Case Report

Closure of Recalcitrant Macular Hole after Choroidal Neovascularization

Cagri Ilhan1, Mehmet Citirik2
1Department of Ophthalmology, Hatay State Hospital, Hatay, Turkey, 2Department of Ophthalmology, University of Health Sciences, Ankara Ulucanlar Eye Education and Research Hospital, Ankara, Turkey

Abstract

Purpose: To report the closure of a recalcitrant macular hole (MH) following the development of choroidal neovascularization.

Methods: A 67-year-old female patient in this case report was diagnosed with a MH and operated twice, but anatomical closure of MH could not be achieved. The patient was followed up without further treatment, as she rejected any additional procedure.

Results: Six months later, a lesion consistent with choroidal neovascularization appeared in the central macula, and the recalcitrant MH closed spontaneously. The MH defect remained closed in the following years.

Conclusion: Besides being a new example of the presence of choroidal neovascularization after MH surgery, the most important aspect of this case report is to report the closure of a recalcitrant MH following the development of choroidal neovascularization.

Keywords: Choroidal neovascularization, Macular hole, Vitrectomy

INTRODUCTION

Macular hole (MH) is one of the conditions associated with the abnormal posterior vitreous detachment that causes full-thickness tissue loss, including the internal limiting membrane (ILM) and photoreceptor layer in the central macula. The anatomical success rate in MH surgery is high with ILM peeling and gas tamponade. For persistent cases, reinstallation of a gas tamponade is a widely used treatment option; however, the closure rates are not as high as primary surgery. Endophthalmitis, retinal pigment epithelium (RPE) abnormalities, macular edema, retinal detachment, or choroid neovascularization (CNV) are some surgical complications that limit anatomical and functional outcomes.

In the literature, several CNV cases occurring after successful MH surgery have been reported. In this presented case, CNV developed after two unsuccessful MH surgeries, and the presence of CNV contributed to the simultaneous closure of this recalcitrant MH defect. This case report aims to draw attention to the closure of a recalcitrant MH following the development of chorioretinal structural changes associated with CNV.

CASE REPORT

A 67-year-old female patient was referred with a complaint of low vision in her left eye. The best corrected visual acuity (BCVA) values were 20/20 in the right eye and 20/200 in the left eye. Intraocular pressure values were within the normal limits, and there was no abnormal finding in anterior segment examinations with slit-lamp biomicroscopy. On dilated fundus examination, the right eye was completely normal, and a large MH appearance was observed in the left eye [Figure 1]. There was no history of ocular trauma, surgery, chronic disease, or...
Systemic hypertension for 5 years was present as the only comorbidity. Surgery was planned for the idiopathic MH in the left eye.

One week later, uneventful phacoemulsification, posterior chamber intraocular lens implantation, pars plana vitrectomy, ILM peeling after brilliant blue staining, and perfluoropropane ($C_3F_8$) gas tamponade were successfully performed under local anesthesia. In addition to standard postoperative medical care including antibiotic, steroid, and cycloplegic eye drops, postoperative face-down positioning was recommended for 1 week. No intraoperative or postoperative complication was observed. At the postoperative 2nd-month visit, intraocular gas completely resorbed, but BCVA was 20/200, and the large MH appearance persisted [Figure 1]. Because of no anatomical and functional improvement, a reoperation was planned for the patient. One month later, the ILM peeling area was widened after brilliant blue staining, and a free ILM flap was created and placed over the MH to cover it. Finally, intraocular $C_3F_8$ gas tamponade was successfully performed. The same postoperative care procedure was repeated, and no complication was observed. Two months after the second surgery, BCVA was still 20/200, and the same large MH appearance persisted [Figure 1].

Six months after the second surgery, the patient presented with a small decrease in BCVA to 20/400. An elevated mass under the MH edges consistent with CNV was observed on dilated fundus examination and a closed MH on optical coherence tomography [Figure 2]. The patient was followed up monthly without treatment, as she rejected any additional procedure. Two months later, CNV remained limited to that area, and the MH remained closed. Similar optical coherence tomography findings and intraretinal cysts were observed 2 months later [Figure 3].

Four years after the last visit, the BCVA was still 20/400 without any treatment. Closed MH, fibrovascular changes associated with CNV lesion, and intraretinal cysts were observed on optical coherence tomography [Figure 4]. Written informed consent was obtained from the patient to share her medical records and photographs for academic purposes.

**Discussion**

Pathogenesis and risk factors for CNV after MH surgery are not completely understood. Preexisting drusen and age-related degenerative changes in Bruch’s membrane are important risk factors for the development of CNV after MH surgery. RPE abnormalities secondary to MH surgery, induced by intraocular manipulation, direct trauma, light toxicity, and inflammatory processes, are other important predisposing factors for the development of CNV. Nevertheless, CNV is a rare condition after MH surgery, and only a minority of surgery-related RPE abnormalities progress to CNV. Banker et al. reported that RPE abnormalities occurred in 33% of 95 patients who underwent MH surgery, and CNV developed in only one of them. Use of trypan blue or indocyanine green could be another factor in the development of CNV secondary to MH surgery because those dyes are associated with toxicity to the neurosensory retina and RPE. Triamcinolone acetonide or brilliant blue are known as safer options, and covering the MH site with viscoelastic material before staining may limit dye-related toxicity. In this regard, using brilliant blue in...
repeated surgery was no additional risk for the development of CNV in this patient. In this presented patient, the absence of preexisting drusenoid changes was clearly demonstrated with different imaging modalities.

Tabandeh et al. reported that nine eyes of eight patients who underwent successful MH surgery developed CNV. They concluded that most CNV lesions occurred in the foveal region, but the central foveal area corresponding to the previous MH site was spared. CNV can occur as early as 6 weeks after MH surgery. They also found that another common feature of the lesions was a predominantly classic appearance on fluorescein angiography, with a ≤ 2 macular photocoagulation study (MPS) disc diameter. The characteristics of CNV in this patient were fully consistent with the literature. The lesion was diagnosed 6 months after the second MH surgery, and the <2 MPS disc diameter lesion had a predominantly classic appearance.

Most of the CNVs that occur after MH surgery are associated with successful surgeries, and only a small number occur after unsuccessful surgeries. In fact, Spies and Messner reported a case of CNV formation in a patient with untreated MH who had no other risk factors for CNV. At this point, treatment strategies directly aim to regress CNV, regardless of whether MH surgery has been successful or whether the patient has had surgery. Focal laser photocoagulation and photodynamic treatment have been performed to regress CNV, but functional outcomes were not favorable in CNV after MH surgery. Oh et al. reported that after 3-monthly intravitreal ranibizumab injections, the CNV lesion and visual acuity did not change significantly. In this reported case, CNV developed after unsuccessful MH surgery and partially regressed spontaneously within months, without anti-vascular endothelial growth factor treatment. The MH defect remained closed in the following years; however, visual acuity did not significantly increase.

The most important aspect of this case is to report the closure of a recalcitrant MH following the development of chorioretinal structural changes caused by CNV. In the literature, limited reports have clearly shown the macroscopic effects of CNV on retinal structure. In one, CNV occurred after unsuccessful MH surgery complicated with retinal detachment after intravitreal ranibizumab injection. The CNV lesion regressed, and the MH remained open. In contrast, recalcitrant MH closure occurred in this case, following the development of CNV. This can be associated with more extensive retinal morphological remodeling. The new vessels in CNV are highly permeable and cause retinal edema and neuroretinal degeneration. Fibrovascular changes and endothelial-to-mesenchymal transition can be involved in the development and course of CNV. In this process, some endothelial-specific markers such as vascular endothelial growth factor receptor-2 and vascular endothelial cadherin are down-regulated, while some mesenchymal markers,
such as vimentin, α-smooth muscle actin, and type I and type III collagens, are up-regulated in the endothelial cells.\textsuperscript{17,18} Fibrovascular membrane-like structures and their contractions are likely responsible for the closure of recalcitrant MH. Nevertheless, the hypothesis of endothelial-to-mesenchymal transition in CNV is a novel concept and should be clarified by further experimental and animal studies.

In summary, CNV is an unusual condition after MH surgery, and only a minority of cases has occurred after unsuccessful surgery. The closure of recalcitrant MH may occur following the development of chorioretinal structural changes caused by CNV.

**Declaration of patient consent**
The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

**Financial support and sponsorship**
Nil.

**Conflicts of interest**
There are no conflicts of interest.

**REFERENCES**
1. Karatepe AS, Menteş J, Erakgün ET, Afrashi F, Naçacı S, Akkin C, et al. Vitreoretinal interface characteristics in eyes with idiopathic macular holes: Qualitative and quantitative analysis. Turk J Ophthalmol 2018;48:70-4.
2. Vishal MY, Babu N, Kohli P, Rajendran A, Ramasamy K. Retrospective study of changes in ocular coherence tomography characteristics after failed macular hole surgery and outcomes of fluid-gas exchange for persistent macular hole. Indian J Ophthalmol 2018;66:1130-5.
3. Tabandeh H, Smiddy WE, Sullivan PM, Monshizadeh R, Rafiei N, Cheng L, et al. Characteristics and outcomes of choroidal neovascularization occurring after macular hole surgery. Retina 2004;24:714-20.
4. Tabandeh H, Smiddy WE. Choroidal neovascularization following macular hole surgery. Retina 1999;19:414-7.
5. Banker AS, Freeman WR, Kim JW, Munguia D, Azen SP. Vision-threatening complications of surgery for full-thickness macular holes. Vitrectomy for macular hole study group. Ophthalmology 1997;104:1442-52.
6. Oh HN, Lee JE, Kim HW, Yang JW, Yun IH. Occult choroidal neovascularization after successful macular hole surgery treated with ranibizumab. Clin Ophthalmol 2012;6:1287-91.
7. Elsing SH, Postel EA, Jaffe GJ. Surgical intervention in eyes with macular hole and choroidal neovascularization. Invest Ophthalmol Vis Sci 2000;41:183.
8. Kelly NE, Wendel RT. Vitreous surgery for idiopathic macular holes. Results of a pilot study. Arch Ophthalmol 1991;109:654-9.
9. Natarajan S, Mehta HB, Mahapatra SK, Sharma S. A rare case of choroidal neovascularization following macular hole surgery. Graefes Arch Clin Exp Ophthalmol 2006;244:271-3.
10. Lee JE, Yoon TJ, Oum BS, Lee JS, Choi HY. Toxicity of indocyanine green injected into the subretinal space: Subretinal toxicity of indocyanine green. Retina 2003;23:675-81.
11. Kumagai K, Furukawa M, Ogino N, Larson E, Uemura A. Long-term outcomes of macular hole surgery with triamcinolone acetonide-assisted internal limiting membrane peeling. Retina 2007;27:1249-54.
12. Fukuda K, Shiraga F, Yamaji H, Nomoto H, Shiragami C, Enaida H, et al. Morphologic and functional advantages of macular hole surgery with brilliant blue G-assisted internal limiting membrane peeling. Retina 2011;31:1720-5.
13. Spies A, Messner LV. An untreated macular hole with adjacent choroidal neovascularization. Optom Vis Sci 2003;80:619-22.
14. Elsing SH, Postel EA, Gill MK, Jampol LM, Jaffe GJ. Management of eyes with both idiopathic macular hole and choroidal neovascularization. Retina 2001;21:613-8.
15. Otsuka K, Imai H, Shimoyama T, Nagai T, Honda S, Azumi A. Recurrence of macular hole retinal detachment after intravitreal ranibizumab injection for the treatment of choroidal neovascularization from the remaining macular hole edge. Case Rep Ophthalmol 2012;3:424-7.
16. Rossato FA, Su Y, Mackey A, Ng YS. Fibrotic changes and endothelial-to-mesenchymal transition promoted by VEGFR2 antagonism alter the therapeutic effects of VEGFA pathway blockage in a mouse model of choroidal neovascularization. Cells 2020;9:E2057.
17. Dejana E, Hirschi KK, Simons M. The molecular basis of endothelial cell plasticity. Nat Commun 2017;8:14361.
18. Piera-Velazquez S, Li Z, Jimenez SA. Role of endothelial-mesenchymal transition (EndoMT) in the pathogenesis of fibrotic disorders. Am J Pathol 2011;179:1074-80.