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Multimodal Evaluation of Presumed Tuberculous Serpiginous-like Choroiditis

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Key words: presumed tuberculous serpiginous-like choroiditis, optical coherence tomography
angiography, multimodal imaging, fundus autofluorescence, uveitis, swept-source optical
coherence tomography.

Abstract

Purpose: To evaluate multimodal imaging findings in longitudinal follow-up of a patient with presumed tuberculous serpiginous-like choroiditis (TB-SLC).

Method: We evaluated multimodal imaging in a 62-year-old male with TB-SLC. Correlation between optical coherence tomography angiography (OCTA), swept-source OCT (SS-OCT) and fundus autofluorescence (FAF) at defined disease stages and evolution of observed imaging descriptors during long-term follow-up has not been previously reported.

Results: OCTA of the active lesion demonstrated defined areas of choriocapillaris hypoperfusion, suggesting inflammatory vascular occlusive pathology. Over 9-month follow-up, OCTA illustrated sequential improvement in choriocapillaris flow, suggesting vascular remodelling. This correlated with progressive change in FAF signal and transition to diffuse hypoautofluorescence. SS-OCT demonstrated focal choroidal thickening and retinal pigment epithelium elevation in acute phase and resolution in time.

Conclusion: Multimodal imaging, particularly novel non-invasive technologies such as OCTA and SS-OCT, improves our understanding of the pathogenesis and evolution of disease in TB-SLC.

Introduction

Serpiginous choroiditis (SC) is a rare chronic idiopathic inflammatory condition characterised by a geographic lesion pattern with intermittent centrifugal spread with an advancing active edge. Tuberculous choroiditis simulating SC is now recognised as a distinct clinical entity known as tuberculous serpiginous like choroiditis (TB-SLC).¹⁻⁴ Fundus fluorescein angiography (FFA) and indocyanine green angiography (ICGA) are well-established for in part assessing the retina and choroid in TB-SLC and defining active disease. Fundus autofluorescence (FAF) classified disease stages and enhanced depth imaging optical coherence tomography (EDI-OCT) signs have been described.⁵⁻⁷ OCT angiography (OCTA) technology provides non-invasive vascular imaging at specific depths including the retina plexus and choriocapillaris. The role of OCTA in long-term follow-up of TB-SLC has not been previously evaluated. We report a case of TB-SLC and evolution of multimodal imaging findings, including swept-source OCT (SS-OCT) and SS-OCTA, at sequential disease stages.

Case Report

A 62 year-old Caucasian male presented with a 6-week history of photopsia and scotoma in his right eye. Best-corrected visual acuity was 0.0 LogMAR in both eyes. The left eye was normal. In the right eye a creamy yellow serpiginous-like subretinal lesion was seen in the nasal peripapillary region contiguous with the optic disc (Figure 1A). The superior aspect of the lesion was defined with a light surrounding border; the inferior portion demonstrated an ill-defined edge and oedematous appearance, indicating active disease and centrifugal extension.

Multimodal imaging demonstrated active disease (Figures 1-3). FAF revealed a hyperautofluorescent lesion with rapid progression and contiguous extension from imaging

performed in a different centre 4 weeks earlier (Figure 2A and B, Spectralis® Heidelberg Engineering, Heidelberg, Germany). Surrounding ill-defined hyperautofluorescence was evident (Figure 2A); this persisted at the active inferior edge but became a thin defined border of hypoautofluorescence around the rest of the lesion at 1 month (Figure 2B) suggesting transition towards inactivity. Fundus fluorescein angiography (FFA) and ICG delineated the lesion and different disease stages within it: in the inferior portion early FFA hypofluorescence was followed by late leakage indicating active disease contrasted by hypofluorescence and subsequently a bright hyperfluorescent edge around the rest of the lesion suggesting transition to less active disease (Figure 3C-F).

Swept-source OCT (SS-OCT) (Triton®, Topcon Corporation, Tokyo, Japan) at the active edge illustrated hyper-reflectivity of the ellipsoid zone (EZ), retinal pigment epithelium (RPE) elevation and focal choroidal thickening (Figure 4A). Within areas of scarring, irregularity of EZ, hyper-reflectivities within the RPE, choroidal attenuation and outer retinal atrophy were observed (Figure 5A). SS-OCTA (Triton®) segmentation images demonstrated disrupted choriocapillaris vascular flow and hypoperfusion within the lesion corresponding with hypocyanescent areas on ICGA. (Figure 6A and B) The deep and superficial vascular plexus flow was normal.

Uveitis investigations were negative except for positive QuantiFERON®-TB Gold and tuberculin skin test (12mm induration). The patient received anti-tuberculous therapy (ATT) for 6-months alongside corticosteroid therapy (starting dose 80mg/day) tapered with clinical response.

Over 9 months the lesions gradually became inactive: FAF demonstrated transition to an inactive hypoautofluorescent lesion (Figure 2C-F); SS-OCT within the active area showed resolution of RPE elevation, outer retinal atrophy and some restoration of outer retinal

structures (Figure 4); OCTA revealed progressive improvement in choriocapillaris flow and reduction in the size of the hypoperfusion areas suggestive of vascular reperfusion and remodeling (Figure 6). The macula was spared, symptomatic improvement was reported and excellent visual acuity maintained.

Discussion

Optical coherence tomography angiography (OCTA) is an emerging technology in the study of inflammatory choriocapillaris diseases; it provides high-resolution structural information at defined levels including the choriocapillaris, which may not be detectable on FFA or ICGA. In TB-SLC, previous publications have described choriocapillaris hypoperfusion within choroiditis lesions using OCTA at single time points,^{7,8} and correlated with enhanced depth imaging OCT (EDI-OCT) structural change.^{6,7} Evidence on OCTA of paradoxical worsening of choriocapillaris hypoperfusion following initiation of anti-tuberculous therapy in 5 patients has been reported.⁹ Early OCTA detection of secondary choroidal neovascular membrane (CNVM) is also described.⁸ Our case illustrated the use of OCTA for longitudinal choriocapillaris flow evaluation, which has not been previously reported.

Four disease stages, characterised by FAF, have been described in TB-SLC - stage 1 (active): diffuse hyperautofluorescence with an ill-defined hyperautofluorescent halo; stage 2 (subacute): defined surrounding edge of hypoautofluorescence; stage 3: predominant hypoautofluorescence with stippled pattern and stage 4 (inactive): uniform hypoautofluorescence.⁵ We studied SS-OCT, FAF and SS-OCTA during transition through all disease stages. The correlation of these modalities at sequential disease stages, during transition to inactive disease, has not been previously detailed. Progressive restoration of choroidal circulation, with reduction of the lesion size and reduction in hypoperfusion was seen on OCTA, suggesting vascular remodeling during the recovery phase. The

choriocapillaris flow appeared to progressively restore centrally from the lesion edges. This correlated with progressive change in FAF signal and transition to diffuse hypoautofluorescence. At the last follow-up, persistent choriocapillaris flow abnormality was evident and it is uncertain if the flow morphology will normalise with longer follow-up. Interestingly in acute posterior multifocal placoid pigment epitheliopathy, choriocapillaris healing is reported to lag behind resolution of outer-retinal morphological changes;¹⁰ and a similar evolution may be observed in TB-SLC. Certainly, SS-OCT morphological abnormalities including RPE elevation and hyper-reflectivity in the outer retina have evolved within the active lesion ahead of full restoration of choriocapillaris flow.

Enhanced depth imaging (EDI-OCT), using spectral domain OCT for detailed choroidal imaging, has been detailed in this condition.^{6,7} Rifkin et al demonstrated infiltration of the choroid, elevation of RPE and focal choroidal thickening in the active lesion of TB-SLC using EDI-OCT.⁶ We evaluated SS-OCT and found consistent imaging descriptors with focal choroidal thickening and RPE elevation in acute phase and resolution in time. These EDI-OCT features have not been reported in SC and may help differentiate infective SLC from SC.⁶ In a previous study, OCTA in the acute disease phase (stage 1 FAF lesions), areas of reduced choriocapillaris flow within lesions correlated with reduced signal transmission on EDI-OCT and the authors inferred that the observed flow void may be because of a shadowing effect from hyper-reflective overlying retina.⁷ In our patient, we correlated OCTA with SS-OCT at the active edge; hyper-reflective outer retinal changes were observed but there was no loss of SS-OCT signal transmission and we believe this demonstrates true hypoperfusion.

These modalities, used in combination, provide valuable imaging markers of clinical activity and disease evolution with the advantage of being non-invasive and readily repeatable during follow up. Further studies to correlate structural change with function, quantitative analysis of hypoperfusion and response to treatment are necessary.

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Figure Legends

Figure 1: Fundus photographs of a serpiginous-like choroiditis lesion contiguous with the optic disc. (A) At 1 month the lesion has a light defined surrounding border (marked with arrow). The inferior portion of the lesion is active with less well-defined borders and active choroiditis (marked with *) representing contiguous extension. Progressive scarring is evident during follow-up with no lesion extension at (B) 3 months; (C) 5 months (D); 6 months and (E) 9 months. The border has faded and progressive atrophy is observed. The green arrows delineate the orientation of swept-source optical coherence tomography (Figures 4 and 5).

Figure 2: Evolution of fundus autofluorescence over 9 months, from active progressive disease to inactive state. The lesion was classified according to the pattern of autofluorescence.⁵ (A) Baseline. Stage 1 ‘acute’ lesion: defined, diffusely hyperautofluorescent lesion with surrounding ill-defined hyperautofluorescence. (B) 1 month. Stage 1-2 lesion: contiguous serpiginous-like extension compared to (A); the inferior area has persistent hyperautofluorescence and an ill-defined hyperautofluorescent border (short arrows), indicating stage 1 active disease; a hypoautofluorescent thin border has evolved around the rest of the lesion (arrow heads), a defining feature of transition to stage 2 ‘subacute’ disease. (C) 3 months and (D) 5 months: progressive transformation, with stippled

autofluorescence pattern and no lesion extension. (E) 8 months. Stage 3 lesion: predominantly hypoautofluorescent lesion. (F) 9 months. Evolution towards stage 4, inactive lesion, with transformation to uniform hypoautofluorescence within the lesion.

Figure 3: Multimodal imaging of the right eye. (A) Red-free imaging delineates hyper-reflective choroiditis lesion. The inferior active edge is less well-defined than the remaining border. (B) Fundus autofluorescence (FAF) image (see Figure 2B legend). (C), (D) Fundus fluorescein angiography demonstrates different disease stages within the lesion: the active inferior aspect shows early hypofluorescence due to blockage and progressive diffuse staining and leakage indicative of active disease (marked with *) and the rest of the lesion showed hypofluorescence and later edge hyperfluorescence (marked with an arrow) correlating with the hypoautofluorescent thin border seen on FAF. (E and F) Early and late indocyanine green angiography hypocyanescence was present, indicating choroidal disease.

Figure 4: Swept-source optical coherence tomography (SS-OCT) images orientated as per Figure 1B at the active lesion edge. (A) At 1 month, SS-OCT within the advancing active area showed retinal pigment epithelium (RPE) elevation (arrow head), hyper-reflectivity of ellipsoid zone (arrow) (EZ) and choroidal thickening. (B) At 3 months, SS-OCT showed resolution of RPE elevation, persistent focal ellipsoid zone (EZ) hyper-reflectivity and atrophy of the outer retina layers. (C) At 9 months, SS-OCT revealed resolution of EZ hyper-reflectivity and partial restoration of outer retinal structures.

Figure 5: Swept-source optical coherence tomography OCT (SS-OCT) images orientated as per Figure 1A within an area of scarring. (A) At 1 month, SS-OCT showed outer retinal disruption including loss of the ellipsoid zone (EZ), hyper-reflectivities (marked with

arrows), choroidal attenuation and outer retinal atrophy. This is contrasted by normal retinal and choroidal appearance temporal to the optic disc. At 3 months (B) and 9 months (C), SS-OCT showed persistent outer retinal atrophy but less hyper-reflectivity.

Figure 6: Sequential swept-source optical coherence tomography angiography (OCTA) imaging suggests inflammatory vascular occlusive pathology in the acute stage with defined areas of altered flow and non-perfusion at the level of the choriocapillaris that corresponded with areas of hypocyanescence on indocyanine green angiography (A). (B) OCTA, at 1 month, revealed defined areas of choriocapillaris hypoperfusion within the lesion. (C) 3 months and (D) 9 months: Progressive OCTA evolution, over 9 months, with sequential improvement in flow and reduction in size of the non-perfused areas was noted indicating vascular remodelling in the choriocapillaris.