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Case report

Parafoveal cone abnormalities and recovery on adaptive optics in posterior uveitis

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ABSTRACT

Purpose: To determine if adaptive optics (AO) flood illumination imaging can detect subclinical changes in 4 cases of posterior uveitis affecting the outer retina.
Observations: In all 4 cases, the affected eye showed altered areas in the photoreceptor mosaic on AO that corresponded to changes on other imaging modalities. Abnormalities not apparent on other imaging modalities were also noted. In one case of multifocal choroiditis with acute outer retinal atrophy, AO revealed decreased visualization of photoreceptors in the unaffected eye that was not noted on spectral domain-optical coherence tomography. In the patient with multiple evanescent white dot syndrome, focal photoreceptor abnormalities were more apparent on AO compared to other imaging modalities, and these areas normalized on AO during follow-up. Five weeks after initiation of high dose prednisone and azathioprine in a patient with serpiginous choroidopathy, AO images showed recovery in apparent parafoveal cone density.
Conclusions and importance: AO detects subclinical changes in the photoreceptor layer in posterior uveitis that can recover over time. AO may be useful in following outer retinal inflammatory conditions.

1. Introduction

Posterior uveitis (PU) encompasses a heterogeneous group of disorders with a predominant site of intraocular inflammation located in the retina or choroid. Spectral domain optical coherence tomography (SD-OCT) and fundus autofluorescence (FAF) have allowed non-invasive *in vivo* imaging that is able to distinguish and localize abnormalities in the outer retina and RPE in many cases of posterior uveitis. Studies showing the utility of multi-modal imaging in posterior uveitis have been growing in number [1–10].

Adaptive optics (AO) has been used to study a variety of retinal conditions including the normal cone mosaic, acquired and inherited retinal disorders, and color deficiencies [11–17]. There are few case reports and one larger series of AO use in uveitis [2,18–22]. With the exception of the larger case series and one case report utilizing AO-OCT, most case reports utilize custom-built AO-scanning laser ophthalmoscopy (SLO) systems and showed photoreceptor abnormalities in the diseased eye, but to our knowledge seldomly demonstrated improvements in these changes after treatment or time. In our study, we demonstrate the ability of a commercially available AO flood-illuminated camera to document alterations in the parafoveal cones in posterior uveitis, including subclinical changes not seen on other commonly used imaging modalities, and reversibility of these AO abnormalities in some cases.

2. Methods

This research was approved by the Institutional Review Board of the Oregon Health & Science University and adhered to the tenets of the Declaration of Helsinki. All subjects signed an informed consent after the nature and possible consequences of the study

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were explained. Permission was obtained to publish personal information such as age, gender, and ethnicity.

Both eyes of 4 sequentially recruited subjects with posterior uveitis were imaged using the Rtx1 AO camera (Imagine Eyes, Orsay, France). Exclusion criteria included patients with opacification of the ocular media, subjects that had uncontrolled nystagmus, trembling, or movements of the eyes and/or head that prevented target fixation, or incapacity to maintain a stable position while seated. Both eyes were dilated with 1% phenylephrine and 2.5% mydriacyl prior to each imaging session. The same technician conducted all imaging sessions in the study.

The scanning protocol consisted of a series of 25, 4° × 4° images with 40 raw images at each point, acquired with 50% overlap between adjacent images, then automatically registered and combined to reduce noise and enhance image quality using vendor-provided software (ck_v0_1b, Imagine Eyes, Orsay, France) to cover a 12° × 12° field of central macula. Automated cone identification was performed using a custom algorithm developed in MATLAB (Mathworks, Natick, MA, USA), and Voronoi cone density maps produced as previously described [23]. Because Rtx1 is unable to detect individual cones at the fovea where the inter-cone spacing is smaller than the spatial resolution, cone density maps in this study have a gray oval to mask these areas [23]. Because inflammation can potentially change the reflective properties of a cone below the threshold of detection on the cone density map, we used the term “decreased apparent cone density” to illustrate the fact that rather than disappearing, the cones may have diminished wave-guiding ability. AO images were compared to corresponding areas from other imaging modalities including fundus images (Optos 200TX, Scotland, UK), FAF (Optos 200TX), infrared photography (IR) (Spectralis, Heidelberg, Germany), fluorescein angiography (FA) (Optos 200TX), and SD-OCT (Spectralis), when obtained for clinical purposes.

2.1. Findings

2.1.1. Case report 1

A 60 year-old Caucasian woman presented with an acutely enlarging scotoma in the left eye. Her corrected visual acuity was 20/20 in both eyes. Examination revealed outer retinal lesions emanating in a serpentine fashion from the optic nerve OS (Fig. 1C). There were no anterior chamber cells, few anterior vitreous cells, and characteristic fluorescein angiographic findings with early hypofluorescence and late hyperfluorescence most prominent at the edges of lesions (Fig. 1D,E). After tests for infectious etiologies including syphilis and tuberculosis came back negative, the patient was diagnosed with serpiginous choroidopathy. AO imaging at the initial visit of the symptomatic left eye illustrated a significant area of decreased cone visualization in the nasal macula corresponding to locations of ellipsoid zone (EZ) or inner segment-outer segment junction (IS/OS) disruption seen on SD-OCT and hyper-autofluorescence on FAF (Figs. 1F, H and 2B). The transition from normal to abnormal cone reflectivity on AO is shown as a magnified AO inset in Fig. 1G, and corresponds to the transition of abnormal to normal EZ and ELM reflectivity on SD-OCT in Fig. 1H. Additionally, the AO cone density map revealed an overall apparent depression in the parafoveal area compared to normal subjects (example of normal subject shown in Fig. 1A, B), in both eyes that was not represented by any evident SD-OCT or FAF abnormalities (Fig. 2). Five weeks after initiating prednisone and azathioprine, the patient symptomatically improved and AO images in the left eye showed persistent areas of decreased cone visualization in the nasal macula that corresponded to the EZ abnormalities on SD-OCT and was represented by initial hyperautofluorescence on FAF (Fig. 2B,J,L). Persistent AO abnormalities appeared to correspond to areas of

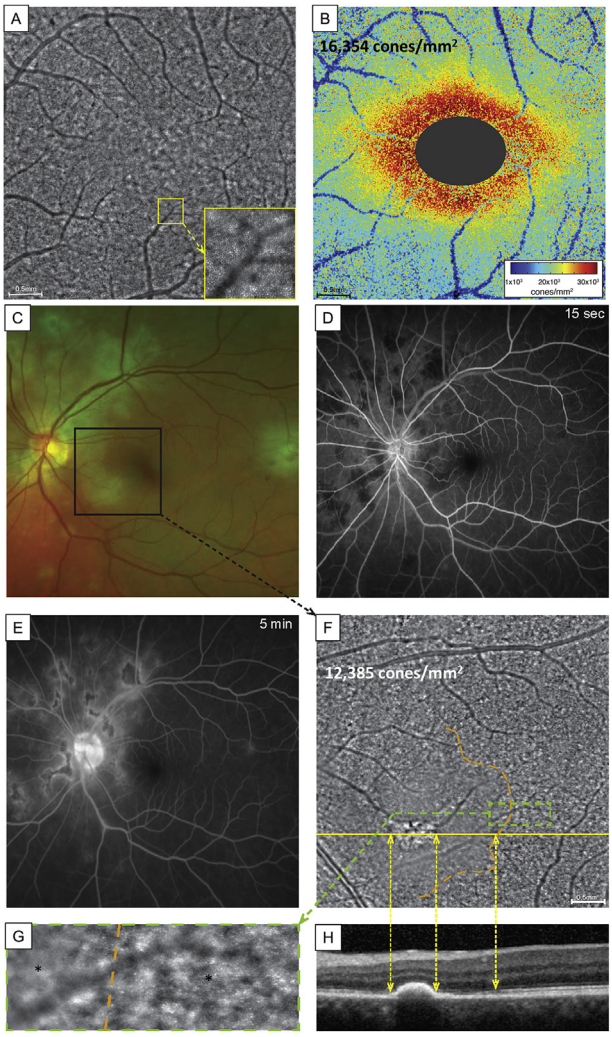

Fig. 1. Reduced cone visualization in adaptive optics (AO) images in serpiginous choroidopathy (Case 1) compared to normal subject. (A) AO composite montage and (B) Voronoi cone density map from a *healthy control subject*. (C) Fundus image and (D,E) fluorescein angiography of Case 1 subject's symptomatic left eye. (F,G) AO composite montage demonstrating focal area of AO hyperreflectivity corresponding to pigment epithelial elevation on spectral domain-optical coherence tomography (SD-OCT) (H) and adjacent area of decreased cone visualization outlined by the orange dotted line. (G) Magnified AO montage showing transition zone from area of abnormal cone mosaic (left side of panel) to area of normal cone mosaic (right side of panel) with asterisks denoting location of 200 μm × 200 μm box where cone densities were quantified at 4477 cones/mm^2 on the left, and 20,825 cones/mm^2 on the right; (H) corresponding SD-OCT changes in the ellipsoid zone and external limiting membrane.

external limiting membrane (ELM) disruption on SD-OCT (dotted arrow, Fig. 2F,J). As shown in the figure, cones in the nasal region remained at low density (from 4451 cones/mm^2 to 5170 cones/mm^2) before and after treatment. The parafoveal apparent cone density, however, showed a recovery in both eyes, suggesting that AO may identify abnormalities in the photoreceptors not seen on SD-OCT, which can recover with treatment (Fig. 2E–J). For instance, despite the minimal improvement in nasal regional cone density, parafoveal cone densities showed a dramatic improvement from 15,847 cones/mm^2 to 21, 979 cones/mm^2 (Fig. 2F,J), a difference of over 6000 cones/mm^2. Global cone densities over the entire 12° x 12° area of retina imaged are listed in the apparent cone density maps or montage in Figs. 1 and 2 and reveal increases in total apparent cone densities of 896 cones/mm^2 OD and 344 cones/mm^2 OS after treatment. Note that global cone densities in the nasal offset montage of the left eye shown in Fig. 1F (image taken at