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Simultaneous development of full-thickness macular hole and neovascular age-related macular degeneration

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ABSTRACT

Purpose: To present a case of full-thickness macular hole (MH) with treatment-naïve neovascular age-related macular degeneration (nAMD).

Observations: A 74-year-old woman presented with sudden visual impairment and floaters in her left eye. Fundus examination revealed retinal hemorrhages and hemorrhagic pigment epithelial detachment at the fovea. Optical coherence tomography angiography revealed both type 1 nAMD and stage 4 MH obscured by blood. After the first intravitreal aflibercept injection, early pars plana vitrectomy in addition to the inverted internal limiting membrane flap technique was performed to close MH without complications. This improved the patient's visual acuity. Throughout the postoperative follow-up period of 18 months, recurrent exudates from nAMD required repetitive aflibercept injections; MH relapse was not observed.

Conclusions: MH can be complicated by acute, treatment-naïve nAMD. Early surgical closure of secondary MH combined with anti-vascular endothelial growth factor therapy for nAMD may yield a satisfactory visual outcome.

1. Introduction

Full-thickness macular hole (MH) sometimes develops secondary to neovascular age-related macular degeneration (nAMD) and requires appropriate management. In particular, MH observed in the acute phase of nAMD is rare, and its pathogenesis and proper treatment strategy are controversial. Herein, we present an unusual case in which treatment-naïve nAMD and MH developed around the same time, and both were effectively managed.

2. Case report

A 74-year-old woman presented to an attending ophthalmologist with complaints of central vision loss, achromatopsia, and floaters in the left eye with sudden onset in the morning. The ophthalmologist identified MH with retinal hemorrhage and pigment epithelial detachment (PED) in the left eye *via* optic coherence tomography (OCT). The best-corrected visual acuity measured by the ophthalmologist had been 30/25 in both eyes 22 days before the symptoms appeared. The patient had glaucoma involving the central visual field in both eyes; latanoprost had been prescribed for treating glaucoma for >10 years. She had undergone cataract surgery in both eyes 6 years before and laser photocoagulation for a retinal break in the left eye several years before. The patient was referred to our department after 3 days. Upon presentation to our department, the best-corrected visual acuity was 30/25 in the right eye and 5/25 in the left eye. The intraocular pressure was 13 and 15 mmHg in the right and left eyes, respectively. Slit-lamp examination revealed clear cornea, anterior chamber with no cells or flare, intraocular lens, and clear vitreous with posterior detachment in both eyes. Dilated fundus examination revealed oval-shaped retinal hemorrhage at the fovea of the left eye adjacent to a hemorrhagic PED with an irregular contour and subretinal hemorrhage (Fig. 1A and C). Moreover, an old retinal break surrounded by a chorioretinal scar was observed in the peripheral fundus. Spectral domain OCT further revealed full-thickness MH filled with blood, epiretinal membrane, and PED (Fig. 1B), in which spectral domain OCT angiography revealed a flow signal suggestive of choroidal neovascularization in PED (Fig. 1E). Fluorescein angiography in the left eye revealed a ring-shaped rim staining of MH in the late phase and late leakage of undetermined source, which corresponded to the vascular network temporal to PED (Fig. 2B).

Based on the diagnosis of nAMD, thrice monthly intravitreal aflibercept injection was scheduled; the first injection was administered 8

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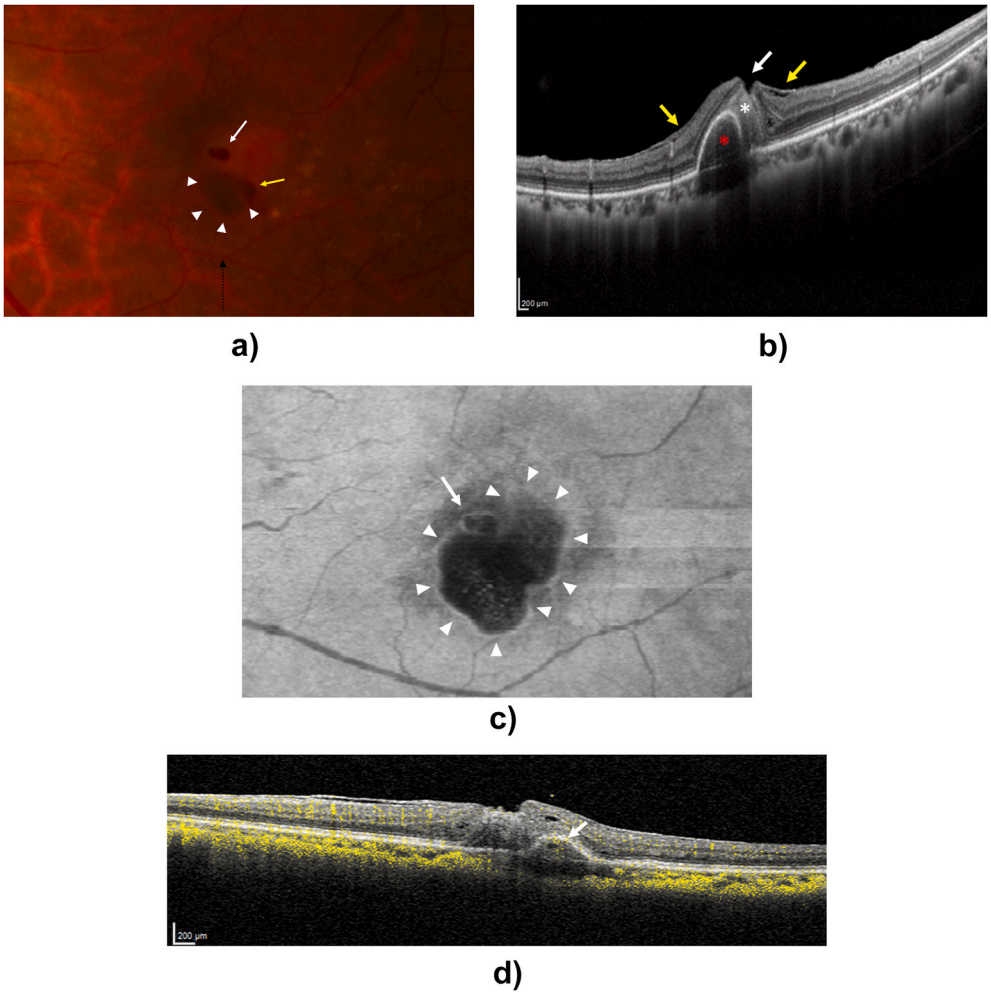

Fig. 1. Baseline multimodal imaging of neovascular age-related macular degeneration and macular hole (MH). A. Color fundus photograph showing retinal hemorrhage at the fovea (white arrow), hemorrhagic pigment epithelium detachment (PED, white arrowheads), and subretinal hemorrhage (yellow arrow). B. Spectral domain optical coherence tomography (SD-OCT) line scan via the fovea (indicated by a black dotted arrow in panel A) demonstrating MH (197 × 265 µm, white arrow) filled with blood (white asterisk), adjacent PED (red asterisk), and epiretinal membrane (yellow arrows). C. *En face* macular image (mean from the external limiting membrane to Bruch's membrane) obtained by SD-OCT cube scan depicting the oval-shaped MH (white arrow) and irregular contour of PED (white arrowheads). D. Vertical line scan via PED, demonstrating the flow signal under pigment epithelium (yellow arrow). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

days after the initial presentation. At 7 days after the first dose, the best-corrected visual acuity in the left eye was 15/50; the height of the PED reduced and the blood inside the MH resolved (Fig. 3A). At 24 days after the initial presentation, pars plana vitrectomy was performed for the persisting MH. During surgery, the posterior vitreous was totally detached, which was consistent with the slit-lamp examination finding at presentation. Epiretinal membrane peeling with the triamcinolone-assisted inverted internal limiting membrane (ILM) flap technique and subsequent fluid-gas exchange using 20% sulfur hexafluoride gas tamponade were performed. The patient remained in the prone position for 3 days postoperatively. MH was closed without complications (Fig. 3B), and visual acuity in the left eye improved to 20/25 2 weeks postoperatively. In the postoperative follow-up period of 18 months, after planned intravitreal aflibercept injections administered twice, *pro re nata* aflibercept injections were administered three times for exudation relapses due to nAMD; visual acuity in the left eye was maintained at 20/25 without MH recurrence.

The patient provided written informed consent to publish this case, including images.

3. Discussion

We encountered a rare case of MH and nAMD detected within a day of symptom onset. Good visual acuity of 30/25 in the left eye was previously confirmed 22 days before the onset of sudden visual loss and floaters, which probably excludes preexisting chronic MH. That is, at the earliest, MH probably formed several weeks before the symptoms appeared. The sudden onset of floaters indicates that fresh retinal hemorrhage from active choroidal neovascularization was diffused in the preretinal region via MH.

The mechanism of MH formation secondary to nAMD appears multifactorial. MH complication in the acute phase of nAMD is rare, and in most reported cases, MHs are detected at least several months after the development of neovascular lesion[1] or chief complaint.[2,3] MH secondary to nAMD is also often associated with therapeutic intervention for nAMD, including the injection of anti-vascular endothelial growth factor agent into the vitreous.[4–7] The pathogenesis of these secondary MHs has been attributed to vitreomacular tractional force,[5] pigment epithelium contraction,[6] or retinal vulnerability due to exudative changes or intervention.[4] In the present case, preoperative examinations suggested total posterior vitreous detachment and no vitreomacular traction was observed during surgery; however, the undetected vitreomacular traction or contractive force of the epiretinal membrane may have been aggravated by exudation at the fovea due to choroidal neovascularization, leading to MH formation. Furthermore, exudation itself might cause retinal vulnerability and result in MH formation. However, fresh blood in MH at the time of initial diagnosis suggests that hemorrhage from choroidal neovascularization directly triggered MH formation. Several studies[1,8] reported MH due to subretinal hemorrhage. Wan et al. reported an unusual case of MH following subretinal hemorrhage in a patient[1] with nAMD and suggested that subretinal hemorrhage increased the subretinal pressure and caused foveal dehiscence. This

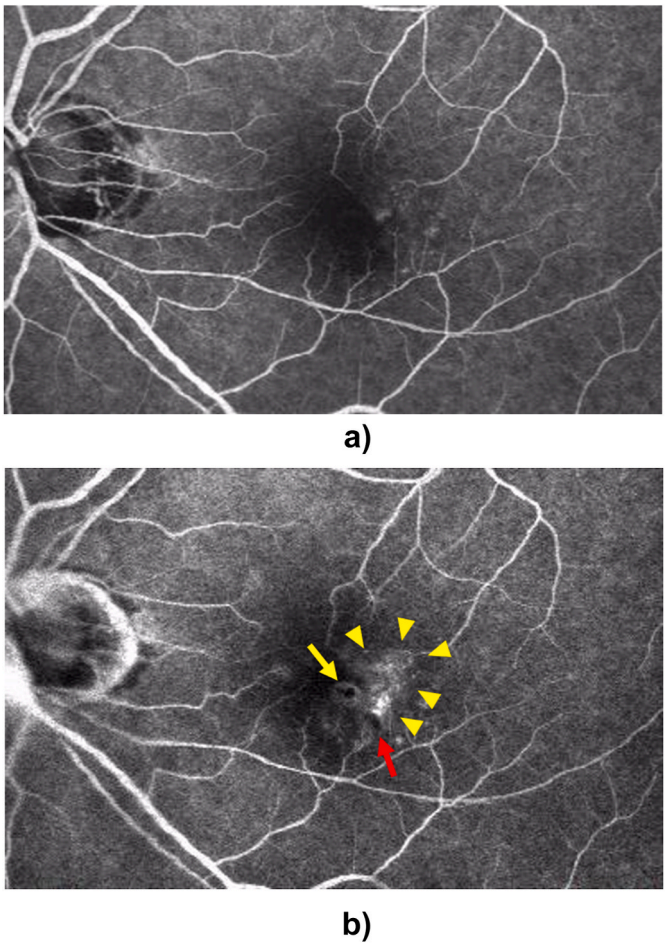

Fig. 2. Images of the early (A) and late (B) phases in fluorescein angiography obtained at presentation. In the late phase, the ring-shaped rim staining of macular hole (yellow arrow), blocking due to subretinal hemorrhage (red arrow), and late leakage of undetermined source temporal to the fovea (yellow arrowheads) were observed. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

increase in pressure is one of the explanations for MH formation following subretinal hemorrhage due to ruptured retinal arteriolar macroaneurysms.[9,10] Baskaran et al. also reported a rare case of MH secondary to a rupture of polypoidal choroidal vasculopathy and argued that massive subretinal hemorrhage directly led to MH.[8] In the present case, overall hemorrhage was not massive and was unlikely to have sufficiently increased the subretinal pressure to cause MH. Instead, retinal hemorrhage from choroidal neovascularization may have directly increased intraretinal stress to cause foveal dehiscence, and this process might have occurred together with the other mechanisms described above. To the best of our knowledge, MH formation secondary to retinal hemorrhage restricted at the fovea has not been reported.

The management of MH secondary to nAMD is controversial. Cases have been reported where MH concomitant with nAMD[3,7,11] or other retinal diseases[12,13] resolved spontaneously or after medical treatment without surgical repair. These phenomena are considered to occur because of relief of the underlying pathogenesis inducing MH such as macular edema.[14] However, there is little evidence on the proportion or clinical characteristics, such as MH size, of such successful cases[1215] compared with overall secondary MH. A retrospective study[12] revealed that MH resolved after topical therapy in eight of nine eyes; the MH diameter was up to 132 μm with an average value of 79.6 μm. Another case series[15] reported diameters of up to 189 μm. Given the expanding nature of idiopathic stage 2 MH[16] and poorer surgical outcomes in larger idiopathic MH cases,[17] larger secondary MHs would be less likely to spontaneously close. Moreover, extremely late surgery may lead to worse preoperative visual acuity[16] and result in limited visual prognosis as demonstrated in idiopathic MH cases.[18,19] In the current case, MH could have resolved with medical treatment only. The attending physician planned early vitrectomy because the complicating epiretinal membrane was considered an aggravating factor[20,21] and early surgical repair was believed to provide good visual outcome as chronic MH was excluded.

Few studies have reported anatomical and functional outcomes following vitrectomy for MH secondary to nAMD.[1,22] The rarity of the condition makes it difficult to evaluate different procedures in vitrectomy. The inverted ILM flap technique has demonstrated a higher or similar closure rate in large MHs than the conventional ILM peeling technique, although its superiority with respect to long-term functional outcome is inconclusive.[23–25] Some studies suggested that the inverted ILM flap technique is effective in MH complicated by other macular pathologies, such as type 2 idiopathic macular telangiectasia[26] and dry age-related macular degeneration.[27] The inverted ILM flap technique was selected in the current case because exudative changes due to nAMD might have hampered MH closure. A relatively good clinical course of the present case suggests the efficacy of the procedure for MH complicated by nAMD.

The case also highlights that MH filled with hemorrhage is difficult to distinguish from intraretinal hemorrhage by funduscopic examination alone. A careful evaluation of the OCT image helped detect MH at the initial presentation.

4. Conclusions

Treatment-naïve nAMD can cause MH in a very acute phase. In such a case, early surgical approach for MH closure may be an option to obtain a better visual outcome.

Patient consent

Written consent to publish this case report was obtained from the patient. This report does not contain any personally identifiable information.

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Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Data availability statement

All data are available on reasonable request to the corresponding author.

Author contributions

Shuichiro Aoki wrote and revised the manuscript; Hiroko Imaizumi performed the clinical evaluation and revised the manuscript. All authors approved the final version of the manuscript for publication.

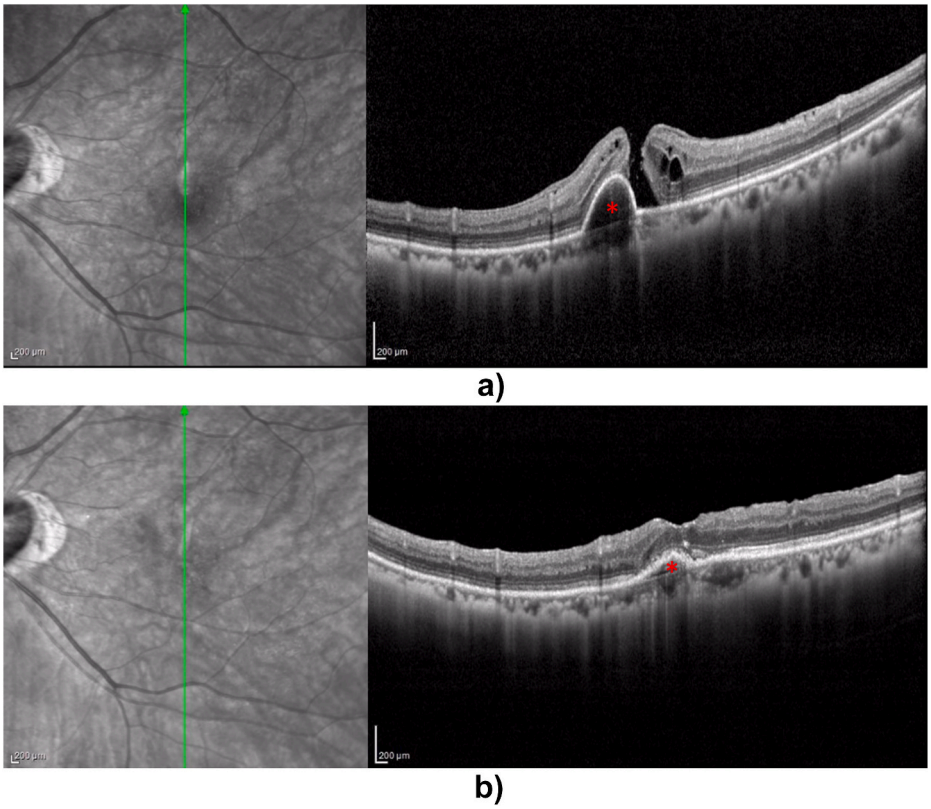

Fig. 3. Vertical line scans at the same location via the fovea by spectral domain optical coherence tomography during the treatment. A. At 7 days after the first intravitreal aflibercept injection, pigment epithelium detachment (red asterisk) reduced its height, and blood in the macular hole disappeared. B. At 2 weeks after pars plana vitrectomy, macular hole was closed with decreased pigment epithelium detachment (red asterisk). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

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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None.

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