Title

Phase-Variance Optical Coherence Tomographic Angiography Imaging of Choroidal Perfusion Changes Associated With Acute Posterior Multifocal Placoid Pigment Epitheliopathy

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Letters

OBSERVATION

Phase-Variance Optical Coherence Tomographic Angiography Imaging of Choroidal Perfusion Changes Associated With Acute Posterior Multifocal Placoid Pigment Epitheliopathy

Acute posterior multifocal placoid pigment epitheliopathy (APMPPE) is characterized by bilateral multiple placoid white-gray lesions of the posterior pole at the level of the retinal pigment epithelium (RPE) and/or choriocapillaris, which self-resolve with recovery of vision.[1,2] The etiology is unknown, but APMPPE has been associated with viral prodromes and vasculitis. The placoid lesions are thought to represent focal RPE inflammation or choriocapillaris ischemia based on fluorescein angiogram findings of early hypofluorescence and late hyperfluorescence.

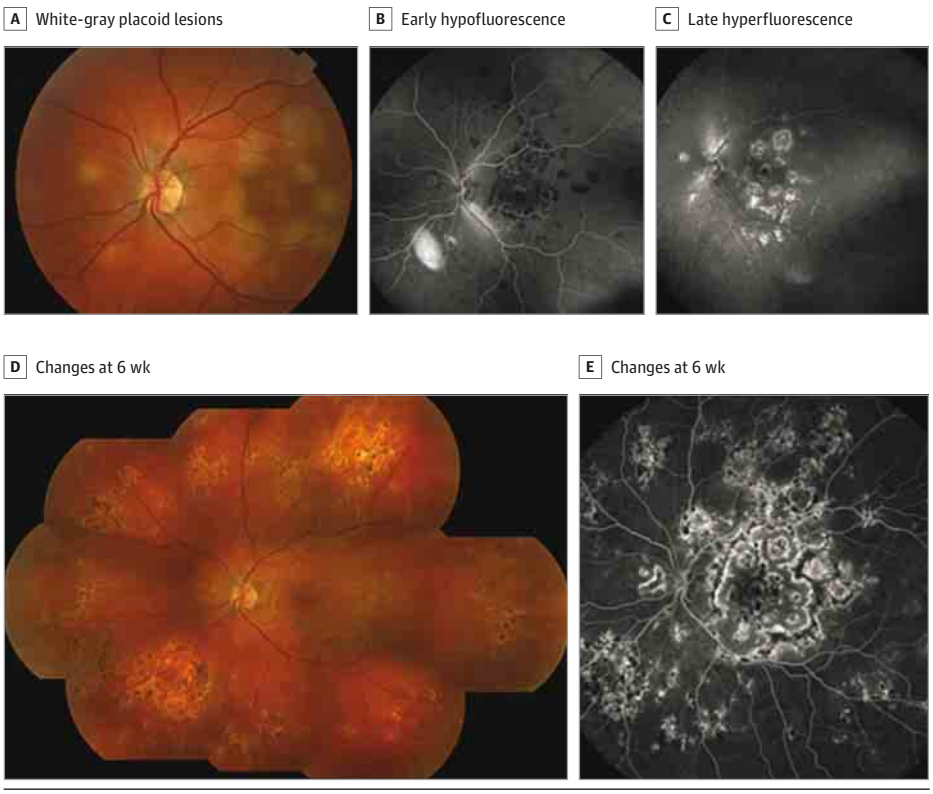
Phase-variance optical coherence tomographic angiography (pv-OCTA) allows noninvasive visualization of the choroidal blood flow in 3 dimensions in vivo.[3,4] A custom-built OCT system (125-kHz line rate, 855-nm central wavelength, and 4.5-μm axial resolution) was used to image choroidal perfusion over a 1.5 × 1.5-mm^2 area (equally spaced 350 A-scans in both x- and y-axes) in acute APMPPE.

Report of a Case | A woman in her mid to late 20s with viral prodrome presented with blurry vision in the left eye for 1 week. Visual acuity was 20/20 OD and 20/400 OS. The right eye was normal, and the left eye had normal anterior segment and vitreous, but fundus showed multiple white-gray placoid lesions posteriorly with early hypofluorescence and late hyperfluorescence on fluorescein angiogram (**Figure 1**). Patchy hypoperfusion of the choriocapillaris and Sattler layer was noted on pv-OCTA corresponding to focal areas of photoreceptor and RPE irregularity on OCT B-scans (**Figure 2A**-C). Serology test results were negative for syphilis, sarcoidosis, and tuberculosis.

After 2 weeks, similar placoid lesions were noted in the right eye. After 6 weeks, placoid lesions resolved bilaterally to develop pigment clumping (Figure 1D) and choroidal perfusion mostly normalized on pv-OCTA. Visual acuity and photoreceptor irregularity on OCT minimally improved (Figure 2D-F). By the 6-month follow-up, visual acuity was 20/20 OD and 20/30 OS, with almost normalized photoreceptor layer on OCT (Figure 2G).

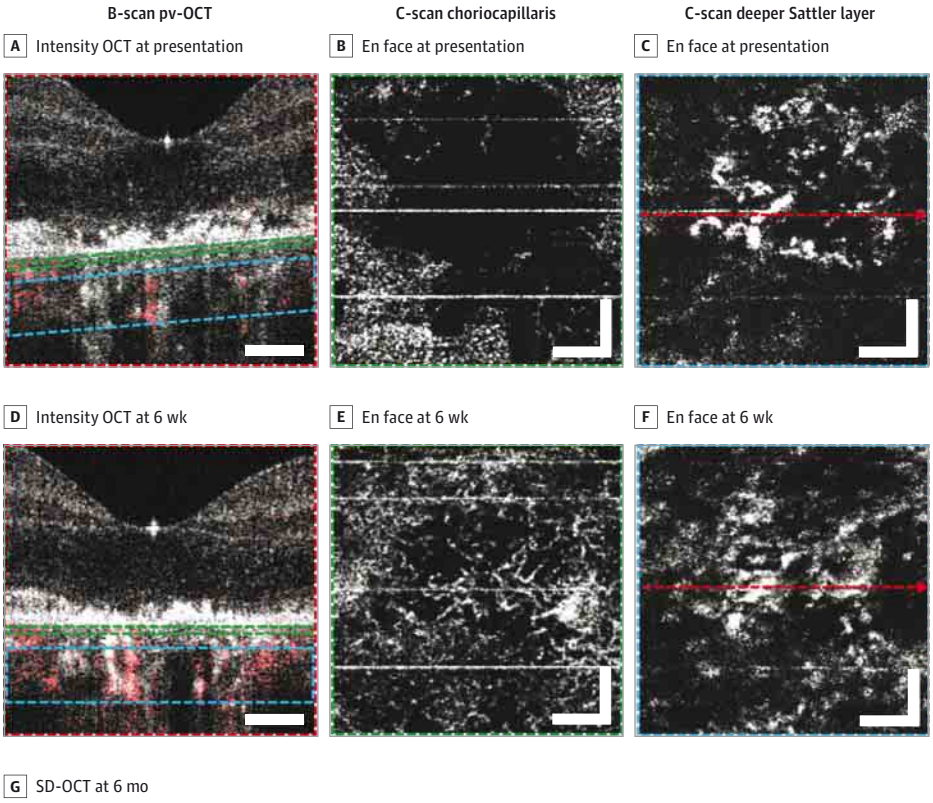
This study conforms to the World Medical Association Declaration of Helsinki[5] and subsequent amendments. The research protocol was approved by the University of California, Davis Office of Human Research.

Figure 1. Fundus Photograph and Fluorescein Angiogram of the Left Eye



At presentation, white-gray placoid lesions are seen (A), with early hypofluorescence (B) and late hyperfluorescence (C) on angiography; pigmentary changes developed by 6 weeks' follow-up (D and E).

Figure 2. Left Macula Phase-Variance Optical Coherence Tomographic Angiography (pv-OCTA)



Choroidal perfusion (red, pv signal) superimposed on intensity OCT (A and D) and en face (B, C, E, and F). The images show patchy hypoperfusion of the choriocapillaris (B, green) and Sattler layer (C, blue) at presentation, resolving at 6 weeks' follow-up (D-F). Image sizes are 1.5 mm × 1.5 mm centered in the fovea; scale bar, 500 µm). G, Spectral-domain OCT (SD-OCT) at 6 months' follow-up. I indicates inferior; N, nasal; S, superior; and T, temporal.

Discussion | Acute posterior multifocal placoid pigment epitheliopathy was first described by Gass in 1968,[1] yet the pathophysiology remains unclear because there is no histopathology of the placoid lesions.[2] During the acute phase, indocyanine green angiography shows hypofluoresence of the lesions without late hyperfluoresence and large choroidal vessels have been seen coursing through hypofluorescent areas on fluorescein angiogram and indocyanine green angiography, findings suggestive of choriocapillaris ischemia.[6]

In this case of APMPPE, serial pv-OCTA visualized the transient patchy hypoperfusion of the choriocapillaris and Sattler layer associated with acute APMPPE. These changes can be compared with published normal pv-OCTA choroidal perfusion maps.[3,4] The resolution of the choroidal hypoperfusion on pv-OCT preceded the resolution of photoreceptor abnormality on OCT and visual recovery. Thus, the pathophysiology of APMPPE likely involves a primary hypoperfusion of the inner choroid with resultant RPE and photoreceptor abnormality and vision loss. Concurrent edema or infiltration of the RPE or choroid is possible.

Perfusion images were produced by en face projection of thin slices from pv-OCTA volumetric data at 8 µm below the Bruch membrane for choriocapillaris visualization and 8 to 16 µm below the Bruch membrane for Sattler layer visualization. By using pv-OCTA signals overlaid on OCT intensity B-scan images, the corresponding retinal structural changes can be studied relative to the perfusion changes (Figure 2A). These focal changes in choroidal flow signal on pv-OCTA do not correlate with shadowing artifacts from overlying RPE changes. The focal lobular areas of choroidal hypoperfusion at the level of the choriocapillaris extend into the deeper Sattler layer and appear to correspond to the placoid lesions.

In conclusion, this case report used pv-OCTA to demonstrate transient inner choroidal flow changes associated with APMPPE.

This and similar OCTA systems can provide new insights into the pathogenesis of this condition. Future larger studies may determine whether these choroidal perfusion changes are universally observed in APMPPE and affect visual prognosis.

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Previous Presentation: This article was presented in part as a poster at the Annual Meeting of the Association for Research in Vision and Ophthalmology; May 7, 2015; Denver, Colorado.

Additional Contributions: We thank the patient for granting permission to publish this information.

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COMMENT & RESPONSE

Zika Virus, Microcephaly, and Ocular Findings

To the Editor We read with great interest the article "Ocular Findings in Infants With Microcephaly Associated With Presumed Zika Virus Congenital Infection in Salvador, Brazil" by de Paula Freitas et al[1] as well as the accompanying Invited Commentary "Zika Virus Infection and the Eye" by Jampol and Goldstein.[2] The authors are to be complimented for addressing the ophthalmologic need and building on their previous report of ophthalmic findings associated with Zika virus (ZIKV) in 3 infants.[3]

The authors in all 3 publications postulate direct ZIKV-induced ocular findings. However, it remains unclear whether the ocular lesions described in these reports are a direct result of ZIKV or a result of microcephaly itself. For 50 years, there has been well-documented history (beginning in this very journal)[4] of both sporadic and heritable (autosomal recessive and autosomal dominant) forms of microcephaly associated with ocular findings similar to those recently attributed to ZIKV infection[1-3]: pigmentary maculopathy, circumscribed chorioretinal atrophy, and optic nerve abnormalities.[4,5] In addition, microcephaly has been associated with microcornea, microphthalmia, falciform folds, cataracts, retinal dysplasia, persistent fetal vasculature, vascular attenuation, nystagmus, and hyperopia,[4,5] and we might expect other findings as the ZIKV epidemic unfolds.

Based on the consistency of the findings here with those previously reported, it is possible that ocular findings described as a direct result of the ZIKV infection may be secondary to the microcephaly.[1-3] It seems plausible that there could be a dual-mechanism process at work in these patients: microcephaly (secondary to ZIKV)–associated ocular abnormalities as well as directly induced ZIKV ocular abnormalities. We look forward to learning more about this potential dual mechanism as we gain additional experience with patients with ZIKV.

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