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Case report

The effect of bevacizumab before vitrectomy for diabetic tractional retinal detachment demonstrated on optical coherence tomography angiography

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Abstract

Purpose: To demonstrate the effect of intravitreal bevacizumab (IVB) on the size and vascularity of the fibro-vascular complex with the optical coherence tomography angiography (OCTA) before pars plana vitrectomy (PPV).

Methods: Observational case series of three eyes with active diabetic fibro-vascular complex and tractional retinal detachment (TRD) who underwent IVB (1.25 mg/0.05 ml) two days before proceeding to PPV. OCTA was carried out prior to IVB, two days after IVB and six weeks after PPV.

Results: OCTA showed a reduction in the size and calibre of the diabetic fibro-vascular complex two days after IVB in all the cases. Consequently, there was less traumatic dissection of the fibro-vascular membranes during PPV and thus reduced chances of intraoperative and postoperative vitreous cavity bleeding. One case showed mild hemorrhage in the posterior vitreous on the second day post-injection which implies the increased traction caused by IVB.

Conclusions: In this case series, we have used OCTA to demonstrate how IVB is highly effective in reducing the vascularity of diabetic fibro-vascular membranes. This finding also suggests that the use of IVB before PPV in the management of diabetic TRD could also be much shorter than the advocated standard practice of one week in most institutions.

Keywords: Bevacizumab; Diabetic tractional retinal detachment; OCTA; Vitreous hemorrhage

Introduction

Tractional retinal detachment (TRD) is a leading cause of vision loss in patients with proliferative diabetic retinopathy (PDR).[1] Pars plana vitrectomy (PPV) is a successful surgical procedure for the complications of PDR such as TRD[2]; nevertheless, postoperative vitreous hemorrhage (VH) represents a significant complication occurring in 20%–30% of cases.[3,4] It has been hypothesized that VH tends to occur after PPV for diabetic TRD because of difficulty of hemostasis

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during surgery, neovascularization stimulated by the sclerotomy site, and residual contracting vitreous.[5,6] Intravitreal bevacizumab (IVB), an inhibitor of vascular endothelial growth factor, performed one to twenty days before vitrectomy has been reported to prevent recurrent VH after vitrectomy for PDR by reducing neovascular activity.[7] The use of IVB has also been shown to reduce overall surgical time and diminish overall intraoperative complications.[8] Optical coherence tomography angiography (OCTA) is a new and promising imaging modality that depict retinal vascular changes and capillary non-perfusion in DR patients.[9] Regression of neovascularization around the optic disc has been shown on OCTA to occur as early as 24 hours after a single IVB administration.[10] Therefore, we have used the OCTA technology to demonstrate the effectiveness of IVB changes on the active proliferative fibro-vascular network in a series of patients prior to PPV surgery for diabetic TRD.

Case report

Three diabetic patients with similar characteristics of active PDR, TRD, and VH were selected. All OCTA enface images were qualitatively reviewed by two independent graders for the size of the retinal fibro-vascular complexes. In all the OCTA images acquired two days after the IVB, a decrease in the reflectivity and the volume of all the retinal fibro-vascular complexes was noticed in all patients with an inter-reviewer agreement of 100%. Patients were imaged with the Deep Range Imaging (DRI) Triton® SS (Swept Source) OCTA (Topcon Corp., Tokyo, Japan) as follows:

- Immediately before IVB 1.25 mg/0.05 ml
- On the second morning after the injection prior to the PPV
- Six weeks after PPV once the gas tamponade (if used) had been absorbed

Topcon IMAGEnet i-base (Topcon Corp., Tokyo, Japan) semi-automated segmentation software demonstrated the findings through the vitreo-retinal segmentation or outer vitreous segmentation. Raster-pattern retinal scans were obtained through the macula, the optic disc, and areas of possible new vessels in the mid-peripheral retina using scanning patterns of 6×6 mm in all patients. During the OCT examination, the choroid and the retina were positioned at the lower border of the image plane and as necessary to achieve a full depth visualization of the new vessel processes in the vitreous cavity. During vitreoretinal or vitreous segmentation analysis, the vitreous was segmented semi-automatically after modifying the reference planes and manipulating the depth of the boundaries to optimize the visualization of new vessel features in the cortical vitreous. OCTA images obtained were then automatically segmented to show the neovascular changes above the internal limiting membrane, the superficial neurovascular plexus, or any other tissular layer that could be arbitrary set as the lower segmentation boundary. The superior boundary was set in the depth of the vitreous cavity in order to obtain full visualization of the new vessels performed.[11] The same boundaries were evaluated before and after the IVB and PPV in all the patients.

Fig. 1 is a 45-year-old female, Fig. 2 is a 55-year-old male, and Fig. 3 is a 30-year-old female. There was absence of reflectivity of retinal fibro-vascular complexes after four to eight weeks from PPV in all three eyes following PPV. VH occurred in one patient two days after IVB (Fig. 2). No VH or postoperative RD was evident in all patients after six weeks from PPV. No intraoperative complications were observed during the PPV. There was no significant bleeding from the segmentation and delamination of the fibro-vascular complex during the PPV.

Discussion

Smith and Steel[7] investigated the use of anti-VEGF for prevention of postoperative vitreous cavity hemorrhage (POVCH) for PDR and concluded in their Cochrane review that the use of pre or intraoperative bevacizumab lowers the incidence of early POVCH with no local or systemic

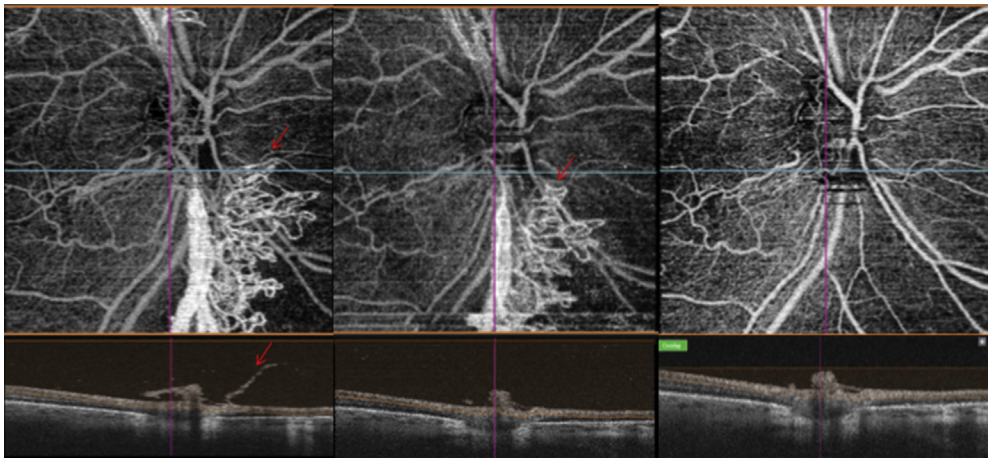

Fig. 1. From the left to the right: Swept-source optical coherence tomography angiography (SS OCTA) (top) and B Scan SS OCT images (bottom) before intravitreal bevacizumab (IVB), two days after IVB and 6 weeks after pars plana vitrectomy (PPV). Red arrow indicates the superior edge of the fibro-vascular membrane before and 2 days after IVB (with the contraction of the membrane).

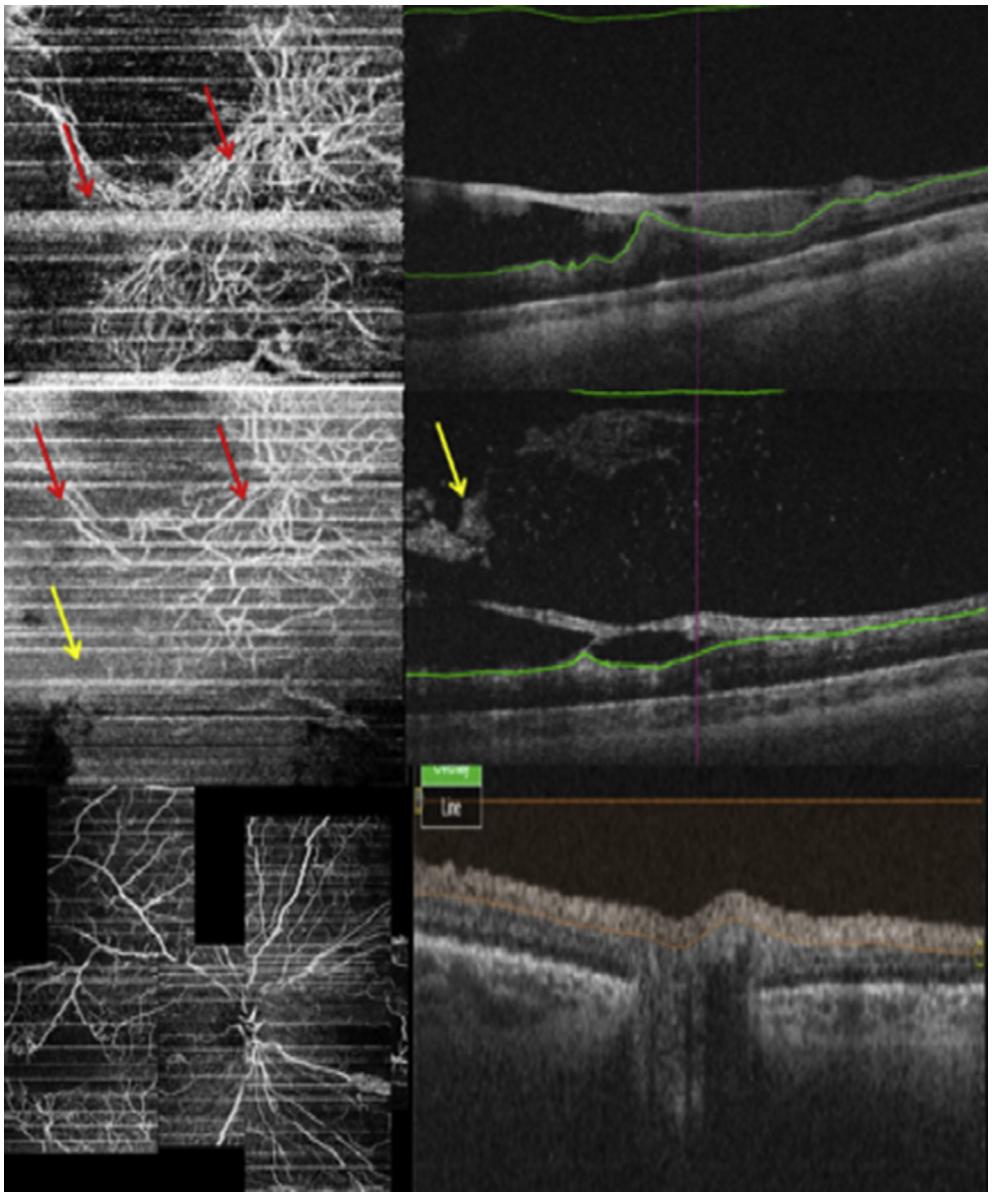

Fig. 2. From left to right: Optical coherence tomography angiography (OCTA) of the fibro-vascular complex and B Scan Swept-source optical coherence tomography angiography (SS OCTA) of the fibro-vascular complex. From top to bottom: before intravitreal bevacizumab (IVB), two days from IVB and 6 weeks from pars plana vitrectomy (PPV). Note the reduced size and branching of the vascular complex after IVB (red arrow) and the mild hemorrhage in the posterior vitreous on the second day post-injection (yellow arrow) implying the increased traction caused by IVB.

complications of IVB. However, the effect on late POVCH was uncertain. Different authors have advocated different timelines for IVB use, from one day to three weeks pre-PPV, including some who give IVB at the end of PPV.[7] A long delay from IVB to PPV also increases the change of progression in pre-existing TRD. These clinical findings influenced our decision to choose a shorter timeframe to proceed to PPV after the IVB. Our observational study has demonstrated that IVB can be effective as early as two days to take effect and this is confirmed with the OCTA findings. An early sign of increased traction was seen in one case. This increased traction was manifested through hemorrhage in the posterior hyaloid face due to the pulling effect on the fibro-vascular membranes. Alternatively, the mechanical effect of the IVB in the vitreous cavity and the mixing of pre-existing epi-retinal blood with the vitreous could also explain the blood in the posterior vitreous. Despite the evidence that anti-VEGFs reduce early POVCH, there is an argument against its use in all diabetic vitrectomies, especially those with fibrotic TRDs where it can be counter-productive. In our case series, IVB was given only before PPV for 'vascular' TRDs and not before other 'routine' diabetic PPV. It was highly effective in our case series by reducing vascularity of diabetic membranes, which in turn lead to an increased ease of surgical dissection and reduced chances of POVCH. Considering that worsening of fibrosis and traction is mostly seen after a week based on previous studies, performing PPV earlier after IVB can be considered an ideal compromise. Inherently, this case series has its obvious limitations which are the small sample size and lack of control group. However, the encouraging result from this case series

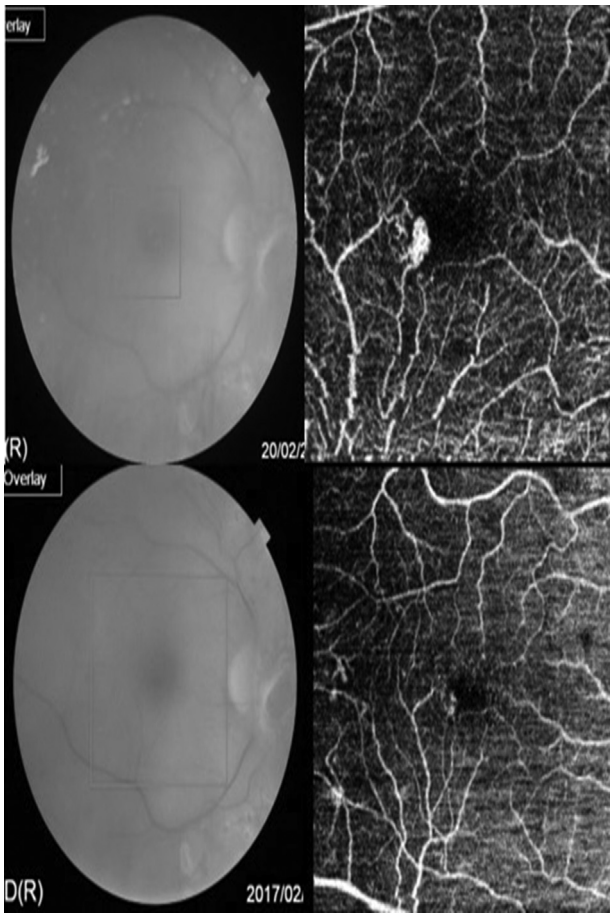

Fig. 3. From left to right: fundus image of the area of active proliferative retinal vessel and optical coherence tomography angiography (OCTA) of the fibro-vascular complex. From top to bottom: before intravitreal bevacizumab (IVB) and two days after IVB (with the decrease size of the active proliferative retinal vessel).

using OCTA provides a platform for a randomized, controlled trial to confirm the optimum time frame for the use of IVB in diabetic TRD before PPV.

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