Increasing Volume of a Retinal Pigmented Epithelial Detachment as a Predictor of Submacular Hemorrhage During Anti-VEGF Therapy

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ABSTRACT: Vascularized retinal pigment epithelium detachments (PEDs) are part of the spectrum of neovascular age-related macular degeneration (AMD). These patients with vascularized PEDs are at a higher risk of experiencing severe vision loss. This case report demonstrates the use of a new spectral-domain optical coherence tomography (SD-OCT) algorithm to measure the area and volume of PEDs. When this algorithm was applied to the scans from a patient with a vascularized PED who developed a large submacular hemorrhage while undergoing ranibizumab therapy, the authors found that the algorithm measured an increase in the area and volume of the PED that preceded the macular hemorrhage. Although further studies are needed, the increase in the volume of a PED may serve as a useful predictor of disease progression and the need for more aggressive anti-VEGF therapy.

INTRODUCTION

A retinal pigment epithelium detachment (PED) is formed by the accumulation of sub-RPE fluid, blood, fibrovascular tissue, or drusenoid material between the basal lamina of the retinal pigment epithelium (RPE) and the inner collagenous layer of Bruch’s membrane. PEDs can be part of the spectrum of age-related macular degeneration (AMD) and are frequently associated with the presence of choroidal neovascularization (CNV) and a higher risk of severe vision loss.5

The introduction of spectral-domain optical coherence tomography (SD-OCT) imaging allows for the acquisition of high-speed, high-resolution, high-density, three-dimensional images that can capture the true geometry of the retina and RPE. Recently, a segmentation algorithm was developed to extract quantitative information from SD-OCT datasets obtained from scans containing elevations of the RPE. This new algorithm creates a virtual RPE floor free of any deformations and subtracts this virtual RPE floor from the true RPE segmentation. The resulting difference map is referred to as the RPE elevation map, which includes both area and volume measurements of a PED. This algorithm has been shown to reproducibly measure the area and volume of drusen and larger PEDs.6-8

The purpose of this report is to demonstrate the potential usefulness of this algorithm in following eyes undergoing SD-OCT–guided re-treatment for neovascular AMD. We used this quantitative algorithm retrospectively in this case to reveal a change in the volume of the PED that was not obvious from the B-scans. This case demonstrates how the changes in the PED measurements could serve as useful predictors of disease progression in similar cases.

CASE REPORT

A 74-year-old woman who was treated for dry AMD at the retina clinic of the Bascom Palmer Eye Institute presented with decreased visual acuity (VA) in her right eye for 15 days. VA was 20/40 in the right eye and 20/25 in the left eye. Anterior segment biomicroscopy and intraocular pressures were normal. Fundus examination revealed juxtafoveal choroidal neovascularization (CNV) with subretinal fluid involving the fovea. SD-OCT confirmed the presence of subretinal fluid with foveal involvement, but a serious PED was not present at baseline. Intravitreal injec-
Treatments of Lucentis (ranibizumab 0.5 mg; Genentech, South San Francisco, CA) were initiated. After 11 months of follow-up in which a treat-and-extend retreatment regimen was used, the patient had received seven intravitreal injections of ranibizumab and the CNV was controlled. The VA was 20/30 and there was no evidence of intraretinal or subretinal fluid (Figure 1). The patient received an injection of ranibizumab at this visit and was asked to return 45 days later. At the next visit, she complained of vision loss, and her VA was now 20/40. Fundus examination revealed the presence of a PED with associated subretinal fluid. Figure 2 shows the color image, horizontal and vertical foveal SD-OCT B-scans, RPE segmentation map, and retinal thickness map at this visit. A PED is evident on the B-scans (B, C) and the RPE segmentation map (D), while the subretinal fluid is visualized on the B-scans (B, C) and the retinal thickness map (E, yellow areas). An injection of ranibizumab was given.

The patient continued to receive monthly injections of ranibizumab (0.5 mg), and the next five monthly visits are depicted in Figure 3, which shows the color fundus images, the horizontal foveal B-scans, the RPE segmentation maps, retinal thickness maps, and RPE elevation maps. At each of these follow-up visits, the amount of subretinal fluid increased and the volume of the PED increased compared with the previous visit. Despite monthly ranibizumab injections for 5 months, the volume measurements of the PED increased from 0.17 mm$^3$ to 0.24 mm$^3$ during this interval. The VA remained stable during this period.

Within 28 days of the last injection, a submacular hemorrhage occurred (Figure 4), with VA decreasing to 20/200. Management options were discussed, and the patient elected to receive additional injections of ranibizumab rather than undergo an attempt to displace or remove the hemorrhage. After 4 monthly injections of ranibizumab, the submacular hemorrhage had almost completely resolved, a fibrotic scar formed, and VA was stable at 20/200 (Figure 5).
DISCUSSION

This report describes the retrospective use of a novel SD-OCT algorithm in following up a patient with neovascular AMD and an associated PED undergoing ranibizumab therapy. While receiving monthly ranibizumab therapy, the amount of subretinal fluid in the macula increased at every visit. By analyzing the scans retrospectively, we found that the volume measurements of the PED increased as well, as documented by the SD-OCT algorithm for the measurement of RPE elevations. Despite the adequate monthly treatment, the increasing amount of subretinal fluid alone served as a poor prognostic sign. However, one of the most dreaded outcomes associated with vascularized PEDs is the formation of a RPE tear and hemorrhage, and tears of the RPE often result from pre-existing PEDs. Approximately 12.5% of vascularized PEDs result in a tear of the RPE. By monitoring the change in the volume of a PED, we may have found a useful new tool for following eyes with vascularized PEDs undergoing treatment and assessing disease progression. If the volume of a PED is found to increase, then this finding might serve as a useful predictor of eyes at risk for RPE tears and hemorrhage. While the increasing amount of subretinal fluid alone was an ominous sign, we might have been more insistent that the patient receive more aggressive ranibizumab therapy, such as biweekly injections, had we used this algorithm at the time the injections were being given.

The increasing height of a PED detected using OCT imaging has previously been described as a risk factor for a RPE tear. This change was difficult to appreciate on sequential visits using the conventional B-scans and maps obtained from the SD-OCT instrument. This new SD-OCT algorithm, which is now commercially available in version 6.0 of the Cirrus operating software (Carl Zeiss Meditec, Dublin, CA), demonstrated a volumetric increase even before the height had unambiguously changed. Moreover, the height may vary depending on whether the B-scan
was reproducibly positioned from visit to visit. In addition, the volume measurements may also detect lateral spread of a PED, which may not be evident on a single B-scan image. The automatic and reproducible algorithm described in the manuscript allowed us to retrospectively identify the growth of the PED at each visit prior to the hemorrhage. This algorithm is a simpler and less ambiguous approach than the manual measurement of PED height using a single B-scan when following these patients undergoing treatment. While PED volume is just one of several components such as fluid, contractile elements, fibrovascular tissue, and proteinaceous material associated with the evolution of vascularized PEDs, the volume measurement may serve as a useful surrogate marker for all these associated components as they increase within the sub-RPE compartment. However, all these components should be studied to see if any one provides a better indicator of hemorrhage risk than volume alone.

In summary, SD-OCT imaging can be used to follow elevations of the RPE, and this new quantitative algorithm may be particularly useful when following and managing patients with vascularized PEDs. Although further studies are needed, the increase in the volume of a PED may serve as a useful predictor for disease progression and the need for aggressive therapy.

REFERENCES