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Retinal Neovascularization Secondary to Proliferative Diabetic Retinopathy Characterized by Spectral Domain Optical Coherence Tomography

Hyung Cho, MD¹, Ahmad A. Alwassia, MD¹, Caio V. Regiatieri, MD, PhD^{1,2}, Jason Y. Zhang, MD¹, Caroline Baumal, MD¹, Nadia Waheed, MD¹, and Jay S. Duker, MD¹

¹New England Eye Center, Tufts Medical Center, Boston, Massachusetts

²Federal University of São Paulo, São Paulo, Brazil

Abstract

Purpose—To characterize diabetic retinal neovascularization and accompanying retinal and vitreal morphological changes using high-resolution spectral domain optical coherence tomography (SD-OCT).

Methods—A cross-sectional retrospective analysis was performed on 16 eyes of 14 nonconsecutive subjects with proliferative diabetic retinopathy that were seen between August 2011 and December 2011 at the New England Eye Center, Boston, Massachusetts. Patients who had neovascularization of the disc (NVD), neovascularization elsewhere (NVE) and intraretinal microvascular abnormalities (IRMAs) were scanned using OCT scans directly over the region of the abnormal vessels.

Results—Characteristic changes of the retinal vasculature, retina and vitreous were seen in the 16 eyes with neovascularization. This study describes OCT characteristics of: 1) NVD; 2) NVE; 3) IRMA; 4) NV causing traction without retinal detachment; 5) NV causing traction with retinal detachment. The morphologic appearance of vitreous traction was found to be consistent with previous histological reports.

Conclusions—It is possible to image diabetic NV using SD-OCT and to visualize the spectrum of retinal, retinal vascular and vitreal changes seen through these areas of abnormal retinal vasculature.

Keywords

Neovascularization of the retina; neovascularization of the disc; intraretinal microvascular abnormalities; diabetes mellitus; proliferative diabetic retinopathy; optical coherence tomography

Corresponding Author/Reprint Requests: Jay S. Duker, MD, New England Eye Center, Tufts Medical Center, 800 Washington Street, Boston, MA 02111, Phone: 617-636-4677, Fax: 617-636-4866, Jduker@tuftsmedicalcenter.org.

Conflict of Interest

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Introduction

In many developed countries, diabetic retinopathy is an increasing cause blindness, especially in the working age population.¹ Individuals with diabetes are 25 times more likely to become blind than persons in the general population.² Ischemia-driven release of cytokines such as vascular endothelial growth factor (VEGF) into the vitreous cavity is known to be one of the main drivers of new vessel formation in retinal proliferative disease.³ Proliferative diabetic retinopathy (PDR) is a major cause of visual loss in diabetic patients and is characterized by neovascularization (NV) that occurs at the vitreoretinal interface and in the vitreous. It can cause vitreous hemorrhage, neovascular glaucoma and tractional retinal detachment which can result in visual loss.⁴

Neovascularization is clinically characterized by fine loops or networks of vessels lying on the surface of the retina and extending into the vitreous cavity. They are usually easily identified on slit lamp exam, but in their earliest stages may be overlooked. Detection of NV requires not only for the vessels to be seen, but that they be differentiated from intraretinal microvascular abnormalities (IRMAs). Compared to NV, IRMA was diagnosed clinically on the following characteristics: they appear deeper in the retina and have blurrier edges, have more of a burgundy color as opposed to red, they are not commonly found around the disc, they usually occur adjacent to cotton wool spots, and may be associated with other signs such as 'omega' venous loops, venous reduplication and white lines which represent occluded arterioles. This is somewhat difficult if IRMAs are extensive or if NVs do not show any of their unique features, such as formation of wheel-like networks, extension across both arterial and venous branches of the underlying retinal vascular network, and accompanying fibrous proliferations. If doubt remains, fluorescein angiography (FA) usually resolves the confusion as NV demonstrates profuse leakiness characteristics of preretinal new vessels, but no signs of leakage in the case of IRMAs.

Optical coherence tomography (OCT) is well established as an accurate imaging study of retinal pathology with good correlation between histology of animals and humans in vivo.⁵⁻⁷ OCT images provide an accurate visualization of the actual retinal architecture in vivo. The clinical and histological findings in neovascularization have been described.^{5,8} However, the spectral domain optical coherence tomography (SD-OCT) correlate of neovascularization has not been previously examined. The purpose of this study is to describe the structure of these preretinal vessels, to assess whether it is possible to differentiate NV and IRMA without the use of fluorescein angiography, and to determine if findings such as traction on the retina from the NV can be seen using SD-OCT.

Patients and Methods

A cross-sectional analysis of 16 eyes of 14 patients with proliferative diabetic retinopathy was performed. This study was approved by the institutional review board of Tufts Medical Center and is adherent to the tenets of the Declaration of Helsinki. All patients were examined by the retina service of the Ophthalmology Department of the New England Eye Center, Tufts Medical Center, Boston, MA, between August 2011 and December 2011. Examination included Snellen best-corrected visual acuity, slit-lamp examination, fundus

biomicroscopy, color fundus photography, fluorescein angiogram, and OCT examination. When neovascularization of the disc (NVD), neovascularization elsewhere (NVE) or IRMA was found on clinical exam using a 78 D lens, an OCT scan centered on the area of abnormal blood vessels was performed. A fluorescein angiogram was performed on all patients.

OCT imaging was performed using Cirrus-HD OCT software version 4.5 (Cirrus HD-OCT; Carl Zeiss Meditec). The software version allows for the acquisition of high-definition 1-line raster scans that are constructed from 20 B-scans obtained at the same location and processed using a unique Selective Pixel Profiling system. The 1-line raster is a 6-mm line consisting of 4096 A-scans with an axial resolution of approximately 5 to 6 μm and a transverse resolution of approximately 15 to 20 μm . The macular cube scan consists of 512 A-scans $\times$ 128 B-scans over a 6 mm $\times$ 6 mm area and provides both a qualitative and quantitative evaluation of the retina.

The SD-OCT cross-sectional images and OCT fundus image were correlated to color fundus photographs and fluorescein angiography and evaluated for characteristic changes of the vessels, retina and vitreous overlying the areas of abnormal vasculature.

Results

Sixteen eyes of fourteen patients with PDR were imaged using the Cirrus HD-OCT. The 14 patients consisted of 9 men and 5 women, with a mean age of 51.2 years (range, 28–68 years). Four patients had type 1 diabetes, and 10 had type 2 diabetes. The average hemoglobin A1C in all enrolled patients is 8.7% (range, 7.5–10.1%). Five of 14 patients had prior vitreous hemorrhage treated with vitrectomy. The images were examined to describe the characteristic appearance of: 1) NVD; 2) NVE; 3) IRMA; 4) NV causing traction without retinal detachment; 5) NV causing traction with retinal detachment (Figures 1–6).

NVD

9 patients presented with NVD (56.2%) and it was possible to identify NVD using SD-OCT in all of the cases. In 5 eyes, when the posterior hyaloid was detached, the NVD was identified as a hyperreflective line protruding from the optic disc (Figure 1c). In 4 eyes, when the posterior hyaloid was still attached, the NVD was seen as a hyperreflective tissue sitting over the optic disc (Figure 2b). In all cases, we were able to observe a connection between the new vessels and the optic disc.

Color fundus photograph of a patient with NVD is shown in figure 1A. (B) Fluorescein angiography of the lesion; note the leakage of fluorescein from the vessels around the disc and into the vitreous. (C) HD 1-line scan through the NVD. The arrow shows the new vessels projecting into the vitreous. The posterior hyaloid is demarcated by the arrow heads.

Color fundus photograph of another patient with NVD is shown in figure 2A. New vessel in disorganized manner is evident (B) HD 1-line scan through the NVD. The arrow points to the NV. It appears as a hyper reflective tissue at the vitreal/optic disc interface. The NV in this case appears as a funnel shaped mass growing from the optic disc. Optical shadowing is

evident in the outer portion of the optic disc as a result of the new vessel growth. The posterior hyaloid is attached to the new vessels (arrow heads). The posterior hyaloid appears thickened in some areas. The NV is connected to the retina at the optic disc nasally and appears as a distinct entity temporally.

NVE

In 6 of the images (37.5%) that were examined, neovascularization of the retina was noted (Figure 3). The NV is seen as hyper reflective loops of relatively homogenous hyperreflectivity. Whether a complete loop is seen or just one end depends on the direction of the NV vessels and the plane of the OCT scan. In this case (Figure 3), the NV is visualized as a C-shaped loop (B). Note the shadowing of the inner and outer retina behind the NV. There is increased reflectivity in the nerve fiber and ganglion cell layers intervening between the NVE loop. The boundary between the different retinal layers appears irregular.

IRMA

In 4 of 16 eyes (25%) that were examined, IRMA was observed (Figure 4). IRMA lesion do not project into vitreous, the posterior hyaloid is attached, and no leakage of fluorescein is found (B-1). The lesions are mainly intraretinal causing loss of the inner retinal architecture; there are focal areas where the IRMA appears to protrude through the ILM but not into the overlying vitreous. Thickening of the attached posterior hyaloid is not seen. NVE is shown in (D). The vessels project through the attached and thickened posterior hyaloid and into the vitreous. Examining the corresponding location on fluorescein angiogram for the NVE lesion demonstrates late leakage (B-2).

NV with traction but without detachment

In 4 of the images (25%) that were examined, traction on the retina was observed, without retinal detachment (Figure 5). This patient has a thickened posterior hyaloid, indicated by the green arrowheads. NV is seen as hyperreflective material within the inner retinal layer and projecting into the vitreous. Structural changes are noted in the inner retinal layers as a result of traction but retinal detachment is not present. In addition, focal dots of hyperreflective material corresponding to vessels are evident in the inner retina. Optical shadowing is again seen in the outer retina behind the more reflective new vessels. The hyperreflective material in the cortical vitreous could represent fibrovascular tissue growth or retinal tissue that has been peeled off the retina as a result of traction.

NV with traction and retinal detachment

In 3 of the images (18.8%) that were examined, traction from the NV was observed with accompanying retinal detachment (Figure 6). The posterior hyaloid is attached and thickened and is displayed as the green arrowhead. The detached retina has lost its architectural organization, and cystic spaces were present. The nerve fiber and ganglion cells layers in the involved area shows increased reflectivity; this represents both new vessel formation and intraretinal bleeding. Tractional retinal schisis is also evident temporally in B, and C.

Discussion

This is the first study to show that SD-OCT evaluation of retinal and disc neovascularization in association with proliferative diabetic retinopathy is possible. In all instances, neovascularization with OCT was able to be imaged. The resolution on the macular cube scan was not always enough to identify the areas of NV in detail. The 1-line raster proved superior to the cube scan in delineating the fine detail of the NV because of image averaging that allows for greater resolution. Newer generation OCTs will allow for the acquisition of macular cube scans with resolution comparable to that of the 1-line scan. In addition, newer OCTs will be able to get more peripheral 1-line scans and will potentially allow for scanning of the entire retina.

In all cases, differentiation between NV from IRMA was possible. The main differentiating factor between NV and IRMA was that in NV, the abnormal vessels broke through the posterior hyaloid, which was able to be imaged by OCT. There were two categories of neovascularization on OCT. In the first category, the posterior hyaloid is attached and oftentimes thickened, with the new vessels protruding through the membrane and into the vitreous cavity (Figure 4d). In the second category, the posterior hyaloid is detached and shows vessels clearly evident on the surface of the retina and protruding into the vitreous with many different shapes/patterns as described above depending on the plane of the OCT scan (Figure 3). New vessels were typically visualized as loops of homogenous hyperreflectivity protruding into the vitreous with shadowing of the inner and outer retina behind the NV. The boundaries between the different retinal layers were often irregular.

The posterior hyaloid can be visualized and can be determined whether it is attached to the newly formed vessels in many cases of patients with retinal NV. If the posterior hyaloid is attached to the NV in the area of the optic nerve, it can make the detachment of the hyaloid more difficult with a higher risk of bleeding during surgery. Areas with traction with and without retinal detachment were able to be identified. This prior knowledge may be important in the clinic to assess progression and for surgical planning.

Considering the varying appearance of neovascularization between individuals and even within one eye, this descriptive analysis confirms that neovascularization evolves along a continuing spectrum, with the vessels, retinal and vitreal changes observed at various stages of change. Spectral domain OCT is a non-invasive technology that can be used to image neovascularization and has clinical utility in that OCT may be useful to monitor subtle changes such as progression of the neovascularization and traction on the retina over time.

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Summary Statement

This is a study that characterizes the morphology of neovascularization in patients with proliferative diabetic retinopathy using spectral domain optical coherence tomography (SD-OCT).

Fig. 1. Color fundus photograph of a patient with NVD is shown in A. (B) Fluorescein angiography of the lesion; note the leakage of fluorescein from the vessels around the disc and into the vitreous. (C) HD 1-line scan through the NVD. The arrow shows the new vessels projecting into the vitreous. The posterior hyaloid is demarcated by the arrow heads.

Fig. 2. Color fundus photograph of another patient with NVD is shown in A. New vessel in disorganized manner is evident (B) HD 1-line scan through the NVD. The arrow points to the NV. It appears as a hyper reflective tissue at the vitreal/optic disc interface.

Fig. 3. Color fundus photograph of a patient with NVE. The NVE is indicated by the arrow. The green horizontal line indicates the plane for the OCT scan shown in (B). The NV is visualized as a C-shaped loop (B). Note the shadowing of the inner and outer retina behind the NV.

Fig. 4.

(A) Red free photo of left eye (B) Fluorescein angiogram (late). There is leakage from the areas of neovascularization. The red line indicates the location of the corresponding OCT scan in (C); the horizontal green line indicates the location of the corresponding OCT scan in (D). IRMA lesion is shown in (C). NVE is shown in (D).

Fig. 5.
(A) Fundus photograph of a patient with NVE. The green horizontal line indicates the location of the corresponding OCT image shown in (B).

Fig. 6.
 (A) Color fundus photograph of a patient with NVE. The red and green horizontal lines indicate the location of the OCT scan in B, and C respectively. (B, C) A retinal detachment as a result of traction from the new vessels is shown (asterisk in B, C).