



Swept source OCTA reveals a link between choriocapillaris blood flow and vision loss in a case of tubercular serpiginous-like choroiditis

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ABSTRACT

Optical coherence tomography angiography (OCTA) is a non-invasive technique that is useful in the diagnosis and management of patients with posterior uveitis. Here we report the use of swept source OCTA (SS-OCTA) in a patient with tuberculosis (TB) associated serpiginous like choroiditis (TB-SLC) that made a full visual recovery following treatment with ATT, local and systemic corticosteroids, and systemic immune modulation. By comparing *en face* images of choriocapillaris (CC) blood flow before and after treatment, we conclude that the patient's visual recovery was associated with resolution of extensive CC flow deficits. This case highlights the utility of SS-OCTA in the multimodal evaluation of patients with choroidal inflammation, and the potential for good visual recovery in patients treated for TB-SLC.

1. Introduction

Tuberculosis (TB) associated serpiginous like choroiditis (TB-SLC) is a variant of serpiginous choroiditis (SC) that is believed to result from an inflammatory reaction to TB bacilli in the retinal pigment epithelium (RPE) or choriocapillaris (CC).¹ TB-SLC is typically unilateral, and can present as a multifocal or diffuse choroiditis that is progressive and often leads to poor visual outcomes.² In addition to dilated fundus exam (DFE), indocyanine green angiography (ICGA) and fluorescein angiography (FA) have historically been the gold standard imaging studies for diagnosing and monitoring disease activity.^{3,4} However, these techniques require invasive imaging and can cause dye related adverse effects. Multimodal evaluation with non-invasive imaging techniques like optical coherence tomography (OCT) and fundus autofluorescence (FAF) have therefore become more common, and are useful in detecting disease activity.^{5,6}

Optical coherence tomography angiography (OCTA)⁷ is another new and powerful non-invasive technique for diagnosis and management of patients with choroiditis. OCTA is well suited to these diseases due to its ability to identify depth related alterations in blood flow, particularly in the CC.^{8,9} While spectral domain systems are used widely to study diseases of the retinal vasculature, swept source OCTA (SS-OCTA) is becoming the modality of choice for use in patients with choroidal

inflammatory diseases due to its longer imaging wavelength and wide-field imaging capabilities.¹⁰ Here, we present a patient with TB-SLC that had complete recovery of visual acuity in the affected eye despite extensive posterior pole scarring on DFE. Furthermore, using *en face* analysis of CC flow, we correlate his exceptional recovery with the resolution of large, multifocal, CC flow deficits in the macula.

2. Case report

A 43-year-old Indian male was referred for further management of unilateral posterior uveitis. He initially presented to his outside ophthalmologist with a 6-week history of painless, blurred vision of the left eye. Snellen visual acuity was 20/20 OD, 20/25 OS, and on exam, placoid choroidal lesions were noted in the macula. The patient was diagnosed with acute posterior multifocal placoid pigment epitheliopathy (APMPPE), and prescribed a tapering dose of oral methylprednisolone (Medrol Dosepak). Of note, this is not standard of care for the treatment of APMPPE. At his one week follow-up, visual acuity was 20/20 OD, 20/20 OS, and the original lesion was inactive with signs of early scarring and no additional treatment or work up was initiated. Three weeks later, the patient experienced recurrent vision loss in the left eye. In contrast to his first episode, he was also experiencing left eye pain and redness. Exam of the left eye revealed rare anterior chamber (AC) and

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anterior vitreous cells as well as new placoid choroidal lesions that extended beyond the macula. The right eye remained asymptomatic and no inflammation was seen on exam. Laboratory work up revealed normal studies including a complete blood count, basic metabolic panel, erythrocyte sedimentation rate, C-reactive protein, angiotensin converting enzyme, negative antinuclear antibody, and negative syphilis testing (RPR, FT-Abs). His QuantiFERON® gold test was positive and chest X-ray was negative. The patient subsequently reported a history of known latent tuberculosis infection (LTBI). He had no history of treatment for latent or active TB. The patient was started on 0.05% difluprednate (Durezol) four times daily, and referred to our uveitis service for additional evaluation and management.

The patient was otherwise healthy without any significant past ocular or medical history aside from latent TB status. He was born in India, but was currently living and working in the United States. He took no medication and had no family history of blindness or ocular diseases.

At presentation, visual acuity was 20/20 OD, 20/80 OS. Pupils were equal, round and reactive, pressure was 14 in the right eye and 17 in the left eye. Visual fields were full to confrontation in both eyes. Exam of the right eye was unremarkable without any signs of inflammation. Exam of the left eye revealed 0.5+ AC cell without flare, keratic precipitates (KP) or synechiae. Fundus exam revealed extensive serpiginoid chorioretinal lesions in the macula with extension into the periphery. Lesions demonstrated multiple levels of activity with more posterior lesions exhibiting sharper borders, hyperpigmentation, and retinal pigment epithelium (RPE) atrophy. Multiple active placoid lesions were present in the temporal periphery that were cream-colored with ill-defined borders. There was no vitritis, retinal vascular sheathing, vascular occlusion or hemorrhages.

Multimodal imaging confirmed the presence of active and inactive chorioretinal lesions throughout the posterior pole and periphery. The creamy lesions with ill-defined borders seen on DFE and pseudocolor images (Fig. 1A) corresponded with areas of early blockage and late leakage on fluorescein angiography (Fig. 1B). FAF also revealed widespread lesions with areas of hyper- and hypo-autofluorescence throughout the posterior pole (Fig. 1C). Widefield SS-OCTA was also performed, and the CC slab evaluated (Fig. 1D). Multiple flow deficits

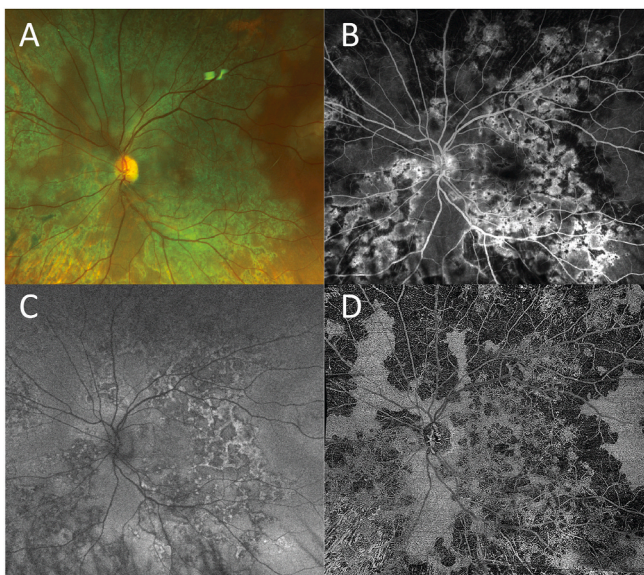


Fig. 1. Multimodal widefield imaging of active TB associated multifocal serpiginoid choroiditis.

Lesions at various stages of activity are identified at presentation on the (A) pseudo-color image photograph, (B) fluorescein angiography, (C) fundus autofluorescence, and (D) SS-OCTA En face choriocapillaris (CC) slab. Images A-C were obtained with an Optos camera. Image D was obtained using the Zeiss Plex Elite. The CC slab was defined as 16 μ m below Bruch's membrane.

throughout the macula and posterior pole were identified that corresponded with the areas of disease activity identified by the other imaging modalities.

The patient was diagnosed with TB-associated serpiginous-like chorioiditis and started on prednisone 60 mg and anti-TB therapy (ATT) with daily Rifampin 600 mg, Isoniazid 300 mg, Pyridoxine 50mg, Pyrazinamide 2g, and Levofloxacin 750mg. After quiescence of all lesions, prednisone was tapered by 10 mg per week. While on 40 mg prednisone daily, a new lesion was noted on DFE, and the patient received a periorbital injection of triamcinolone acetonide. Three weeks later, while still on 40mg prednisone, additional new lesions were noted. Prednisone was increased to 60 mg and mycophenolate mofetil therapy was initiated at 1 g twice daily. Two weeks later, all lesions were inactive and the oral prednisone taper was reinitiated.

Four months after initial presentation, the patient's vision in the left eye had improved to 20/20, the anterior chamber was quiet, and all chorioretinal lesions were inactive with sharp borders, hyperpigmentation and RPE atrophy. His medications included mycophenolate mofetil 1 gm twice daily, Isoniazid 300mg daily, Rifampin 600 mg daily, and prednisone 20 mg daily. OCT of the macula identified resolution of pigment epithelial detachments (PED) and restoration of outer retinal layers when compared to presentation (Fig. 2C and D). Repeat SS-OCTA imaging of the macula identified widespread recovery of normal CC flow when compared to presentation (Fig. 2E and F).

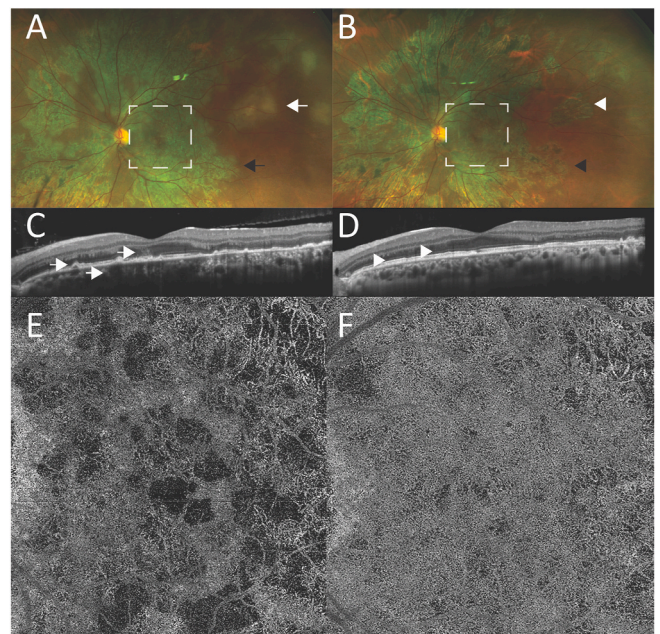


Fig. 2. Visual recovery is associated with resolution of choriocapillaris flow deficits. Pretreatment (left) and posttreatment (right) imaging. (A) Presentation Optos pseudocolor image reveals extensive scarring of the macula (white box) and active appearing choroidal lesions in the periphery. Lesions range in appearance from cream colored areas with ill-defined borders (white arrow) to well-defined serpiginoid areas of RPE atrophy (black arrow). (B) Post treatment pseudocolor image with persistent, extensive scarring of the macula (white box), and inactive peripheral lesions (arrowheads). (C) Heidelberg SD-OCT at presentation with multiple small pigment epithelial detachments (PED), outer retinal layer disruptions impacting the ellipsoid zone, external limiting membrane (ELM) and outer nuclear layers, and increased choroidal signal penetration temporal to the fovea (arrows). (D) Post-treatment SD-OCT reveals PED resolution and improved outer retinal structure (arrowheads). Focal irregularities of outer retinal disruption persist temporal to the fovea. (E) Initial en face 6 mm \times 6 mm macular SS-OCTA choriocapillaris slab depict multifocal flow deficits. (F) Post-treatment SS-OCTA reveals near complete restoration of flow deficits in the central macula. These findings were accompanied by a visual acuity of 20/20 OS at last follow up.

3. Discussion

We report a patient with TB-SLC that made a full visual recovery (20/20) following treatment with ATT, local and systemic corticosteroids, and systemic immune modulation. Due to the extent of macular disease and poor vision at presentation to our clinic (20/80), we did not anticipate this extent of visual improvement. By comparing his imaging studies at baseline to the 4-month follow up images, it is clear that recovery was associated with improved CC flow and normalization of outer retinal structure. TB-SLC is a variant of SC that involves the CC and can be just as devastating to vision and the choroid as autoimmune SC.⁴ Although the exact pathophysiology of TB-SLC is unknown, our patient's presenting imaging supports the CC as a location of significant pathology. Recent studies suggest hypoperfusion leads to the flow deficits detected on OCTA.^{9,11,12} Whether this perfusion deficit is due to vascular destruction, from physical displacement of blood flow caused by an inflammatory infiltrate, or blockage from overlying RPE or retinal inflammation remains an area of controversy and active investigation.¹ We suspect corticosteroid treatment contributed to our patient's favorable outcome, but cannot rule out the timely initiation of ATT, or a more benign natural history in TB-SLC than in autoimmune SC as contributing factors.

Reversible flow deficits have been reported previously in TB-SLC patients treated with corticosteroids, but these lesions were all located in the periphery or were reported without a link to changes in central visual acuity.^{11,12} Brar et al. reported resolution of a large CC flow deficit associated with a peripheral TB-SLC lesion that ultimately developed RPE atrophy similar to our patient despite recovery of CC flow.¹² Nagpal et al. reported on a large case series of patients with SLC that were imaged with widefield OCTA as part of their multimodal evaluation.¹¹ This study found that clinically evident choroidal lesions correlated with hypocyanescent lesions by ICGA and flow deficits by OCTA. Furthermore, following treatment, in the "healing" phase, there was evidence of flow recovery by both imaging modalities. This report focused on the concordance of the lesions identified by each imaging modality and did not report on visual outcomes associated with these changes in flow. To our knowledge, the case presented here is the first to show the association of significant visual recovery with normalization of CC flow despite widespread RPE scarring.

In contrast to TB-SLC, most cases of autoimmune serpiginous choroiditis have inflammation of the choroid that is destructive and can cause permanent loss of the CC in areas of disease activity.^{9,13} In a previous report from our group, we found that new areas of CC flow deficit are detected during a flare of SC disease activity, and that most new areas of CC flow deficit will not recover following corticosteroid treatment. However, some limited areas of the new CC flow deficit can recover flow. One predictive feature associated with CC flow recovery was the absence of hyper-autofluorescence overlying the new CC flow deficits.⁹ In this prior report, the correlated OCTA and FAF findings were not present in foveal lesions so they could not be correlated directly with visual recovery, but outer retinal layers were preserved, suggesting functional potential had been maintained. In the TB-SLC patient described here, the fovea and central macula did not demonstrate hyper-autofluorescence at presentation. His ultimate recovery of vision suggests that like in patients with SC, the combination of OCTA and FAF may help predict patients with the potential for CC flow recovery and better visual outcomes. Additional cases will be needed to determine if this finding is generalizable to other TB-SLC patients, and whether or not detecting CC flow deficits prior to development of FAF lesions identifies the window of opportunity for where and when therapy will be most effective.

One observation about the current case is that we were able to demonstrate recovery of CC flow in a manner reminiscent of reports in patients with APMPE.¹⁴⁻¹⁶ Macular lesions associated with APMPE, which usually portends better visual recovery than SC, have also been shown to demonstrate reversible CC flow loss that correlated with active

disease and visual acuity.¹⁴ Burke et al. showed that in active APMPE, CC flow deficits by OCTA were equivalent to the lesions noted by ICGA and FA. Furthermore, the pathology detected by OCTA and angiography preceded changes visualized on FAF or SD-OCT. During resolution of the flare, OCTA documented reperfusion of the CC.¹⁵ However, CC flow restoration in APMPE lesions is not guaranteed, as some healed lesions have demonstrated persistent flow loss.¹⁶ While it is unknown what factors lead to permanent versus temporary changes in CC perfusion, to what extent these acute changes are reversible, and if reversal of the CC flow deficits with corticosteroid therapy would reliably provide visual recovery, it is reasonable to postulate that the combination of OCTA and FAF may also be helpful in predicting recovery in these patients.

OCTA is a newer diagnostic tool that is becoming a valuable adjunct for posterior uveitis workup due to its ability to detect flow changes within the choroidal microvasculature in a more nuanced way than dye based imaging. Swept source systems may also be helpful in providing information about structural changes in choroidal inflammatory diseases that previously required enhanced depth imaging techniques on spectral domain systems.¹⁷ Both OCTA and FAF have a role in detecting active choroidal lesions, and provide important complementary information to ICGA.^{1,12} Limitations of OCTA in patients with uveitis can include reduction in image quality by media opacity from vitritis or cataract.⁸ Additionally, OCTA cannot detect areas of vascular leakage. It is therefore important to utilize OCTA images in conjunction with other imaging modalities, especially at presentation. However, for select cases such as the TB-SLC patient presented here, OCTA may be an acceptable option for longitudinal monitoring without the need for repeat fluorescein angiography.

In conclusion, we highlight the utility of SS-OCTA for posterior uveitis cases by correlating restoration of CC flow and visual recovery in our patient. This is the first TB-SLC case to our knowledge that associates visual recovery with CC normalization. Continued use of OCTA in SLC and other inflammatory diseases of the choroid will help clarify the relationship between uveitis etiology and the predictive capacity of OCTA on the potential for flow deficit recovery with treatment.

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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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Declaration of competing interest

There are no conflicts of interest related to this manuscript.

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