THE **RETINA** PARTNERS

Encino Santa Monica Valencia Thousand Oaks Century City

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Case of the Month – September 2020

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A 75-year-old female presented with a 3 day history of sudden central vision loss in the right eye. She had an ocular history significant for "non-specific RPE changes" in the macula of the right eye. Her medical history was significant only for hyperlipidemia, for which she was taking a statin and baby aspirin. Vision was measured as counting fingers in the right and 20/25 in the left. Intraocular pressures were 15 in both eyes. Anterior segment examination was significant only for mild, symmetric cataract. Fundus imaging of the right eye is shown below.

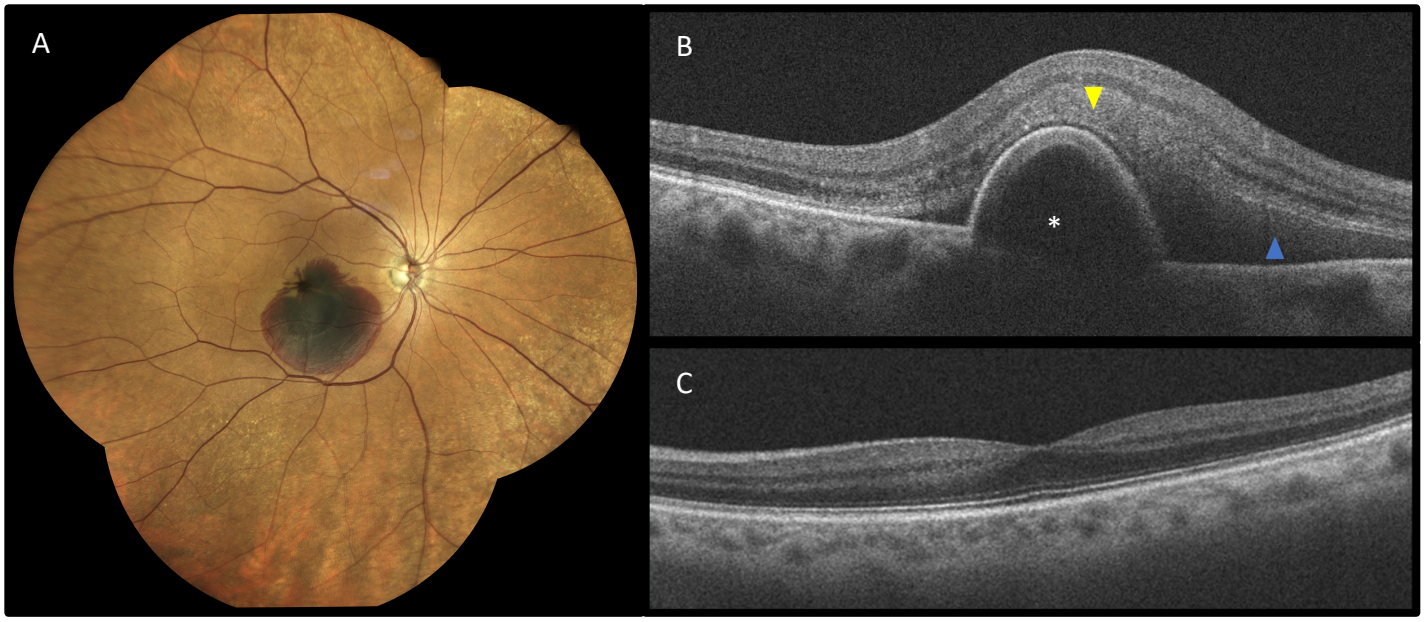

Figure 1: A. Color fundus photo of the right eye shows a macular hemorrhage with subretinal and intraretinal blood. There are peripheral drusen and RPE changes, but the visible macula appears free of these changes. B. OCT through the hemorrhage also reveals a large pigment epithelial detachment (asterisk) and confirms the presence of blood within the subretinal space (blue arrowhead) and within the retina (yellow arrowhead). C. OCT through the fovea of the left eye is normal, notably without significant RPE alterations or drusen.

Differential Diagnosis: Macular hemorrhage secondary to choroidal neovascular membrane, ruptured retinal arterial macroaneurysm, valsalva retinopathy, choroidal rupture/trauma

Clinical Course:
Based upon imaging, examination and history there was high suspicion for hemorrhage secondary to choroidal neovascular membrane. Treatment options were discussed, all of which included intravitreal injection of anti-VEGF for active CNVM. In addition, the options of in-clinic pneumatic/tissue plasminogen activator (TPA) displacement of hemorrhage vs. surgical displacement with vitrectomy, subretinal TPA and gas were discussed. Pneumatic displacement was recommended. The patient underwent injection of Eylea, 25 ug of tissue plasminogen activator and 0.4cc pure SF6 gas. She was instructed to position face down. Follow up images are shown below.

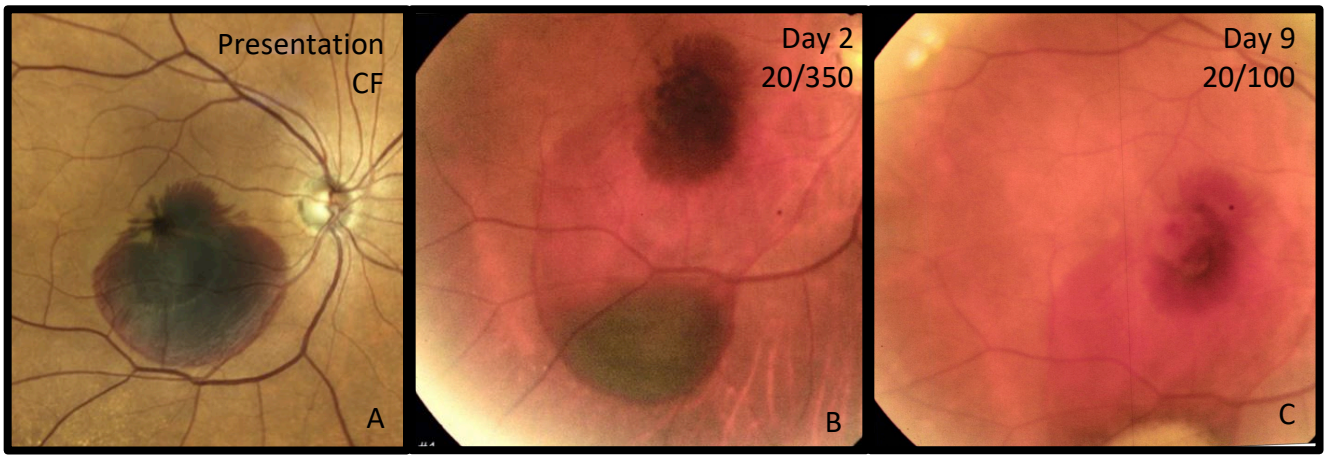

Figure 2: Color photographs of the fovea over the first 1.5 weeks shows progressive displacement of the subretinal hemorrhage, and resorption of the intraretinal hemorrhage. Vision progressively improved.

Clinical Course (continued): As shown in figure 2, the subretinal hemorrhage component displaced quickly following the procedure. The intraretinal hemorrhage component took longer to resolve, and did not displace, as was expected. Vision improved to 20/100 by day 9 following pneumatic. The patient was continued on anti-VEGF therapy monthly until active exudation was noted to resolve, and transitioned to a treat and extend regimen. Her visual acuity at final follow up stabilized at 20/50.

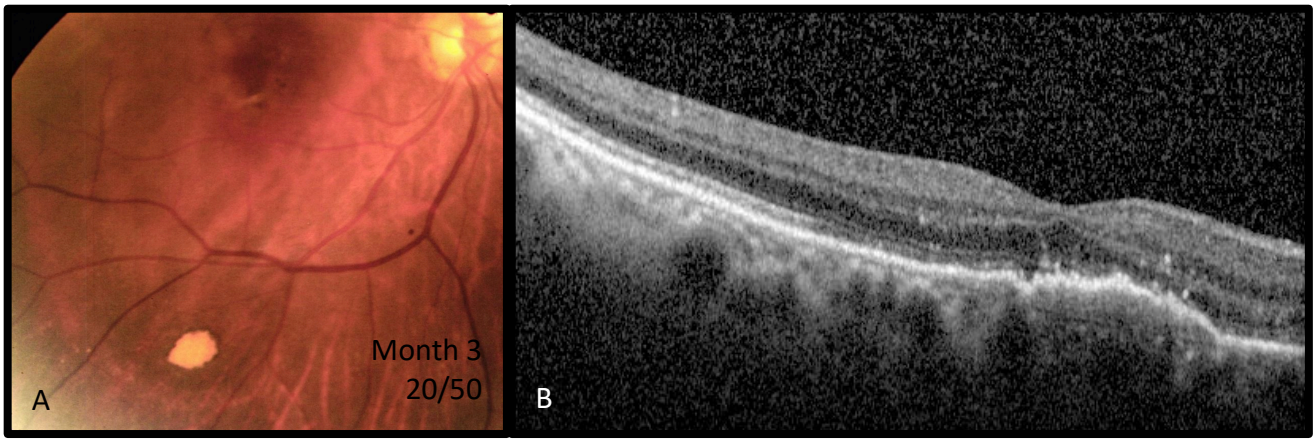

Figure 3: A. Color photo of the macula at 3 month follow up shows near complete resolution of subretinal hemorrhage, with small remaining depigmented hemorrhage inferior to the arcade. There are mild RPE changes within the fovea, but notably, no significant drusen or other signs of age related macular degeneration. B. OCT through the fovea of the left eye shows a consolidated, irregular pigment epithelial detachment with remaining overlying hyper-reflective foci within the retina. There is no intraretinal fluid, no subretinal fluid and no hemorrhage remaining.

Discussion:
Submacular hemorrhage is a severe complication of retinal and choroidal disease, which can cause irreversible and severe central vision loss. Most frequently, submacular hemorrhage results from choroidal neovascularization (CNV). Since CNV most often develops in the setting of age related macular degeneration, this is the most common underlying etiology of submacular hemorrhage. However, any disease which can lead to CNV can also cause submacular hemorrhage (myopic degeneration, angioid streaks, POHS etc.). Less commonly, submacular hemorrhage may be the direct result of traumatic choroidal rupture, ruptured retinal arterial macroaneurysm, Terson's syndrome, valsalva retinopathy or shaken baby syndrome.

Untreated submacular hemorrhage, especially when large, has a very poor prognosis. Vision loss results from multiple mechanisms including direct iron toxicity, blockage of nutrient exchange between the RPE and photoreceptors, sheering forces as the clot retracts, and the eventual development of subretinal fibrosis. Damage to the outer retina occurs quickly. In fact, animal studies have demonstrated toxic effects to the outer retina within 24 hours of subretinal hemorrhage, and complete loss of photoreceptors at 7 days. It is not unexpected then that the largest natural history study of patients presenting with submacular hemorrhage in the setting of age related macular degeneration showed that approximately 90% of patients had a final visual acuity of 20/200 or worse two years following their presentation. However, the etiology of hemorrhage appears to be a significant factor in prognosis, and those patients who have healthier underlying RPE and macula prior to the bleed may fare better than this.

The generally poor prognosis of untreated submacular hemorrhage has led to the development of several treatment strategies. First and foremost, if choroidal neovascularization is causative, this should be treated with anti-VEGF agents, as is the standard treatment for active CNV. In addition, an attempt to remove or displace the submacular hemorrhage from the central macula can be made. If done early in the course, theoretically, this can limit the damage done to the valuable outer retinal structures and RPE of the central macula.

Proof of this concept was first reported in 1987 by Thomas Hanscom, MD and Kenneth Diddie, MD. In their surgical case series, two patients underwent vitrectomy with retinotomy, direct aspiration of hemorrhage, cryotherapy and fluid-gas exchange within days of vision loss. Hemorrhage was successfully removed in both, and both patients experienced a significant improvement in their visual acuities. While this technique would eventually be supplanted by others, this early report demonstrated that vision could indeed be improved with successful and early hemorrhage removal.

Today, the focus of surgical intervention has shifted from removal of hemorrhage to displacement of the hemorrhage out of the macula. This can be done using vitrectomy with gas tamponade with or without subretinal injection of tissue plasminogen activator or with in-clinic intravitreal gas injection (pneumatic) with or without intravitreal tissue plasminogen activator. Multiple case series have reported a high degree of success in hemorrhage displacement using both techniques. Reported visual results are variable, but overall vision tends to improve in comparison to vision at presentation. While no comparative randomized controlled trials exist to definitively guide treatment decisions, generally, vitrectomy seems to be favorable in cases with thick submacular hemorrhages as the ability to displace large amounts of blood is greatest, and visual results without intervention are very poor. For intermediately sized hemorrhages, as in our case, pneumatic or vitrectomy are both options. In contrast, cases with scant subfoveal hemorrhage may be best treated with anti-VEGF alone to limit risk associated with surgical interventions.

The decision to surgically intervene requires careful discussion and weighing of the risks and potential benefits. Both procedures carry a risk of retinal detachment and vision loss (among others) and both require some degree of post-operative positioning to succeed, which may not be possible for some elderly patients. Finally, the timing of presentation is critical. The more time between the hemorrhage and intervention, the less likely that vision can be restored. Patients presenting more than 7 days from the event may therefore have minimal benefit from displacement, and risks may outweigh any potential benefit. Even when patients present early and surgical

intervention is selected, all parties involved must understand that a submacular hemorrhage may represent a catastrophic visual event with or without intervention.

Our patient was lucky in several respects. First and likely most importantly, she had minimal coexisting macular disease. As Figure 3 shows, once the hemorrhage cleared, only mild RPE changes were revealed, and notably she had no drusen. Her CNV was idiopathic, rather than secondary to age related macular degeneration, and therefore she likely had much healthier retina and RPE than most prior to the hemorrhage. Second, the subfoveal component of her hemorrhage was not terribly thick allowing for near complete and rapid displacement with pneumatic. Finally, she presented relatively early in the course, and intervention was performed immediately.

In summary, submacular hemorrhage is most commonly encountered in the setting of exudative macular degeneration. It often represents a catastrophic event with a guarded visual prognosis. However, when intervention is performed early, in the appropriate patient, some may recover significant functional vision.

Take Home Points

- Submacular hemorrhage is a severe complication of macular and choroidal disease, most frequently seen in the setting of exudative macular degeneration.
- Early surgical displacement of the hemorrhage may be attempted using vitrectomy, or in-clinic pneumatic procedure
- The prognosis in such cases is guarded, dependent upon size of the hemorrhage, timing of intervention and underlying health of the retina and RPE

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