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CASE REPORT

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Retinal atrophy and eccentric macular hole after internal limiting membrane peeling: a case report

Shu Zhang[1], Zhiyan Liu[2*], Chenjia Zhang[1] and Xiangli Wang[1]

Abstract

Background Postoperative eccentric macular hole (MH) formation is a relatively rare complication after pars plana vitrectomy (PPV) with internal limiting membrane(ILM) peeling for epiretinal membrane (ERM) or MH treatment. Herein, we report a case of eccentric MH formation following PPV with ILM peeling for MH.

Case presentation A 62-year-old male presented with a 3-month history of blurred vision and metamorphopsia in the left eye. Preoperative optical coherence tomography (OCT) confirmed a full-thickness MH (minimum linear diameter: 675 µm). The patient underwent 25-gauge PPV with ILM peeling using indocyanine green (ICG, 0.25%) and inverted ILM flap placement. Postoperative OCT at one week confirmed MH closure. However, subsequent follow-ups revealed progressive inner retinal disorganization, atrophy, and cavitation. At five months, a parafoveal full-thickness eccentric macular hole (EMH) developed inferiorly. No additional interventions were pursued due to stable hole size and absence of retinal detachment.

Conclusions This case highlights rare postoperative retinal atrophy and EMH formation following ILM peeling for MH repair. Potential contributors include ICG-induced photochemical toxicity, Müller cell damage from ILM peeling, and fluid shear stress. The findings underscore the need to optimize ICG protocols (reduced concentration, shorter exposure) and prioritize safer alternatives like brilliant blue G (BBG). Long-term postoperative monitoring is critical to detect delayed complications, emphasizing the balance between surgical efficacy and minimizing iatrogenic retinal injury.

Keywords Eccentric macular hole, Retinal atrophy, Pars plana vitrectomy, Optical coherence tomography, Case report

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Background

Macular hole (MH) is a full-thickness defect in the fovea. It was first described by Herman Knapp in 1869 [1]. Contraction of the premacular vitreous cortex and tangential vitreous traction forces have been suspected to play an important role in MH development [2]. The first successful surgery for idiopathic full-thickness macular holes (FTMHs) was introduced by Kelly and Wendel [3]. To date, vitrectomy combined with ILM peeling and gas tamponade has become a routine technique for MH surgery, with a high success rate of 95% [4, 5].

The preoperative minimum linear diameter (MLD) of the MH is the strongest predictor of anatomical closure. Smaller holes (MLD ≤ 500 μm) have significantly higher closure rates (97–98%) compared to larger holes (MLD > 500 μm; 90% closure). Holes exceeding 600 μm show the poorest closure rates (87%) [6]. However, in challenging cases, such as large MHs, chronic MHs, and secondary MHs from ocular trauma or severe myopia, surgical closure rates are lower [7]. The inverted ILM flap technique improves anatomical and functional outcomes in large and complicated MHs [8]. Postoperative complications of PPV include cataracts, retinal breaks, retinal detachment, MH reopening, and infections [9]. Postoperative eccentric MH formation is a rare complication after PPV with ILM peeling for ERM or MH treatment [9, 10]. Herein, we report a case of eccentric MH formation following PPV with ILM peeling for MH.

Case presentation

A 62-year-old male presented with blurred vision and metamorphopsia in his left eye for 3 months. The patient had no significant history of systemic illnesses, current or prior medications, allergies, or relevant family/genetic disorders. There was no documented history of surgeries, specialized treatments, or chronic therapies. His refractive error was −1.50 diopters in the left eye and −2.75 diopters in the right eye (KR-800, Topcon, Japan), and axial length was 23.33 mm in the left eye and 23.46 mm in the right eye (IOLMaster 500, Carl Zeiss Meditec, Germany). Clinical examination revealed a best-corrected visual acuity (BCVA) of 20/400 in the left eye and 20/40 in the right eye. Intraocular pressure was 16 mmHg bilaterally. Anterior segment slit-lamp examination showed cataracts in both eyes graded as N1C1P0. Fundus examination revealed an idiopathic full-thickness MH in the left eye, with a minimum linear diameter of 675 μm on vertical scan and maximum basal diameter of 921 μm on horizontal scan, confirmed by OCT (Fig. 1). No significant abnormalities were detected in the right eye by Optos photography (Daytona P200T, OPTOS, UK) and macular OCT scan (Cirrus 6000, Carl Zeiss Meditec, Germany) (Fig. 2).

The patient underwent 25-gauge PPV with a 10,000 cuts per minute rate using the CONSTELLATION Vision System (Alcon, USA) and Resight 700 viewing system (Carl Zeiss Meditec, Germany). No cataract surgery was undertaken as the crystalline lens did not impede retinal surgical procedures. After core vitrectomy, Triamcinolone acetonide was used to assist surgical posterior vitreous detachment (PVD), The posterior vitreous adhered tightly to the retina without peripheral adhesions. Indocyanine green (2.5 mg/mL) stained the ILM for 10 s, followed by immediate lavage. The ILM was peeled using forceps, and an inverted ILM flap covered the MH. Fluid-air exchange was performed, and the patient maintained a face-down position for 7 days postoperatively. The intraoperative lighting source was a xenon lamp, with a total surgical duration of 30 min. The procedure was performed smoothly by an experienced surgeon without complications.

One-week postoperative OCT demonstrated MH closure with BCVA of 20/200 and intraocular pressure of 13 mmHg. A thin layer over the fovea indicated stable

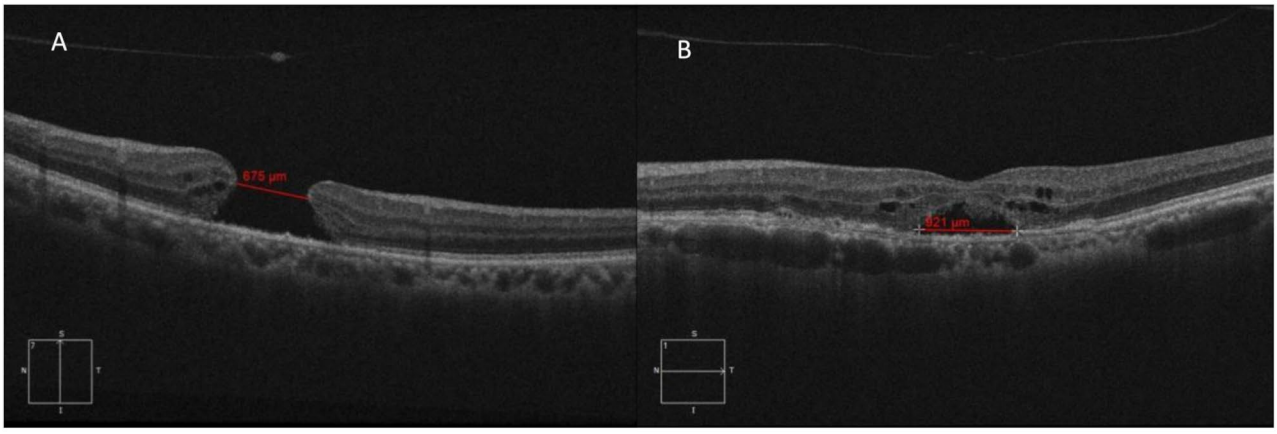

Fig. 1 Preoperative OCT image of the left eye demonstrating an idiopathic full-thickness MH, with a minimum linear diameter of 675 μm on vertical scan **(A)** and a maximum basal diameter of 921 μm on horizontal scan **(B)**, accompanied by disorganization of the retinal outer layers in the macular area

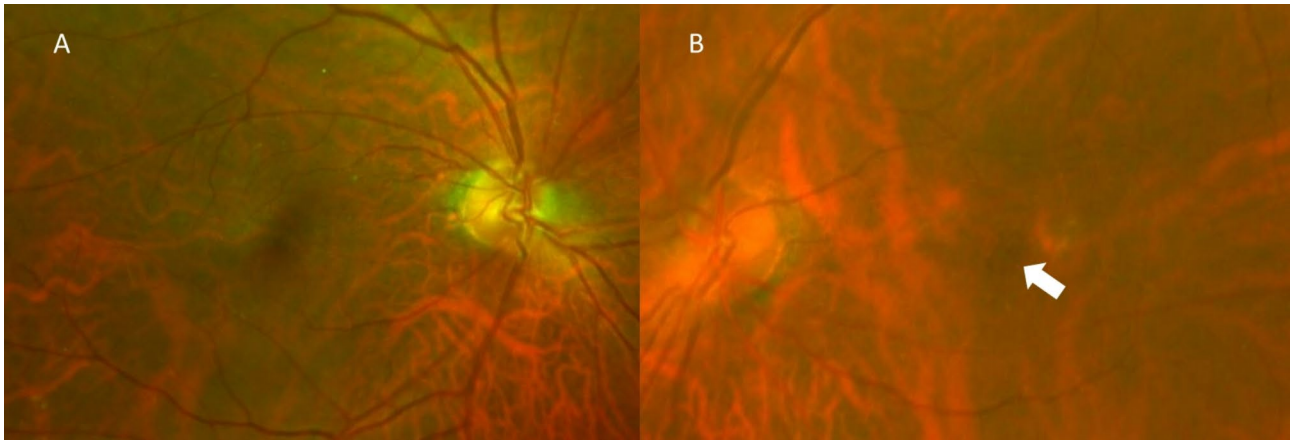

Fig. 2 Fundus examination revealed no significant abnormalities in the right eye **(A)**, and an idiopathic full-thickness MH in the left eye (indicated by the arrow) by Optos photography **(B)**

ILM positioning. At one month, OCT revealed disorganization of the inner retinal layers and macular atrophy. Two months postoperatively, severe inner retinal atrophy and cavitation were observed. Five months post-PPV, a parafoveal full-thickness MH was identified inferiorly by OCT on vertical scan. During the follow-up period, horizontal OCT scans revealed progressive thinning of the temporal retina, disorganization of the outer retinal structures, and no evidence of EMH formation (Fig. 3). Fundus photography and autofluorescence revealed dissociated optic nerve fiber layer (DONFL) in the ILM peeling area, which was more pronounced inferiorly (Fig. 4). BCVA remained 20/400 with stable symptoms. No additional interventions were performed due to the absence of retinal detachment and static hole size.

Discussion

The presence of an eccentric MH is a rare finding in patients after ILM peeling, with a reported incidence of less than 0.6% of cases [9, 11]. In this case, we report an eccentric MH that developed following PPV with ILM peeling for MH treatment. There is no general consensus regarding the pathogenesis of postoperative eccentric MH formation, but various theories have been proposed, including surgical trauma, intraocular dye use during peeling, ILM removal-induced weakening of retinal glial structures, and residual ILM contraction [9, 12].

A plausible explanation for eccentric MH formation is iatrogenic retinal trauma during ILM grasping with forceps. ILM peeling may damage the nerve fiber layer and Müller cells, leading to delayed degeneration of adjacent retinal neurons. Additionally, ILM removal can induce glial apoptosis, weakening the glial architecture and ultimately causing macular hole formation [13]. Ultrastructural studies reveal remnants of necrotic Müller cell processes attached to the removed ILM. Eccentric MHs may also occur without ILM peeling, potentially due to retinal blade use during ERM removal or traction from perifoveal hyaloid adherence during ERM removal [9].

In this case, postoperative OCT at one week demonstrated disrupted and progressively worsening the photoreceptor inner and outer segment lines and external limiting membrane layers. By two months, significant retinal atrophy, inner retinal cavitation, and nerve fiber layer dimpling were observed, suggesting surgical trauma from ILM peeling played a key role. ILM peeling-induced cell damage may activate regenerative glial proliferation (promoting hole closure) or trigger Müller cell decapitation and apoptosis [14]. Histopathology confirms Müller cell fragments adherent to excised ILM [9]. Müller cells, critical for retinal integrity, span the retinal thickness and interact with photoreceptors and ganglion cells. ILM peeling inevitably damages their footplates, potentially causing inner retinal loss and functional decline [15].

Toxicity from ILM-staining dyes, such as indocyanine green (ICG), may also contribute. ICG's safety depends on concentration, pH, exposure duration, illumination, and other factors. ICG induces dose-dependent toxicity to retinal cells, including retinal pigment epithelium (RPE), ganglion cells, and Müller cells. High concentrations (≥ 0.5%) cause inner retinal disorganization, RPE atrophy, and photoreceptor damage; ICG acts as a photosensitizer, absorbing light (380–550 nm wavelengths) and generating free radicals, exacerbating oxidative damage. Synergistic effects between ICG and intraoperative light sources (halogen, xenon) increase photothermal and photochemical damage. Halogen light sources cause more DNA damage and induce higher levels of inflammatory cytokines than other sources. Prolonged light exposure or close proximity of the endoilluminator to the retina amplifies toxicity; ICG triggers apoptosis in RPE and retinal ganglion cells via upregulation of pro-apoptotic proteins (Bax, p53) and mitochondrial dysfunction. Light exposure combined with ICG enhances

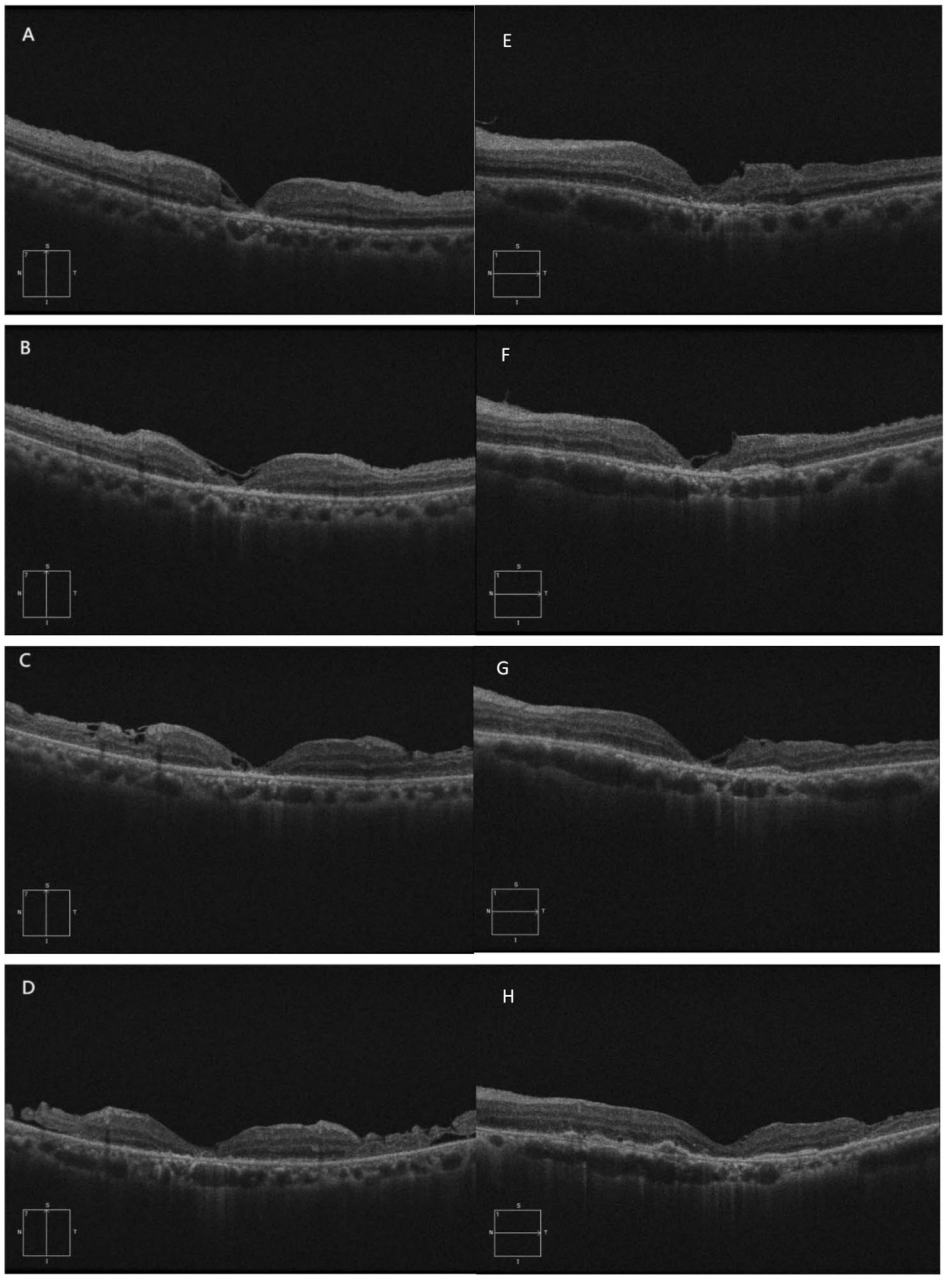

Fig. 3 Development of an eccentric retinal hole after surgery. One week postoperatively, OCT imaging demonstrated MH closure **(A)**. At one month postoperatively, OCT revealed disorganization of the inner retinal layers and macular atrophy **(B)**. Two months postoperatively, severe inner retinal atrophy and cavitation were observed **(C)**. Five months post-PPV, a parafoveal full-thickness MH was identified inferiorly by OCT on vertical scan **(D)**. Horizontal OCT scans revealed progressive thinning of the temporal retina, disorganization of the outer retinal structures, and absence of EMH formation **(E-H)**

cell cycle arrest and apoptotic pathways; hypoosmotic ICG solutions (diluted in balanced salt solution) exacerbate RPE damage by inducing osmotic stress, Isoosmotic solvents (5% glucose) reduce toxicity compared to standard saline-based dilutions; accidental subretinal ICG migration during peeling causes persistent cystoid macular edema or RPE atrophy. Repeated ICG applications or prolonged incubation times increase retinal exposure and toxicity risks. ICG toxicity is multifactorial, involving biochemical, photochemical, and mechanical mechanisms. While it enhances surgical precision, its risks necessitate stringent protocols to minimize retinal damage. Further research is needed to optimize ICG use and develop safer alternatives. Compared to ICG, brilliant blue G (BBG) exhibits lower retinal ganglion cell and RPE toxicity and phototoxic effects. If ICG is used, recommendations include: minimal concentration (0.05-0.2%), brief exposure(a few seconds), avoidance of repeated bare

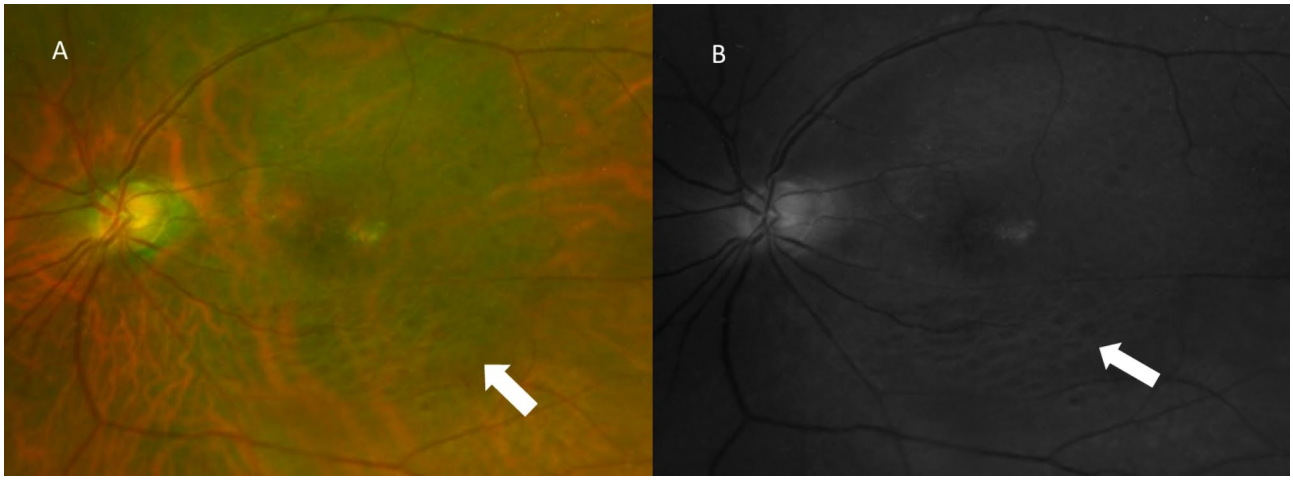

Fig. 4 Fundus photography **(A)** and autofluorescence **(B)** reveal DONFL in the ILM peeling area, which is more pronounced inferiorly (indicated by the arrows)

retinal injections, macular hole distancing to prevent RPE contact and maintaining the light pipe away from the retina [16, 17].

Direct mechanical trauma is unlikely here, as atrophy occurred diffusely across the peeled ILM area, not just at forceps sites. In our case, the use of a high ICG concentration (0.25%) combined with prolonged intraoperative light exposure (30 min) likely induced photochemical damage through oxidative stress and dose-dependent cytotoxicity, leading to widespread injury to retinal ganglion cells, Müller cells, and RPE. Synergistic interactions between ICG's photosensitizing properties and xenon light illumination exacerbated structural degradation, culminating in neurosensory atrophy and secondary MH formation. By one month, nerve fiber layer dimples and atrophy-consistent with ILM peeling-emerged. This is supported by ultrastructural analysis revealing ILM removal with adjacent retinal structure loss [9]. Progressive inner retinal thinning and cavitation culminated in MH formation, implicating combined Müller cell injury and ICG toxicity.

Preoperative fluid changes may constitute an additional potential etiological factor for postoperative eccentric macular hole development. Incomplete preoperative PVD may generate shear stress at the edges of the partial vitreous liquefaction due to fluid flow dynamics. Persistent vitreous traction or dynamic fluid currents (vortex flow during eye movement) could weaken perifoveal retinal structures, predisposing to precursor lesions for eccentric hole formation [18]. Persistent shear stress on the bare retinal surface caused by balanced salt solution and aqueous dynamics renders postoperative atrophic areas vulnerable to secondary hole formation [19]. Serial OCT showing atrophy preceding eccentric hole formation supports fluid-driven mechanisms.

Intervention is unnecessary unless MH enlargement or vision decline occurs, as progression to retinal detachment is rare [9.10]. No treatment was administered in our case, with stable MH size and vision at nine months.

Conclusion

Our case report highlights the rare occurrence of retinal atrophy and EMH following PPV with ILM peeling for MH closure. While initial surgical success was achieved, progressive inner retinal disorganization, atrophy, and subsequent parafoveal MH formation underscore the potential role of ICG toxicity as a predominant etiological factor. Mechanical trauma from ILM peeling, which disrupts Müller cell footplates and weakens retinal integrity, alongside postoperative fluid dynamics (shear stress), may have accelerated pathological progression. However, these factors likely operated synergistically with ICG toxicity as the primary driver of tissue damage.

This case emphasizes the need for stringent ICG protocols: minimizing concentration (≤0.2%), limiting exposure time, avoiding direct RPE contact, and prioritizing safer alternatives like BBG. Although ILM peeling remains the gold standard for MH management, surgeons must balance its benefits against ICG-associated risks. Long-term postoperative monitoring is critical to detect delayed complications. These findings advocate for refined surgical strategies to mitigate iatrogenic damage and highlight the multifactorial interplay underlying complex postoperative outcomes. Novel 3D visualization surgical systems (such as Ngenuity) do not require intraoperative injection of staining agents and can clearly delineate the internal limiting membrane through color filters alone, thereby achieving enhanced surgical outcomes.

Abbreviations

MH	Macular hole
PPV	Pars plana vitrectomy
ILM	Internal limiting membrane
ERM	Epiretinal membrane
BCVA	Best-corrected visual acuity
OCT	Optical coherence tomography
ICG	Indocyanine green
BBG	Brilliant blue G
RPE	Retinal pigment epithelium
DONFL	Dissociated optic nerve fiber layer

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Not applicable.

Author contributions
All authors (SZ, ZL, CZ, XW) have made substantive intellectual contributions to this manuscript. SZ performed the surgery and wrote the manuscript. ZL made the diagnosis and revised the manuscript. CZ examined the patient and obtained consent of the patient and revised the manuscript. XW acquired data and revised the manuscript. All authors read and approved the final manuscript.

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Data availability
The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
No ethical approval required.

Consent for publication
Written informed consent was obtained from the patient for publication of this Case Report and any accompanying images.

Competing interests
The authors declare no competing interests.

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