Case Reports in Ophthalmology

Case Rep Ophthalmol 2024;15:326–334
DOI: 10.1159/000538026
Received: November 14, 2023
Accepted: February 16, 2024
Published online: April 12, 2024

Case Report

Treatment of Failure of Macular Hole Closure due to Post-Vitrectomy Macular Edema Using Sub-Tenon Triamcinolone Acetonide Injection: A Case Report

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Keywords

Macular hole · Cystoid macular edema · Sub-Tenon triamcinolone acetonide · Pars plana vitrectomy · Inverted internal limiting membrane flap

Abstract

Introduction: Post-vitrectomy cystoid macular edema (CME) can lead to failure of macular hole (MH) closure. We report 2 cases of failure of MH closure due to post-vitrectomy CME, which were successfully treated using sub-Tenon triamcinolone acetonide (STTA) injection. ***Case Presentations:*** Case 1 involved a 72-year-old male patient with a Gass Stage 3 MH in the right eye. He underwent pars plana vitrectomy (PPV), internal limiting membrane translocation, and sulfur hexafluoride (SF6) gas injection with cataract surgery in his right eye. The MH did not close postoperatively; further, CME developed at the edge of the MH. Accordingly, the patient underwent an STTA injection. Approximately 2 weeks after the STTA injection, the CME disappeared and the MH closed, which has remained closed 1 year after PPV. Case 2 involved a 78-year-old female patient with Gass Stage 3 MH in the left eye. The patient underwent the same surgical procedure as that performed in case 1. Further, she presented with failure of MH closure caused by CME; therefore, an STTA injection was performed. Approximately 6 weeks after STTA injection, the CME disappeared and the MH closed; further, there was maintained improvement of best-corrected visual acuity for 6 months. ***Conclusions:*** STTA injection could be considered before reoperation in cases involving failure of MH closure due to postoperative CME.

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Introduction

A macular hole (MH) refers to a full-thickness anatomical break or defect in the fovea, which results in blurred and distorted central vision. MH most commonly involves idiopathic causes; however, it has secondary causative factors, including high myopia, cystoid macular edema (CME), inflammation, and trauma [1]. Several theories regarding the pathogenesis of MH have been proposed, with some suggesting traction of the vitreous and internal limiting membrane (ILM) [2, 3] as well as vitreous humor retention in the middle and outer retinal tissues due to the breakdown of the inner retinal structure in the macula (Tornambe's hydration theory) [4]. In some cases, the MH closes spontaneously and requires no treatment; however, in other cases, pars plana vitrectomy (PPV) is necessary for improving visual function. The current standard protocol of PPV for MH is combined with peeling of the ILM and gas tamponade [4], achieving an anatomical closure rate of 80–100% [5–8]. Complications following PPV for MH include failure of MH closure, MH recurrence, intraocular complications (retinal rupture, elevated intraocular pressure, and cataract induction), and vision loss due to the use of gas bubbles and silicone oil [2]. Failure of MH closure following PPV surgery occurs in 10% of cases [6–9] and is usually treated through surgical therapy, including revisional PPV with or without ILM peeling enlargement as well as inverted ILM flap and intraocular tamponade with gases or silicone oils [5]. Additionally, there have been reports of MH closure through medical treatment. Specifically, Kokame et al. [2] reported closure of initially developed and recurrent MH after PPV using only medical therapy, including steroid eye drops and other eye drops. Accordingly, MH closure may be achieved by improving macular edema with drug treatment. This article describes 2 cases of MH closure failure due to post-vitrectomy CME that were successfully treated using sub-Tenon triamcinolone acetonide (STTA) injection.

Case Presentation

Case 1

A 72-year-old male patient with vision loss for 6 months in his right eye visited an ophthalmologist. He had a history of hypertension, diabetes mellitus, and allergic conjunctivitis; additionally, he had used fluorometholone 0.1% eyedrops four times a day. He showed decreased right eye visual acuity; moreover, a fundus examination revealed an MH in the right eye. The patient was referred to our hospital for MH treatment. At the time of the initial visit, his best-corrected visual acuity (BCVA) was 20/320 and 20/25 in the right and left eyes, respectively, indicating decreased visual acuity in the right eye. The intraocular pressure in both eyes was 18.0 mm Hg. Further, the ocular axis length in the right and left eyes was 23.19 and 22.94 mm, respectively. Slit-lamp examination and optical coherence tomography (OCT) revealed a Gass Stage 3 MH in the right eye, without diabetic retinopathy or maculopathy in either eye (shown in Fig. 1a, b, g, h). OCT showed that the minimal diameter of the MH was 286 μm and the maximal diameter was 910 μm. The patient underwent PPV, ILM translocation, and sulfur hexafluoride (SF6) gas injection with cataract surgery in the right eye. After induction of sub-Tenon's anesthesia with 0.6 mL of 2% lidocaine, cataract surgery was performed. Subsequently, 25-gauge, 4-port PPV was performed using the Constellation® system (Alcon Laboratories, Inc., Fort Worth, TX, USA). Further, triamcinolone-assisted posterior vitreous detachment creation was performed using a vitreous cutter. Specifically, 20 mg per 1 mL of triamcinolone was used (MaQaid, 40 mg/vial; Wakamoto Seiyaku, Tokyo, Japan). Brilliant blue-assisted ILM peeling (Coomassie BBG 250; Sigma-Aldrich, St. Louis, MO, USA) was circumferentially performed around the MH. The ILM flap was not completely

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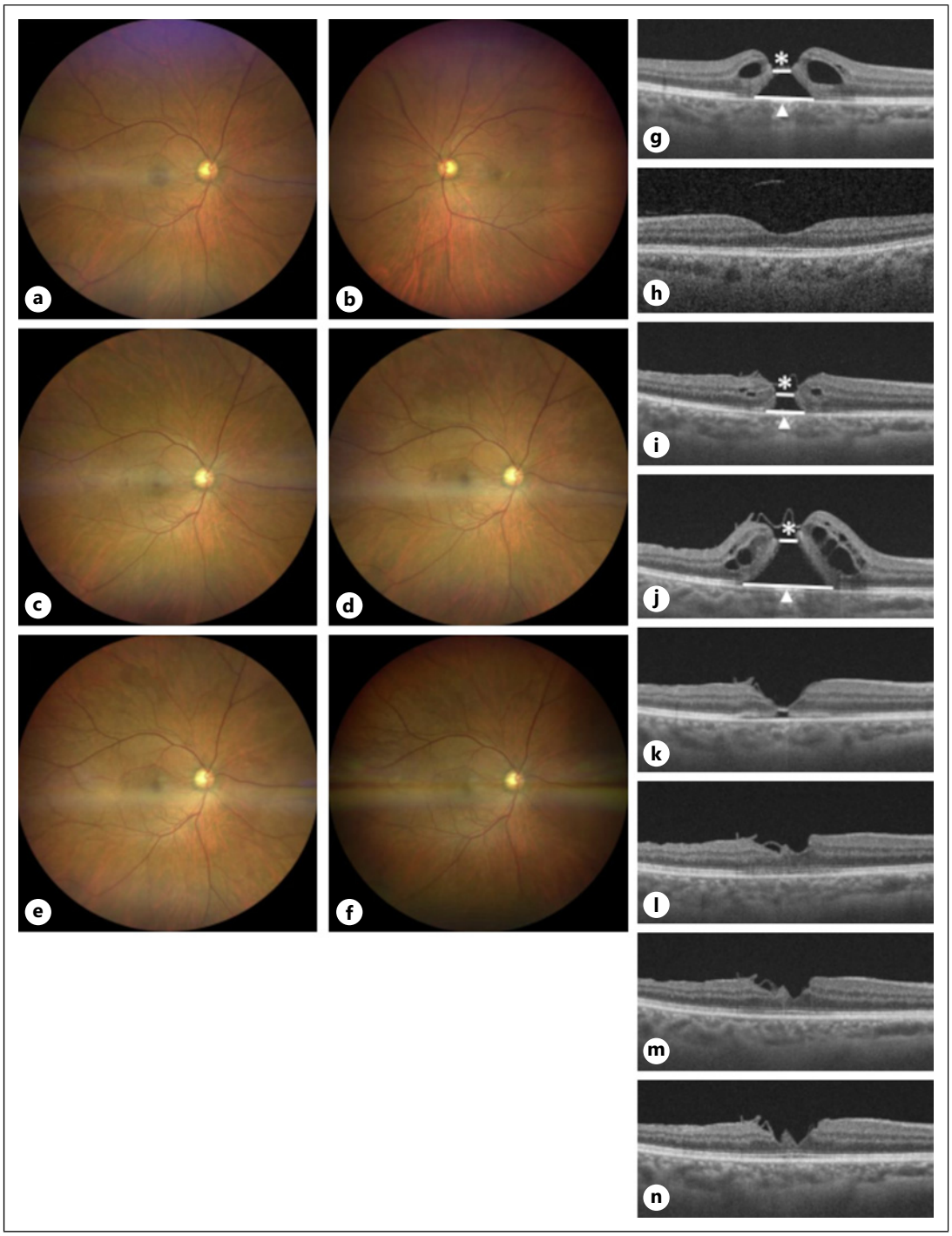

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removed and was placed on the MH; subsequently, purified sodium hyaluronate/sodium chondroitin was placed on top of the ILM. After completion of the vitrectomy, 1.5 mL of 100% SF6 gas was injected into the vitreous cavity. Moreover, 0.3 mL subconjunctival injections of dexamethasone sodium phosphate (Dexart, 6.6 mg/vial; Fuji Pharma, Tokyo, Japan) and dibekacin sulfate (kanamycin injection, 50 mg/vial; Meiji Seika Pharma, Tokyo, Japan) were administered. The patient maintained a face-down position until postoperative day 8. Starting

from the next day after surgery, topical medications were initiated, including 1.5% levofloxacin (levofloxacin ophthalmic solution; Rohto Nitten Co., Ltd., Nagoya, Japan) four times per day, 0.1% bromfenac sodium hydrate (bromfenac Na; Nihon Generic Co., Ltd., Tokyo, Japan) twice per day, and betamethasone 0.1% (betamethasone sodium phosphate PF ophthalmic and otorhinologic solution 0.1%; Rohto Nitten Co., Ltd., Nagoya, Japan) four times per day for 6 months. OCT performed on postoperative day 2 yielded unclear images due to SF6 gas; further, the MH could not be clearly visualized. OCT performed on postoperative day 4 (shown in Fig. 1i) revealed that the MH was open, with slight edema at its edge. OCT showed a minimal diameter (*) of 306 μm and maximal diameter (arrowhead) of 656 μm. The ILM flap remained over the MH. Fundus examination and OCT on postoperative day 18 (shown in Fig. 1c, j) revealed that the ILM flap remained in the MH; however, the edema at the edge of the MH had worsened. OCT showed a minimal diameter (*) of 290 μm and maximal diameter (arrowhead) of 1,502 μm. The MH remained open, and the BCVA was 20/200. Since the cause of the MH closure failure was most likely macular edema associated with postoperative inflammation, STTA was performed. Accordingly, 40 mg of preservative-free triamcinolone acetonide (TA; MaQaid, 40 mg/vial; Wakamoto Seiyaku, Tokyo, Japan) was dissolved in 1.0 mL of saline solution; moreover, 20 mg/0.5 mL TA was injected into the sub-Tenon cavity. OCT performed 2 weeks after STTA injection (postoperative month 1) indicated that the macular edema had disappeared (shown in Fig. 1k); further, MH closure has been achieved. However, the residual pocket of subretinal fluid remained until the sixth postoperative month, with the MH remaining closed (shown in Fig. 1d, e, l, m) and the BCVA of the right eye improving to 20/100. One year after surgery, OCT revealed disappearance of the subretinal fluid, and the BCVA remained at 20/100 (shown in Fig. 1f, n).

Case 2

A 78-year-old female patient with vision loss in her left eye for 1 month visited an ophthalmologist. She had a history of hypertension, rheumatoid arthritis, cataracts, and dry eye; moreover, she was taking 4 mg/day of prednisolone. Her left eye showed decreased visual acuity, and she was referred to our hospital for treatment of macular vitreous traction syndrome. At the initial visit, the BCVA in the right and left eyes was 20/16 and 20/125, respectively, indicating decreased visual acuity in the left eye; further, the intraocular pressure was 13.0 mm Hg in both eyes. The ocular axis lengths in the right and left eyes were 21.52 mm and 21.69 mm, respectively. Slit-lamp examination and OCT revealed a Gass Stage 3 MH in the left eye (shown in Fig. 2a, b, g, h). OCT showed that the minimal diameter of the MH was

Fig. 1. Fundus photography and horizontal OCT at initial and postoperative examination in case 1. **a** Fundus photograph of the right eye with a MH. **b** Fundus photograph of the left eye. **c** Fundus photograph of the right eye on postoperative day 18. **d** Fundus photograph of the right eye on postoperative month 3. **e** Fundus photograph of the right eye on postoperative month 6. **f** Fundus photograph of the right eye on postoperative year 1. **g** OCT of the right eye with a MH. OCT showing a minimal diameter (*) of 286 μm and maximal diameter (arrowhead) of 910 μm; with a full-thickness neurosensory defect at the macula, there is the presence of cystic changes involving the margins of dehiscence. **h** OCT of the left eye. **i** OCT of the right eye performed on postoperative day 4. OCT showing a minimal diameter (*) of 306 μm and maximal diameter (arrowhead) of 656 μm, the presence of full-thickness defect at the macula along with cystoid changes. **j** OCT of the right eye performed on postoperative day 18. OCT showing a minimal diameter (*) of 290 μm and maximal diameter (arrowhead) of 1,502 μm, the presence of full-thickness defect at the macula along with cystoid changes. The cystic changes are worsening. **k** Postoperative month 1. With the disappearance of edema, the rim of the MH is attached and the MH is closed. The residual pocket of subretinal fluid is remained. **l** OCT of the right eye performed on postoperative month 3. OCT reveals disappearance of the subretinal fluid. **m** OCT of the right eye performed on postoperative month 6. **n** OCT of the right eye performed on postoperative year 1.

312 μm and the maximal diameter was 555 μm. She underwent PPV, ILM translocation, and SF6 gas injection with cataract surgery in the left eye. The same surgical technique as in case 1 was used. Photocoagulation was performed intraoperatively given the presence of lattice degeneration in the upper retina. The patient was placed on supine rest until postoperative day 9. After surgery, the same eye drops used in case 1 were administered. OCT performed on postoperative day 3 showed unclear images owing to SF6 gas; moreover, the macular area could not be clearly visualized. OCT performed on postoperative day 5 (shown in Fig. 2i) revealed that the MH was open. On postoperative day 18, fundus examination and OCT (shown in Fig. 2c, j) revealed that the ILM flap remained in the MH; however, edema was observed at the edge of the MH. Additionally, the MH was open, and the BCVA was 20/125. OCT showed a minimal diameter (*) of 221 μm and maximal diameter (arrowhead) of 959 μm. Given the similar pathogenesis to that in case 1, 20 mg/0.5 mL of STTA was performed. One week after STTA injection (postoperative day 25), the macular edema persisted and the MH remained open (shown in Fig. 2k). OCT showed a minimal diameter (*) of 189 μm and maximal diameter (arrowhead) of 885 μm. Six weeks after STTA injection (postoperative month 2), OCT showed that the MH was closed; however, the residual pocket of subretinal fluid persisted (shown in Fig. 2d, l), but BCVA improved to 20/100. OCT showed a maximal diameter (arrowhead) of 663 μm. OCT revealed remaining subretinal fluid at 4 postoperative months (3 months after STTA) (shown in Fig. 2e, m). OCT showed a maximal diameter (arrowhead) of 663 μm. At 6 postoperative months, OCT revealed the subretinal fluid was decreased and the MH remained closed (shown in Fig. 2f, n), and the BCVA of the left eye remained 20/100. OCT showed a maximal diameter (arrowhead) of 242 μm.

Discussion

This article describes our experience with two cases of MH closure failure due to post-vitrectomy CME, with successful treatment using STTA injections. In both cases, the macular edema improved, the MH closed approximately 1 month after STTA, and vision acuity improved.

The relationship between post-vitrectomy MH closure failure and CME remains unclear. Postoperative failure of MH closure occurs in 10% of cases [6–9]. Risk factors for closure failure include MH size >500 μm [6], disease duration >6 months, ethnicity, high myopia, inadequate ILM detachment or gas tamponade, inability of patients to maintain postoperative posture, traumatic etiology, flat edge of the MH, history of uveitis, and concurrent macular diseases such as drusen. Further, the rate of MH recurrence ranges from 3.3% to 11.4% [10], with risk factors including axial length >26 mm, concomitant atrophic age-related macular degeneration, history of intraoperative retinal tears, and cataract surgery after MH repair [10]. The risk of recurrence may increase to 20%, particularly if CME occurs after cataract surgery. A study found that 61.5% of patients presented CME at the time of MH recurrence [3]. The risk factors for CME include concomitant cataract surgery, epiretinal membrane, uveitis, and exudative macular degeneration. In case 1, the patient had an MH for >6 months, which is a risk factor for postoperative failure of MH closure. In case 2, the patient had rheumatoid arthritis and was taking oral prednisolone (4 mg/day) and methotrexate; however, there was no evidence of preoperative intraocular inflammation. Further, the patient in case 1 had a history of diabetes mellitus; however, there was no preoperative evidence of diabetic retinopathy or macular edema. However, both patients developed postoperative CME, which is a risk factor for MH recurrence. About the possible etiology of CME, since there are reports that concomitant cataract surgery can cause CME, we believe that cataract surgery did influence the development of CME in the two cases we reported here. While we did not find any reports

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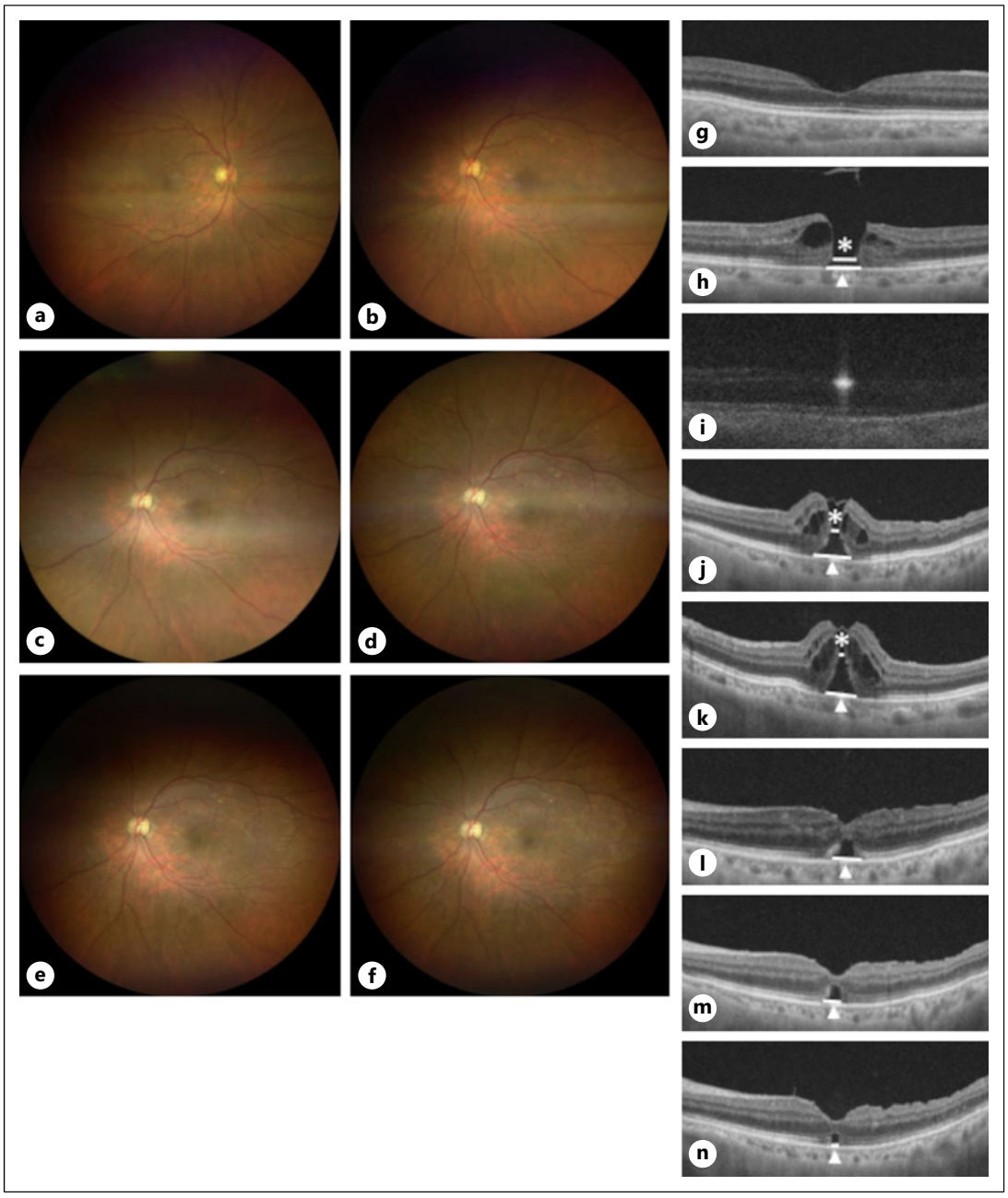

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that the invasion of ILM peeling itself is a risk factor for CME development after MH surgery, it is possible that mechanical invasion and inflammation of the macular edema due to ILM peeling could cause CME. In our cases, postoperative CME may have led to the failure of MH closure.

Currently, vitrectomy with ILM peeling and gas tamponade is the standard protocol for temporary repair of MHs [5]. Persistent MH after ILM peeling is a common complication that is usually surgically treated; however, there remains no consensus regarding the timing and type of reoperation [9]. The reoperative procedures included the following: (1) revision vitrectomy with or without ILM peeling enlargement and intraocular tamponade with gases

or silicone oils; (2) subretinal fluid injection; (3) autologous platelet-rich plasma (injection); (4) autologous ILM free flap transplantation; (5) lens capsular flap transplantation; (6) autologous retinal transplantation; and (7) human amniotic membrane graft. However, the success rates of these invasive procedures remain unclear. In our cases, inverted ILM flaps were used to further promote MH closure. The inverted ILM flap technique is considered superior to conventional ILM peeling in terms of closure of MH across different sizes, including large and myopic MH. In our cases, the use of an inverted ILM flap did not achieve MH closure; however, the STTA injections were successful.

Similar to our cases, there have been reports of the achievement of MH closure through medical therapy without surgery. Kokame et al. [2] indicated that the effectiveness of medical treatment in MH closure can be explained by Tornambe's hydration theory, which suggests that the breakdown of the inner retinal structure results in the accumulation of vitreous fluid in the middle and outer retinal tissues. Subsequently, it is proposed that the expansion of the accumulated fluid, the bulging and slight retraction of the inner retinal layers, and the drawbridge effect contribute toward MH formation [4]. Tornambe's hydration theory may also apply to recurrent MH with CME. Anti-inflammatory treatment with steroids reduces edema at the edge of the hole and releases the drawbridge effect, which ameliorates recurrent MH. Kokame et al. [2] reported seven cases of first-episode or recurrent MH that were closed through medical therapy without surgery. These 7 patients were treated with eye drops (prednisolone in 5 eyes, nepafenac in two eyes, ketorolac in three eyes, and dorzolamide/timolol in one eye). In addition, bevacizumab and triamcinolone vitreous injections were administered for CME in one eye, with bevacizumab vitreous injection being continued due to coexisting exudative age-related macular degeneration. Drug treatment for MH should be considered in the absence of significant traction by the vitreous or preretinal membranes. Both patients in our report developed CME and failed MH closure despite the use of steroids and nonsteroidal anti-inflammatory drug eye drops. The eventual improvement of CME with STTA could have eliminated the drawbridge effect described in Tornambe's hydration theory and promoted MH closure. In the 2 cases presented here, no obvious preretinal membrane was observed, but STTA was performed after the vitreous traction was released by vitrectomy. This may have enhanced the effectiveness of STTA.

This article describes 2 cases of MH closure failure following CME after vitrectomy using the ILM flap technique. In both cases, STTA injections achieved MH closure. In conclusion, STTA injections could be considered before reoperation in patients with MH closure failure

Fig. 2. Fundus photograph and horizontal OCT at initial and postoperative examination in case 1. **a** Fundus photograph of the right eye. **b** Fundus photograph of the left eye with a MH. **c** Fundus photograph of the left eye on postoperative day 18. **d** Fundus photograph of the left eye on postoperative month 2. **e** Fundus photograph of the left eye on postoperative month 4. **f** Fundus photograph of the left eye on postoperative month 6. **g** OCT of the right eye. **h** OCT of the left eye with a MH. OCT showing a minimal diameter (*) of 312 μm and maximal diameter (arrowhead) of 555 μm; with a full-thickness neurosensory defect at the macula, there is the presence of cystic changes involving the margins of dehiscence. **i** OCT of the left eye on postoperative day 5. OCT showing the presence of full-thickness defect at the macula. **j** OCT of the left eye on postoperative day 18. OCT showing a minimal diameter (*) of 221 μm and maximal diameter (arrowhead) of 959 μm, the presence of full-thickness defect at the macula along with cystoid changes. **k** OCT of the left eye on postoperative day 25. OCT showing a minimal diameter (*) of 189 μm and maximal diameter (arrowhead) of 885 μm, the presence of full-thickness defect at the macula along with cystoid changes. The cystic changes are worsening. **l** OCT of the left eye on postoperative month 2. OCT showing a maximal diameter (arrowhead) of 663 μm; with the disappearance of edema, the rim of the MH is attached and the MH is closed. The residual pocket of subretinal fluid is remained. **m** OCT of the left eye on postoperative month 4. OCT showing a maximal diameter (arrowhead) of 663 μm. **n** OCT of the left eye on postoperative month 6. OCT showing a maximal diameter (arrowhead) of 242 μm. Subretinal fluid is decreased, and the MH remains closed.

due to postoperative CME. The CARE Checklist has been completed by the authors for this report and can be accessed as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000538026).

Acknowledgment

We would like to thank Editage (www.editage.com) for English language editing.

Statement of Ethics

Written informed consent was obtained from the patients (patients 1 and 2) for publication of the details of their medical case and any accompanying images. This study protocol was exempted from the need for approval by the Institutional Review Board of Yamaguchi University Hospital. Ethical approval is not required for this study in accordance with local or national guidelines.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Funding Sources

This study was not supported by any sponsor or funder.

Author Contributions

Aiko Haraguchi designed the study and wrote the initial drafts of the manuscript. Ogata, Ohta, and Higashijima examined patients and documented the course of treatment. Makiko Wakuta, Nobuaki Ariyoshi, Masahiko Funatsu, and Yuki Wasai contributed to data collection and interpretation and critically reviewed the manuscript. Kazuhiro Kimura is the corresponding author, contributed to the analysis and interpretation of the data, and assisted in manuscript preparation. All the authors have read and approved the final manuscript.

Data Availability Statement

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

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