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ANATOMIC AND FUNCTIONAL IMPROVEMENT OF A DRUSENOID PIGMENT EPITHELIAL DETACHMENT: A CASE REPORT

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Background/Purpose: Age-related macular degeneration is the most prevalent cause of permanent vision loss in the developed world. Drusenoid pigment epithelial detachments are a biomarker of age-related macular degeneration disease progression and typically result in poor visual prognosis. Low luminance visual acuity (LLVA) has been previously been shown to correlate with the severity of age-related macular degeneration. However, the degree of spontaneous improvement of this functional outcome is still under investigation.

Methods: Observational clinical case report.

Results: A drusenoid pigment epithelial detachment that increased in size with the development of hyperreflective foci spontaneously improved with restoration of normal foveal contour over the span of 41 months without progression to geographic atrophy or choroidal neovascularization. Although best-corrected visual acuity remained stable both before and after the pigment epithelial detachment resolution, low luminance visual acuity decreased from a baseline of 59 (20/63 –1) to 39 (20/160 –1) letters over 17 months. However, over the subsequent 24 months, low luminance visual acuity improved by 35 letters to 74 letters (20/32 –2).

Conclusion: Drusenoid pigment epithelial detachments can resolve without treatment. Low luminance visual acuity seems to correlate with the anatomic improvement and can improve spontaneously by more than six lines of vision.

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In the developed world, age-related macular degeneration (AMD) is the most common cause of permanent vision loss[1] and has two different advanced forms: neovascular (wet) and atrophic (dry) geographic atrophy (GA). A pigment epithelium detachment (PED) is currently a poorly understood finding, both as it relates to disease pathophysiology and vision prognosis. There are three different kinds of PEDs: neovascular, serous, and drusenoid.

Although more research into the pathophysiologic mechanisms underlying the development of PEDs is needed, it is thought that they may be the result of a variety of degenerative and other processes.[2] Previous research has suggested that serous PEDs may be caused by the prevention of diffusion of fluid from the retinal pigment epithelium to choriocapillaris due to the formation of an age-related hydrophobic barrier in Bruch membrane.[3] However, there are other pathologic mechanisms that may be involved as well. It has been demonstrated that soft drusen are primarily composed of lipoprotein particles secreted by the retinal pigment epithelium and then not properly recycled, leading to the formation/expansion of drusen, retinal pigment epithelium migration, druse collapse, and atrophy.[1] Drusenoid PEDs, however, are thought to be the aggregate of large drusen, and because of the hydrophobic nature of the drusen, a similar barrier in Bruch membrane is created as with serous PEDs and causes the accumulation of fluid.[1]

With new therapies emerging for the intermediate stages of AMD, the ability to accurately and repeatedly

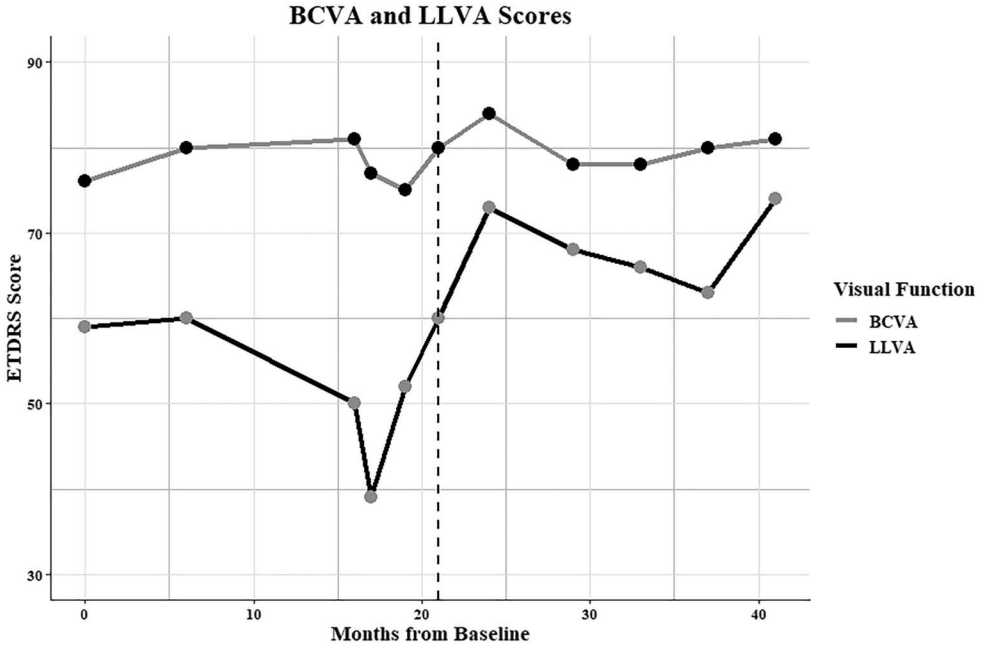

Fig. 1. Best-corrected visual acuity and LLVA ETDRS scores in the involved eye versus months from baseline. Time frame of anatomic resolution of the drusenoid PED (dashed vertical line).

assess the efficacy of treatments is critical. Currently, best-corrected visual acuity (BCVA) is the most common measure of visual function; however, it is insufficient for assessing disease severity in intermediate AMD because BCVA is not affected until later stages of the disease.

Low luminance visual acuity (LLVA) is measured by placing a 2.0 log unit neutral density filter over best-corrected vision and reading a normally illuminated Early Treatment of Diabetic Retinopathy Study (ETDRS) chart. Low luminance visual acuity has been found to be significantly reduced in eyes with non-foveal GA, despite BCVA being good, and predicted subsequent loss of vision.[4] In addition, low luminance deficit, the difference between the ETDRS letter score under photopic and low luminance conditions, is a strong predictor for AMD progression.

In this case report, spontaneous optical coherence tomography (OCT)-based improvement of a drusenoid PED with the return of a foveal contour and the absence of either GA or choroidal neovascularization was demonstrated. Furthermore, although there was loss of LLVA, a spontaneous improvement of 13 letters was observed after the resolution of the PED by this functional assessment and continued to improve over the 24-month follow-up period to a total gain of 35 letters. These results indicate the anatomic and functional vision improvement possible in PEDs associated with intermediate AMD and denote the degree of amelioration that is possible in this disease.

Case Report

A 73-year-old white man presented with a history of AMD. The subject's personal, family, and systemic history were unremarkable. Baseline BCVA was 76 ETDRS letters (20/32 +1) and LLVA was 59 letters (20/63 −1) (Figure 1). Slit-lamp exam revealed trace nuclear sclerosis cataracts OU. Spectral domain OCT (Heidelberg, Heidelberg, Germany) showed a drusenoid PED central to the fovea, vitreomacular adhesion without foveal distortion, and an absence of fluid or choroidal neovascularization (Figure 2). Fundus autofluorescence (Heidelberg) showed intraretinal hyperfluorescence areas around the fovea (Figure 3).

During the first 17 months, extensive intraretinal hyperreflective foci appeared over the PED (Figure 2), BCVA remained stable at 80 letters (20/25), and LLVA decreased from baseline over Months 6, 16, and 17, with letter scores to 60 (20/63), 50 (20/100), and 39 (20/160 −1) respectively (Figure 1). However, at Month 19, LLVA improved to 52 (20/100 +2) letters with BCVA holding at 75 letters (20/32) (Figure 1). By Month 21, anatomical resolution of the drusenoid PED by OCT was seen (Figure 2) and LLVA had improved to 60 letters (20/63). Hyperfluorescence areas around the fovea, as shown in fundus autofluorescence images, decreased after PED improvement at Month 21 (Figure 3). A vitelliform lesion was present at the apex of the drusenoid PED at baseline and Month 17 (Figure 2). At Months 21 and 41 no evidence of GA or choroidal neovascularization, confirmed by fundus photography (Canon CF-1, Canon U.S.A, Melville, NY) was seen. At Month 41, OCT-Angiography was conducted with a Zeiss

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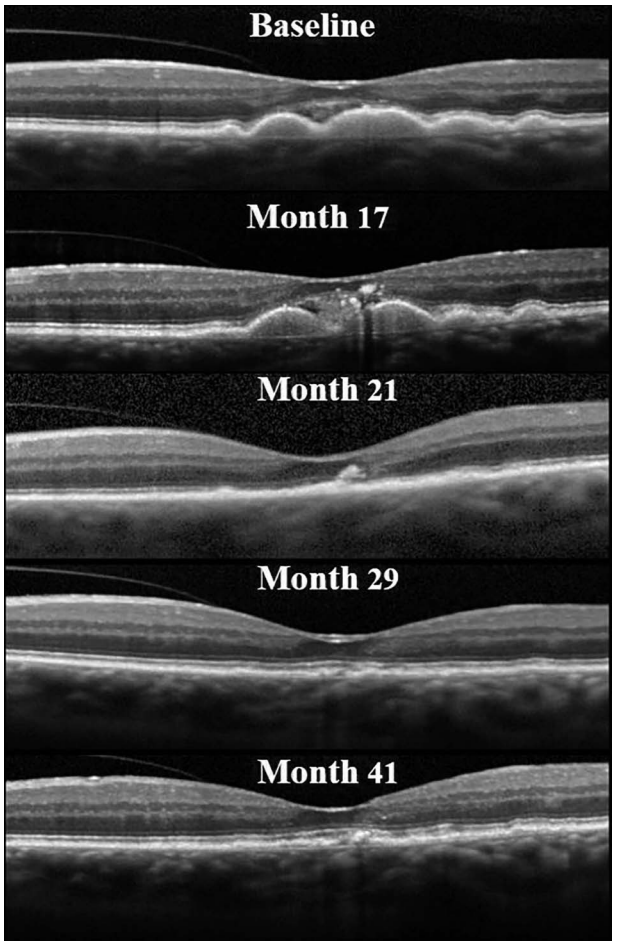

Fig. 2. Optical coherence tomography line scans of the fovea show the evolution of the drusenoid PED over the span of 41 months.

Plex Elite 9000 (Carl Zeiss, Jena, Germany) and showed no evidence of choroidal neovascularization. Interestingly LLVA continued to improve to 73 (20/40 +2) and 74 (20/32 −2) letters at Months 24 and 41 respectively.

Discussion

Although BCVA may remain unchanged, LLVA has been shown to be significantly reduced in early AMD[5] and has been demonstrated to be highly repeatable[6] with 6.5 letter variation.[4] In this case report, the patient's LLVA decreased to an ETDRS letter score of 39 (20/160 −1) from a baseline of 59 letters (20/63 −1), then improved by 35 letters after resolution of the drusenoid PED. Anatomical improvements, as shown by the spectral domain OCT, are aligned with the LLVA improvements (Figure 3). This suggests that LLVA may be a sensitive approach to structure/function analysis.

Certain features on the patient's baseline OCT were indicators of a risk of the development of

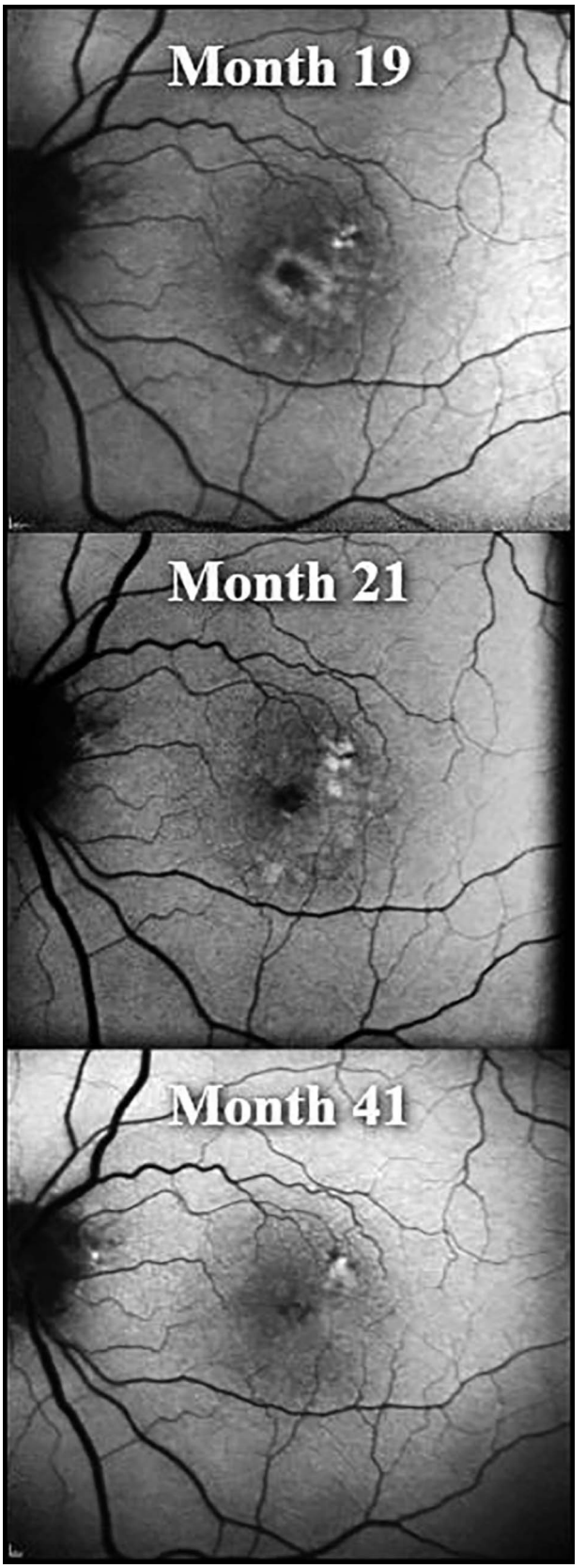

Fig. 3. Fundus autofluorescence image at baseline, Month 12, and Month 41.

subsequent GA, such as the height of the drusenoid PED and hyperreflective foci.[7] Through natural history studies, it is known that the prognosis of a drusenoid PED is not favorable. The Age-Related Eye Disease study found that of the 282 eyes observed with a drusenoid PED, 42% progressed to advanced AMD, with 45% of those patients developing GA and the other 55% developing neovascular AMD.[2] In addition, in this case, numerous intraretinal hyperreflective foci were noted at baseline (Figure 2). Hyperreflective foci have also been associated with an increased risk in developing atrophy at their location,[8] and as the number of hyperreflective foci increases, the risk of atrophy at that location also increases.[9]

As this case demonstrated, the use of LLVA outcome has implications when considering different functional measures as intermediate AMD clinical trial endpoints. Not only can spontaneous improvement in large drusenoid PEDs occur, but increases in functional outcomes, such as LLVA, can occur well beyond the limits of variability. This needs to be taken into account both when designing clinical trials and when considering the potential extent of future therapeutic interventions.

Key words: drusenoid PED, geographic atrophy, macular degeneration, pigment epithelium detachment.

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