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Acute Submacular Hemorrhage Resulting from Neovascular Age-Related Macular Degeneration in a Monocular Patient

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Abstract

Purpose: To present the management and outcomes of a case of an acute submacular hemorrhage secondary to neovascular age-related macular degeneration (nAMD). **Methods:** A single case was retrospectively evaluated. **Results:** A 79-year-old man with a history of submacular hemorrhage from nAMD and persistent disease activity in the left eye presented with an acute submacular hemorrhage in his better-seeing right eye, which was previously closely monitored for an extrafoveal serous pigment epithelial detachment without exudation. The patient received intravitreal antivascular endothelial growth factor (anti-VEGF) and subsequently had pars plana vitrectomy with subretinal tissue plasminogen activator and gas tamponade. After 5 days of face-down positioning, the hemorrhage was successfully displaced from the fovea. Recurrent disease activity 2 weeks postoperatively prompted intensive biweekly anti-VEGF therapy. By postoperative month 5, the patient's visual acuity improved from 20/400 to 20/70 OD. **Conclusions:** This case highlights the importance of close monitoring of patients with nAMD who exhibit aggressive disease as well as the efficacy of prompt surgical intervention and increased anti-VEGF frequency for large submacular hemorrhages.

Keywords

submacular hemorrhage, wet (neovascular) AMD, anti-VEGF agents

Introduction

Submacular hemorrhage is an uncommon yet devastating complication of neovascular age-related macular degeneration (nAMD) that can cause permanent vision loss. The prognosis of a submacular hemorrhage depends on its size, thickness, and location. Although smaller hemorrhages may resolve completely with observation or intravitreal (IVT) antivascular endothelial growth factor (anti-VEGF) therapy, larger hemorrhages can persist, leading to subretinal fibrosis. The ideal treatment for large submacular hemorrhages is still up for debate, with several possible options, including observation, IVT anti-VEGF, pneumatic displacement with or without IVT tissue plasminogen activator (tPA), subretinal tPA, and submacular surgery.[1,2]

We report a case of a large submacular hemorrhage secondary to nAMD in a monocular patient who was treated with subretinal tPA and anti-VEGF injections every 2 weeks and had excellent visual recovery. We also discuss management strategies that can be of benefit in such uncommon and challenging cases.

Case Report

A 79-year-old man with a history of AMD was followed by our retina service for the past 2 years. He initially presented with nAMD in the left eye with severe persistent disease activity despite monthly aflibercept (9 injections) followed by monthly faricimab (12 injections). His right eye had intermediate non-neovascular AMD and had been stable for some time; however, a progressively worsening pigment epithelial detachment (PED) was noted on optical coherence tomography (OCT) over the past few visits (Figure 1). Given the lack of intraretinal fluid (IRF) or subretinal fluid (SRF) in the right eye, close observation with a low threshold for initiating anti-VEGF treatment was recommended.

Unfortunately, the patient presented 2 weeks later with sudden-onset, painless vision loss in the better-seeing right eye. The visual acuity (VA) was 20/400 OD (baseline 20/40) and counting fingers (stable) OS. The intraocular pressure was symmetric and within normal limits in both eyes (11 mm Hg and 10 mm Hg, respectively). The pupils were equal, round, and reactive with

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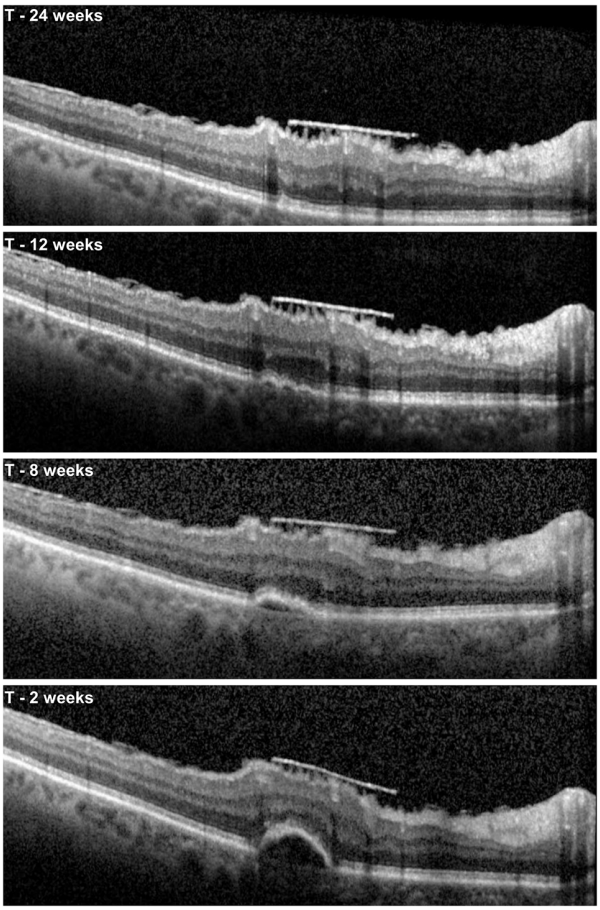

Figure 1. Progressive extrafoveal serous pigment epithelial detachment in a patient with previously stable non-neovascular age-related macular degeneration (AMD) and a history of neovascular AMD in the fellow eye who subsequently developed a large submacular hemorrhage 2 weeks after the last follow-up.

no relative afferent pupillary defects. An anterior segment examination was notable for bilateral intraocular lenses with mild posterior capsule opacification. A dilated fundus examination of the right eye showed a large submacular hemorrhage occupying most of the macula (Figure 2A), with a subretinal component and subretinal pigment epithelium (RPE) component on OCT (Figure 3A). A dilated fundus examination of the left eye showed subretinal fibrosis.

The patient was administered IVT faricimab, and after extensive discussion regarding the risks, benefits, and alternatives, he elected to proceed with vitrectomy and subretinal tPA. The next day, the patient was brought to the operating room, and a core vitrectomy and peripheral vitrectomy were performed. An extendable 41-gauge subretinal injection needle was used to deliver approximately 0.1 mL of 500 µg/mL tPA at the superotemporal edge of the submacular hemorrhage; the solution was slowly injected into the subretinal space. A partial fluid–air exchange was performed followed by an air–gas exchange with 26% sulfur hexafluoride and IVT bevacizumab (see Supplemental Video). Postoperatively, the

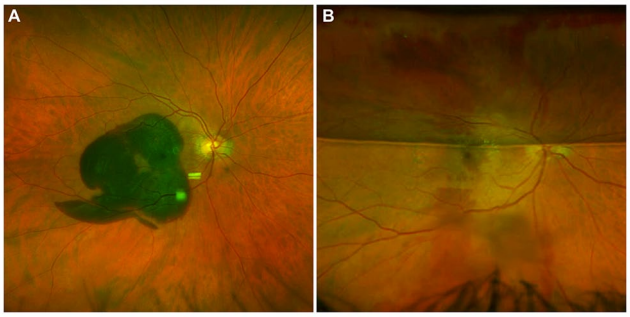

Figure 2. Color fundus photograph of a patient with a large submacular hemorrhage (A) at presentation and (B) 5 days after pars plana vitrectomy with subretinal tissue plasminogen activator, partial fluid–air exchange, and 26% sulfur hexafluoride gas.

patient was instructed to position 45 degrees forward for at least 3 days to displace the hemorrhage.

On postoperative day 5, the submacular hemorrhage was displaced from the fovea (Figure 2B and Figure 3B). On postoperative week 2, recurrent disease activity was noted on OCT (Figure 3C) and the patient was started on biweekly IVT injections, alternating faricimab and aflibercept. At the last follow-up 5 months after surgery, the patient's VA had improved to 20/70 OD with stable OCT findings (Figure 3D).

Conclusions

This case highlights several critical decision points in the management of nAMD and the challenges involved in monitoring and treating this patient population.

PEDs are a common manifestation of both non-neovascular AMD and nAMD and can present as serous, drusenoid, or fibrovascular.[3] Serous PEDs are found in approximately 10% of patients with AMD and can remain stable, collapse into macular atrophy, or develop into choroidal neovascularization (CNV).[4–7] The serous PED in our patient was extrafoveal and not associated with IRF or SRF to suggest active CNV. However, his age and history of aggressive disease in the fellow eye rendered him at higher risk. Thus, despite close monitoring and a readiness to initiate treatment, it is likely that early detection of the CNV complex through multimodal imaging, such as fluorescein angiography (FA), indocyanine green angiography (ICGA), or OCT angiography (OCTA), could have facilitated prompt intervention.[8,9]

Even in the absence of CNV, it is debatable whether the patient would have benefited from anti-VEGF treatment, especially if the PED continued to grow or began to affect his vision. There are no established guidelines for treating avascular PEDs; however, IVT anti-VEGF is effective and most studies have not shown a difference in outcomes depending on the PED subtype.[10] However, although treatment with anti-VEGF can temporarily decrease the volume of avascular PEDs, the effect is not permanent and does not necessarily improve functional outcomes.[11] Furthermore, anti-VEGF therapy can be associated with the development of RPE tears or atrophy, which in turn

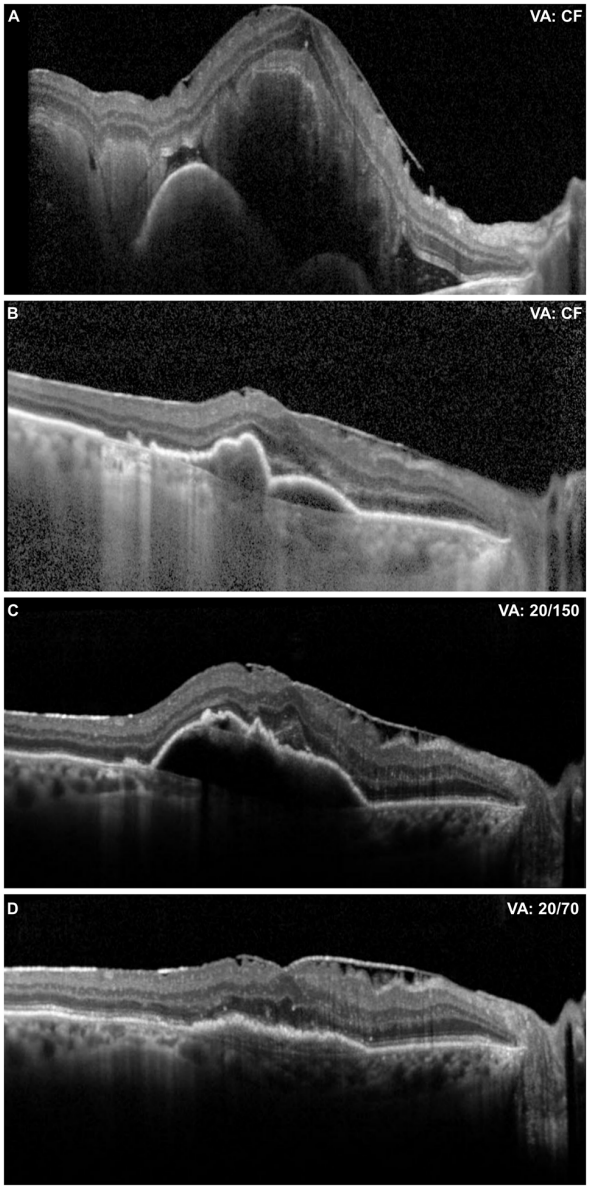

Figure 3. Optical coherence tomography of a patient with a large submacular hemorrhage (A) at presentation, (B) 5 days after pars plana vitrectomy with subretinal tissue plasminogen activator, partial fluid–air exchange, and 26% sulfur hexafluoride gas, (C) 2 weeks after surgery, and (D) 5 months after surgery.

can lead to vision loss. The situation can be especially challenging in patients such as ours, where a thorough discussion regarding the risk–benefit profile becomes paramount.

The management of submacular hemorrhage is even more controversial because no large-scale prospective studies have evaluated the best treatment modalities for this relatively rare condition and the visual prognosis is often guarded regardless of treatment.[1] IVT anti-VEGF monotherapy has shown favorable outcomes in several case series, although large, thick hemorrhages may require additional interventions.[2] Pneumatic displacement can be an effective treatment and can be performed immediately in the office; however, the positioning requirement may limit its usefulness, especially in older patients. Although pneumatic displacement is often combined with IVT tPA, animal studies suggest that IVT tPA does not reach the subretinal space. Clinical studies have also shown better outcomes with subretinal tPA.[12] Subretinal tPA is more technically challenging; however, intraoperative OCT can be an invaluable tool to help ensure correct placement.[13] Given the toxic effect of a subretinal hemorrhage on the photoreceptors and RPE,[14,15] prompt surgical intervention may improve outcomes, especially in cases of thick or dense hemorrhages.

This case emphasizes the importance of tailoring management for persistent or aggressive disease. Before being treated with subretinal tPA, our patient received IVT faricimab, a bispecific antibody targeting both angiopoietin-2 (Ang2) and VEGF-A. Although there are no current data specifically on the effectiveness of faricimab for submacular hemorrhage, preclinical studies using animal models suggest that Ang2 inhibition may be beneficial in reducing the subretinal fibrosis associated with CNV.[16] Despite receiving IVT faricimab, the patient had recurrent disease activity with enlargement of the PED and new SRF just 2 weeks after injection. His other eye already had a history of significant persistent disease activity despite monthly injections. Therefore, given his monocular status, the decision was made to pursue intensive anti-VEGF therapy with biweekly injections. The rationale for biweekly dosing in refractory cases is supported by a pharmacokinetic and clinical rationale because the optimal dosing interval for anti-VEGF depends on the overall disease burden.[17–19] As such, physicians should be cognizant of the need to individualize treatment regimens for patients who present as nonresponders or short-term responders.[18]

In conclusion, this case presents the challenges associated with treating patients with nAMD and underscores the importance of frequent monitoring, the use of multimodal imaging (eg, FA, ICGA, OCTA), early intervention, and intensive (and unconventional) management of complicated cases.

Ethical Approval

This case report was conducted in accordance with the Declaration of Helsinki. The collection and evaluation of all protected patient health information were performed in a US Health Insurance Portability and Accountability Act–compliant manner. Ethical approval was not sought because the Duke Institutional Review Board does not consider review of medical records for publication of a single case report to be research involving human subjects.

Statement of Informed Consent

Informed consent, including permission for publication of all photographs and images included herein, was obtained before the procedure was performed.

Declaration of Conflicting Interests

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Supplemental Material

Supplemental material is available online with this article.

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