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PHOTORECEPTOR ATROPHY IN ACUTE POSTERIOR MULTIFOCAL PLACOID PIGMENT EPITHELIOPATHY DEMONSTRATED BY OPTICAL COHERENCE TOMOGRAPHY

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Acute posterior multifocal placoid pigment epitheliopathy (APMPPE) is a self-limited inflammatory disorder that typically affects young, healthy patients. Funduscopy examination is characterized by multiple cream-colored lesions in the posterior pole bilaterally. Symptoms may include metamorphopsia, scotomata, and rapid loss of visual acuity. Resolution of the lesions may be followed by retinal pigment epithelial (RPE) changes.^{1–3}

It is unclear whether the disease is primarily an RPE abnormality or is caused by a disruption of the choroidal vasculature.^{1–3} Because of its transience, no histopathologic studies have been reported. The presumptive location of the lesions has therefore been based on clinical examination and angiography.

We present ultrahigh-resolution optical coherence tomography (UHR-OCT) of the macula in three patients with APMPPE. One patient was imaged acutely and two were imaged after the lesions had healed. UHR-OCT provides 3 μ m of axial resolution, compared to 10 μ m achieved with conventional OCT, allowing for better visualization of the retinal architecture.^{4,5} The OCT signal is reflected back variably by different anatomic and pathologic structures with the retina, generating the different signal intensities visualized in an OCT image. Since very little of the OCT signal travels through the RPE in a healthy retina, an increase in signal backscattering by the choroid suggests loss of the normal RPE barrier to the OCT laser beam. In all three cases, the images show disruption and atrophy of the normally highly backscattering photoreceptor outer segments. After the acute phase, lesions demonstrate an increase in signal backscattering from the choroid, consistent with RPE atrophy.

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Summary Statement: This case series documents three patients with acute posterior multifocal placoid pigment epitheliopathy (APMPPE), one in the acute phase and two after disease resolution. Images obtained with ultrahigh resolution optical coherence tomography, capable of 3 μ m axial resolution, show photoreceptor disruption in all cases and show retinal pigment epithelial atrophy in healed cases.

Case Reports

Case 1

A 31-year-old white man reported 10 days of blurred vision in his right eye and 3 days of a paracentral scotoma in his left eye. He also reported myalgias 1 week before the onset of his visual changes. His visual acuity was 20/80 in the right eye and 20/20-1 in the left. Intraocular pressures and anterior segment examination were normal, with no cells in the anterior chamber or vitreous. Dilated fundus examination showed multifocal yellowish-white plaques in the posterior pole bilaterally (Figure 1, A and B). Some of the lesions in the right eye appeared to be fading centrally and demonstrated hyperpigmented borders (Figure 1B). The lesions were hypofluorescent early in the fluorescein angiogram (FA) and stained late. Indocyanine green (ICG) angiography showed hypofluorescence of the lesions throughout the study.

UHR-OCT images of the more acutely affected left eye showed an intact RPE (Figure 2A). There is an increase in choroidal backscattering in the right eye, indicating a focal disruption of the overlying RPE (Figure 2B). The highly backscattering line above the RPE, representing the junction between the inner and outer segments of the photoreceptors (IS/OS junction), was disrupted in several areas in both eyes. The outer nuclear layer (ONL) contained areas of increased backscattering that corresponded clinically to the yellowish-white plaques observed during the acute phase of the disease. In the right eye, the ONL appeared thinned in the areas of increased signal backscattering. These outer retinal lesions could represent inflammation or degenerating photoreceptor cells.

Case 2

A 23-year-old white man had 6 days of blurred peripheral vision in his right eye and blurred central vision in his left eye. He noted frontal headaches, rhinorrhea, and a dry cough that coincided with the onset of his visual disturbance. His visual acuity was 20/20 in the right eye and counting fingers at 5 feet in the left. Intraocular pressures were normal. Slit lamp examination was significant for trace cells in the anterior chamber and vitreous bilaterally. Dilated fundus examination showed multiple creamy white placoid lesions in the posterior pole bilaterally (Figure 1C, right eye only). FA showed early blocking and late staining of the lesions. ICG angiography showed hypofluorescence of the lesions throughout the study. Over the next 3 years, the patient's visual acuity in the left eye improved to 20/50-2. The posterior pole of both eyes demonstrated placoid areas of RPE atrophy and hyperpigmentation with a few patches of subretinal fibrosis. UHR-OCT images obtained 3 years after the lesions had healed (Figure 3, right eye shown) showed areas of disruption of the IS/OS junction bilaterally and thinning of the ONL bilaterally. In addition, there was an increase in backscattered signal in several areas of the choroid bilaterally, indicating focal disruptions of the overlying RPE.

Case 3

A 60-year-old white woman reported 3 weeks of black paracentral scotomata in her right eye and decreased central vision in her left eye. Her visual acuity was 20/40 in the right eye and hand motion in the left. Intraocular pressures and anterior segments were normal, with no cells in the anterior chamber of either eye. Trace anterior vitreous cells were present bilaterally. Dilated fundus examination showed multiple creamy white placoid lesions in the posterior pole bilaterally. FA showed early blocking and late staining of the lesions. ICG angiography showed hypofluorescence of the lesions throughout the study. After several weeks, the lesions faded and were replaced by areas of RPE atrophy (Figure 1D, right eye). Over the next year, her vision remained stable in the right eye and improved to counting fingers in the left. UHR-OCT performed 1 year after resolution of the disease showed disruption of the IS/OS junction bilaterally and thinning of the ONL bilaterally, as in the previous cases (Figure 4, right eye). In addition, the choroid was highly backscattering in several areas bilaterally, indicating areas

of RPE atrophy. There was a focal area of RPE sparing in the right macula; the RPE in the left macula was diffusely atrophic. The fundus photographs (Figure 1D), which show the severe RPE atrophy in Case 3, explain why the choroidal backscattering in Case 3 is more intense than in Case 2.

Discussion

UHR-OCT in each of the three patients shows disruption and atrophy of the photoreceptor layers of the neural retina. These outer retinal structural changes occur early in the disease; RPE disruption is demonstrated after the lesions have healed.

In the left eye of Case 1, during the acute inflammatory phase of the disease, moderately backscattering lesions were observed in the ONL of the retina. Garg and Jampol observed similar lesion backscattering on standard resolution OCT in a patient with APMPE and serous macular detachments.⁶ UHR-OCT demonstrates more clearly that these lesions are located in the outer retina.

Images of the resolving lesions in the right eye of Case 1 show atrophy of the ONL and the inner and outer photoreceptor segments. This finding is also visible in the healed lesions of Cases 2 and 3. Therefore, photoreceptor atrophy occurs as the lesions begin to heal and persists after resolution of the disease. This observation suggests that the moderately backscattering lesions in the outer retina seen acutely represent inflamed or damaged photoreceptor cell bodies, which atrophy later in the course of the disease.

Degeneration of the RPE is apparent on UHR-OCT images from the right eye in Case 1 and both eyes of Cases 2 and 3, visualized as an increase in the backscattered signal of the underlying choroid. Hence, structural RPE changes are not visible until the lesions are healing or healed; however, it is possible that RPE dysfunction, which is not detectable by OCT, occurs in the acute setting.

The pathogenesis of APMPE remains unclear. In the three cases presented, UHR-OCT demonstrates early and late photoreceptor disruption, which has not been demonstrated previously in this disease. In the acute setting, areas of increased backscattering are seen in the ONL, likely representing early degenerative changes of the photoreceptors. Fluorescein and ICG angiography demonstrate hypofluorescence of these lesions. The choroidal fluorescence may be blocked by the inflamed or damaged photoreceptor cell bodies seen concurrently on UHR-OCT. Alternatively, the hypofluorescence could be due to choroidal ischemia, which would also result in ischemia of the RPE and outer retina and could account for the photoreceptor and RPE disruption seen on the UHR-OCT.

As the lesions begin to resolve, photoreceptor loss is evident. Healed cases continue to demonstrate areas of severe photoreceptor atrophy. Loss of the RPE is also evident during healing and after disease resolution; however, OCT imaging cannot detect RPE dysfunction, which may occur earlier. Future histologic studies would be helpful in corroborating the structural changes seen on UHR-OCT, and serial UHR-OCT imaging in patients with APMPE might shed more light on the pathogenesis of the disease.

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Fig 1. Fundus photographs from Cases 1 (**A, B**), 2 (**C**), and 3 (**D**). Corresponding ultrahigh resolution optical coherence tomography images are shown in Figs. 2–4.

Fig 2.

Case 1. Six-millimeter macular ultrahigh-resolution optical coherence tomography scans reveal an area of increased backscattering in the outer nuclear layer of the acutely affected left eye (A, white arrow), and thinning of the outer nuclear layer in the resolving lesions of the right eye (B, blue arrows). The highly backscattering line representing the inner/outer photoreceptor segment junction is disrupted in several areas bilaterally (red asterisks). Increased signal backscattering is seen below a focal area of photoreceptor disruption, indicating RPE disruption (B, under the blue arrow to the right). Retinal layers are labeled: nerve fiber layer (NFL), ganglion cell layer (GCL), inner plexiform layer (IPL), inner nuclear layer (INL), outer plexiform layer (OPL), outer nuclear layer (ONL), external limiting membrane (ELM), inner/outer segment junction (IS/OS), retinal pigment epithelium (RPE).

Fig 3.

Case 2, right eye. Six-millimeter macular ultra-high-resolution optical coherence tomography scan 3 years after resolution of the disease shows thinning of the outer nuclear layer (blue arrows) and disruption of the line representing the inner/outer segment junction bilaterally (red asterisks). Increased choroidal signal backscattering is also noted under areas of photoreceptor atrophy, indicating loss of the normal signal attenuation that would be produced by an intact retinal pigment epithelium.

Fig 4. Case 3, right eye. Six-millimeter macular ultra-high-resolution optical coherence tomography scan 1 year after disease resolution shows thinning of the outer nuclear layer (blue arrows). Disruption of the line representing the inner/outer segment junction is noted in the right eye (to the right of the red asterisk). Increased signal backscattering in the choroid is also noted under areas of photoreceptor degeneration, indicating degeneration of the RPE.