

Vitreous Punctate Spots in Eyes with Intermediate and Posterior Uveitis Using Spectral Domain Optical Coherence Tomography

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Abstract

Purpose:- To assess inflammatory cells in the vitreous which are seen as punctate spots on Nidek Spectral Domain Optical Coherence Tomography in eyes with intermediate and posterior uveitis.

Materials and Methods:- This prospective study involved 73 eyes having intermediate and posterior uveitis which were imaged with Spectral Domain Optical Coherence Tomography (SDOCT) at baseline and 1 month after the treatment. The punctate spots were seen as hyper-reflective dots in the retina and vitreous. These were larger with greater density than the nonpunctate, irregular condensations seen in the vitreous cavity, reflecting normal age-related vitreous syneretic changes. The presence and severity of vitreous haze were classified according to the National Eye Institute system. The vitreous haze scale and SD-OCT findings were compared at baseline and 1 month after treatment.

Results:- At baseline, SD-OCT showed inflammatory cells as numerous punctate spots in the vitreous cavity and retina in all eyes with decrease in their number on follow up.

Conclusion:- The inflammatory cells in the vitreous and retina in eyes with intermediate and posterior uveitis were objectively documented using SD-OCT. SD-OCT is a useful imaging tool to correlate the reduction in inflammatory cells with vitreous haze seen clinically following treatment.

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Introduction

The annual incidence of uveitis is between 17 and 52 per 1,00,000 of the population, with up to 35% of patients reported to have significant visual impairment or legal blindness.¹⁻⁵ To assess the severity of vitreous inflammation in patients of intermediate and posterior uveitis, the current gold standard is the National Eye Institute (NEI) system for grading of vitreous haze.⁶⁻⁷ This system, often referred as the "Nussenblatt scale," is based on the comparison of clinical findings of the patient's eye on indirect ophthalmoscopy with a series of six photographs representing various degrees of fundal vitreous haze.

Nussenblatt scale (by NEI) had few limitations such as:

- (1) Interval between grades were not quantified.
- (2) subjective or interobserver variation.
- (3) haziness due to media is not accounted for.
- (4) poor discrimination at lower levels of vitreous haze.

Finally the scale was not validated as the standard for grading fundus photographs. Davis et al⁶ proposed a method of photographic grading of vitreous haze using a 9-level scale created by photographing a normal fundus through Bangerter occlusion filters to create increasing optical blur, simulating increasing grades of vitreous haze. This method proved highly reproducible and better than the Nussenblatt scale.^{7,8} The advancement in SDOCT enabled high-resolution images with reduced motion artifact and increased image acquisition speed. In conventional use, SD-OCT has its peak sensitivity in the vitreous above the retina, and this property can be used to image cells in the posterior vitreous. Lately, however, the use of OCT for direct visualization of

vitreous inflammatory cells in patients with uveitis has been described.⁵ Commercially available devices have a resolution in the range of 5 μm to 7 μm , which exceed the size of leukocytes, such as macrophages, which can be up to 25 μm in diameter in tissue.⁵ Certainly, highly reflective objects can be visualized by optical systems even if their size is smaller than the theoretical resolution. As a preliminary investigation, we examined the SD-OCT findings in eyes with posterior and intermediate uveitis to ascertain if reflective patterns consistent with cells in the vitreous could be visualized. The recent introduction of Spectral-Domain (SD) OCT technology allows better visualization of the hyaloid.

Materials And Methods

This prospective study compared and analysed the SD-OCT findings in 73 eyes with active intermediate and posterior uveitis. All patients underwent a complete ophthalmic examination, including slit-lamp biomicroscopy and color fundus photography with a fundus camera (Topcon Retinal Camera TRC. 50DX) at baseline. The grading of vitreous inflammation was done according to Davis scale at baseline and 1 month after treatment. SD-OCT system (Spectralis OCT, Heidelberg Engineering, Heidelberg, Germany) was done for both the eyes. This system acquires 40,000 A-scans per second with 7 μm axial resolution and 14 μm transverse resolution. High resolution single and volume scans were taken along vertical and horizontal axis through the center of the fovea and also along the retinal areas with maximum activity (wherever applicable) at baseline and at 1 month. The length of scan lines set in volume scan was 9042 microns with automatic real time (ART) of 9. The space between two scan lines in the volume scan was 240 microns. For OCT at 1 month,

follow up acquisition mode was used which automatically placed the follow up scans in exactly the same location as that of the initial scan. The standard white on black SD-OCT images were also seen on black on white image mode and the findings were analysed. Image measurements were made with Heidelberg Viewer Module software (version 5.8.3). Similar to the definition given by Saito et al.⁹ SD-OCT findings of punctate spots (PS) were defined as hyperreflective dots in the vitreous and retina. The PS in the vitreous were larger and had a greater density. These were differentiated from the large, nonpunctate, irregular condensations within the vitreous cavity, which appeared to reflect normal age-related vitreous synergetic changes. These SD-OCT images were then compared with clinical vitreous haze scale. We looked at the status of vitreous cells clinically and on SD-OCT images at baseline and 1 month after the treatment. In addition, we also examined eyes on Nidek RS-3000 OCT and generated 3D images which have a better depiction of vitreous cells.

Results

We evaluated 73 eyes with intermediate and posterior uveitis, 43 females and 30 males, with a mean age of 36.1 years (mean \pm SD, 36.1 ± 13.64 years; range, 10–64 years). Table 1 shows the number of patients with their diagnosis. All 73 eyes showed vitreous cells on slit-lamp biomicroscopy. At baseline, all 73 eyes underwent SD-OCT scanning which showed punctate spots in the vitreous and retina. At 1 month after instituting the appropriate treatment, all patients responded to the treatment, as evident by decrease in vitreous cells on clinical examination. Also, SD-OCT showed a decrease in the number of punctate spots in the retina and vitreous correlating with the clinical examination. Six eyes of 6 patients were also studied on Nidek RS-3000 with a 3D reconstruction.

Table 1: Types of Uveitis

	Number of eyes
Pars Planitis	49
Toxoplasmosis	16
Serpiginous choroiditis	7
Cysticercosis	1

Parsplanitis

The study included 49 eyes with parsplanitis. Patients presented with complaints of unilateral floaters and blurring of vision. The best corrected visual acuity ranged from 20/60 to – 20/20. As per Davis' scale, grade 4 vitreous haze with 1 + cells was found in 36 eyes. Ten eyes had grade 3 vitreous haze with 1 + cells and the remaining 3 eyes had grade 1 vitreous haze with 1 + cells. The diagnosis of pars planitis was made on the basis of presence of snow ball opacities in the peripheral fundus and/or snowbanking in the inferior fundus along with vitritis. On clinical examination, 19 patients had cystoid macular edema at presentation. At baseline, SD-OCT scans revealed collection of punctate spots in the vitreous and outer retina. SD-OCT scans showed cystoid spaces in 19 eyes with clinical cystoid macular edema with subfoveal fluid collection in 2 eyes. However, when the standard white on black SD-OCT images were subjected to black on white

image, punctate spots were enhanced and seen more clearly, especially intraretinally (Figure 1a). Oral steroids (1mg/kg body weight) were started. Posterior sub-tenon triamcinolone injection was given in patients with macular edema, along with oral steroids. As the vitritis resolved at 1 month after treatment, the number of punctate spots in the vitreous and retina also decreased as evident in Figure 1b, correlating with decrease in clinical vitritis. Cystoid edema resolved but one patient still had mild subfoveal fluid.

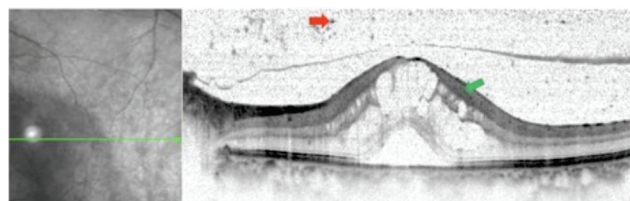


Figure 1 (a): A horizontal black on white OCT image enhancing the visible punctate spots in the vitreous (red arrow) and within the underlying retina (green arrow). Note cystoid macular edema and sub retinal fluid.

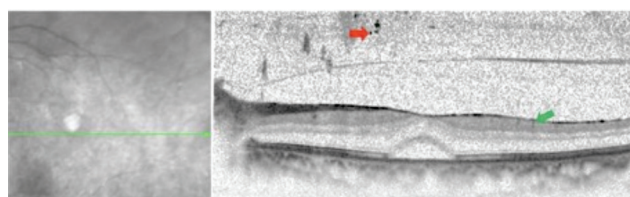


Figure 1 (b): A horizontal black on white SD OCT image enhancing the decreased number of punctate spots in the vitreous (red arrow) and within underlying retina (green arrow). Note the resolution of macular edema and decrease in sub retinal fluid.

Toxoplasmosis

Toxoplasmic retinochoroiditis was diagnosed in 16 eyes. Unilateral blurring of vision with floaters were the chief complaints. BCVA ranged from 20/200 – 20/20. There was grade 2 vitreous haze with 2 + cells in 9 eyes. The remaining 7 eyes had grade 1 vitreous haze with 1 + cells. Fundus examination revealed focal vitritis overlying yellowish white retinal lesions. A chorioretinal scar was present adjacent to the active lesion in 7 patients. The macula was affected in 14 eyes. SD-OCT showed many punctate spots in the vitreous. The density of these punctate spots was greater closer to the underlying retina, particularly over the area of focal retinitis. The punctate spots were also seen within the retina, which were of the same size and reflectivity as that of the punctate spots seen within the vitreous. Black on white image further enhanced the visualisation of these spots (Figure 2a). Anti-toxoplasma three drug regime was started which included clindamycin 300 mg QID for a day and then TDS, sulphamethoxazole 800 mg and trimethoprim (160 mg) BD and pyrimethamine 50 mg OD, with folic acid 5 mg every 3 days for 4 weeks. Oral steroids (1mg/kg body weight) were started after 2 days. At 4 weeks after the initiation of treatment, SD-OCT clearly showed a decrease of punctate spots in the vitreous and underlying retina (Figure 2b), which correlated with decrease in clinically observed vitritis.

Serpiginoid Choroidopathy

Seven patients with serpiginoid choroidopathy presented

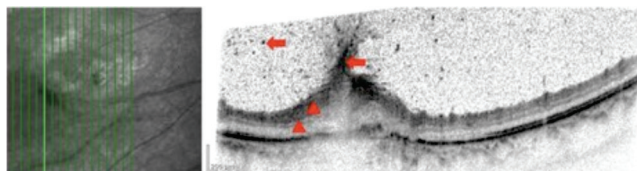


Figure 2 (a): A vertical black on white OCT image enhancing the punctate spots in the vitreous (arrow) and within the underlying retina (arrowheads). The density of the punctate spots was greater over the most intense areas of retinitis.

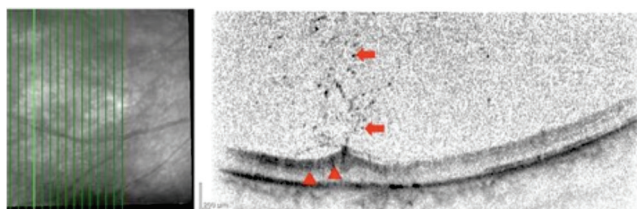


Figure 2 (b): After antitoxoplasma regime, a vertical black on white OCT image enhancing the punctate spots in the vitreous (arrow) and within the underlying retina (arrowheads). Note the density of punctate spots over the area of most active retinitis has reduced.

with unilateral blurring of vision with visual acuity ranging from 20/120-20/40. There were trace cells with grade 1 vitreous haze in 5 eyes. The remaining 2 eyes had 1 + cells with grade 1 vitreous haze. Fundus examination showed ill-defined patches of gray-yellow, placoid sub-retinal infiltrates extending in a finger like projection from the peripapillary area. The macula was affected in 5 eyes. At presentation, SD-OCT images revealed intravitreal and intraretinal cellular infiltrates over the area of active lesion. Black on white SD-OCT image showed multiple PS in the retina, especially in the inner retinal layers (Figure 3a). Intravenous methylprednisolone 1g for 3 days, followed by oral steroids (1mg/kg body weight) was started in 5 patients who had involvement of the macula. Oral steroids (1mg/kg body weight) were started in the remaining two patients. At 1 month post-treatment, there was no evidence of active inflammation on clinical examination, a finding in keeping with results from SD-OCT analysis, which showed absence of punctate spots in the vitreous and retina. (Figures 3b).

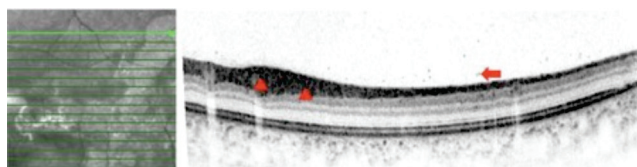


Figure 3 (a): Baseline horizontal black on white OCT image passing through the area of active lesion enhancing the punctate spots in the vitreous (arrow) and within the underlying retina (arrowheads).



Figure 3 (b): At 1 month after treatment a horizontal black on white OCT image corresponding to (Figure 3A) arrow showing absence of punctate spots in the vitreous and underlying retina.

Cysticercosis

A 24-year old male presented with complaints of blurring of vision in the right eye since 20 days. BCVA was 6/6. There were 2 + cells with grade 4 vitreous haze. Clinically the fundus showed a cyst-like lesion in the juxtapapillary area with a small haemorrhage which eventually increased in size, with a dense white spot (scolex) at one region. SD-OCT showed numerous punctate spots in the vitreous and retina with mild subfoveal fluid. Intraretinal PS were seen more clearly with black on white image (Figure 4a). Anti-parasitic drugs with oral steroids were started. At 4 weeks, there was a reduction in the number of punctate spots in the vitreous and retina, correlating with decrease in vitreal inflammation seen clinically, but the size of the cyst increased further (Figure 4b) and the BCVA dropped to 20/200. As a result, the patient underwent successful vitrectomy for cyst removal.

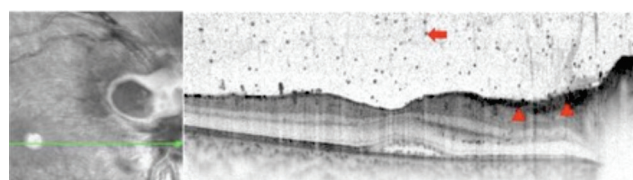


Figure 4 (a): A horizontal black on white OCT image enhancing the numerous punctate spots in the vitreous (arrow) and within underlying retina (arrowhead) with mild subfoveal fluid.

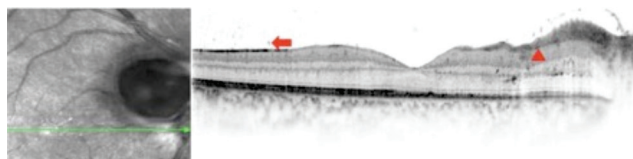


Figure 4 (b): A horizontal black on white OCT image corresponding to figure 4A showing gross reduction in punctate spots in the vitreous (arrow) and within underlying retina (arrowhead).

Discussion

Characteristics of inflammation in the vitreous cavity, as in the anterior chamber, are increased cells and protein. Vitreous is rarely a source of the inflammatory cells, the most common sources being the choroid, retina, and ciliary body. However, in certain infections, the focus of the inflammation may be in the vitreous. Quantification of vitreous cells and haze is challenging as compared to aqueous cells and flare. The vitreous is larger, and cells or haze may be localized to only a part of the vitreous. Therefore, quantification may depend on how the eye was examined. For example, the anteroposterior location of small numbers of cells in a relatively clear vitreous can be determined with the use of the slit lamp, but in a severely inflamed eye, the mid and posterior vitreous may be obscured by anterior vitreous cells and haze. Small pupil size, corneal opacity, and cataract will also make the grading process more difficult. Location of the cells depends on the ocular disease and its severity. The location of the cells also has a role in classifying the inflammation, for example, patients with pars planitis, who usually have cells in the anterior vitreous, will develop many cells in the posterior vitreous, if the inflammation is severe. Studies on grading of inflammation have evaluated various parameters. Curiously, grading the number of cells within

the vitreous cavity by ophthalmoscopy shows a relatively poor coefficient of reproducibility.^{6,9} Indeed, Davis et al have addressed some of these issues by using an extended 9-point graded photograph-to-photograph technique that was assessed in the Multicenter Uveitis Steroid Treatment trial.⁶ Although the study noted excellent interobserver and intraobserver intraclass correlations (correlation coefficients, 0.84-0.93), the correlation between the photographic and the NEI vitreous haze scores was weaker ($r=0.51$; $P<0.001$). SD-OCT is often referred to in literature as an "optical biopsy method" due to its ability to provide information on ocular subsurface structures with retinal layer by-layer analysis, otherwise obtainable only by histology.⁷ In conventional use, SD-OCT has its peak sensitivity in the vitreous above the retina, and this property can be used to image cells in the posterior vitreous. In the current study, 3D imaging on SD-OCT was used to image the vitreous architecture and the vitreo-macular interface. It could visualise the details of the vitreoretinal interface and the vitreous body, not discernible clinically or in the B-scan OCT image. This imaging can be used to objectively assess the reduction of vitritis following treatment in inflammatory pathologies involving the vitreous. In this study, we first obtained horizontal and vertical line and volume OCT scans through the center of the fovea and along the retinal areas with maximum activity (wherever applicable). At baseline, SD-OCT showed inflammatory cells as PS in the vitreous and retina of all eyes. Punctate spots were seen as hyper-reflective dots in the vitreous that were larger with greater density than the usual background speckle. At 4 weeks after treatment, reduced vitreous and retinal cellular infiltration was correlated with a decrease in the number of the punctate spots visible by SD-OCT in all eyes. The punctate densities seen were uniform in size, located over areas of retinitis, had a greater density near the retina, the presumed source of the cells, and change in number was noted over short durations of time. Black on white images of SD-OCT enhanced the visibility of these PS, especially intraretinally, which to the best of knowledge of authors, has not yet been reported. This study showed that SD-OCT can be a useful objective tool to document reduction in inflammatory cells in the vitreous and retina following treatment in eyes with intermediate and posterior uveitis. Recently Saito et al¹⁰ reported similar results, but in a limited number of eyes. Their study included 7 eyes with 3 different pathologies. The present study included 73 eyes with 4 different pathologies. The limitation of the current study is short-term follow up of 4 weeks. Although all treated eyes showed reduced PS in the vitreous and retina at 4 weeks, longer follow ups are required to compare and document the recurrence of disease activity on SD-OCT. Another study by Keane et al⁵ provides preliminary evidence that OCT derived measurements may help in defining vitreous signal intensity as an outcome measure in patients with uveitis. If validated in future studies, such measures may serve as an objective, quantitative disease activity end point, with a potential to improve the "signal:noise" ratio of clinical trials in this area, thus enabling smaller studies for the same power. The incorporation of automated vitreous analysis in commercial OCT systems may, in turn, facilitate monitoring and retreatment of patients with uveitis in clinical practice.

The present study demonstrates the novel use of SD-OCT as an objective tool to document and monitor inflammatory cells in eyes with intermediate and posterior uveitis.

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