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En Face Optical Coherence Tomography and Optical Coherence Tomography Angiography for the Diagnosis and Monitoring of Syphilitic Posterior Placoid Chorioretinopathy

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Abstract

Purpose: To describe a case of syphilitic posterior placoid chorioretinopathy, a rare ocular manifestation of syphilis requiring prompt diagnosis and treatment. **Methods:** A single case was evaluated. **Results:** Multimodal imaging including spectral-domain optical coherence tomography (SD-OCT), en face OCT, and OCT angiography (OCTA), were used to confirm a diagnosis in a patient presenting with symptoms of syphilitic posterior placoid chorioretinopathy. SD-OCT showed nodular hyperreflective thickening of the retinal pigment epithelium (RPE), an attenuated ellipsoid zone, loss of the outer segment/RPE junction, and trace hyperreflective vitreous material. En face OCT showed hyperreflective lesions at the avascular complex layer, and flow voids suggestive of nonperfusion within the choriocapillaris were seen on OCTA. SD-OCT showed resolution of disease after 1 week of treatment with penicillin, but en face OCT and OCTA findings persisted for 1 month before finally resolving. **Conclusions:** En face OCT and OCTA enable the early detection of placoid lesions and microvascular changes commonly seen in syphilitic posterior placoid chorioretinopathy, allowing for the development of an appropriate treatment plan.

Keywords

syphilitic posterior placoid chorioretinopathy, optical coherence tomography angiography, monitoring, treatment, en face

Introduction

From 2000 to 2023, the incidence of primary and secondary syphilis cases in the United States dramatically increased approximately 10-fold, from 5,973 cases in 2000 to 59,016 cases in 2023.[1] Ocular manifestations of syphilis are relatively rare, occurring in approximately 10% of cases of secondary syphilis.[2] Posterior uveitis is the most common diagnosis in HIV-negative patients, whereas panuveitis is the most common clinical manifestation found in patients coinfected with HIV.[3] Among the posterior segment manifestations, syphilitic posterior placoid chorioretinopathy is an uncommon presentation, characterized in 1990 by Gass et al[4] as the presence of more than 1 placoid yellowish lesion involving the posterior pole of the retina. Treatment with intravenous penicillin G generally results in improvement in visual acuity (VA). Left untreated, however, syphilitic posterior placoid chorioretinopathy can lead to irreversible vision loss.

Its clinical resemblance to other posterior segment diseases, including acute posterior multifocal placoid pigment epitheliopathy, serpiginous choroiditis, and viral retinitis, makes the diagnosis of syphilitic posterior placoid chorioretinopathy challenging. Fluorescein angiography (FA) of the retina and choroidal vasculature may show late-phase hyperfluorescent lesions, hypocyanesence attributable to nonperfusion within the choriocapillaris may be seen with indocyanine green angiography (ICGA), and fundus autofluorescence (FAF) may show hyperautofluorescence resulting from the loss of photoreceptors at the outer retina.[5]

Spectral-domain optical coherence tomography (SD-OCT) is among the least invasive and most useful form of imaging for

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the evaluation of syphilitic posterior placoid chorioretinopathy, the features of which include disruption of the inner segment/outer segment junction, nodular hyperreflective thickening of the retinal pigment epithelium (RPE), loss of the linear outer segment/RPE junction and, in some cases, loss of the external limiting membrane, subretinal fluid, and punctate hyperreflectivity within the choroid.[6,7] With treatment, these changes, including those to the ellipsoid zone (EZ) and elevated hyperreflective lesions in the outer retina and RPE, are shown to be reversible.[7]

Traditional imaging modalities such as fundus photography, FA, ICGA, and SD-OCT have been instrumental in the evaluation of syphilitic posterior placoid chorioretinopathy, but their ability to provide sufficient depth and detail of the retinal and choroidal vasculature may be insufficient. Because it is thought that syphilitic posterior placoid chorioretinopathy lesions develop as a result of inflammation at the level of the choriocapillaris, OCT angiography (OCTA), which allows for high-resolution noninvasive visualization of the retinal and choroidal vasculature, plays a crucial role in diagnosis and treatment monitoring.[8] By selectively imaging blood flow within specific retinal layers, OCTA provides detailed information about the microvascular architecture and perfusion status of the retina and choroid, allowing a deeper imaging of the capillary plexi compared with SD-OCT.

En face imaging obtained with OCTA is used to visualize deeper retinal pathology.[9] In patients presenting with symptoms of syphilitic posterior placoid chorioretinopathy, flow voids indicating areas of hypoperfusion that correspond to placoid lesions can be identified.[10] Previous case reports[5,10] have described the persistence of these hypoperfusion defects at the level of the choriocapillaris, lasting from 3 months up to 10 months after treatment, despite an improvement in VA and resolution of SD-OCT findings.

To our knowledge, there have been no reports showing changes on OCTA with close serial monitoring. We present a patient being treated for syphilitic posterior placoid chorioretinopathy in whom OCT and OCTA were used to closely monitor their progress.

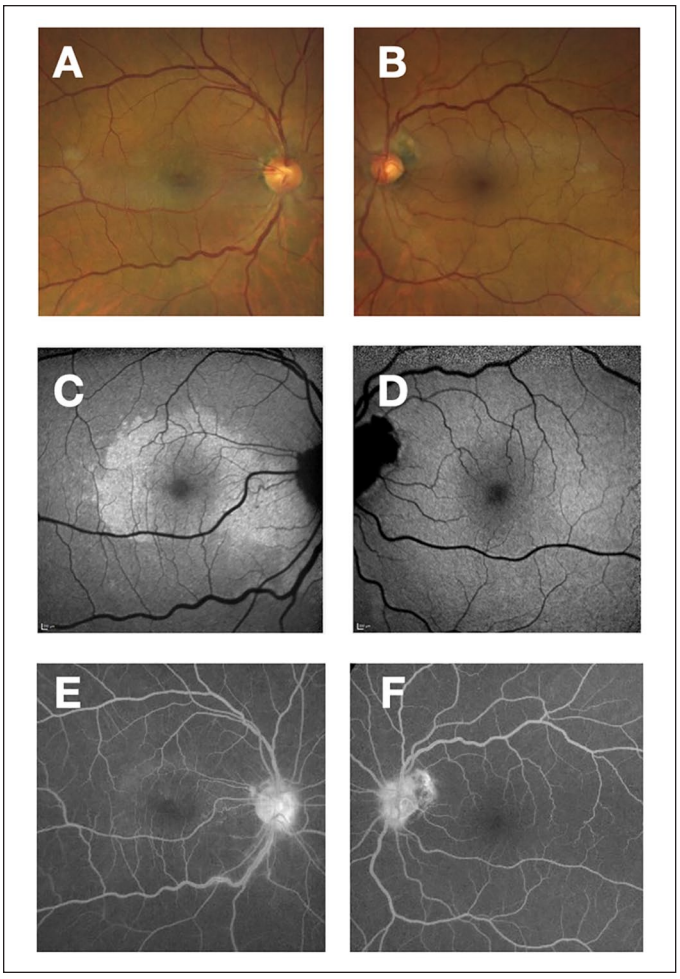

Figure 1. Color fundus photograph of the right (A) and left (B) eye. A. Multiple punctate yellow-white lesions were scattered within the macula. Fundus autofluorescence of the right (C) and left (D) eye. C. Hyperautofluorescence was noted circumferentially within the parafovea in a ring-like pattern with extension into the perifovea. Fluorescein angiogram, late phase of the right (E) and left (F) eye. E. Hyperfluorescent staining of the optic disc and circumferential staining around the fovea was evident; engorgement, staining, and leakage were also noted from the proximal segment of the inferior retinal vein.

Case Report

A 65-year-old man presented with blurring in the central vision of his right eye for 1 day and no systemic symptoms. The VA was 20/20 OS and 20/30 OD, which he patient described as "looking through gray." A slitlamp examination and entrance testing were otherwise unremarkable. On funduscopic examination, multiple faint white-yellow chorioretinal lesions were found unilaterally throughout the macula of the right eye while the macula of the left eye was unremarkable. FAF showed a ring of hyperautofluorescence within the parafovea of the right eye, and late-phase FA revealed optic disc staining and subtle circumferential staining of the parafovea, along with staining of an inferior retinal vein originating at the disc, in addition to late-phase leakage within the macula (Figure 1, A–F).

SD-OCT scans (Spectralis, Heidelberg Engineering) of the right eye showed nodular hyperreflective thickening of the RPE paracentrally, attenuation of the EZ, loss of a clear outer segment/RPE junction, and trace hyperreflective material in the vitreous. En face OCT of the right eye revealed multiple discrete hyperreflective lesions at the level of the avascular complex, and en face OCTA showed flow voids, or areas of nonperfusion, at the level of the choriocapillaris that were more pronounced in the right eye (Figure 2, A–J).

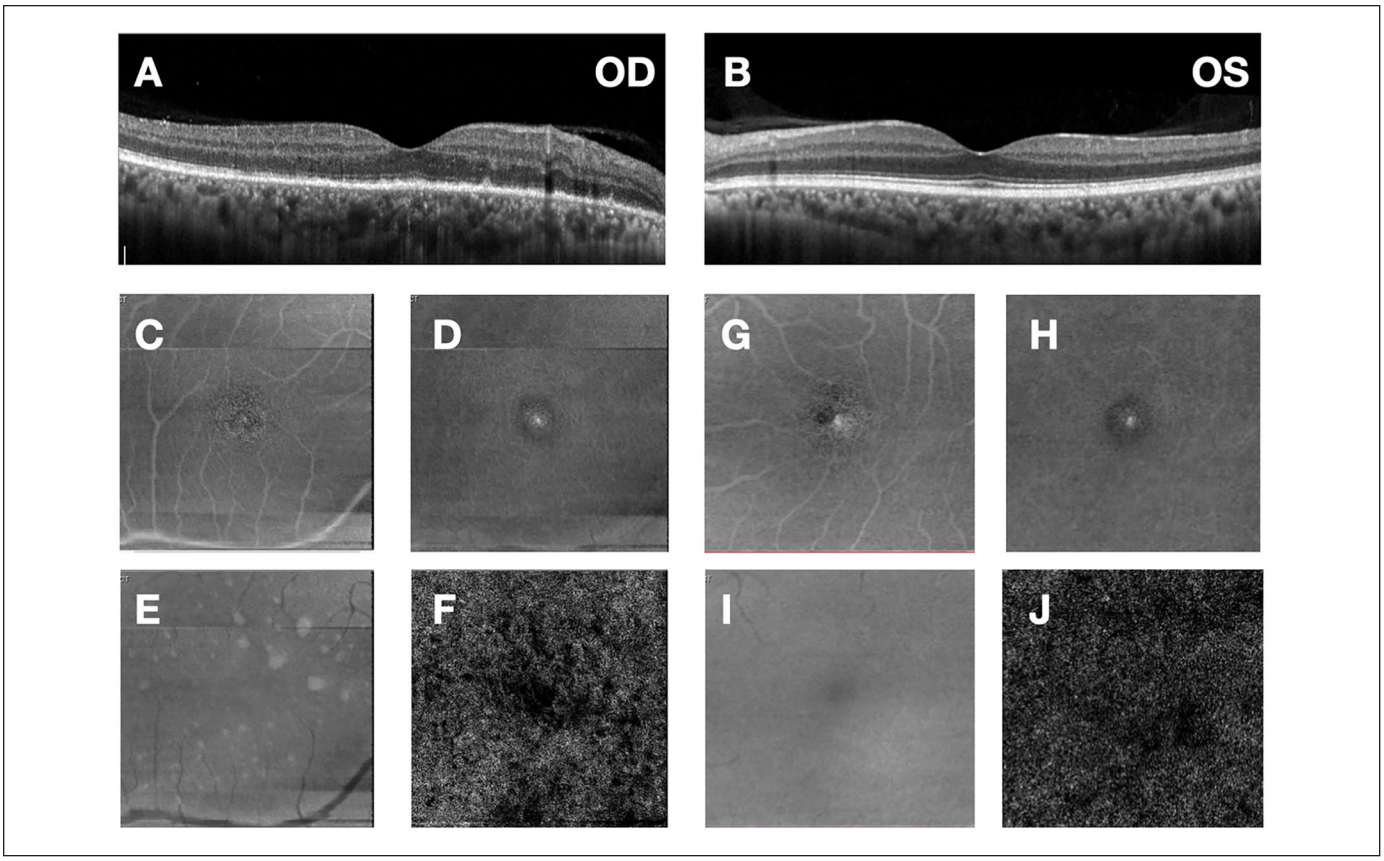

Figure 2. SD-OCT scans showing nodular hyperreflective changes of the RPE, loss of a clear outer segment/RPE junction, attenuation of the ellipsoid zone, and trace hyperreflective material in the vitreous OD (A) compared to a relatively normal macula OS (B). En face OCT images at the level of the superficial vascular plexus (C, G), deep vascular plexus (D, H), and avascular complex (E, I) layers for OD and OS, respectively. E. Multiple discrete hyperreflective lesions at the level of the avascular complex noted OD. En face OCTA at the level of the choriocapillaris (F, J) of OD and OS, respectively. F. Scattered flow voids were appreciated within the choriorcapillaris in areas corresponding to the overlying fovea and parafovea OD compared to the patient's OS.

The patient was found to be positive for *Treponema* antibodies on fluorescent treponemal antibody absorption tests but negative for *Treponema* antibodies by rapid plasma reagin. With guidance from our infectious diseases specialists, the patient was subsequently admitted for treatment with intravenous penicillin G (4 million units) every 4 hours for a total of 10 days.

On day 3 of treatment, SD-OCT showed improvement in the nodularity of the RPE and restoration of the outer segment/RPE junction. By day 7, the changes detected by SD-OCT had completely resolved in the right eye, and the previously attenuated EZ appeared intact (Figure 3, A–D). Throughout treatment, slow improvement of the hyperreflective lesions in the right eye was seen on en face OCT at the level of the avascular complex. Nineteen days after beginning treatment, a few lesions remained. At day 33 (23 days after completing treatment), the lesions had resolved (Figure 4, A–H). In addition, the flow voids seen on en face OCTA within the choriocapillaris were slowly improving, with near-complete resolution of the perfusion deficits in the right eye (Figure 5, A–E). At the patient's first follow-up visit after finishing treatment, the VA had returned to 20/20 OD, with a fundus examination showing complete resolution of the visible lesions.

Conclusions

With early diagnosis and treatment, syphilitic posterior placoid chorioretinopathy has an excellent functional prognosis. Thus far, traditional multimodal imaging has provided clinicians with several ways of differentiating the disease from similarly appearing posterior segment lesions. However, there are limitations to several of these techniques. In particular, FA and ICGA are invasive, time consuming, and do not easily provide detailed analysis of the individual deep vascular layers of the retina. In light of these limitations, noninvasive imaging modalities such as en face OCT and OCTA could aid in the early diagnosis of syphilitic posterior placoid

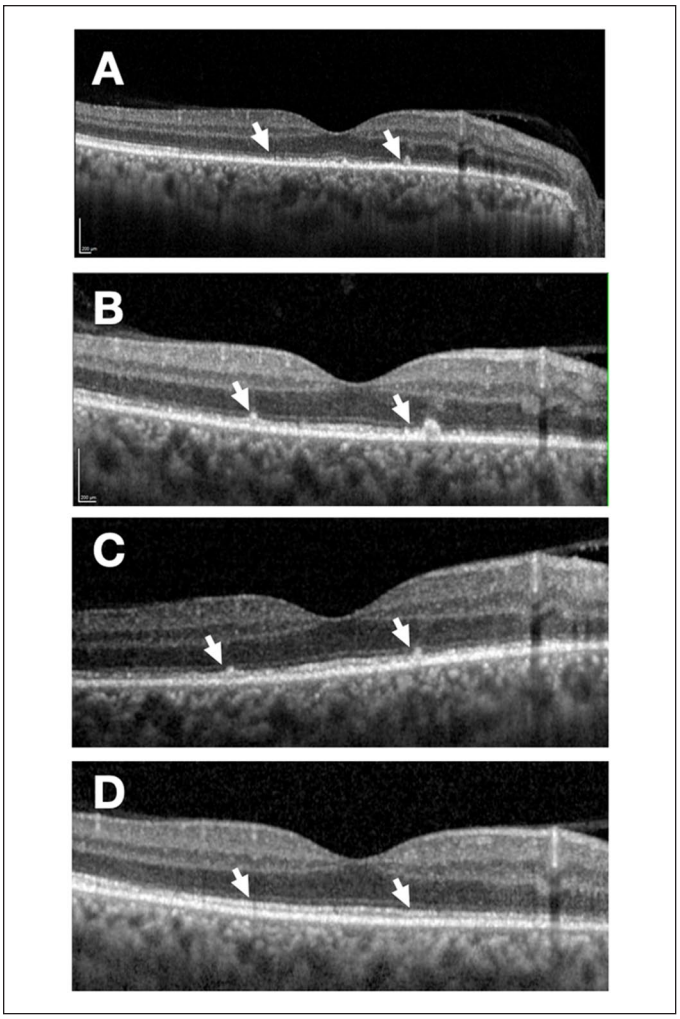

Figure 3. SD-OCT images of the right eye showing hyperreflective nodularity at the level of the RPE (arrows) and loss of outer segment/RPE junction before treatment with IV penicillin (A), at day 1 after treatment (B), day 3 after treatment (C), and day 7 after treatment (D). C. Improvement in the RPE nodularity (arrows) and restoration of the outer segment/RPE junction at day 3 after treatment. D. Resolution of the RPE, photoreceptor outer segment, and ellipsoid zone laminations was observed at day 7 after treatment with IV penicillin therapy.

chorioretinopathy. In our patient, the SD-OCT findings of attenuated EZ, nodular hyperreflective thickening of the RPE, and loss of the outer segment/RPE junction were consistent with previously described cases.[6,10] Gass et al[4] proposed that inflammatory changes or immune complex dysfunction at the level of the choroid–RPE–photoreceptor complex were responsible for the pathophysiology of syphilitic posterior placoid chorioretinopathy. Neri and Pichi[11] speculated that these hyperreflective spots may represent changes to RPE metabolism as the result of focal areas of inflammation-related choroidal occlusions.

To our knowledge, there is only 1 other documented case in which hyperreflective lesions at the level of the avascular complex have been seen on en face OCT. Moll-Udina et al[10] noted hyperreflective dots at the level of the ellipsoid layer that resolved in 14 days. However, the lesions noted in their patient appeared more granular than those in our patient, and their study assessed only 2 timepoints. The macular placoid lesions steadily improved over 33 days, and the resolution of clinical findings on fundus examination and on multimodal imaging ultimately correlated with visual improvement. These lesions potentially corresponded to the same areas of nodular RPE thickening seen on cross-sectional SD-OCT, but this is unlikely because the nodularity on SD-OCT resolved by day 7 after beginning treatment, whereas the avascular complex lesions in our patient persisted. More studies are needed to determine whether these avascular complex lesions are consistently found across cases of syphilitic posterior placoid chorioretinopathy. If so, they could be a useful marker of disease progression and treatment efficacy.

Because choroidal perfusion deficits are thought to be influenced by the pathophysiology of syphilitic posterior placoid chorioretinopathy, en face OCTA may play a substantial role in diagnosis and treatment monitoring. Our patient presented with a central area of nonperfusion at the level of the choriocapillaris in both eyes that was seen on en face OCTA. This deficit was fully resolved in the right eye after 1 month of treatment, and improvement was also seen in the left eye. A similar perfusion deficit of the choriocapillaris was noted in the case reported by Moll-Udina et al.[10] Still, that defect persisted at 3 months' follow-up, which the authors suspected may be attributed to an initial choriocapillaris infarction. This explanation more than likely describes a pathophysiologic feature of this disease that causes asymmetric differences in perfusion, as seen in our patient. Localized inflammation from circulating *Treponema pallidum* could also lead to small vaso-occlusive events.

Serial OCTA scans enable documentation of changes in the size of avascular complex lesions and perfusion at the choriocapillaris over time, providing valuable insights into the efficacy of treatment modalities such as systemic antibiotics and corticosteroids. Residual inflammatory activity or secondary complications such as choroidal neovascularization can also be identified, necessitating adjunctive therapy or closer follow-up.

Limitations of OCTA for the evaluation of syphilitic posterior placoid chorioretinopathy include software-related retinal segmentation deviation, anatomic-related and motion-related image artifacts, and the inability to visualize deeper choroidal vessels. En face OCT and OCTA represent valuable adjunctive tools to enable early detection of placoid lesions and microvascular changes associated with syphilitic posterior placoid chorioretinopathy. Future studies incorporating multimodal imaging approaches and quantitative analysis techniques will further enhance the diagnostic accuracy and prognostic value of OCTA.

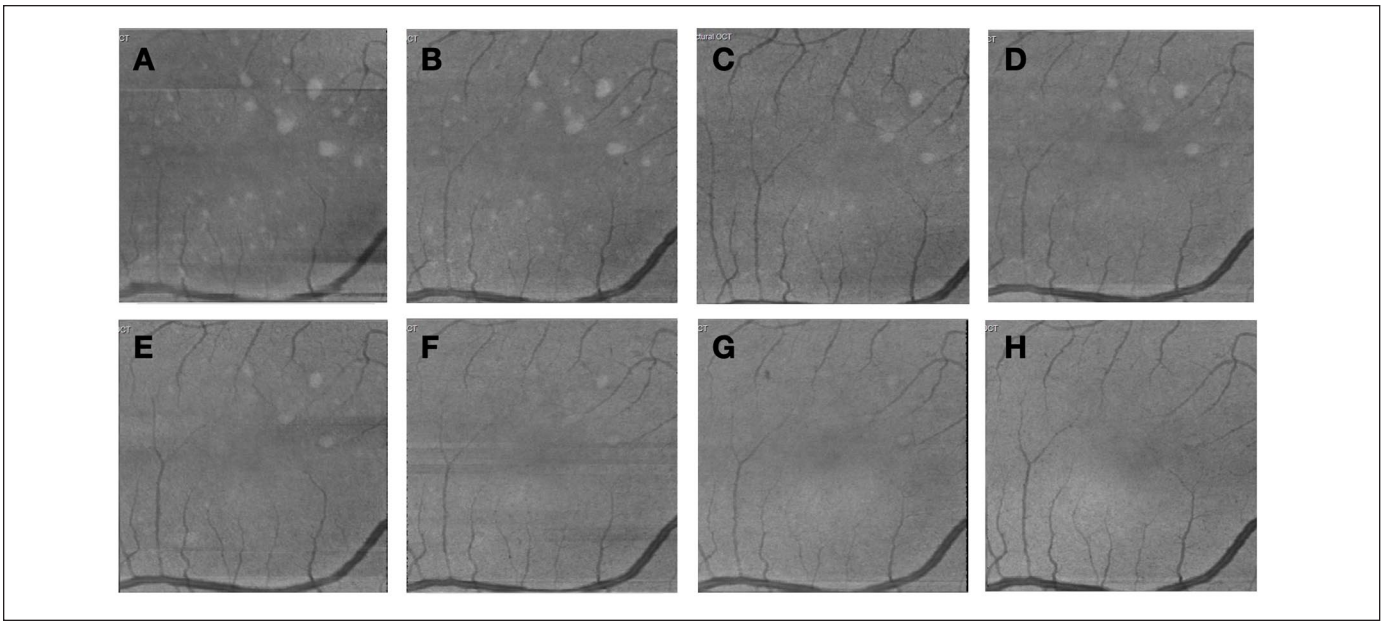

Figure 4. Near-infrared en face OCT fundus images of the right eye demonstrating multiple hyperreflective lesions at the level of the avascular complex before treatment with IV penicillin (A), at day 1 after treatment (B), day 3 after treatment (C), day 5 after treatment (D), day 7 after treatment (E), day 12 after treatment (F), day 19 after treatment (G), and day 33 after treatment (H). H. Resolution of the hyperreflective lesions at day 33 after treatment with IV penicillin.

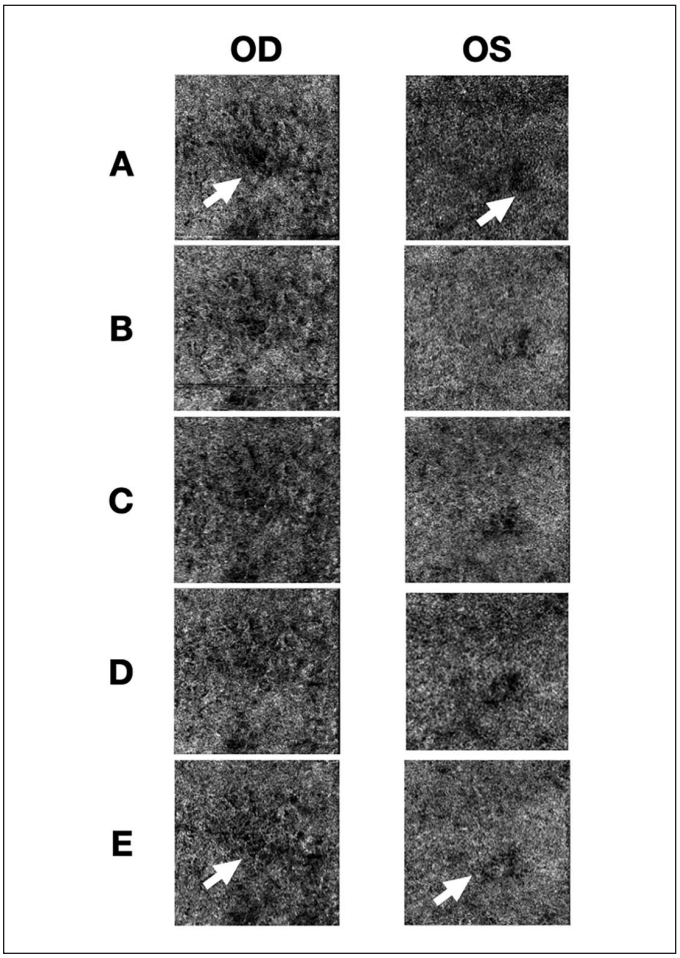

Figure 5. (continued)

Figure 5. Longitudinal changes in flow voids seen on OCTA showing gradual improvement with resolution of flow voids developing concurrent to parental Penicillin use. Flow voids, OD more pronounced than OS seen in figure A, gradually resolve over 33 days. En face OCTA images of both eyes at the level of the choriocapillaris demonstrating flow voids (arrows) suggestive of non-perfusion before treatment with IV penicillin (A), at day 7 after treatment (B), day 12 after treatment (C), day 19 after treatment (D), and day 33 after treatment (E).

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Statement of Informed Consent

The patient provided verbal informed consent to publication of the case.

Declaration of Conflicting Interests

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