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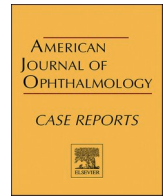
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## A case of iatrogenic CNV following macular surgery

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### ABSTRACT

**Purpose:** To report a case of iatrogenic trauma related choroidal neovascularization (CNV)

**Methods:** A 66 year old female presented with complaints of distortion of vision in the right eye. A diagnosis of epiretinal membrane (ERM) foveoschisis was made and the patient was recommended surgery. During surgery an inadvertent touch of the retina occurred. Post operatively, an iatrogenic choroidal neovascular membrane was diagnosed.

**Results:** Post-operative optical coherence tomography (OCT) and optical coherence tomography angiography (OCTA) revealed a CNV which was treated with intravitreal Bevacizumab. The visual acuity improved remarkably. The intraretinal and subretinal fluid resolved and the macula was almost completely dry at final visit.

**Conclusion:** ERM surgery is one of the common procedures in vitreoretinal surgery. Iatrogenic CNV is a reported but rare complication following inadvertent trauma during surgery. We report a successful outcome of iatrogenic CNV treated with intravitreal injections of Bevacizumab.

### 1. Introduction

Epiretinal membrane (ERM) peeling is a commonly performed vitreoretinal surgery. Like any surgical procedure it has its own set of complications including retinal trauma, retinal breaks, endophthalmitis, retinal detachment, post-surgical cataract in phakic eyes and rarely iatrogenic choroidal neovascularization (CNV).<sup>1</sup> We did a literature search for iatrogenic CNV following macular surgery and it reveals very few case reports and generally poor outcomes with treatment.<sup>2</sup> Optical coherence tomography angiography (OCTA) is less commonly reported but a useful non-invasive technique in managing iatrogenic CNV post macular surgery.

#### 1.1. Case report

A 66 year old female presented with distortion of vision in the right eye. Her best corrected visual acuity was 20/50 in the right eye and 20/25 in the left eye. Slit lamp examination revealed an early cataract in both eyes. Fundus exam revealed an epiretinal membrane (ERM) with a foveoschisis in the right eye (Fig. 1). The left eye also had an epiretinal membrane.

We advised surgical membrane peeling for the right eye.

After a routine 25 gauge pars plana vitrectomy, we stained the internal limiting membrane (ILM) using indocyanine green (ICG) dye. The ILM was peeled using a pinch-and-peel technique with ILM forceps. An accidental touch occurred at the perifoveal region with the extrusion soft tip cannula during the fluid-air exchange and we noted intra-op bleeding from the site of trauma (Fig. 2). The bleeding was controlled by raising the IOP and no further complications were noted. The eye was left under a complete fill of 20 % SF6 gas tamponade.

At 4 week follow up, we noted a significant 8 line drop in the right eye vision which was now 20/320. The gas bubble had diminished significantly by that time and the media was clear. On fundus exam, we noted retinal edema and subretinal fluid and an elevated foveal contour most probably secondary to subretinal serous fluid.

We performed optical coherence tomography (OCT) imaging that revealed increased macular thickness, subretinal fluid, and subretinal hyperreflective material (SHRM) suspicious for the presence of CNV (Fig. 3). This was a standard 30° horizontal raster scan of the macula (number of B-Scans = 97) using high speed mode. This was confirmed with an optical coherence tomography – angiography (OCTA) scan (Fig. 4). OCTA scans were acquired with a scan pattern of 3 × 3 mm

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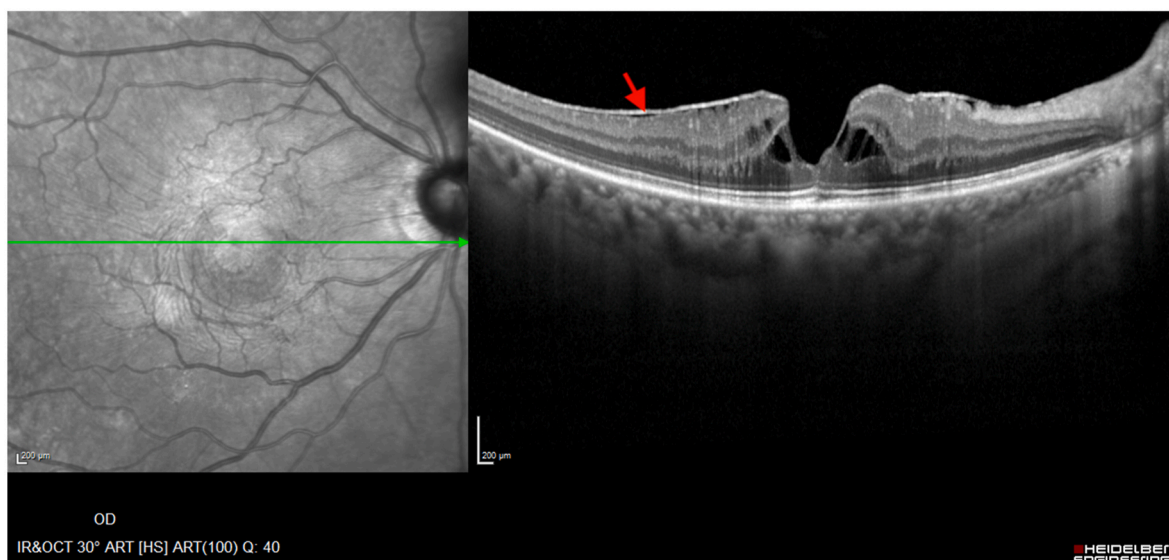
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**Fig. 1.** Pre-operative OCT showing ERM foveoschisis and distorted foveal contour. The image reveals splitting of the retinal layers at the fovea. The ERM (red arrowhead) appears as a hyperreflective band adherent to the retinal surface, exerting tangential traction. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)



**Fig. 2.** Surgical still photograph showing retinal bleed localized at the site of trauma, characterized by a distinct area of hemorrhage on the retinal surface, and the soft tip cannula positioned adjacent to the affected region.

(field of view:  $10^\circ \times 10^\circ$ ) in High Resolution (HR) mode. The scans included 512 B-scans, each consisting of 512 A-scans per B-scan. The spacing between B-scans was  $11.7 \mu\text{m}$ . Automatic Real-Time (ART) averaging of 5 frames was applied to improve signal quality. Both the OCT and OCTA were performed with a confocal scanning laser ophthalmoscope (Spectralis HRA-OCT; Spectralis, Heidelberg Engineering, Heidelberg, Germany).

The patient was treated using two monthly intravitreal anti-VEGF injections of Bevacizumab  $1.25\text{mg}/0.05 \text{ ml}$  (Avastin; Genentech, South San Francisco, CA, USA) for the CNV at the time of reporting.

At the most recent two-month follow-up, OCT showed that the intraretinal and subretinal fluid had almost resolved (Fig. 5) and the patients visual acuity improved to 20/80 (30 letter improvement) with the presence of a posterior subcapsular cataract. OCTA (Avascular layer) also showed decreased signal intensity post treatment (Fig. 6). The avascular layer slab represents an en-face image segmented from the outer plexiform layer (OPL) to the retinal pigment epithelium (RPE). Reduced flow signals were detected within this slab compared to initial scans.

## 2. Discussion

Wet AMD is the most common cause of CNV reported in literature.<sup>2</sup> Amongst other causes, iatrogenic trauma is an uncommon cause of CNV with only a handful of cases reported worldwide. Most cases of iatrogenic CNV have been due to laser injury.

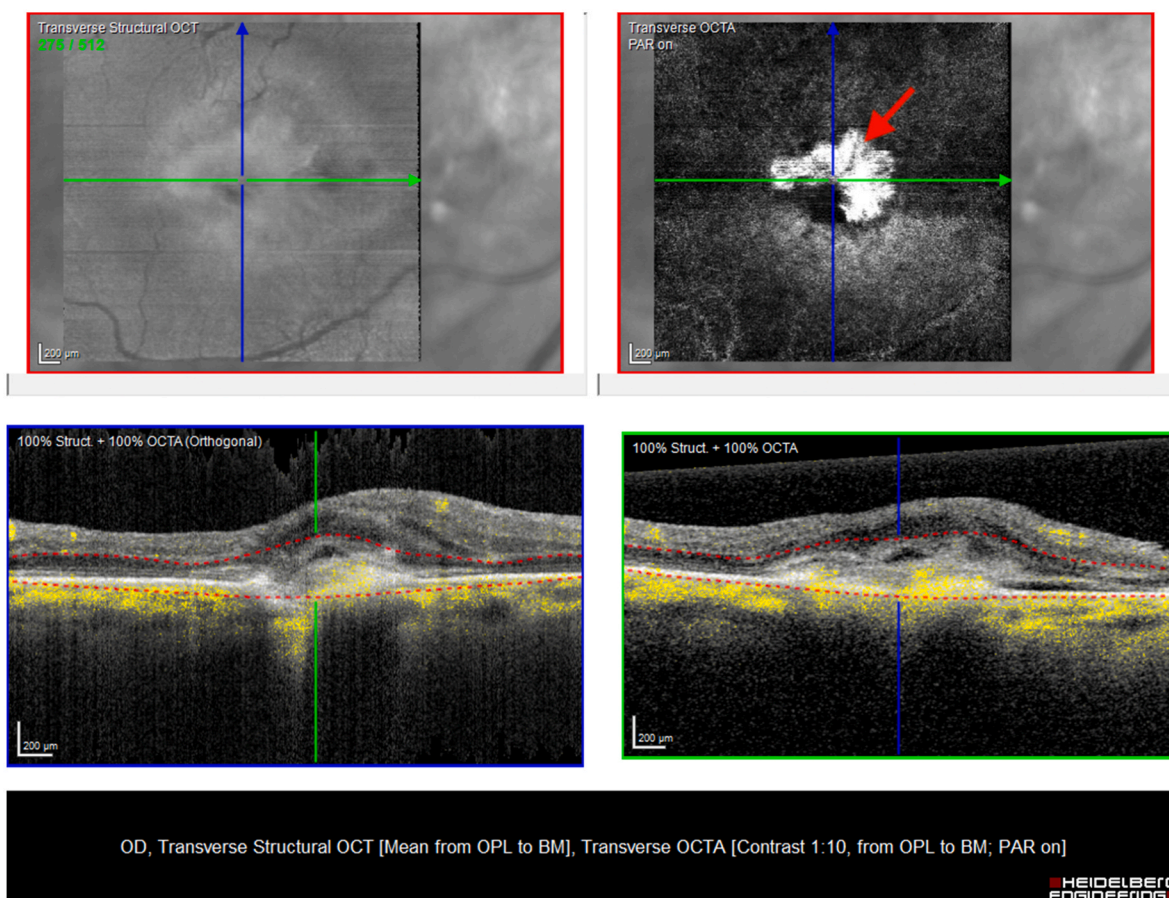
Kelly and Wendel reported approximately 10 % of the patients who underwent macular hole surgery were found to have postoperative RPE mottling and suggested that it could be due to intraocular manipulation, direct trauma, or light toxicity.<sup>1</sup>

Our case is a true iatrogenic trauma-related CNV due to inadvertent trauma.

In the case series published by Tsokolas G et al.,<sup>2</sup> all 3 of their patients developed CNV two to four months post macular surgery. Our patient was diagnosed as an iatrogenic CNV at the 4 week visit itself. They have hypothesized that surgical retinal trauma, triggers a inflammatory response in a similar manner as wet AMD. They used membrane blue in their surgical cases while we used indocyanine green (ICG). All three of their patients underwent routine surgery with standard

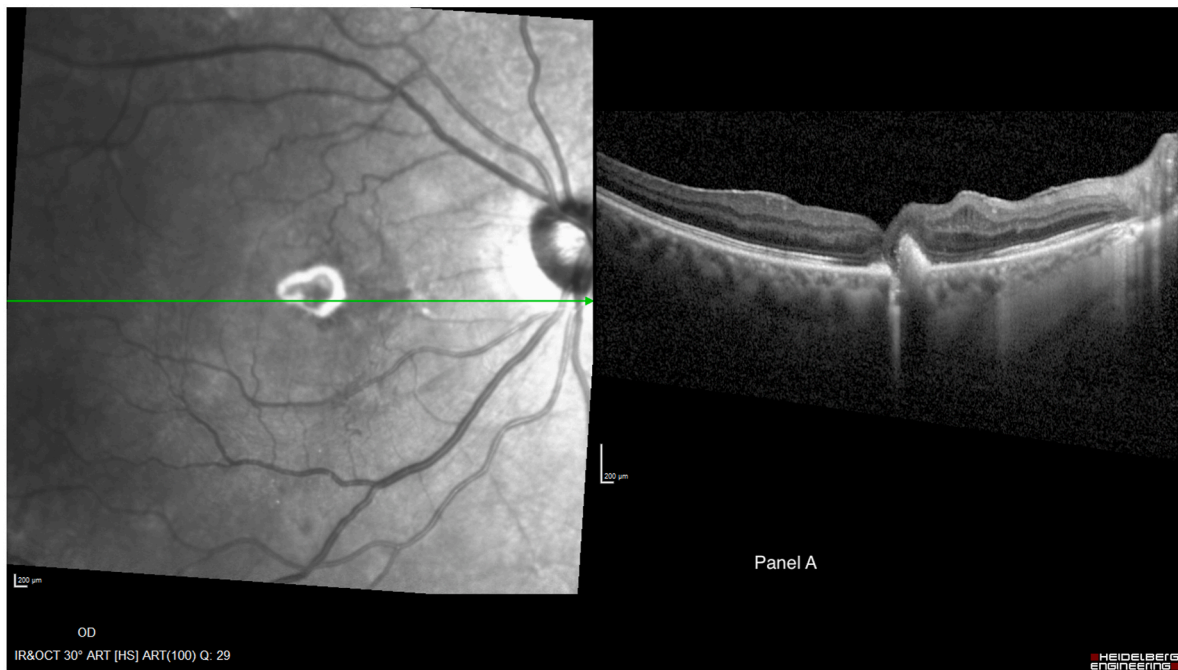


**Fig. 3.** Postoperative OCT image showing CNV. The image highlights a hyperreflective subretinal lesion with associated subretinal fluid, indicative of active neovascular leakage. Adjacent retinal layers exhibit disruption, with irregularities in the outer retina and the retinal pigment epithelium (RPE).

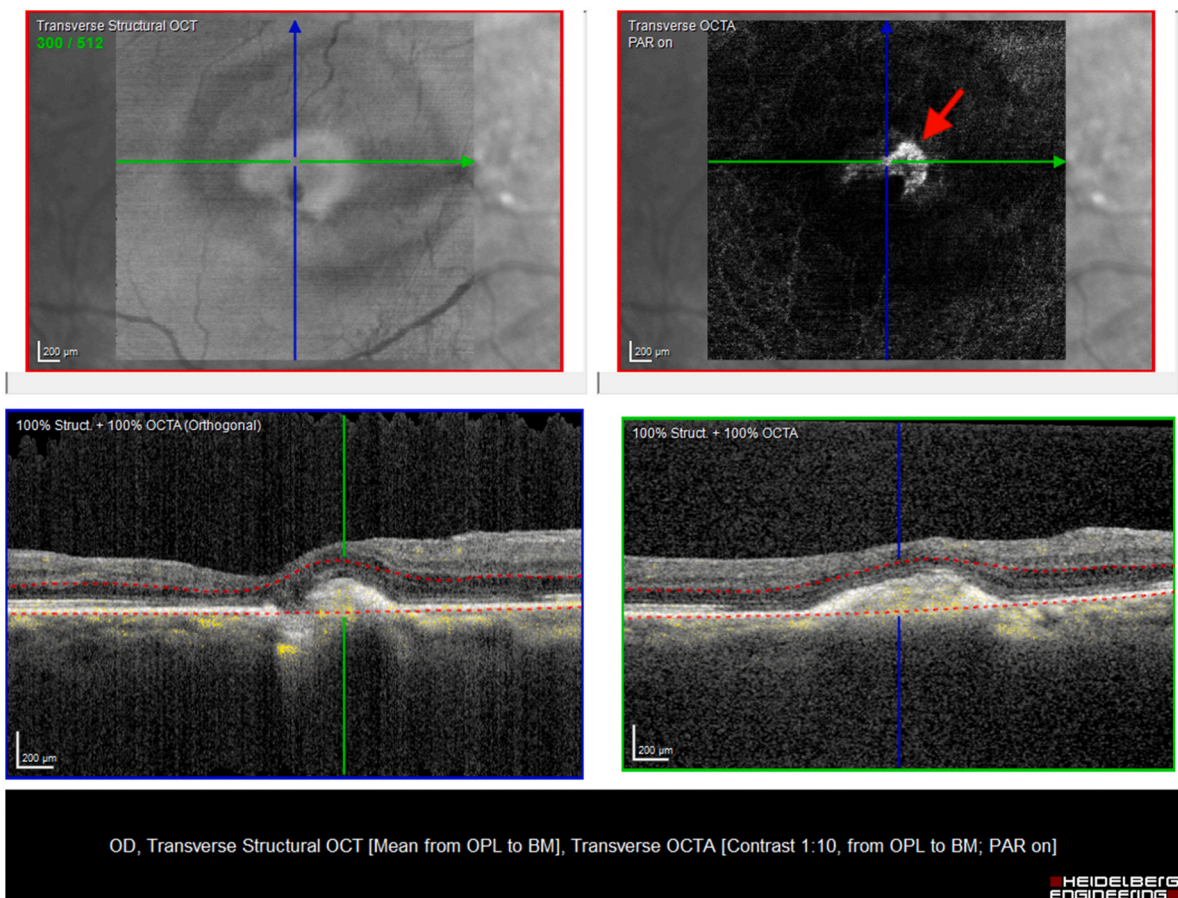


**Fig. 4.** OCTA scan of avascular layer showing neovessels (red arrowhead) The scan reveals abnormal vasculature, characterized by a dense, high-flow network consistent with neovascularization. These findings provide detailed visualization of pathological blood vessels not discernible on structural OCT. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)





**Fig. 5.** Post-treatment OCT image demonstrating resolution of subretinal fluid. The image shows reduced thickness and improved continuity of retinal layers. These findings reflect a favorable response to treatment, with reduced activity of the underlying CNV.



**Fig. 6.** Post-treatment OCTA of avascular layer showing partial regression of neovessels (red arrowhead) The scan reveals a reduction in the size and density of the abnormal vascular network, though remnants of the neovascularization persist. These findings indicate an incomplete but favorable therapeutic response, with decreased vascular activity. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

operating time and no obvious retinal trauma, while our patient sustained definite retinal trauma with a soft tip extrusion cannula which resulted in an immediate retinal bleed. Pre existing RPE degeneration was also one of the factors which was postulated to be an important factor in hyper stimulated VEGF production following surgical insult. Our patient had no pre existing RPE damage which may have been a factor in the improved visual acuity and good treatment response to anti VEGF.

Korobelnik et al. have previously reported the delayed development of an extrafoveal, subretinal choroidal neovascular membrane 2 years after an uncomplicated removal of an epiretinal membrane.<sup>3</sup>

Price et al. have described an iatrogenic choroidal neovascularization associated with subretinal gene therapy surgery. During initiation of a balanced salt solution pre-bleb, a faint and transient subretinal hemorrhage was observed at the retinotomy site. They detected a CNV and a break in Bruch's membrane at the retinotomy site one month later. The asymptomatic CNV was observed without treatment and resolved spontaneously.<sup>4</sup>

Similarly, Eugene et al. reported three cases of choroidal neovascularization (CNV) that occurred following surgical disruption of Bruch membrane during macular surgery.<sup>2</sup> They reported that disruption of Bruch membrane during macular surgery may lead to the development of CNV even though the health of Bruch membrane is presumably different in patients with age-related macular degeneration (ARMD) compared with patients with ERM alone.

Appanraj et al. reported a case of iatrogenic CNV following retinal detachment surgery which was successfully treated with intravitreal anti-VEGF.<sup>5</sup> Literature search of previous cases after ERM peel or macular surgery had variable visual outcomes despite anti VEGF treatment. Our patient had a good functional response to anti VEGF injections. Although, it is important to state that a short follow up period of two months is a limitation of this report.

Previous studies seem to suggest reduced half-life and efficacy of anti-VEGF agents in vitrectomized eyes.<sup>6</sup> Increased clearance of anti-VEGF in vitrectomized eyes may require more frequent dosing although the majority of studies were retrospective, uncontrolled, and based on small numbers of patients.<sup>6</sup>

Some studies indicate that combined lensectomy could significantly affect intravitreal clearance because drug clearance through the anterior chamber could be altered after combined lensectomy and vitrectomy.<sup>7</sup> Our patient was phakic and did not undergo cataract surgery at the time.

OCTA in such cases can guide the physician towards a definitive diagnosis of an iatrogenic CNV and is helpful to exclude other trauma related pathologies like choroidal rupture or subretinal hemorrhage.

### 3. Conclusion

Surgeons need to be aware of this rare complication which might lead to poor visual outcomes for these patients. Most cases presented in literature did not improve much following treatment with anti-VEGF injections.<sup>1</sup> An OCTA in the early post-operative stage of such patients may alert the physicians to the development of a CNV and help in the early diagnosis and treatment leading to better visual outcomes.

### CRedit authorship contribution statement

**Akshay Prashant Agnihotri:** Investigation, Data curation, Conceptualization. **Ines D. Nagel:** Writing – review & editing. **Anna Heinke:** Writing – review & editing. **Zachary A. Koretz:** Writing – review & editing, Writing – original draft. **William R. Freeman:** Writing – review & editing, Data curation, Conceptualization.

### Patient consent

Written consent to publish this case has not been obtained. This report does not contain any personal identifying information.

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### Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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