Case report

Rapid displacement of subretinal hemorrhage from a choroidal neovascular membrane with intravitreal C3F8 gas and face-down positioning*

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ABSTRACT

Purpose: To describe a case of rapid displacement of subretinal hemorrhage (SRH) from a choroidal neovascular membrane (CNV) with intravitreal injection of C3F8 gas.

Observations: A 66-year-old patient presented in clinic with count fingers (CF) vision from a fibrovascular scar in the right eye (OD) and 20/30 vision in the left eye (OS) with butterfly dystrophy. His left eye developed a CNV and was managed with monthly intravitreal anti-VEGF agents for 29 months. Five days after a ranibizumab treatment, the patient developed a moderate subfoveal hemorrhage. The vision decreased from 20/30 to 20/50. He elected to monitor the disease process. Eleven days later the vision decreased to 20/200, and he consented to intravitreal injection of 0.3 cc of 100% C3F8 with face-down positioning. The patient received an anterior chamber paracentesis to manage the intraocular pressure. The patient had near complete displacement of subretinal hemorrhage and fluid in less than 2 hours. He then had repeat OCT and fundus photos to document the rapid displacement. His vision returned to 20/30-2 twelve days later, at which point the subretinal fluid and blood had been completely displaced from the macula.

Conclusions and Importance: The patient had rapid displacement of subretinal hemorrhage and fluid with intravitreal C3F8. New blood filling the space of pre-existing neurosensory fluid from the active CNV likely enhanced displacement. Timely intervention before stable clot formation was helpful for ease of displacement of the subretinal hemorrhage.

1. Introduction

Anti-VEGF agents are the first-line treatment for managing choroidal neovascular membranes (CNV) from neovascular age-related macular degeneration. Rarely patients with pattern dystrophies, including butterfly dystrophy, may develop a CNV and these patients may also be successfully managed with anti-VEGF agents. When a CNV is complicated with sub-retinal hemorrhage (SRH), the management options vary dramatically. Massive subretinal hemorrhages, such as those reaching the arcades or beyond with thickness greater than 500 μm, have been successfully managed by anti-VEGF agents alone, with intravitreal gas alone or with intravitreal gas and tissue plasminogen activator (TPA) in the office. Furthermore, vitrectomy surgery may be performed. There are various surgical techniques including the removal of clot using retinotomy with TPA and gas. Recent advances in surgical techniques have included displacement of massive SRH with 41 gauge subretinal insertion of filtered air with subretinal TPA with or without anti-VEGF agents to help clear the SRH. Resolution or displacement of the subretinal hemorrhage outside of the fovea is the most significant factor for visual improvement. The timing of treatment for the subretinal hemorrhage is important as well. While combination therapy has proven efficacious for various time points, there is evidence that displacement of SRH with gas alone may be achieved if the time from SRH onset to treatment is shorter, and may result in fewer complications.

This case report details a patient with SRH which was displaced within 2 hours after pneumatic displacement of intravitreal C3F8 gas resulting in improvement of vision to levels before the SRH.

2. Case report

In December 2008, a 66-year-old male presented with a fibrovascular scar in his right eye. He also had butterfly dystrophy in his left eye. The vision was counting fingers in his right eye and 20/30 in his left eye. In August 2010, he noticed metamorphopsia and decreased vision in his left eye. The vision had decreased to 20/40 from a new
CNV. He was initially treated with 3 intravitreal injections of bevacizumab (Avastin, Genentech, San Francisco, CA.). At that point, the subretinal fluid and vision worsened, so he was switched to ranibizumab (Lucentis, Genentech, San Francisco, CA.). Although his vision was stabilized, he continued to display chronic subretinal fluid despite monthly ranibizumab injections. In January 2013, his vision had improved to 20/30, and he was given his monthly ranibizumab injection. Five days following this injection, he developed a subfoveal hemorrhage associated with the CNV and underwent fluorescein angiogram (FA). His vision decreased from 20/30-2, prior to the hemorrhage, to 20/50-2. Various treatment options were discussed with the patient and the patient elected to monitor the process. He returned 4 days later and the vision decreased to 20/60-2. The patient again elected to monitor the process. One week later the vision was 20/200 (Fig. 1A-D). At this point, the patient consented to intravitreal C3F8 gas and face-down positioning. At each of these time points, he had SD-OCT and fundus photos (FF).

During previous anti-VEGF treatments, the patient would stop perfusing the central retinal artery (CRA) each time the volume of the intravitreal injections was greater than 0.05ml. Even when only 0.05ml were given, at times the CRA would close. Therefore, he was carefully monitored after injections for perfusion of the CRA. He would often use a drop of brimonidine the night before treatment. After injecting 0.3 cc of 100% C3F8, the CRA was closed and the patient had an anterior chamber (AC) paracentesis to manage the intraocular pressure (IOP). Although his AC was shallow, the IOP was still 52. The patient was monitored after injections for perfusion of the CRA. He would often use a drop of brimonidine the night before treatment. After injecting 0.3 cc of 100% C3F8, the CRA was closed and the patient had an anterior chamber (AC) paracentesis to manage the intraocular pressure (IOP). Although his AC was shallow, the IOP was still 52. The patient was instructed to maintain a face-down position, while he was seated in the office and he was monitored for the next 2 hours, to allow for reformation of the anterior chamber. Prior to subsequent AC paracentesis, repeat fundus biomicroscopy was performed to evaluate the optic nerve. At this point, it was noted that there was nearly complete displacement of the subfoveal hemorrhage and fluid. Following the repeat AC paracentesis, the IOP decreased to 12. The patient was then re-imaged with FF and SD-OCT. Overall, the patient was found to have near complete displacement of the subretinal hemorrhage in less than 2 hours with intravitreal C3F8 (Fig. 2). The patient reported better vision. Four days later the patient’s vision improved to 20/40-2, and 8 days later had returned to 20/30-2. At this point, the subretinal fluid and blood had been completely displaced from the macula (Fig. 3).

3. Discussion

This patient had rapid displacement of subretinal hemorrhage with intravitreal C3F8 gas. Several factors may have contributed to the rapid displacement. There was pre-existing neurosensory fluid from the active CNV and when the CNV bled, this space was filled with blood and subretinal fluid. The pressure of gas on this pre-existing fluid with hemorrhage may have facilitated its displacement. Since, fibrin cross-linking does not occur during the first 3 weeks within the subretinal space, there was sufficient time to intervene on the SRH in our patient. Extensive SRH often requires surgery and the addition of various agents. Extensive SRH often requires surgery and the addition of various agents.1,3,4,7,8 Vitrectomy with subretinal filtered air of 0.2ml, subretinal TPA 0.4ml at 12.5 μm/ml with or without the addition of subretinal anti-VEGF agents, has been highly successful in displacing massive subretinal hemorrhage.3,4 However, smaller SRHs and certain larger SRHs may be better managed with anti-VEGF agents, TPA and gas, alone or in combination.7 This is to prevent complications from the SRH such as apoptosis of the photoreceptors due to mechanical stress.7 Guthoff et al. assessed the addition of bevacizumab to combination iPA and gas for symptomatic SRH with an average of around 11 days from SRH onset to treatment, documenting improved visual outcomes and stability with the addition of bevacizumab at 4 weeks and 7 months.2 However, our patient developed the SRH during active anti-VEGF therapy. Therefore, another anti-VEGF injection was inappropriate. Because the clinical course continued to worsen for his remaining eye with previous visual function (his fellow eye only had counting fingers vision), our initial approach was to displace the SRH using C3F8 gas alone. Pre-existing neurosensory fluid from the active CNV was present at the time. This space was filled with the new blood and the pneumatic pressure of the gas may have enhanced the resorption and displacement. However, if the patient did not respond to gas displacement at this point then the patient would have required surgical evacuation. The patient’s vision returned to levels prior to the SRH and no complications were noted.

Time to intervention likewise appears to play an important role in the resolution of SRH and preservation of vision. Previous groups have demonstrated the utility of using TPA for clot lysis and displacement using air or nonexpansile gasses. Lewis et al. found that TPA used before seven days was significantly more effective in clot liquefaction and removal compared to eight to fourteen days.5 More recently, Fang et al. demonstrated in that the addition of TPA to gas for SRH displacement versus gas alone leads to significant differences in visual function only if time to intervention fell outside of 14 days based on subgroup analysis.6 Thus, they recommended that TPA should only be used if the initial SRH was not cleared using gas alone.6 This may be due the time required for fibrin cross-linking within the subretinal space for clot formation. Therefore, as with our patient, intervention before fibrin cross-linking and stable clot formation is essential for ease of displacement of the subretinal hemorrhage.

4. Conclusion

CNV activity and anatomy, as well as timing of treatment, are important considerations in the management of SRH. Hemorrhage may be successfully displaced using C3F8 gas alone, particularly when pre-existing anatomical spaces allow for ease of displacement and when there is pre-existing neurosensory retinal fluid. Additionally, early intervention likely results in greater success before stable clot formation occurs.
Future studies assessing these factors may help guide the choice of therapy among the array of regimen options and improve visual outcomes while mitigating complications.

5. Patient consent

Verbal consent to publish the case report was obtained. This case report does not contain any personal information that could lead to the identification of the patient.

Acknowledgements and disclosures

Conflicts of interest

Dr. Adrean reports grants from Genentech, grants of Ohr, grants from Regeneron, grants from SciFluor, grants from Ophthotech, grants from Allergan, outside the submitted work.

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![Fig. 2. Displacement of SRH using C3F8 gas. A) Funduscopic photo and SD-OCT images showing SRH immediately prior to treatment and B) 2 h following treatment using C3F8 gas. The subretinal fluid was almost completely displaced at 2 h.](image1)

![Fig. 3. Improvement of retinal anatomy. SD-OCT imaging demonstrating resolution of subretinal fluid status post pneumatic displacement with C3F8 at days 4 and 8. Vision OS improved to 20/40 post-treatment day 4 and returned to baseline of 20/30 post-treatment day 8.](image2)
Authorship

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

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