocular findings are summarized in Table 1. The mean age of the patients was 56 years (age range, 50–60 years). All patients presented with bilateral macular lesions within 1 to 2 weeks of subjective symptoms. The mean initial BCVA was 20/144 (range, 20/25–20/400). Two patients (4 eyes) developed extramacular lesions later in the follow-up. The

### Table 1. Demographic Characteristics and Ocular Findings

<table>
<thead>
<tr>
<th>Patient No./ Sex/Age, y and Eye</th>
<th>Duration of Symptoms Before Initial Visit, d</th>
<th>BCVA at First Visit</th>
<th>Anterior Chamber Cells</th>
<th>Vitreous Cells</th>
<th>Foveal Involvement</th>
<th>Extramacular Lesions</th>
<th>Development of CNV or Atrophy</th>
<th>Treatment</th>
<th>BCVA at Last Visit</th>
<th>Duration of Follow-up, wk</th>
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<tr>
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Abbreviations: BCVA, best-corrected visual acuity; CNV, choroidal neovascularization.
Figure 1. Evolution of the Placoid Lesions Into Atrophy in Patient 1

A, Fundus view of the right eye shows a large macular placoid lesion with beginning pigmentary and atrophic changes. B, Fundus view of the left eye shows a smaller placoid macular lesion. C and D, Three weeks later, macular lesions expanded with some atrophy and pigmentation.

Figure 2. Fundus Autofluorescence (FAF) and Indocyanine Green Angiography (ICG-A) Patterns in the Healing Phase in Patient 1

A and B, A mottled FAF pattern was seen as the macular lesion started to heal. C and D, ICG-A reveals dense hypofluorescent macular lesions with linear intervening hyperfluorescence (choroidal vessels) and hypofluorescent satellite lesions.
central foveal subfield was spared in only 1 patient bilaterally. The mean follow-up time was 28 weeks (range, 2-92 weeks). Unlike our earlier experience in which most patients (90%) developed CNV, only 1 patient (20%) developed CNV bilaterally. On last follow-up visit, mean BCVA was 20/125 (range, 20/25-20/400).

**Patient 1**

A 59-year-old man presented with acute vision loss for 1 week in the right eye and for 2 days in the left eye. He had an external ear infection 2 weeks earlier. His BCVA was 20/400 in both eyes. The anterior chamber was quiet, and few vitreous cells were seen in both eyes. Fundus photography revealed a large macular placoid lesion with pigmentary changes at the fovea in the right eye (Figure 1A) and a smaller placoid macular lesion in the left eye (Figure 1B). On FAF imaging, macular lesions had a mottled pattern of hyperautofluorescent areas with intervening hypoautofluorescent spots (Figure 2A and B). Dense hypofluorescent macular lesions with linear intervening hyperfluorescence and few satellite lesions were evident on ICG-A (Figure 2C and D). The SD-OCT images of the right eye revealed severely thinned fovea, collapsed ONL, and absence of the external limiting membrane (ELM) and ellipsoid layers (Figure 3A). The RPE layer was disrupted with areas of thickening. The SD-OCT image of the left eye revealed parafoveal hyperreflective bands in the ONL and disruption of the ELM and ellipsoid layers, with an underlying sliver of hyporeflectance (Figure 2B). Focal deposits of hyperreflective material were seen over the RPE layer. In 3 weeks, expansion of the macular lesion in both eyes was noted with progressive atrophy and pigmentation (Figure 1C and D). The SD-OCT images of the right eye revealed progressive thinning and outer retinal atrophy (Figure 3C). The SD-OCT images of the left eye revealed thinned fovea, thinned ONL, loss of the ELM and ellipsoid layers, and resolution of the hyporeflective space with progressive parfoveal RPE atrophy (Figure 3D). At the 10-week follow-up visit, the patient reported no improvement. His BCVA remained at 20/400 in both eyes. The SD-OCT image of the right eye revealed
severely thinned fovea and extensive outer retinal atrophy (Figure 3E). The SD-OCT image of the left eye revealed recovery of the outer retinal layers nasal to the fovea with progressive central thinning and atrophy (Figure 3F). At the initial visit, a Cirrus OCT C-scan positioned at the ONL revealed delineated circular hyperreflectance at the lesion periphery and a hyporeflective center (Figure 4A), whereas a C-scan positioned at the choroid revealed hyporeflectance with a central hyperreflective area (Figure 4B). On last follow-up visit, a C-scan positioned at the choroid revealed a significant resolution of choroidal darkness with hyperreflective areas (Figure 4C).

**Patient 2**

A 52-year-old woman presented with acute onset of blurred spots in her central vision in both eyes of 1-week duration. Her BCVA was 20/30 in both eyes. There was no anterior chamber or vitreous inflammation. Fundus photography revealed a large macular annular placoid lesion encircling the fovea in the right eye (Figure 5A) and similar findings in the left eye. The macular lesions were hypofluorescent in the early stage of the FA (Figure 5C) and hyperfluorescent in late stages (Figure 5D). On FAF imaging, the macular lesions were delineated and revealed hyperautofluorescence with hypoaustofluorescent margins (Figure 5B). The SD-OCT images revealed a thinned ONL.

**Figure 5. Fundus Autofluorescence (FAF) Changes as Disease Progressed Into Atrophy in Patient 2**

A. Fundus view of the right eye shows large macular annular placoid lesion encircling the fovea. B. An FAF image shows hyperautofluorescence with hypoaustofluorescent margins. Early frames of fundus angiography show a hypofluorescent macular lesion (C), with increasing hyperfluorescence in late frames (D). Four months after treatment, a fundus view shows resolution of the placoid lesion with atrophic and pigmentary changes (E), whereas on FAF, lesions decreased in size and became hypoautofluorescent (F).
with a hyperreflective band associated with loss of the ELM and ellipsoid layers. The RPE was atrophied and disrupted with overlying hyperreflective focal deposits. The central foveal subfield thickness revealed preserved ELM and ellipsoid layers (Figure 6A). The patient was prescribed 60 mg of oral prednisone for 2 days, then 40 mg daily. Five weeks later, while taking 40 mg of prednisone, she reported no improvement in her vision, and her BCVA remained at 20/30 OU. The SD-OCT images of the right eye revealed progressive thinning of the ONL with resolution of the hyperreflective lesions (Figure 6B). In addition, the focal deposits over the RPE layer located temporal to the fovea resolved with some improvement of the integrity of the ellipsoid layer (Figure 6B). Treatment with azathioprine was initiated, but it was quickly discontinued secondary to intolerance. Mycophenolate mofetil was started at a daily dose of 1000 mg, which was increased to 2000 mg daily. Four months later, the patient reported improvement in her vision, and her BCVA remained at 20/25 in both eyes. Ophthalmoscopic examination revealed resolution of the placoid lesion and improved integrity of the RPE layer, and persistent thinning of the ONL at the parafoveal regions (Figure 6C).

Patient 3
A 50-year-old woman presented with sudden onset of progressive blurred vision in her left eye of 2-week duration. She had rheumatoid arthritis and type 2 diabetes mellitus for 13 years. Her uncorrected visual acuity was 20/80 OU which improved to 20/30 on testing vision through a pinhole. There was no anterior chamber or vitreous inflammation. Ophthalmoscopic examination findings were normal in the right eye, and resolution of the placoid lesion was noted to have decreased in size and were hypofluorescent (Figure 5F). On the last follow-up visit, the SD-OCT image revealed significant restoration of the ELM and ellipsoid layers, improved integrity of the RPE layer, and persistent thinning of the ONL at the parafoveal regions (Figure 6C).

A, A spectral domain optical coherence tomography (SD-OCT) image of the right eye reveals a thinned outer nuclear layer (ONL) with a hyperreflective band associated with loss of the external limiting membrane (ELM) and ellipsoid layers (black arrowheads). The RPE shows disruption with overlying hyperreflective focal deposits (white arrowheads). The central foveal subfield with preserved ELM and ellipsoid layers is also seen. B, Five weeks after treatment with oral prednisone, the right eye has progressive thinning of the ONL with resolution of the hyperreflective lesions (black arrowhead). Resolution of focal RPE deposits with some restoration of the integrity of ellipsoid layer is also seen (arrowhead). C, Four months after treatment with mycophenolate mofetil, significant restoration of the ELM and ellipsoid layers and improved integrity of the RPE layer (black arrowheads) with areas of persistent ONL (white arrowhead) thinning seen.
Patient 4
A 58-year-old woman presented with blurred vision in both eyes of 1-week duration. She reported a hepatitis C virus infection that began in 1970. Her BCVA was 20/400 OD and 20/25 OS. There was no anterior chamber or vitreous inflammation. In early frames of the FA, the right eye had a hypofluorescent macular lesion, which was hyperfluorescent with leakage in late frames (Figure 10A and B). Meanwhile, the FA of the left eye revealed a hypofluorescent macular lesion with focal areas of leakage (Figure 10C). On both eyes, CNV was seen at presentation. The SD-OCT image of the right eye revealed CNV with RPE elevation, subretinal fluid (SRF), and disruption of the ELM and ellipsoid layers (Figure 11A). The SD-OCT image of the left eye revealed an ONL hyperreflective band and focal disruption of the ellipsoid layer (Figure 11B). She underwent photodynamic therapy, bevacizumab injection, and intravitreal injection of dexamethasone in the right eye. Three weeks later, the SRF had almost completely resolved, with more elevation of the pigment epithelial detachment (Figure 11C).

The SD-OCT image of the left eye revealed more disruption of the ELM and ellipsoid layers and accumulation of intraretinal fluid (IRF) (Figure 11D). Hypofluorescence with a larger area of leakage was seen on FA (Figure 12A). Dense hypofluorescent macular lesions that were not visible on FA were seen on ICG-A (Figure 12B). Two areas of hypofluorescent macular lesions that were not visible on FAF were seen on ICG-A (Figure 12B). Two areas of hypofluorescent macular lesions that were not visible on FAF were seen on ICG-A (Figure 12B). Two areas of hypofluorescent macular lesions that were not visible on FAF were seen on ICG-A (Figure 12B). Two areas of hypofluorescent macular lesions that were not visible on FAF were seen on ICG-A (Figure 12B). Two areas of hypofluorescent macular lesions that were not visible on FAF were seen on ICG-A (Figure 12B). Two areas of hypofluorescent macular lesions that were not visible on FAF were seen on ICG-A (Figure 12B). 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Patient 5
A 60-year-old woman presented with vision loss in both eyes of 1-week duration. Her BCVA was 20/50 OU. There was no anterior chamber or vitreous inflammation. Fundus photography of both eyes revealed placoid macular lesions. The SD-OCT image revealed hyperreflective lesions in the ONL, disruption of the ELM and ellipsoid layers with a sliver of hyporeflectance, RPE atrophy, and focal hyperreflective deposits in the outer retina (Figure 13E).

Figure 8. Outer Retinal and Choroidal Changes in Patient 3

A and B, Fundus views show resolution of the placoid lesions with atrophic and pigmentary macular changes.

Figure 9. Evolution of the Placoid Lesions Into Atrophy in Patient 3

A and B, Fundus views show resolution of the placoid lesions with atrophic and pigmentary macular changes.

Figure 10. Bilateral Choroidal Neovascularization (CNV) at Presentation in Patient 4

At presentation, early fluorescein angiograph frames of the right eye show an early hypofluorescent lesion (A), which exhibits late hyperfluorescence with leakage from the CNV (B). C, The left eye shows hypofluorescent macular lesion with focal areas of leakage from CNV (black arrowheads).
Discussion

We used the following multimodal imaging approach to describe the imaging characteristics of PPM: FA, ICG-A, SD-OCT, and FAF. On FA, all placoid lesions in PPM had typical findings as described previously1,2 and were hypofluorescent in early frames, with increasing hyperfluorescence in later frames (Figure 5C and D). In patient 4, leakage in the right eye was secondary to a type 1 CNV that was also seen on SD-OCT (Figure 10B and Figure 11A). Meanwhile, the left eye had hyperfluorescence in late frames with focal leakage (Figure 10C).

The ICG-A revealed sharply delineated, dense, early hypofluorescent lesions, which persisted on late ICG-A in all patients. A few extramacular satellite lesions were seen only on ICG-A (Figure 2C and D). Golchet et al3 speculated that the hypofluorescence observed on FA and ICG-A can be due to choroidal hypoperfusion, blockage by the placoid lesions, or a mixed mechanism. Khairallah and Ben Yahia10 believed that choroidal ischemia was the reason for the hypofluorescence observed in this disease entity. We sought to further investigate these competing theories by studying the shape of the lesion seen in the outer retina and choroid on SD-OCT en face scans. In patient 4, with the use of Cirrus SD-OCT advanced visualization analysis, a C-scan positioned at the ONL delineated the placoid macular lesion observed clinically in the left eye (Figure 4A). Hyperreflectance was seen at the periphery of the lesion, which corresponded to the ONL reflectivity, being darker where the ONL was more hyperreflective (Figure 4B). At the last visit after multiple treatments for 18 months, the right eye shows extensive subretinal scarring and residual intraretinal cysts (E), whereas the left eye shows resolution of the IRF with nearly complete restoration of the ELM and ellipsoid layers (F).
Figure 13. Acute Spectral Domain Optical Coherence Tomography (SD-OCT) Findings in All Cases

A, The SD-OCT images of acute placoid lesions from patient 1 (A), patient 2 (B), patient 3 (C), patient 4 (D), and patient 5 (E) show hyperreflectivity within the outer nuclear layer and disruption of the external limiting membrane and ellipsoid layers, appearing as a hyporeflective space at the level of the outer segments.

Table 2. Differences in Various Imaging Modalities Among PPM, APMPPE, SC, and AMN

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<th>Modality</th>
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<th>APMPPE</th>
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<td>Early hypofluorescence and late hyperfluorescence&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Early hypofluorescence, late hyperfluorescence and staining of some lesions&lt;sup&gt;1,4&lt;/sup&gt;</td>
<td>Early hypofluorescence of the central portion of the lesion surrounded by hyperfluorescence at the margins with late staining&lt;sup&gt;1,5,15&lt;/sup&gt;</td>
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<td>ICG-A</td>
<td>Sharply delineated dense hypofluorescent lesions in early and late frames&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Hypofluorescence in both early and late frames&lt;sup&gt;3,16,17&lt;/sup&gt;</td>
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<td>FAF</td>
<td>Hyperautofluorescence, hypoaufotofluorescence (1 patient), and no changes (1 patient) (current study)</td>
<td>No changes in some lesions&lt;sup&gt;2&lt;/sup&gt;; mixed hypoaufotofluorescence and hyperautofluorescence in some lesions&lt;sup&gt;2&lt;/sup&gt;; hypoaufotofluorescence&lt;sup&gt;8&lt;/sup&gt;</td>
<td>Hyperautofluorescence in active area&lt;sup&gt;16,19&lt;/sup&gt; and hyperautofluorescence heralded the development of CNV&lt;sup&gt;5&lt;/sup&gt;</td>
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<td>SD-OCT</td>
<td>Hyperreflectivity of the ONL, disruption of the ELM and ellipsoid layer (all cases), and hyporeflective silver at the level of the outer segments in some cases (current study); homogeneous solid isoreflective pattern of the choroidal capillaries located beneath the severely disrupted RPE (some cases) (current study)</td>
<td>ONL hyperreflectivity and disrupted ellipsoid and normal RPE layers&lt;sup&gt;19&lt;/sup&gt;; dome-shaped elevation with disruption of the ellipsoid layer, distinct separation between ellipsoid and RPE layers, later accentuation of RPE hyperreflectivity, and union of the RPE and ellipsoid layers&lt;sup&gt;19&lt;/sup&gt;; outer retinal hyperreflectivity with choroidal thickening&lt;sup&gt;19&lt;/sup&gt;; SRF in some cases&lt;sup&gt;6,10&lt;/sup&gt;</td>
<td>Increased reflectivity of the choroid and disruption of the ellipsoid and RPE layers&lt;sup&gt;16,19&lt;/sup&gt;</td>
<td>ONL and OPL/Henle layer hyperreflectivity and focal disruption of the interdigitation line&lt;sup&gt;20&lt;/sup&gt;</td>
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<td>FA</td>
<td>Normal except for hyperfluorescence if atrophy or scarring develop (current study); persistent hypofluorescence in some cases&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Late staining of scarred lesions</td>
<td>Late staining of scarred lesions&lt;sup&gt;13,15,19&lt;/sup&gt;</td>
<td>Normal</td>
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<tr>
<td>ICG-A</td>
<td>Persistent hyperfluorescence in some cases&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Partial or complete resolution of hypofluorescent areas&lt;sup&gt;6,17&lt;/sup&gt;</td>
<td>Hypofluorescence&lt;sup&gt;1,15&lt;/sup&gt;</td>
<td>Normal</td>
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<td>FAF</td>
<td>Mixed hyper- and hypoaufotofluorescence in atrophic lesions (current study)</td>
<td>Areas of pigmentation were hyperautofluorescent while the depigmented areas were hypoaufotofluorescent&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Hypoaufotofluorescence in areas of chorioretinal atrophy&lt;sup&gt;18,19&lt;/sup&gt;</td>
<td>Normal</td>
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<td>SD-OCT</td>
<td>Many lesions showed complete restoration of the outer retinal architecture, whereas some showed only partial restoration or progression to atrophy (current study)</td>
<td>Resolution of the ONL hyperreflectivity with thinning and outer retinal atrophy&lt;sup&gt;7&lt;/sup&gt;; reformation of 2 distinct visible layers of ellipsoid and RPE layers&lt;sup&gt;7&lt;/sup&gt;</td>
<td>Retinal atrophy, subretinal fibrosis, cystic changes, marked attenuation of the ellipsoid, thinned RPE&lt;sup&gt;7,21&lt;/sup&gt;</td>
<td>ONL thinning&lt;sup&gt;20&lt;/sup&gt;</td>
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Abbreviations: AMN, acute macular neuroretinopathy; APMPPE, acute posterior multifocal placoid pigment epitheliopathy; CNV, choroidal neovascularization; ELM, external limiting membrane; FA, fluorescein angiography; FAF, fundus autofluorescence; ICG-A, indocyanine green angiography; ONL, outer nuclear layer; OPL, outer plexiform layer; PPM, persistent placoid maculopathy; RPE, retinal pigment epithelium; SC, serpiginous choroidopathy; SDOCT, spectral domain optical coherence tomography; SRF, subretinal fluid.
At this stage, a C-scan positioned at the choroid revealed almost complete resolution of the choroidal darkness and appearance of hyperreflective areas, consistent with increased choroidal illumination secondary to RPE atrophy (Figure 4C). In addition, the similar shape of the observed pattern of macular and extramacular placoid lesions on FP, FA, SD-OCT, and ICG-A supports the masking effect by those lesions. Evidence in support of choroidal involvement was seen in patient 3, in whom we observed a homogeneous solid dark pattern of the choroidal capillaries located beneath the severely disrupted RPE in areas of PPM involvement, suggesting either choroidal ischemia or infiltration, as was observed in patient 3 (Figure 8D and E). Two weeks later, choroidal capillaries revealed normalization of the SD-OCT pattern (regularly alternating hyperreflective and hyporeflective patterns), which was associated with some recovery of the outer retina and RPE (Figure 8F). Similar choroidal findings were observed in APMPPE, where some investigators had suggested delayed choroidal filling in addition to extensive choroidal nonperfusion.12

On SD-OCT, acute placoid lesions revealed hyperreflectivity in the ONL and disruption of the ELM and ellipsoid layers with a hyporeflective space in the outer retina, related to loss of the ellipsoid layer and interdigitation zone on OCT of these eyes (Figure 13). On follow-up visits, SD-OCT revealed a range of changes among the patients. Some patients exhibited total recovery of the outer retinal architecture and near complete restoration of the ELM and ellipsoid layers (patient 4) (Figure 11F). These changes correlated with resolution of the placoid lesions on fundus photos and ICG-A. In patient 1, there was an evolution to atrophy in 1 week (Figure 3D). Also in this patient, both eyes had significant foveal thinning and outer retinal scarring without any signs of recovery (Figure 3E and F). In patient 2, the nasal parafoveal regions had resolution of retinal changes and few areas of retinal atrophy, with improvement of the ELM and ellipsoid integrity at the foveal subfield (Figure 6C). Patient 4 developed CNV with scarring and SRF in the right eye and IRF in the left eye (Figure 11A and D). After receiving anti-vascular endothelial growth factor treatments for 2 years, SRF and IRF resolved with significant scarring in the right eye (Figure 11E) and significant outer retinal layer restoration in the left eye (Figure 11F). We have noted that the size of the ONL hyperreflective lesion, the degree of disruption of the ELM and ellipsoid layers, the presence or absence of the hyporeflective sliver at the level of the ellipsoid layer, and the existence of the hyperreflective focal deposits at the level of the RPE do not predict the prognosis or the extent of recovery. Similar SD-OCT changes in the ONL, ELM, ellipsoid layer, and RPE layer are observed in the acute and resolution phases in APMPPE.6-10

This study identified 2 distinct patterns on FAF imaging in acute lesions of PPM. In the first pattern, acute placoid lesions demonstrated hyperautofluorescence, which became hypoautofluorescent as the disease progressed to atrophy (patient 2, Figure 5B and F). These changes corresponded with the RPE disruption with overlying focal hyperreflective deposits on SD-OCT in the acute stage (Figure 6A). In the second pattern, in 1 patient, a pattern of minimal hypoautofluorescent FAF changes in the face of prominent lesions on ICG-A was seen (patient 4, Figure 12B and C). The PPM healing phase was similarly associated with variable FAF findings. These highly variable findings in acute and healing FAF suggest different patterns of RPE involvement in PPM. This variability appears to correlate with the severity of acute RPE involvement. Interestingly, we found that all patients, even those without acute FAF changes, had some degree of RPE involvement as the disease progressed.

In summary, we describe the imaging characteristic of PPM on FA, ICG-A, SD-OCT, and FAF. Although long-term prognosis was highly variable, the patients had similarities on the different imaging modalities, especially in the acute stage of the disease. We speculated that acute retinal changes in PPM involve the ONL, ELM, and ellipsoid layer with secondary involvement of the RPE layer and choroid in some patients, depending on the severity of the disease. On the basis of our imaging findings, choroidal hypofluorescence on ICG-A may be secondary to choroidal hypoperfusion or infiltration by inflammatory material but also could be due to optical blockage by the placoid lesions or possibly related to a mixed mechanism of all or some of these factors. Given similarities in clinical findings among PPM, APMPPE, serpiginous choroidopathy, and acute macular neuroretinopathy, Table 2 summarizes the differences in various imaging modalities. Imaging findings in the acute stages of PPM resemble the findings in acute APMPPE on all imaging modalities. Clinical and historical findings at presentation that would favor a diagnosis of PPM are older age (mean age was 56 years in the current study), presence of bilateral symmetric lesions, CNV at presentation. Although APMPPE lesions usually resolve and pigment within days to a few weeks with minimal atrophy, the occurrence of significant atrophy and, most importantly, persistent placoid lesions in the same location beyond 3 months would strongly favor PPM.

Unlike our original series in which CNV predominated,1 atrophy was the predominant outcome (60%) in the current series, whereas CNV developed bilaterally in only 1 patient (20%). This change in disease pattern may reflect a change in community referral patterns or variability in the disease itself. Further long-term imaging studies are needed and may help to clarify the exact location and pathogenesis of this rare disease.
Multimodal Imaging in PPM

Original Investigation Research

syndromes.

autofluorescence imaging of the white dot

5

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