Imaging drusens using Spectral Domain Optical Coherence Tomography

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Abstract

Purpose: The purpose was to evaluate pathological changes of photoreceptor layer and retinal pigment epithelium in eyes with drusens using Spectral Domain Optical Coherence Tomography (SD-OCT).

Methods: Twenty-nine eyes of 29 patients with (drusens) dry age-related macular degeneration and 43 eyes of 43 controls were included in this study. All subjects underwent complete ophthalmic examination including SD-OCT. Central foveal thickness (CFT), photoreceptor layer (PRL) thickness and retinal pigment epithelial (RPE) thickness were measured and compared between the groups. P value < 0.05 was considered statistically significant.

Results: Best corrected visual acuity (BCVA) ranged between 20/20 and 20/200. RPE (36.10 ± 5.48 μm Vs 39.27 ± 4.30) and PRL thickness (53.93 ± 7.36 μm Vs 61.20 ± 4.50 μm) were significantly reduced in patients with drusens compared to controls. Increase in age was a significant risk factor for drusens (OR: 1.22, p < 0.001) and increased PRL thickness was a protective factor (OR: 0.720, p = 0.002). PRL thickness was significantly associated with BCVA (p = 0.019).

Conclusion: With an increased resolution of SD-OCT, the involvement of the outer retinal layers was more clearly defined. SD-OCT may allow for the early detection of exudative changes.

Keywords: Age related macular degeneration, Spectral Domain Optical Coherence Tomography, Photoreceptor layer, Retinal pigment epithelium

Introduction

Age-related macular degeneration (AMD) is the leading cause of irreversible blindness in industrialized countries. Drusen is the earliest visible abnormality in AMD. Drusens are regarded histopathologically as deposits of extra cellular material lying between the basement membrane of the retinal pigment epithelium (RPE) and the inner collagenous zone of Bruch’s membrane. Spectral Domain Optical Coherence Tomography (SD-OCT) has been used extensively to characterize drusen structure in AMD. AMD is characterized by the progressive degeneration of photoreceptors, RPE, and choroid. Histopathological studies show both hyper pigmentation and hypo pigmentation of the macular RPE and abnormalities in the photoreceptors including photoreceptor cell loss.

The aim of the present study was to evaluate the pathological changes of photoreceptor layer (PRL) and RPE in eyes with drusens in early AMD using SD-OCT.
Materials and methods

Twenty-nine eyes of 29 patients with drusens and 43 eyes of 43 controls were included in this prospective case control study. All patients underwent a thorough clinical examination that comprised of best corrected visual acuity (BCVA) assessment which was measured using ETDRS chart, biomicroscopy of the anterior and posterior segment and indirect ophthalmoscopy. Only eyes with media sufficiently clear to allow good quality SD-OCT scans were included. Subjects with pathology other than drusen were excluded from this study. The study was approved by the organization’s Institutional Review Board, and informed consent was obtained from the subjects in accordance with the Helsinki Declaration.

SD-OCT images were generated using Copernicus instrument (Optopol, Poland) with 2 mm axial depth and 4–10 mm transverse width. The resolution was about 6 μm in the axial direction and 12–18 μm in the transverse direction. Retinal structural details in cases with drusens were obtained using 7 mm scan with 6 B-scans and 2743 A-scans per B-scan in the macula, each separated by 30 degrees. Based on the reflectivity of SD-OCT cross section images, PRL, RPE and central foveal thickness (CFT) were measured manually using the calipers. CFT was measured as a distance between the vitreoretinal interface and the inner border of RPE. PRL thickness was defined as the distance between the medium reflective membrane which represents external limiting membrane and the inner border of RPE. In all the subjects, the integrity of all inner and outer retinal layers was assessed using SD-OCT.

Statistical analysis was performed using SPSS ver15.0 statistical package. Kolmogorov–Smirnov Z test was done to test the distribution of data. We found that the data were normally distributed. Independent t-test was used to compare the PRL, RPE and the foveal thickness between the groups. Pearson correlation was performed to see the correlation between the variables. Multiple logistic regression was performed to assess the risk factors for presence of drusens. Linear regression was performed to assess the association of thickness parameters with visual acuity. P value less than 0.05 was considered statistically significant.

Results

Mean age of the study sample was 54.87 ± 11.07 years. Men and women were equally distributed in the study. BCVA ranged from 20/20 to 20/200. The inner retinal layers were normal, whereas the outer retinal layers showed structural alterations in eyes with drusens (Fig. 1). Table 1 shows the clinical parameters among the study sample. No significant difference in CFT was found between the groups (p = 0.535). Mean PRL thickness was significantly reduced in patients with drusens compared to controls (53.93 ± 7.36 vs 61.2 ± 4.5 μm, p < 0.001). Mean RPE thickness in patients with drusens was significantly reduced (36.10 ± 5.48 vs 39.27 ± 4.30 μm, p = 0.001). Multiple logistic regression analysis was done to assess the risk factors for presence of dry AMD. It was found that increased age was a significant risk factor for drusens (OR: 1.22, p < 0.001) and increased PRL thickness was a protective factor (OR: 0.720, p = 0.002) when adjusted for age, gender, CFT, PRL and RPE thickness.

BCVA was significantly reduced with reduced PRL thickness (r = −0.564, p = 0.002) (Fig. 2) and CFT (r = −0.410, p = 0.017) among patients with drusens. No correlation was found between BCVA and age (r = −0.024, p = 0.904) as well as age and PRL thickness (r = −0.119, p = 0.540) in our study sample. In multivariate model including age, PRL and CFT, only PRL thickness (p = 0.019) had significant association with BCVA (Table 2).

![Figure 1. SD-OCT showing Drusens. Drusen appears as irregular elevations of the highly reflective RPE layer and showing the thinning of the photoreceptor layer overlying the drusen.](image)

Table 1. Clinical parameters of the study sample.

| Parameters                        | Controls     | Cases        | p   |
|-----------------------------------|--------------|--------------|-----|
| Visual acuity (log MAR)           | 0.00 ± 0.00  | 0.25 ± 0.24  | <0.001 |
| Central foveal thickness          | 168.41 ± 16.63 | 165.58 ± 21.83 | 0.535 |
| Photoreceptor layer thickness     | 61.20 ± 4.50 | 53.93 ± 7.36 | <0.001 |
| Retinal pigment epithelum thickness | 39.27 ± 4.30 | 36.10 ± 5.48 | 0.008 |
Discussion

The high resolution and lack of motion artifacts in SD-OCT scans allowed the assessment of multiple morphologic parameters and thus made precise assessment of the early retinal changes in AMD possible. SD-OCT due to its better resolution revealed structural changes in the retinal layers in the eyes with drusens. Although the integrity of the inner retinal layers was maintained, the outer retinal layers showed alterations in eyes with drusens.

Histological studies have revealed that most drusens consist of focal collections of eosinophilic material lying between the RPE and Bruch’s membrane. Therefore, they represent focal detachment of the RPE. The detached RPE may show evidence of varying degrees of thinning and degeneration. Dysfunction of thinning RPE may affect the neighbouring photoreceptor cells, as the photoreceptor function is dependent on that RPE for its contribution to the visual cycle and also in the process of constant phagocytosis of shed distal outer segment stacks, a process that generates photoreceptor cell renewal. If lipofuscin (LF) inhibits degradative metabolism, it would be assumed that the rate of phagocytosis of photoreceptor outer segment (POS) discs is impaired. Cells with LF-loaded secondary lysosomes would phagocytose less amount of shed POS. If these RPE cells were incapable of clearing obsolete tips of POS to a sufficient degree, it would result in the abnormal photoreceptor function. These may be the mechanisms or account for the association of increased LF in RPE and impaired photoreceptor function. Schuman et al. in their study using SD-OCT have reported thinning of PRL by 27.5% over drusen compared to age matched control eyes. This supports our study results which showed the thinning of RPE and PRL thickness in case of eyes with drusens. Godara et al. in their case report have reported thinning of outer segment of PRL above the drusen.

There was reduced reflectance of the boundary between the inner and outer segments of the photoreceptors (IS/OS) around the drusen (Fig. 3b). There are two possible reasons for this. Firstly, in cases of non-neovascular AMD, the PRL is damaged because of the dysfunctional RPE. This may be associated with structural changes in the PRL and the IS/OS that may reduce its reflectivity, mainly in the areas overlying drusen. Secondly, the elevation of RPE, over the dome-shaped drusen, may also change the reflectance of the IS/OS by disrupting the original arrangement of the photoreceptors. In this study we also found the hyper-reflective foci

![Figure 2](image_url)

**Figure 2.** Significant negative correlation was demonstrated between the photoreceptor layer thickness and the visual acuity.

**Table 2.** Multivariate model to predict visual acuity in patients with drusens.

|                | Beta   | Standard error | p      |
|----------------|--------|----------------|--------|
| Constant       | 1.602  | 0.487          | 0.003  |
| Age            | -0.002 | 0.005          | 0.675  |
| PRL thickness  | -0.017 | 0.007          | **0.019** |
| FT             | -0.002 | 0.002          | 0.394  |

Dependent variable: Visual acuity. Bold values are statistically significant; p value < 0.05.

**Figure 3.** SD-OCT image showing (a) hyper-reflective foci over drusen. (b) Reduced reflectivity of IS/OS junction around the drusen.
over drusen (Fig. 3a) which may represent retinal pigment migration or liberation that may signal the progression of the disease. Further studies should correlate the structural changes with that of the retinal sensitivity and also study these structural changes at different stages of AMD.

Function of RPE is the main factor influencing both the integrity of the photoreceptors over drusen and the life cycle of the drusen themselves. In the present study, the thinning of the PRL resulted in a significantly reduced visual acuity. The range of visual acuity found in our study sample was high when compared to the other studies even in cases with only drusen. This is very important finding, because we do not exactly know why patients with drusen alone sometimes have symptom of decreased vision. Studies also reported that drusen becomes clinically associated with a higher risk of vision loss when they exceed 64 μm in width, but in our study we did not measure the size of drusen. Godara et al. in their study have illustrated adaptive optics fundus imaging to quantitatively analyse the integrity of photoreceptors among patients with drusen.

We conclude that BCVA, PRL an RPE thickness were significantly reduced among patients with drusens and also we report that PRL thickness was significantly associated with BCVA. SD-OCT provides the cross sectional images of the nonexudative AMD with drusens with unprecedented resolution and detail. The images obtained using SD-OCT will be able to pick the early changes in PRL layer which have further impact on the visual acuity and help in further understanding the pathology of the disease. Loss of RPE cells results in the death of the overlying PRL causing impairment in visual acuity. By monitoring these drusens using the imaging modalities and assessing their impact on the photoreceptors and inner retinal layers might be quantified and helps in the management decisions involved in treating AMD.

**Conflict of interest**

The authors declared that there is no conflict of interest.

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