Choroidal ischemia drives macular neovascularization in persistent placoid maculopathy

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Persistent placoid maculopathy (PPM) is a rare, mostly bilateral, placoid chorioretinopathy affecting mainly Caucasian men in their 50s and 60s. Golchet et al. were the first to describe PPM in 2006 in six patients. The features of this disorder are similar to acute posterior multifocal placoid pigment epitheliopathy (APMPPE) but with a more protracted course and poorer outcomes and more frequent development of macular neovascularization. In contrast to serpiginous, the lesions are more central without progressive creep and with less chorioretinal scarring.

The pathogenesis of PPM is not yet fully understood but is likely related to inflammation causing choriocapillaris (CC) hypoperfusion and ischemia with secondary outer retina and retinal pigment epithelium (RPE) disruption and atrophy. Klugas et al. were the first to describe optical coherence tomography angiography (OCTA) findings in patients with placoid spectrum diseases such as APMPPE and PPM and showed evidence of choriocapillaris (CC) ischemia with OCTA that colocalized with regions of CC ischemia with indocyanine green angiography (ICGA) and with areas of outer retinal disruption with en face OCT. Inner choroidal ischemia may be the driving etiology of placoid diseases such as APMPPE and PPM and OCTA is a simple, practical tool to capture this finding and to help differentiate the different forms of placoid disorders.

In this case report, we describe a case of PPM with serial OCTA scans during 26 months of follow up, showing the presence and progression of inner choroidal ischemia driving the development of macular neovascularization.

1. Case report

A 65-year-old man with no previous ocular history was referred for the evaluation of a 5-day history of vision loss OD. Past medical history was positive for hypertension, allergic rhinitis, benign prostatic hyperplasia and emphysema. On examination, visual acuity was 20/40 OD and 20/20 OS, with normal anterior segment examination. Dilated fundus examination revealed yellow-white plaque-like lesions in the central macula OD and in the superior macula OS (Fig. 1). Spectral-domain OCT through the lesions illustrated hyperreflective outer retinal lesions associated with ellipsoid zone disruption and OCTA demonstrated patches of inner choroidal flow deficit that co-localized with the yellow-white macular lesions (Fig. 2). After inflammatory and infectious diseases such as tuberculosis were excluded, a diagnosis of APMPPE was rendered and the patient was closely monitored.

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Three weeks later, the patient presented with progressive vision decrease in each eye. Visual acuity was 20/60 OD and 20/20–2 OS. An increase in the number of placoid lesions was noted in each eye (Fig. 3A and B). Fundus autofluorescence (AF) showed corresponding areas of hyper-AF with smaller patches of mottled hypo-hyper AF (Fig. 3C and D). OCT demonstrated drusen like deposits and EZ loss in the macula OU (Fig. 3G and H). OCTA of the inner choroid showed larger areas of progressive choriocapillaris flow deficit OU and ICGA confirmed the presence of widespread inner choroidal ischemia in each eye (Figs. 2 B, Fig. 3E–F). The patient was started on a regimen of oral Prednisone (1 MG/KG), and the visual acuity improved with resolution of the placoid lesions and improved flow deficit with repeat OCTA three weeks later (Fig. 2C). Because of persistent choroidal ischemia with serial OCTA (Fig. 2D and E) however, the patient was diagnosed with PPM and started on immunosuppressive therapy while the prednisone was slowly tapered. Azathioprine (50 MG daily) was eventually replaced with mycophenolate mofetil (Cellcept) 2000 MG daily under the supervision of a rheumatologist.

Three months from the baseline presentation, the patient presented with progressive vision decrease in each eye. Visual acuity was 20/60 OD and 20/20–2 OS. An increase in the number of placoid lesions was noted in each eye (Fig. 3A and B). Fundus autofluorescence (AF) showed corresponding areas of hyper-AF with smaller patches of mottled hypo-hyper AF (Fig. 3C and D). OCT demonstrated drusen like deposits and EZ loss in the macula OU (Fig. 3G and H). OCTA of the inner choroid showed larger areas of progressive choriocapillaris flow deficit OU and ICGA confirmed the presence of widespread inner choroidal ischemia in each eye (Figs. 2 B, Fig. 3E–F). The patient was started on a regimen of oral Prednisone (1 MG/KG), and the visual acuity improved with resolution of the placoid lesions and improved flow deficit with repeat OCTA three weeks later (Fig. 2C). Because of persistent choroidal ischemia with serial OCTA (Fig. 2D and E) however, the patient was diagnosed with PPM and started on immunosuppressive therapy while the prednisone was slowly tapered. Azathioprine (50 MG daily) was eventually replaced with mycophenolate mofetil (Cellcept) 2000 MG daily under the supervision of a rheumatologist.

Patient’s vision was stable 26 months from the baseline visit and visual acuity was 20/30 OD and 20/20 OS with minimal recurrent fluid OU and no evidence of recurrent choroidal ischemia in either eye. The patient continued to receive aflibercept injections OD every 8 weeks and was maintained on Cellcept 2000 MG daily under continued supervision by the rheumatologist without complications.

2. Discussion

Although the presenting findings of PPM and APMPPE are similar, the latter is associated with a good visual prognosis and a low incidence of MNV. PPM however, has a worse visual prognosis and can be complicated by secondary MNV in 38–50% of cases and macular atrophy in 23% of cases. The presence of persistent inner choroidal ischemia is
a critical factor differentiating these 2 disorders and OCTA is a valuable, practical tool to distinguish these 2 subtypes of placoid disease.\(^4\,7\)

Inner choroidal ischemia has been suspected to be the driving etiology of placoid diseases, such as APMPPE and PPM, based on the fluorescein angiographic and ICGA findings of choroidal hypofluorescence noted early in these studies,\(^2\,4\,5\) although the role of blockage must be accounted for.\(^7\,9\) OCTA however, has more definitively confirmed the presence of inner choroidal ischemia in these disorders and specifically, Klufas et al.\(^4\) showed that blockage from the outer retinal plaques was not a significant factor causing the identified choriocapillaris (CC) flow deficits which were more importantly attributed to CC hypoperfusion.

In this case report, OCTA was an essential tool to identify the presence of CC ischemia and provided a very practical method to document the development of progressive and persistent inner choroidal ischemia occurring in each eye of our patient. Moreover, OCTA was an important modality to identify the formation of MNV in each eye requiring the initiation of antiVEGF therapy. Of great interest, the application of serial
OCTA facilitated the exact co-localization of inner choroidal ischemia with the development of MNV in each eye.

The mechanisms leading to angiogenesis and the development of MNV are complex and include ischemic and inflammatory pathways. The elaboration of angiogenic growth factors can be caused by several factors but the role of ischemia in driving proliferative retinal and macular disease cannot be understated. This case report is unique in that it illustrates exact co-localization of areas of CC ischemia, as documented with OCTA, with subsequent development of macular neovascularization originating from the choroid and demonstrates the importance of persistent inner choroidal ischemia in eyes with PPM in driving the development of MNV. Immunosuppressant therapy should be initiated in patients showing persistent choroidal ischemia. Whether earlier immunosuppressive therapy can alter the course of macular neovascularization and vision loss requires further study.

Patient consent

Consent to publish the case report was not obtained. This report does not contain any personal information that could lead to the identification of the patient.

Intellectual property

We confirm that we have given due consideration to the protection of intellectual property associated with this work and that there are no impediments to publication, including the timing of publication, with respect to intellectual property. In so doing we confirm that we have followed the regulations of our institutions concerning intellectual property.

Research ethics

We further confirm that any aspect of the work covered in this manuscript that has involved human patients has been conducted with the ethical approval of all relevant bodies and that such approvals are acknowledged within the manuscript.

IRB approval was obtained (required for studies and series of 3 or more cases).

Written consent to publish potentially identifying information, such as details or the case and photographs, was obtained from the patient(s) or their legal guardian(s).

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Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.
Declaration of competing interest

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