Case Reports in Ophthalmology

Case Rep Ophthalmol 2025;16:107–113
DOI: 10.1159/000543599
Received: October 28, 2024
Accepted: January 13, 2025
Published online: January 17, 2025

Case Report

Development of Macular Atrophy after Macular Hole Surgery in an Eye with Retinitis Pigmentosa

Yuki Goto[a] Kazuki Kuniyoshi[a] Kensuke Goto[b] Tomoyasu Kayazawa[a] Taro Kominami[b] Fukutaro Mano[a] Masuo Sakamoto[a] Chiharu Iwahashi[a] Shunji Kusaka[a]

[a]Department of Ophthalmology, Kindai University Faculty of Medicine, Osakasayama, Japan; [b]Department of Ophthalmology, Nagoya University Graduate School of Medicine, Nagoya, Japan

Keywords
Retinitis pigmentosa · Macular hole · Vitreoretinal surgery · *EYS* · Indocyanine green

Abstract
Introduction: Macular hole is a rare complication in patients with retinitis pigmentosa that significantly reduces visual acuity. Although vitreous surgery for macular holes generally yields favorable outcomes, postoperative macular atrophy has been reported. We report the second case of retinitis pigmentosa in a patient who developed a 13-year progressive macular atrophy after macular hole surgery. ***Case Presentation:*** A 64-year-old Japanese woman, who had been diagnosed with retinitis pigmentosa at 52 years of age, presented to our hospital with blurred vision in her left eye. Phacovitrectomy of the left eye was performed after a full-thickness macular hole was revealed by optical coherence tomography. We stained the internal limiting membrane during surgery using 0.05% indocyanine green and peeled it around the macular hole. Nevertheless, slight atrophy of the retinal pigment epithelium appeared in the left macula 17 days after surgery. The macular hole closed 1 year after surgery, and the macular atrophy gradually became more apparent and enlarged. Thirteen years later, atrophy had expanded to 2.5-disc diameters, and the left decimal best-corrected visual acuity was 0.1; no macular degeneration appeared in the right eye. Genetic examination revealed compound heterozygous variants in the *EYS* gene. ***Conclusion:*** Macular atrophy can develop after dye-assisted macular hole surgery for patients with retinitis pigmentosa. Potential risk factors for

Correspondence to:
Kazuki Kuniyoshi, kazuki@med.kindai.ac.jp

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the development of postoperative macular atrophy include dye toxicity, light toxicity, surgical intervention in the macula, postoperative inflammation, and genotype. However, the exact cause of atrophy remains uncertain.

Introduction

Macular hole (MH) is a rare complication that occurs in patients with retinitis pigmentosa [1, 2], and it significantly reduces their visual acuity. Since the initial report of vitreous surgery for MH [3], vitrectomy has been widely accepted as the standard procedure. Dye-assisted internal limiting membrane (ILM) peeling around the MH during vitreous surgery has improved the anatomical closure rate up to more than 90% [4]. The reported results of macular surgery for patients with retinitis pigmentosa are favorable [5–8]; however, macular atrophy after surgery has been reported [9]. Here, we report on the second case of retinitis pigmentosa in a patient who developed a 12-year progressive macular atrophy after MH surgery. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000543599).

Case Presentation

A 64-year-old Japanese woman presented to our hospital with blurred vision in the left eye. She was diagnosed with retinitis pigmentosa at the age of 52 years because of diffuse retinal degeneration, constricted visual field, and non-recordable electroretinograms in both eyes. Additionally, the patient had an intraocular lens in the right eye, cataract in the left eye, and decimal best-corrected visual acuity (dBCVA) of 1.0p × IOL × S -3.5D = C -0.75D Ax 100° and 0.1 × S -9.0D = C -2.5D Ax 90° in the right and left eyes, respectively.

Phacovitrectomy of the patient's left eye was performed after a full-thickness MH (Fig. 1a) was revealed by optical coherence tomography. We stained the ILM during surgery using 0.05% indocyanine green (ICG) and peeled it around the MH. The surgical procedure was uneventful.

Nevertheless, slight atrophy of the retinal pigment epithelium was observed in the left macula 17 days after surgery. The atrophy had 2-disc diameters (DDs), and the dBCVA of the left eye was 0.4. Although the MH was still open 1 month after surgery (Fig. 1b), we continued to monitor it and did not perform any treatment because the patient's vision improved. The MH closed 1 year after surgery, and the macular atrophy gradually became more apparent and enlarged. Thirteen years later, the atrophy had expanded to 2.5 DD (Fig. 1e) and the dBCVA of the left eye decreased to 0.1. However, there was no macular degeneration, and the dBCVA remained unchanged (1.0) in the right eye (Fig. 1f). The diameters of the V4e isopter in the Goldmann kinetic visual fields were gradually constricted; however, they were similar in both eyes. Genetic examination of the patient revealed compound heterozygous variants of c.2528G>A (p.Gly843Glu) and c.179delT (p.Leu60fs) in the *EYS* gene.

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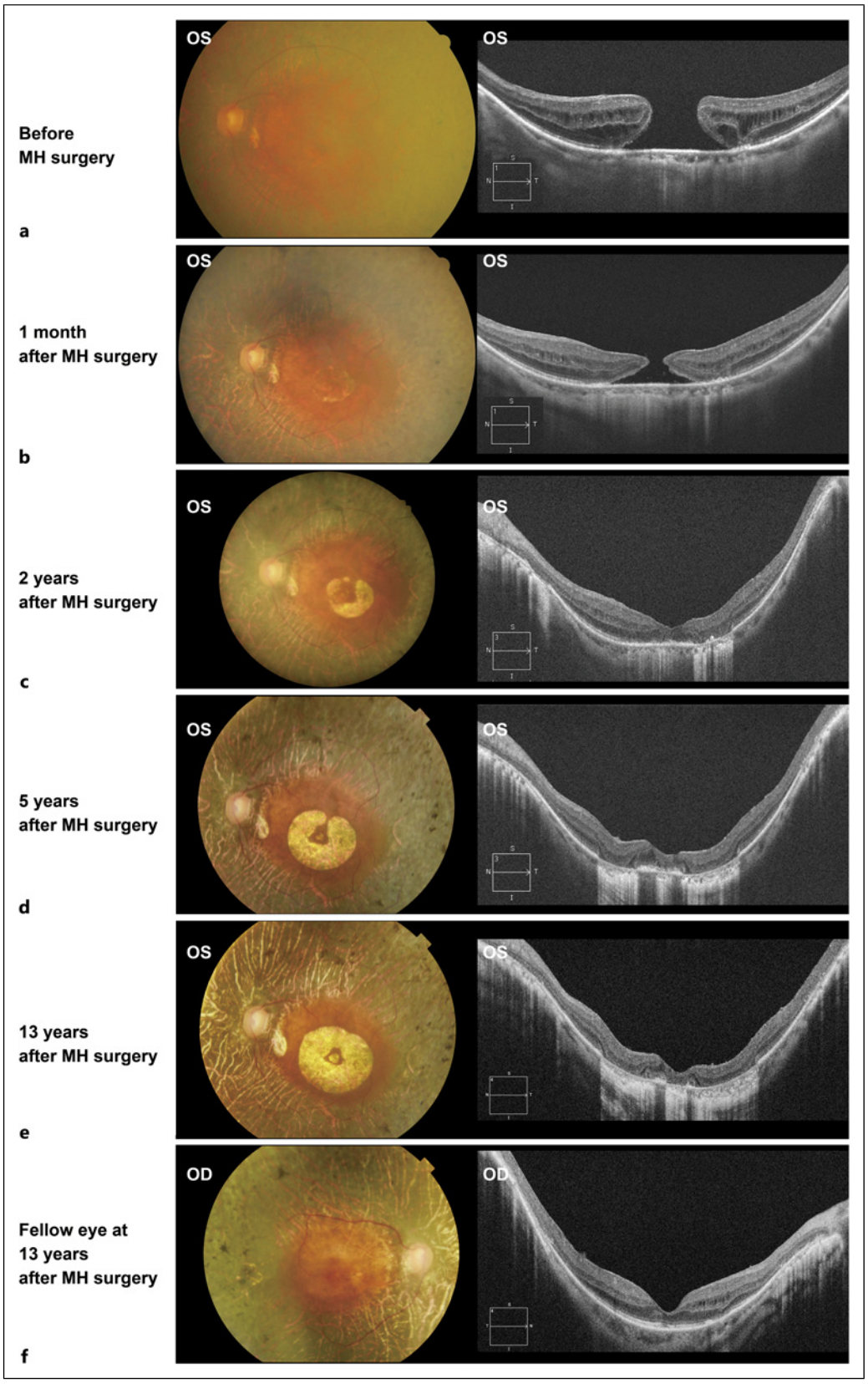

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Discussion

Similar to our case, Miura et al. [9] reported macular atrophy after vitrectomy for 2 patients with retinitis pigmentosa; 1 patient underwent ICG-assisted MH surgery, and the other underwent epiretinal membrane peeling without dye staining. Nevertheless, both patients developed macular atrophy in the operated eye but not in the fellow eye [9]. These results suggested that macular atrophy can develop in patients with retinitis pigmentosa after macular surgery with or without dye-assisted ILM peeling. Potential risk factors for the development of postoperative macular atrophy include surgical intervention in the macula, postoperative inflammation, dye toxicity, light toxicity, and genetic predisposition.

Surgical intervention, including ILM peeling, can cause postoperative macular degeneration. This is especially prevalent in eyes with vulnerable retinas, such as those with retinitis pigmentosa and/or high myopia, as observed in our patient. Furthermore, postoperative inflammation can damage the retina. Because retinal degeneration after uveitis can mimic retinitis pigmentosa [10], postoperative reactivation of uveitis should be considered as a possibility.

Regarding dye and light toxicity, the dye sprayed onto the posterior retina can migrate into the subretinal space through the full-thickness MH; this may damage the photoreceptors and retinal pigment epithelium cells, causing postoperative macular atrophy. Notably, ICG toxicity is enhanced by light exposure [11, 12]. Moreover, intraoperative and postoperative light exposure may cause retinal damage. The photoreceptor cells, particularly in *EYS*-associated retinitis pigmentosa, reported to be especially vulnerable to light exposure [13].

In addition, genetic risk factors for atrophic (dry) age-related macular degeneration should be considered. In this patient, no pathogenic variant was identified in the *ABCA4* gene, which is associated with dry age-related macular degeneration. Single nucleotide polymorphisms related to atrophic age-related macular degeneration were not evaluated in the patient.

The *EYS* gene, the causative gene for retinitis pigmentosa in our patient, is a major contributor to retinitis pigmentosa not only in Japanese populations [14–21] but also in other populations [22–28]. The missense variant c.2528G>A (p.Gly843Glu) in the *EYS* gene is the most frequently identified variant in Japanese populations [14–20], whereas another truncating and nonsense variant, c.179delT (p.Leu60fs), is relatively rare [21]. A recent study revealed that epiretinal membrane development occurs more frequently in patients with *EYS*-associated retinitis pigmentosa compared to those with *RHO*- or *USH2A*-associated retinitis pigmentosa [29]. These findings suggest that ophthalmologists may frequently perform macular surgery in patients with retinitis pigmentosa who share a genetic background similar to that of our patient.

In conclusion, macular surgery in patients with retinitis pigmentosa may lead to postoperative macular atrophy. Future studies involving further examinations of the risk factors for macular atrophy are needed because macular atrophy does not always occur in patients with retinitis pigmentosa after macular surgery [6–8].

Fig. 1. Photographs of the fundus (left column) and optical coherence tomography images (right column) of the left (OS) and right (OD) eyes before (**a**) and 1 month (**b**), 2 years (**c**), 5 years (**d**), and 13 years (**e**) after MH surgery. Macular atrophy appeared after surgery and gradually expanded to 2.5-DDs over a 13-year period (**b–e**). The right macula was unremarkable and maintained a decimal best-corrected visual acuity (dBCVA) of 1.0 (20/20 vision) (**f**).

Acknowledgments

The authors thank the patient for providing her consent for the publication of her medical information.

Statement of Ethics

All procedures performed in this study involving human participants were approved by the Ethics Review Board of each institute (Kindai University: R04-203, Nagoya University: 2020-0598) and adhered to the tenets of the Declaration of Helsinki and its later amendments or comparable ethics standards. Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Funding Sources

Part of this research was supported by a Grant-in-Aid for Scientific Research from the Japan Society for the Promotion of Science (grant 22K09825) and a grant from the Japanese Retinitis Pigmentosa Society (JRPS) to K.K.

Author Contributions

Yuki Goto: writing – original draft, conceptualization, and data curation. Kazuki Kuniyoshi: writing – original draft, conceptualization, data curation, formal analysis, funding acquisition, investigation, methodology, project administration, resources, supervision, validation, visualization, and writing – review and editing. Kensuke Goto and Taro Kominami: data curation, formal analysis, investigation, methodology, visualization, and writing – review and editing. Tomoyasu Kayazawa: conceptualization, methodology, project administration, visualization, and writing – review and editing. Fukutaro Mano and Masuo Sakamoto: conceptualization, methodology, project administration, visualization, and writing – review and editing. Chiharu Iwahashi: conceptualization, methodology, project administration, and writing – review and editing. Shunji Kusaka: conceptualization, formal analysis, investigation, methodology, project administration, supervision, validation, and writing – review and editing.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its online supplementary material files. Further inquiries can be directed to the corresponding author.

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