# Intravitreal bevacizumab for iatrogenic choroidal neovascular membrane following vitreoretinal surgery for retinal detachment

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We report the successful use of intravitreal bevacizumab in the iatrogenic choroidal neovascular membrane (CNVM) following vitreoretinal surgery. A 69-year-old male underwent vitrectomy surgery with silicone oil (SO) tamponade for rhegmatogenous retinal detachment. During fluid air exchange, there was an accidental retinal touch at an area in the papillomacular bundle with the silicone tip cannula. He had persistent subretinal bleed at the area 1 month after surgery. The optical coherence tomography (OCT) showed a subretinal elevated lesion and fluorescein angiography (FFA) showed an active CNVM. The patient was treated with intravitreal bevacizumab in the SO-filled eye. At 1-month postinjection, the OCT revealed reduction in the size of CNVM. The patient underwent SO removal with the second dose of intravitreal bevacizumab. CNVM regressed with no recurrence on follow-up at 1 year. Iatrogenic CNVM is a rare complication following successful vitreoretinal surgery. Prompt diagnosis and treatment with intravitreal bevacizumab may be required for a favorable outcome.

**Key words:** Avastin, choroidal neovascular membrane, intravitreal anti-VEGF agents, laser, silicone oil, vitrectomized eye

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Iatrogenic choroidal neovascular membrane (CNVM) is an uncommon condition usually associated with retinal laser or iatrogenic trauma during vitrectomy. Very few cases of iatrogenic CNVM have been reported in the literature, and the functional outcome has generally been poor in these reports despite treatment with laser photocoagulation, intravitreal bevacizumab, photodynamic therapy, and surgical removal of neovascular membranes. We report this case to highlight this rare complication following vitrectomy and its response to antivascular endothelial growth facor (VEGF) therapy.

## Case Report

A 69-year-old male presented with a sudden onset of floaters in his right eye (RE) since a week. Medical history was noncontributory. His Snellen's best-corrected visual acuity (BCVA) was 20/30 in the RE and 20/20 in the left eye. Both eyes were pseudophakic. The fundus examination in the RE revealed an inferotemporal rhegmatogenous retinal detachment with an attached macula. The left eye fundus was normal. The patient underwent primary vitrectomy surgery with silicone oil (SO) tamponade in his RE. An inadvertent retinal touch occurred in the papillomacular bundle, superonasal to the fovea while performing fluid air exchange with silicone tip cannula. A mild intraretinal hemorrhage was noted intraoperatively following the injury. Postoperatively,



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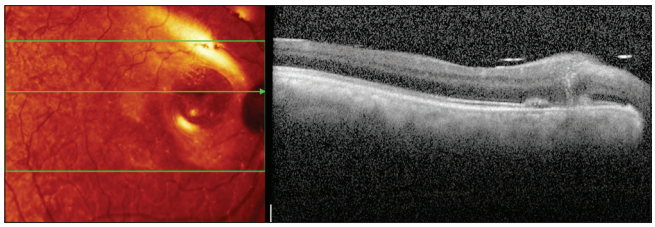

**Figure 1:** Right eye SD-OCT showing retinal edema with RPE discontinuity at the site of instrument touch at 1 month after vitrectomy

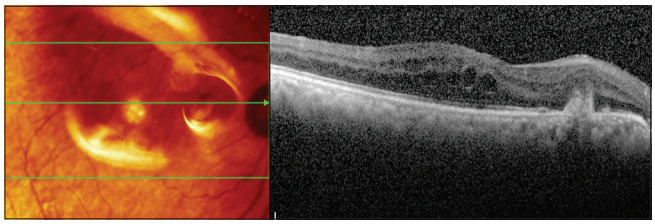

**Figure 3:** SD-OCT at 1 month post bevacizumab injection OCT showing CNVM with cystic spaces in oil-filled eye

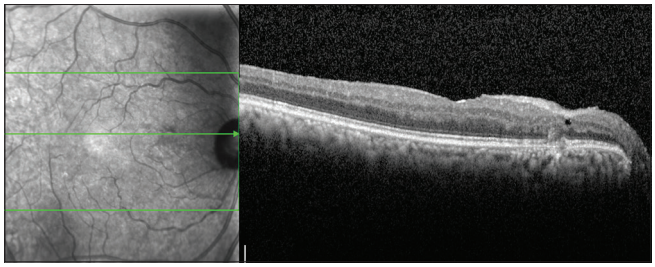

**Figure 5:** SD-OCT showing regressed CNVM at 6 months follow-up

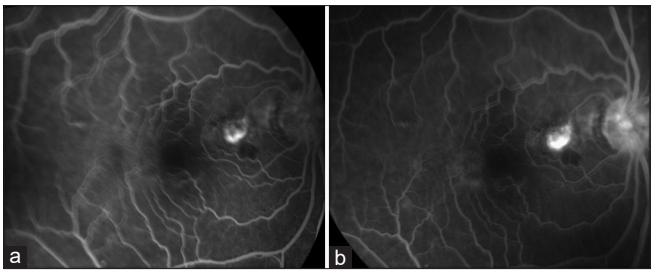


**Figure 2:** (a and b) FFA showing hyperfluroscence, which is increasing in intensity and size suggestive of leakage

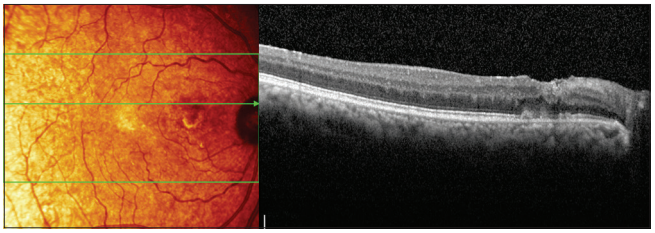

**Figure 4:** SD-OCT at 1 month postinjection OCT showing resolving retinal edema with regressing CNVM

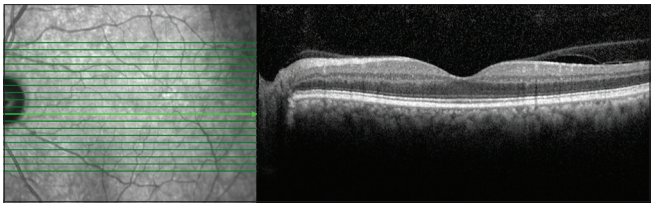

**Figure 6:** SD-OCT of the left eye shows normal foveal contour

the patient had a good anatomical outcome with no secondary glaucoma or inflammation.

His BCVA was 20/30 at the 1-month follow-up. A large subretinal hemorrhage at the site of the previous injury was noted at this visit. Spectral-domain OCT (SD-OCT) showed disruption of retinal pigment epithelium with irregular pigment epithelial detachment (PED) with minimal subretinal fluid (SRF), suggestive of a CNVM. Disruption of the superficial retinal layers was seen adjacent to the PED, indicating the site of intraoperative injury [Fig. 1]. Fundus fluorescein angiography (FFA) revealed an extrafoveal, well-defined area of early hyperfluorescence, increasing in intensity beyond its borders, confirmative of CNVM [Fig. 2a and b]. The patient underwent intravitreal bevacizumab (1.25 mg in 0.05 ml) injection in SO-filled globe.

One month postinjection, BCVA in RE dropped to 20/40. Cystoid macular edema (CME) was noted at the fovea. There was a mild increase in the size of the PED, but the SRF had resolved [Fig. 3]. SO removal with a second dose of intravitreal bevacizumab injection (1.25 mg) was done 3 months after vitrectomy. During his subsequent follow-up after 1 month, CNVM was regressing well and BCVA improved to 20/30. The OCT showed a decrease in the size of PED and CME. No SRF was noted [Fig. 4]. Three months following intravitreal injection, a scar developed at the site of CNVM and the patient maintained BCVA of 20/30 in the RE [Fig. 5]. No further bevacizumab injections were needed in the next 1-year follow-up.

## Discussion

CNVM occurs when there is damage to Bruch's membrane and/or retinal pigment epithelium (RPE), and new blood vessels, originating from the choroid, grow into the subRPE or subretinal space.[1] The disruption of Bruch's membrane following direct surgical injury may initiate a reparative response of the retinal pigment epithelium leading to the synthesis of VEGF.[2] Goh *et al.* postulated that the inflammatory process following surgical intervention would contribute to additional oxidative stress (OS) to the neurosensory retina, and a preexisting surgically induced abnormal RPE activation can result in unfamiliar VEGF upregulation.[2] AntiVEGF therapy by inhibiting the release of proangiogenic cytokines has been proven to be effective in the treatment of CNVM of various etiologies, revolutionizing the treatment paradigm. Bevacizumab has been widely used off-label in VEGF-mediated ocular diseases because of its relatively low cost and noninferior efficacy to the US Food and Drug Administration (FDA)-approved drug for CNVM secondary to wet age related macular degeneration (AMD) (ranibizumab).

Pharmacokinetic profiles of intravitreal-injected drugs are important in determining the optimal dosing frequency to achieve maximum therapeutic intraocular concentration with a minimal number of injections.[3] A drug when injected into the posterior segment of the eye in the presence of SO tamponade could behave significantly different when compared with a vitreous-filled eye or eye following vitrectomy without

tamponade.[4] SD - OCT of the other eye showed normal foveal contour [Fig. 6]. Xu *et al.* in their study in rabbit eyes observed that following an intraSO injection of bevacizumab, the visible droplets migrate in the SO for 1 to 3 days before integrating into the vitreous fluid that existed between the SO and retinal surface.[4,5] Also, the integration process was gradual that slowed down the distribution of bevacizumab into various ocular tissues, which resulted in larger T max (time at which maximum concentration is achieved) and smaller C max (maximum concentration) with a relatively sustained bevacizumab levels in the ocular tissues; however the terminal half-lives were found to be similar to eyes with native vitreous. The possible complication of oil emulsification occurring at the vitreoretinal surface could make the process complex.[5] Thus, in this case, bevacizumab in SO-filled globe might have required more time to achieve the maximum concentration, leading to a suboptimal response following the first bevacizumab injection and SO removal with repeat injection might have enhanced the antiVEGF effect, leading to regression of CNVM following the second injection.

Goh *et al.* published a similar case of iatrogenic CNVM following the epiretinal membrane (ERM) removal in a 69-year-old woman who was treated with four intravitreal bevacizumab injections, but the treatment was discontinued because of disciform scar and poor prognosis.[2] However, our patient had a good visual outcome, as the CNVM was extrafoveal and, probably, the prompt intervention along with early oil removal hastened its recovery. Literature search, in PubMed, revealed six case reports of CNVM after idiopathic ERM peeling and fourteen cases following macular hole surgery.[6-10] Despite treatment, functional outcome in all these cases was poor. To the best of our knowledge, this is the first reported case of CNVM following retinal detachment surgery with a good visual outcome.

## Conclusion

Iatrogenic CNVM is an uncommon complication following successful vitreoretinal surgery; however, surgeons should be aware of this complication as astute diagnosis and treatment are required to prevent visual deterioration.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

### Conflicts of interest

There are no conflicts of interest.

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