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Swept-Source OCT Angiography of Serpiginous Choroiditis

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Purpose: To examine and quantify choriocapillaris lesions in active and quiescent serpiginous choroiditis (SC) using swept-source (SS) OCT angiography (OCTA) and en face image analysis.

Design: Prospective, observational case series.

Participants: Patients with a clinical diagnosis of SC.

Methods: A SS-OCTA prototype was used to image active and quiescent serpiginous lesions longitudinally before and after anti-inflammatory treatment. En face slabs of choriocapillaris flow or outer nuclear layer structure were generated from OCTA and OCT data, respectively.

Main Outcome Measures: Qualitative and quantitative analyses on lesion boundary and area using a semiautomated MATLAB algorithm. Lesions also were compared with traditional multimodal imaging.

Results: Six eyes of 3 patients were imaged. Choroidal lesions were identified and analyzed in 4 of 6 eyes. Lesions with well-defined boundaries were identified in the choriocapillaris slab in areas of both active and inactive choroiditis. The choriocapillaris slab lesion size and shape showed good correlation with lesions identified on indocyanine green angiography. The choriocapillaris slab lesion area increased with disease activity and decreased with corticosteroid treatment. During active disease, the choriocapillaris slab lesion area was larger than both the outer nuclear layer (ONL) slab and fundus autofluorescence lesion areas. Active choriocapillaris slab lesions not associated with corresponding abnormal autofluorescence resolved without clinical scarring after treatment. In inactive scars, the areas of retinal and choriocapillaris lesions were similar and did not change over time.

Conclusions: En face analysis of SS-OCTA choriocapillaris flow voids provide a noninvasive method for the detection of lesions in patients with SC. The presence of lesions in the choriocapillaris in the absence of retinal pigment epithelium and outer retinal abnormalities supports the hypothesis that choriocapillaris is the primary site of pathologic features in SC and may be a sensitive early sign of disease activity. We propose a simple grading system of SC lesions based on SS-OCTA and fundus autofluorescence findings. Swept-source OCTA is a promising noninvasive method for monitoring patients with SC. *Ophthalmology Retina 2017;■:1–8 © 2017 by the American Academy of Ophthalmology. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).*

Supplemental material available at www.ophthalmologyretina.org.

Serpiginous choroiditis (SC) is a rare form of bilateral, chronic, or recurrent posterior uveitis that is thought to involve primarily the choriocapillaris, with subsequent involvement of the retinal pigment epithelium (RPE) and outer retina.[1–3] It causes severe permanent vision loss when involving the fovea and parafovea. This has led to a practice pattern of initiating aggressive immunosuppressive treatment on diagnosis, with evidence of progressive expansion of old lesions or with identification of new lesions.[1,4,5] The identification of disease activity before permanent structural damage would provide the opportunity to prevent vision loss.

Currently, SC is diagnosed based on clinical appearance and characteristic changes of active lesions using fluorescein angiography (FA),[1,6] with indocyanine green angiography (ICGA) as an adjunct that can identify subclinical lesions.[7,8] Both these studies suggest primary inflammatory pathologic features at the level of the choriocapillaris. More recently, fundus autofluorescence (FAF) has been reported to highlight active lesions with foci of hyperautofluorescence, presumably reflecting acute RPE injury overlying the choriocapillaris inflammation.[9] However, inactive scars become hypoautofluorescent.[1,6,8] Nevertheless, none of these methods provide high-resolution imaging of the choriocapillaris, which seems to be fundamentally affected in SC.

OCT angiography (OCTA) has emerged as a noninvasive imaging method to detect the presence or absence of blood flow signal in the retina.[10] Unlike dye-based angiography methods, OCTA allows vascular analyses to be stratified by retinal layer. OCT angiography has provided insights into pathogenic mechanisms of retinal disease, including uveitic conditions.[11] Compared with dye angiography, OCTA also has the benefit of providing high-resolution digital images that are amenable to reproducible quantification.

Most currently available OCTA devices use spectral-domain (SD) OCT technology. Unfortunately, diseases of

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the choroid and choriocapillaris are difficult to study with SD technology because of RPE attenuation of the 840-nm central wavelength used in this imaging method.[12] Despite this limitation, SD-OCTA has identified flow voids in the choroid of patients with placoid chorioretinal diseases such as acute posterior multifocal placoid pigment epitheliopathy.[13] Swept-source (SS) OCT and OCTA use a longer central wavelength (1050 nm) that provides improved signal penetration through the RPE and produces high-resolution images of the choriocapillaris and choroidal vessels.[14,15] Swept-source OCTA has the potential to provide the benefits of noninvasive vascular imaging to identify and monitor diseases that are believed to originate in the choriocapillaris.

In this study, we sought to examine the usefulness of SS-OCTA to detect choriocapillaris involvement in patients with SC. Furthermore, we compared SS-OCTA with other standard imaging methods including FA, ICGA, SD-OCT, and FAF to determine their relative usefulness in characterization of active and quiescent SC.

Methods

This single-institution prospective, observational case series was approved by the institutional review board at the University of Washington. Patients with a diagnosis of peripapillary SC, macular SC, or multifocal or ampiginous choroidopathy were recruited for OCTA imaging as part of this study between September 2016 and March 2017. Informed consent was obtained, and the tenets of the Declaration of Helsinki and the regulations of the Health Insurance Portability and Accountability Act of 1996 were followed.

Swept-source OCTA and SS-OCT images were obtained using a PLEX Elite 9000 (Carl Zeiss AG, Dublin, CA). This device uses a central wavelength of 1050 nm with a 100-kHz A-scan rate and a spectral bandwidth of 100 nm. The axial and lateral resolutions are approximately 5 μm and approximately 14 μm, respectively. An optical microangiography (OMAG) algorithm was used to construct images demonstrating surrogate markers of vascular flow, the technical aspects of which are detailed elsewhere.[16] Fields of view sizes included 3 × 3-mm, 6 × 6-mm, 9 × 9-mm, and 12 × 12-mm imaging windows. A 3 × 3-mm cube contains 300 A-scans per B-scan, and a total of 1200 B-scans, 4 repeats each, whereas the 6 × 6-mm, 9 × 9-mm, and 12 × 12-mm cubes hold 500 A-lines per B-scan, with a total of 1000 B-scans, 2 repeats, centered at the fovea or the optic disc. Pixel spacing and the number of repeated B-scans were compromised in larger scans to maintain similar scanning time as 3 × 3-mm cube. The specific scanning window size chosen for analysis was selected based on the size and location of the region containing pathologic features. OCT angiography images of the choriocapillaris slab (measured from 15 to 35 μm below the RPE best-fit line), OCT images of the RPE slab (from 0 to 10 μm anterior to the RPE best-fit line), and OCT images of the outer nuclear layer (ONL) slab (from 55 to 105 μm anterior to the RPE best-fit line) then were generated for en face analysis for the same field of view. A semiautomated MATLAB algorithm (MathWorks, Natick, MA) was used to identify and measure lesion area on the en face slabs. Lesion area was determined manually by one expert grader with fellowship training in both medical retina and uveitis (K.P.-V.), area was calculated, and the lesions in the various slabs then were overlaid for comparison.

Clinical images were collected for comparison with OCT and OCTA research images. Clinical images were ordered at the discretion of the treating physician and included color fundus photography (FF450Plus; Carl Zeiss AG), spectral-domain OCT (Spectralis HRA+OCT; Heidelberg Engineering, Heidelberg, Germany), FAF (FF450Plus [Carl Zeiss AG] or Spectralis HRA+OCT [Heidelberg Engineering]), FA (FF450Plus; or P200DTx [Optos PLC, Dunfermline, United Kingdom]), and ICGA (Spectralis HRA+OCT). Indocyanine green angiography and FAF images for patient 1 were exported as TIFF image files and analyzed using the semiautomated MATLAB algorithm to determine lesion size.

Patients were diagnosed with SC after an evaluation for other infectious and inflammatory causes that included a careful uveitis review of systems and laboratory testing with a complete blood count, comprehensive metabolic panel, Treponema pallidum immunoglobulin (Ig) G and M for syphilis, an interferon-γ release assay for tuberculosis (QuantiFERON-TB Gold, Qiagen, Hilden, Germany), and a chest radiograph. A complete ophthalmic examination was performed, and uveitis was categorized according to Standardization of Uveitis Nomenclature criteria.[17] Initial treatment consisted of an oral tapering course of corticosteroid with concomitant immunosuppressive treatment, consistent with expert consensus recommendations.[18]

Results

Three patients were identified with SC: patient 1 with macular SC, patient 2 with classic peripapillary SC, and patient 3 with multifocal SC. Patient 1 was a 55-year-old white man with a 3-month history of central scotoma and photopsias in the left eye. Fundus imaging, FAF, FA, ICGA, and SS-OCTA were performed (Fig 1), and he was diagnosed with macular SC of the left eye after the evaluation for infectious and inflammatory conditions. The right eye had mild peripapillary atrophy (not shown). Late ICGA images were used to outline the region of choriocapillaris defect and to quantify the area involved in the left eye (Fig 1D). The total area of choriocapillaris defect detected by ICGA was determined to be 17.4 mm^2 (Table 1). The lesion shape in the choriocapillaris slab approximated the ICGA boundary, and lesion area was similar at 17.5 mm^2. The ONL slab boundary fell within the boundary of the choriocapillaris lesion (Fig 1G), and the lesion area was smaller (14.4 mm^2). The RPE lesion, as identified by FAF, demonstrated a similar shape as the choriocapillaris lesion (Fig 1H), and the lesion area was similar (17.6 mm^2).

Patient 2 was a 41-year-old white man with a 4-month history of scotoma and photopsia in the left eye. He had been diagnosed with probable SC before presentation, but had not received any treatment. On examination, an inactive serpiginous scar extending from the optic nerve into the macula was noted in the right eye (Fig 2A, C, available at www.ophthalmologyretina.org). In the left eye, there was concern for an area of active peripapillary choroiditis that demonstrated late leakage on fluorescein angiography and hyperautofluorescence at the superotemporal optic nerve border (Fig 2, available at www.ophthalmologyretina.org). Treatment with prednisone and mycophenolate mofetil was initiated, but during the prednisone taper at 10 mg daily, he experienced a recurrence in the left eye (Fig 3F). Oral corticosteroids were increased and tacrolimus started, and the flare was controlled (Fig 3K). On the choriocapillaris slab, the area of the lesion nasal to the retinal vessels did not change in boundary or area over the 3 visits (Fig 3C, H, M, red dotted lines). There was also no change in the ONL slab in this region (Fig 3D, I, N, green dotted lines) or the appearance on FAF (Fig 3B, G, L). In this area, the boundary of the lesion as defined by all 3 imaging methods was