Nanovitreoretinal Subretinal Gateway Device to Displace Submacular Hemorrhage: Access to the Subretinal Space Without Vitrectomy

Submacular hemorrhage (SMH) is a complication of choroidal neovascularization (CNV) that markedly diminishes vision and has limited potential for spontaneous recovery.[1] Numerous techniques in the management of SMH have been described. In this article, we present the first series of patients with foveal-involving SMH as a complication of neovascular age-related macular degeneration (nAMD) treated with subretinal hemorrhage displacement through subretinal injection without vitrectomy; a procedure facilitated by the nanovitreoretinal (NVR) subretinal gateway device (Vortex Surgical, Chesterfield, MO).

Methods

In 2019, 2 patients underwent displacement of subretinal hemorrhage with recombinant tissue plasminogen activator (tPA) and air without vitrectomy using the NVR device. Patients' medical records were reviewed, and data were collected on demographic characteristics, ocular history, and best-corrected Snellen visual acuity at presentation and at last follow-up. The etiology and type of hemorrhage were noted, along with visual acuities at baseline, after SMH but preoperative and postoperative time points (Table 1). This retrospective chart review was approved by the Institutional Review Board and adhered to the declaration of Helsinki.

Surgical Technique

The delivery of a subretinal therapeutic cocktail is performed with an instrument designed to target the subretinal space without vitrectomy; therefore, no vitrectomy is performed. In its resting state, the NVR device consists of a handpiece with a slide-action extension mechanism and a 30-gauge (g) needle at the distal tip that ensheaths a fine subretinal cannula with a diameter 25% smaller than currently available 41-g cannulas (Figure 1A). Tubing extends from the back of the handpiece that enables coupling with viscous fluid control of standard vitrectomy systems. Actuating the slide-action control on the handpiece proportionally extends the subretinal cannula (Figure 1B).

The injection cocktail is prepared, consisting of a combination of 0.1 mL of tPA at a concentration of 25 μg/0.1 mL (total, 25 μg) and filtered air. The handpiece containing the subretinal cannula is connected to a syringe with the injection cocktail, which is subsequently connected to the Constellation vitrectomy machine (Alcon, Fort Worth, TX), facilitating fluid injection using viscous fluid control. The subretinal cannula is temporarily extended outside of 30-g needle before entering the eye for testing of adequate fluid flow through the tip of the instrument, which typically occurs at 6 to 10 pounds per square inch (PSI).

A 25-gauge chandelier endoilluminator (Alcon, Fort Worth, TX) is inserted through the pars plana in either of the inferior quadrants. The needle tip of the device (with the subretinal tip now withdrawn into the 30-g needle) is inserted through the pars plana in either of the superior quadrants, and the

Table 1. Characteristics of Two Patients With Foveal-Involving SMH undergoing Displacement With the NVR subretinal Gateway Device

Etiology	Pre-SMH Acuity	Post-SMH Acuity	Postoperative Acuity
nAMD	20/50	CF 1 foot	20/50 (8 week)
nAMD	unknown	20/80-2	20/40-2 (9 week)

nAMD, neovascular age-related macular degeneration; mixed, both subretinal and subretinal pigment epithelial components.

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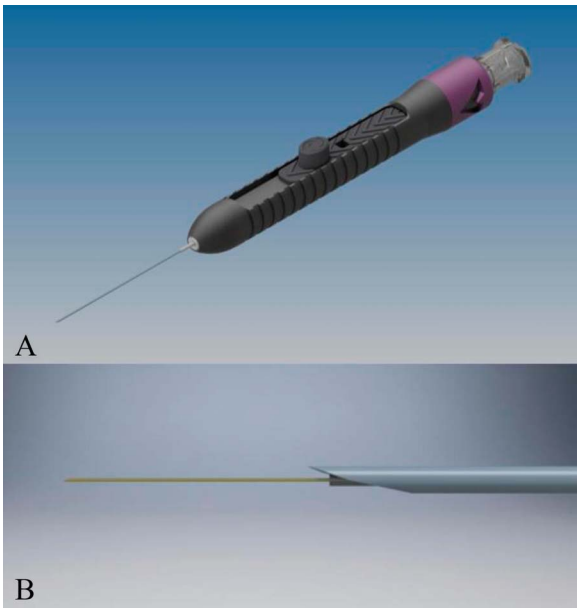

Fig. 1. A and **B.** Nanovitreoretinal device in its resting state and with subretinal cannula extended.

needle itself is advanced to the mid-vitreous cavity, The subretinal cannula is then extended with the slide action on the handpiece, facilitating further extension of the subretinal tip toward and through the retinal surface. The beveled tip of the cannula is inserted into the SMH, and the fluid/air cocktail is injected into the subretinal space. Liquefaction of the clot by tPA enhances its mobility within the subretinal space, while the fluid volume injected within the subretinal space helps create space for movement of the clot inferiorly that is further facilitated by subretinal air. Once the retina is seen to adequately elevate with the infusion (typically at 6–10 PSI), the tip is withdrawn with the slide action on the handpiece, and the needle is subsequently removed from the eye in the same trajectory as it entered. Scleral depression is performed followed by removal of the chandelier and suturing its sclerotomy with one 8-0 polyglactin (vicryl) suture. An anterior chamber tap is performed, followed by the injection of 0.5 cc of 100% sulfur hexafluoride (SF-6) gas into the vitreous cavity, thereby completing the procedure (Supplemental Video 1, http://links.lww.com/IAE/B111). Both patients received intravitreal ranibizumab (Lucentis; 0.5 mg) at the end of the case as well. Patients were advised to maintain chin-down positioning for 3 days.

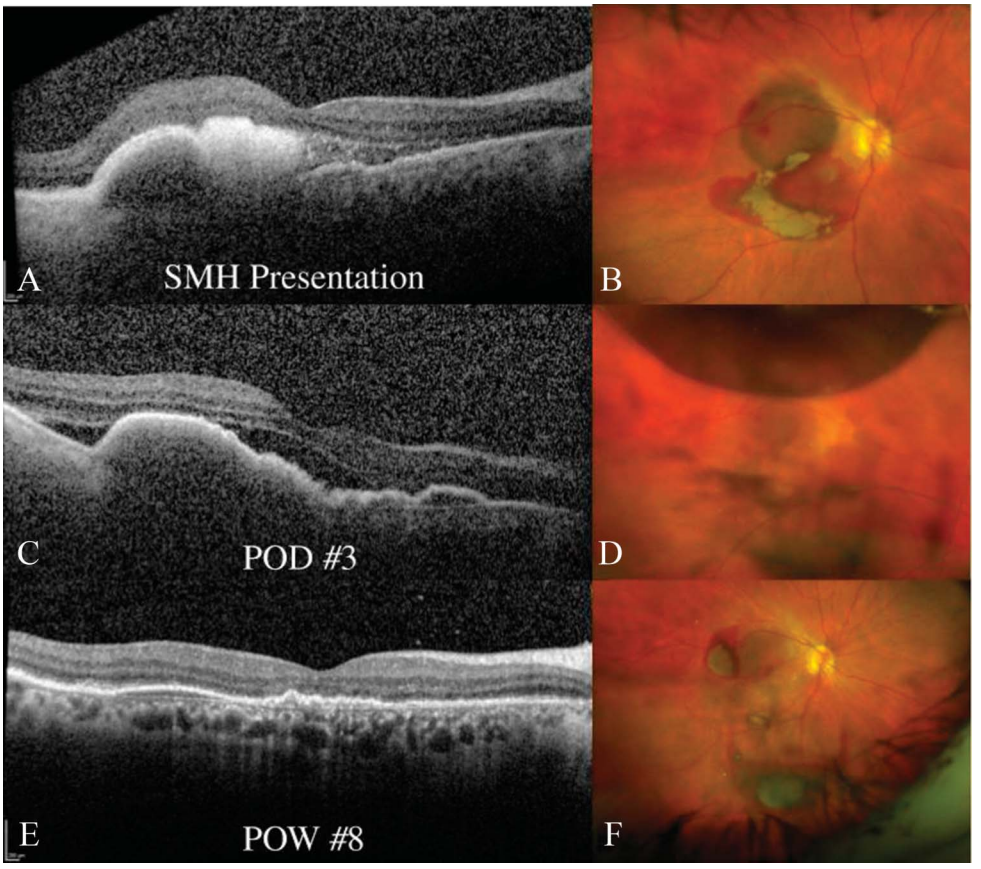

Fig. 2. A–F. Multimodal retinal imaging of Patient 1 at presentation of SMH, postoperative day (POD) 3, and postoperative week (POW) 8.

Results

Patient 1

Patient 1 had an ocular history of nAMD in the right eye, intermediate nonexudative AMD in the left eye, pseudophakia in both eyes, and the presence of posterior vitreous detachment (PVD) in both eyes. She had received 10 intravitreal aflibercept (Eylea; 2 mg) injections before developing SMH in the right eye, with a baseline best-corrected Snellen visual acuity (BCVA) of 20/50 that decreased to counting fingers (CF) at 1 foot with the SMH in the right eye (Figure 2, A and B). She elected to observe for 1 month before deciding to proceed with surgery. She underwent the surgical technique described above and tolerated the procedure well without elevated IOP or retinal tear or detachment occurring in the postoperative period with great displacement (Figure 2, C and D). At postoperative week 8, her BCVA has returned to baseline (20/50), and her macular anatomy had significantly improved (Figure 2, E and F).

Patient 2

Patient 2 had an ocular history of nAMD in the right eye, intermediate nonexudative AMD in the left eye, pseudophakia in both eyes, and the presence of PVD in both eyes. He presented to an outside retinal specialist with BCVA of 20/250 and SMH at the time of nAMD diagnosis and received 1 intravitreal aflibercept (Eylea; 2 mg) injection in the right eye. He presented later to our practice with vision of 20/80-2 and a foveal-involving SMH in the right eye (Figure 3, A and B). He underwent the surgical technique described above and tolerated the procedure well with no postoperative complications (Figure 3, C and D). At postoperative week 9, his BCVA improved to 20/40-2 and his macular anatomy had improved (Figure 3, E and F).

Discussion

The evolution of SMH management correlates with many significant milestones in vitreoretinal surgical innovation including the origin of submacular surgery in 1988 with Eugene de Juan and Machemer,[2] the introduction of pneumatic displacement by Heriot at the 1996 Vail Vitrectomy meeting,[3] the pars plana vitrectomy approach with subretinal injection of tPA for displacement by Haupert et al in 2001,[4] and the additional use of anti–vascular endothelial growth

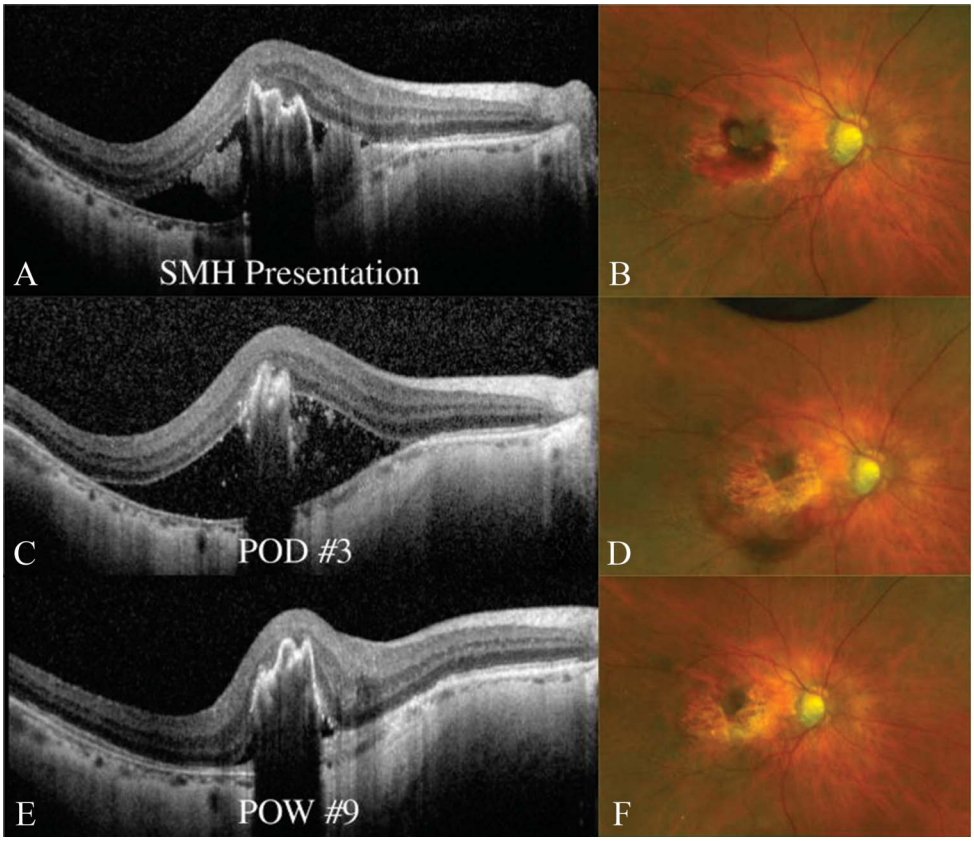

Fig. 3. A–F. Multimodal retinal imaging of Patient 2 at presentation of SMH, postoperative day (POD) 3, and postoperative week (POW) 4.

factor agents.[5] Subretinal injection of tPA and air with and without anti–vascular endothelial growth factor was introduced in 2013 by Martel and Mahmoud.[6] The multicenter US study[7] in 2018 showed 100% rate of displacement with this technique with 75% of those displaced beyond the arcades and additional 20% beyond the equator. Subretinal pigment epithelial hemorrhage was also displaced in 74%. Before the data presented herein, accessing the subretinal space without performing a vitrectomy was not possible.

First introduced by Mahmoud at the 2019 Vail Vitrectomy meeting,[8] the NVR subretinal gateway device (Vortex) was designed by Wood, Rao, and Mahmoud to enable access to the subretinal space without performing a vitrectomy. The 30-gauge needle that ensheaths the subretinal cannula is familiar to vitreoretinal specialists performing intravitreal injections with equivalent pars plana introduction and subsequent passage into the vitreous cavity, thereby obviating the need for cannulas or sclerotomies. The subretinal cannula further extends over the posterior pole and into the subretinal space, minimizing peripheral vitreous traction on approach by virtue of its size, material, and design. Piercing the retina surface is facilitated by its beveled tip and creates a very small, self-sealing retinotomy given the cannula's diameter is 25% smaller than currently available 41-g cannulas. Pharmacologic agents are delivered through automated injection as described above, and visualization is provided by chandelier illumination. This technique allows those receiving anti–vascular endothelial growth factor injections to maintain their vitreous, thereby avoiding the decrease in effective drug half-life that accompanies a vitrectomy created by faster diffusion gradients and fluid currents.[9] The procedure takes the approach of targeted minimalism: performing what is necessary to achieve the surgical goal without additional maneuvers. To date, patients undergoing the procedure have achieved good anatomical and functional results without the creation of iatrogenic retinal breaks or retinal detachment.

Conclusion

Although the NVR device and associated technique is effective in the management of SMH, its use may serve as a gateway tool increasing access to the subretinal space for the delivery of gene-based therapies and stem cell therapies. Further studies are needed to confirm the findings presented herein. This is a rapidly growing space within vitreoretinal surgery,[10] and the minimal approach described herein with small self-sealing retinotomy creation may represent advantages in the delivery of these therapeutic agents in the future.

Key words: submacular hemorrhage, subretinal hemorrhage, subretinal surgery, displacement, macular degeneration, choroidal neovascularization, nanovitreoretinal, subretinal gene therapy, subretinal stem cell delivery.

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References

1. Avery RL, Fekrat S, Hawkins BS, Bressler NM. Natural history of subfoveal subretinal hemorrhage in age-related macular degeneration. Retina 1996;16:183–189.
2. de Juan E Jr, Machemer R. Vitreous surgery for hemorrhagic and fibrous complications of age-related macular degeneration. Am J Ophthalmol 1988;105:25–29.
3. Heriot WJ. Intravitreal gas and TPA: an outpatient procedure for submacular hemorrhage. Presented at the: American Academy of Ophthalmology Annual Vitreoretinal Update; March 10-15, 1996; Chicago, IL.
4. Haupert CL, McCuen BW II, Jaffe GJ, et al. Pars plana vitrectomy, subretinal injection of tissue plasminogen activator, and fluid-gas exchange for displacement of thick submacular hemorrhage in age-related macular degeneration. Am J Ophthalmol 2001;131:208–215.
5. Chang W, Garg SJ, Maturi R, et al. Management of thick submacular hemorrhage with subretinal tissue plasminogen activator and pneumatic displacement for age-related macular degeneration. Am J Ophthalmol 2014;157:1250–1257.
6. Martel JN, Mahmoud TH. Subretinal pneumatic displacement of subretinal hemorrhage. JAMA Ophthalmol 2013;131:1632–1635.
7. Sharma S, Kumar JB, Kim JE, et al. Pneumatic displacement of submacular hemorrhage with subretinal air and tissue plasminogen activator: initial United States experience. Ophthalmol Retina 2018;2:180–186.
8. Mahmoud T. Nano Subretinal Gateway Device to displace submacular hemorrhage without PPV and access SR space for gene therapy and other indications. Presented at the: Vail Vitrectomy Meeting; February 9-12, 2019; Vail, CO.
9. Jung JJ, Hoang QV, Arain MZY, Chang S. Aflibercept antivascular endothelial growth factor therapy in vitrectomized eyes with neovascular age-related macular degeneration. Acta Ophthalmologica 2016;94:e249–e250.
10. Ochakovski GA, Bartz-Schmidt KU, Fischer MD. Retinal gene therapy: surgical vector delivery in the translation to clinical trials. Front Neurosci 2017;11:174.