Post-Game Film Review
With the Wills Retina Coaches:
Submacular Hemorrhage

BY EHSAN RAHIMY, MD

In a previous installment of this column, we gave readers a glimpse into the inner workings of the monthly surgical conferences held by the senior retina fellows at Wills Eye Hospital (see “Post-Game Film Review With the Wills Retina Coaches: PVR and Retinal Detachment” on page 22 of the January/February 2015 issue of Retina Today). Due to the positive feedback, we decided to continue the post-game film review series. Joining us for this session to discuss the management of submacular hemorrhage are Allen Chiang, MD; Allen Ho, MD; Jason Hsu, MD; Richard Kaiser, MD; Joseph Maguire, MD; and Arunan Sivalingam, MD. Links to the videos are provided for readers to follow along.

—S. K. Steve Houston III, MD; Ehsan Rahimy, MD; and David C. Reed, MD

SUBMACULAR HEMORRHAGE AND ANTICOAGULANT USE

This case involves an 85-year-old man with acute-onset loss of visual acuity in his left eye, down to 20/200 (Figure 1). At the time of the examination, he was taking apixaban (Eliquis, Bristol-Myers Squibb), a relatively new agent in the class of novel anticoagulants (NOACs), for atrial fibrillation.

Preoperative Management

Joseph Maguire, MD: When I see an extensive bleed such as the one in this case, I think of three potential scenarios: polypoidal choroidal vasculopathy, a retinal angiomatous proliferation (RAP) lesion, a patient on anticoagulation, or some combination of these. One often sees small hemorrhages with age-related macular degeneration (AMD), but large hemorrhages are less common.

Ehsan Rahimy, MD: Do you routinely ask about anticoagulant use with your AMD patients?

Dr. Maguire: You should look at your review of systems and what medications the patient is taking.

Allen Ho, MD: If I see a large hemorrhage such as this in the setting of AMD, I assume there is an underlying tear of the retinal pigment epithelium (RPE), unless the differential diagnosis leads me elsewhere (eg, a macroaneurysm). Optical coherence tomography (OCT) can be helpful in confirming this.

Dr. Rahimy: Given the imaging findings, how would you manage this case? Would you consider an in-office pneumatic displacement, or would you go straight to the OR?
Arunan Sivalingam, MD: You can tell from the OCT that the hemorrhage is mostly subretinal without much under the RPE, so this patient is a good candidate for surgical evacuation.

Dr. Ho: This is an 85-year-old man who might not be a good candidate for surgery because of other systemic comorbidities. I am fine with trying a pneumatic displacement in the office, but for the larger bleeds I would prefer to do a surgical displacement because I feel I can clear the macula of hemorrhage more effectively. In thinner hemorrhages, though, I would advise against surgery and try an anti-VEGF injection.

Richard Kaiser, MD: In terms of management, OCT is helpful. First, I like to see if the central retinal thickness has at least doubled when deciding whether or not to operate. This is because a thin hemorrhage may look ominous on examination but not necessarily respond well to surgery. Second, looking at the layers where the hemorrhage is located is useful. If the bleeding is 100% under the RPE, then the odds of actually helping this patient surgically are much lower, whereas, in this particular case, you can clearly see most of the bleeding exists between the retina and the RPE.

Dr. Maguire: I often use OCT to estimate where to enter the subretinal space during surgery. The safest place to inject tissue plasminogen activator (tPA) under the retina is usually the area with the thickest blood. You do not want to enter under the RPE.

Dr. Rahimy: Going into the surgery, do you have a different mindset knowing that this particular patient is on a NOAC?

Dr. Ho: Yes. For starters, a patient on an anticoagulant should get you thinking about the anesthesia approach. I will consider a conjunctival cutdown block on the field instead of a peribulbar or retrobulbar injection. Additionally, in the discussion of risks and benefits, I address the possibility of recurrent hemorrhaging intraoperatively or postoperatively. Most of the time, our surgical maneuvers do not induce a repeat hemorrhage that could be exacerbated by being on an anticoagulant, but I am mindful about that possibility during the procedure.

Dr. Sivalingam: If the patient is on warfarin sodium (Coumadin, Bristol-Myers Squibb) or aspirin, I do not really do a cutdown. If, however, the patient is on a NOAC, I would be hesitant to do a retrobulbar block.

Dr. Kaiser: I think the newer-generation anticoagulants make me more nervous because we know less about them. It seems as though the reports continue to change as far as how long they last as well as their side effects.
With a patient taking warfarin sodium, if I know that he or she has discontinued use for at least 5 days, then I feel comfortable with my normal approach. If the patient has not discontinued use, which is often the case under these circumstances, I am still comfortable taking my same approach. It is a different story, however, with NOACs.

Intraoperative Management

A representative video from a similar case is provided (Video 1; eyetube.net/?v=ilohe).

**Video 1**

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**Dr. Rahimy:** In this case, we amputated the trocar valves with the cutter to facilitate insertion of a 41-gauge cannula. When you approach the retina, where are you looking to make your initial puncture?

**Dr. Sivalingam:** I usually inject just outside the hemorrhage. Whether it is superior or inferior does not matter as much to me. I look for where there is a little bit of liquefied hemorrhage and go just outside of that area to start infusing.

**Dr. Kaiser:** I take a different approach. Why do people rob banks? Because that is where the money is! I go straight into the blood. When I make that initial pop, I can feel that I am through. I then pull back a little just in case I am under the RPE before injecting. Afterward, I like making multiple injections; small blebs all over. I will get pretty close into the center of the macula, and, as I do that circumferentially, I will create a gutter to try to have a place to displace the blood to. I like the gutter to be inferior, or at least temporal, so I can lay the patient on his or her side. But I think there is an advantage to the mechanical disruption of this clot with the velocity of the injection, in addition to the effect of the tPA.

**Dr. Rahimy:** Do the others agree? Do you perform multiple injections?

**Dr. Ho:** I do not know that multiple injections of tPA are necessary, but I agree that you want to get in the right tissue plane. Therefore, I also inject directly into the blood. Sometimes little air bubbles will be visible in the submacular space, but this is not necessarily a bad thing because they confirm that the injection is in the correct location.

I inject inferiorly to start because I want to open up a space for the blood to displace inferiorly with gravity. I find that the more fluid I put in the submacular space, the more the hemorrhage clears, and the better these patients do. As such, I am very generous with the fluid. You can do that with multiple injections or with one. As long as it encircles and extends beyond the clot itself, then I am pleased.

**Dr. Sivalingam:** The only reason I would be careful about going within the blood is that there may be elevated RPE in the region (as there is in this case on the OCT). As long as you are sure you are not injecting beneath the RPE, then it is okay. But that is why I go a little bit outside the area of bleeding, just to make sure I am in the subretinal space.

**Dr. Kaiser:** I think it can be difficult to find that plane in situations where there is not a hemorrhage in the retina. I worry that if I inject into a retina where there is no hemorrhage, then it is harder to discern whether I am under the RPE. That is why I choose to go into the blood. If you pick your first bleb in lighter color blood—the area that is a little bit brighter, not the dark blood—then I think you are more likely to end up in the subretinal space. But I think we are all saying the same thing, it is just different ways of getting there.

The other point I want to bring up has to do with air bubbles, which Dr. Ho mentioned, and I think that is interesting. In an episode of the Retina Today Journal Club, Tamer Mahmoud, MD, PhD, from Duke, described a technique of intentionally injecting subretinal air mixed with an anti-VEGF agent and tPA into the clot (Video 2; eyetube.net/?v=jetim). He explained that there is a mechanical disruption of the clot with air, and he advocates for that procedure when there is a massive hemorrhage, arcade to arcade, probably two to three times as thick as the hemorrhage in this case. We need to know more about what exactly to put underneath the retina, because I myself am not sure that tPA does much. I agree with Dr. Ho that volume, and the resultant mechanical disruption, are what matters.

**Dr. Rahimy:** There are also different injection platforms. An assistant can push that tPA for you through a
syringe, or you can use the viscous fluid injection device without the help of an assistant. Dr. Hsu, can you discuss why you prefer the latter method?

**Dr. Hsu:** I prefer using the viscous fluid injection device because I am not depending on an assistant to push the fluid. I control the rate of infusion into the subretinal space. For this technique, you connect the infusion to the oil tubing outside the eye. I usually titrate the injection speed so it is a steady drip. When I can, I like injecting along the inferior border of the subretinal hemorrhage, even right on top of the hemorrhage, because a little more space has already been created there.

**Dr. Maguire:** I think it helps to look for the edges of the hemorrhage on the preoperative OCT and plan to inject there. Usually, the RPE elevation is in the center of the bleed. I prefer to go to the edge, where there is normal retina, because there is tension from the adjacent retinal elevation. You can usually inject at that location more easily, and it is typically safer. I use the viscous fluid injector just as Dr. Hsu does because it gives me control, and I do not have to rely on anyone else. Additionally, I mix fluorescein into the tPA so it turns orange because I like to make sure there is diffuse distribution while making the fewest number of holes. Because the tPA goes where the fluorescein goes, I can actually see its distribution. Also, as you are injecting, it really helps to put your light pipe down close to the retina to make sure you are not piercing through a small hole and causing more bleeding.

**Dr. Hsu:** One thing I notice when fellows are initially trying to maintain pressure while attempting to penetrate through, is that the tip of the injector flexes and becomes slightly bent. When this happens, the flow is not as good, and there is a risk of entering the sub-RPE space.

**Dr. Maguire:** Do people use a wide-angle visualization system pretty routinely when they are popping through, or do they use a contact lens?

**Dr. Hsu:** I will zoom in initially to pop through and make sure I am in the right space, but, once I start injecting, I want to see where that fluid is going, so I zoom out and get the full widefield view.

**Dr. Ho:** I think it is important to use wide-angle viewing to get a picture of the entire hemorrhage because you want to know the extent of your injected fluid.

**Dr. Rahimy:** What is your goal for the bleb size?

**Dr. Ho:** My preference is for the clot to be completely surrounded by fluid for 360°. Again, in my experience, the more fluid you have there, the more likely you are to displace the hemorrhage. So I would not be too concerned if there is a significant elevation of a dome of fluid because, the next day, you will see that the RPE has pumped out almost all of the fluid.

**Dr. Rahimy:** Each of you has your own preferences, but, down the line, do you do a partial or complete air-fluid exchange after? Do you use air or an alternative gas tamponade? Any positioning in the postoperative period?

**Dr. Kaiser:** I do a partial (75-80%) air-fluid exchange. I always use air, because I think whatever displacement you are going to get, you will get within the first 24 hours. An 80% air bubble will last around 7 days, so you are easily covering the first 24 to 48 hours. For postoperative positioning, I have the patient sitting up and looking down. Because these patients tend to be older with more cachectic necks and/or backs, they should not be completely face down, but looking down enough so that blood is displacing to the gutter inferiorly while having a little bit of pneumatic pressure on the retina itself.

**Dr. Ho:** I use a complete air-fluid exchange with a short-acting gas tamponade (16% SF$_6$). The rationale is that, if the blood has not been displaced after the first day, then there is still some residual gas where I might want to position the patient to use a gas bubble. With respect to postoperative positioning, I opt for normal head up and instruct the patient to sleep on his or her side.

**Dr. Maguire:** Like Dr. Kaiser, I do 75% to 80% air-fluid exchange. I use short-acting SF$_6$ as well. As for positioning, as long as the patient is not flat on his or her back, I find that the blood displaces.
Allen Chiang, MD: I agree with the other surgeons. For positioning, I instruct patients to maintain a reading position. I think it is important that these patients sleep on the same side as the eye being operated on because occasionally, when you make that bleb, you may not get it to dissect exactly as you would like and the fluid goes wherever it wants. You may not get it as inferior as you want, and I have had good success with patients lying on that side so that the blood displaces temporally out of the macula.

Dr. Sivalingam: I do complete air-fluid exchange with 16% SF₆, and then I have them lie face down as much as possible for the first 24 hours.

Dr. Hsu: I just use the cutter to do a partial 80% air-fluid exchange. I think if the blood is going to displace, then it is going to do so within the first 24 hours. After that, I instruct patients to maintain a reading position, maybe a little bit looking down, but not much.

Postoperative Management

Dr. Rahimy: Back to our original patient. At his postoperative week 1 visit, his hemorrhage had cleared entirely, his vision had returned to 20/50, and he was now back on his anticoagulant. However, at his postoperative 1-month visit, he was noticing a new kidney bean–shaped central scotoma. Visual acuity dropped a line to 20/60 (Figure 2). What do you do at this point? Inject an anti-VEGF agent? Is an in-office pneumatic displacement a consideration? Do you return to the OR?

Dr. Hsu: There is not much subfoveal hemorrhage on the OCT. I would not be confident in going back in to displace the superior hemorrhage into the fovea. I would inject an anti-VEGF agent and monitor him closely.

Dr. Kaiser: I have never had a patient rebleed that quickly, so I think this points to what we said before about this being a whole new generation of drugs that we do not quite understand, at least from a retina standpoint. But based on that new OCT, I would hold off.

Dr. Chiang: I would also inject an anti-VEGF agent and bring him back in 1 week for close monitoring. We also need to be mindful of the potential need for an increased frequency of injections because the rate of medication clearance will be greater in this vitrectomized eye.

Dr. Rahimy: If you find that a patient with submacular hemorrhage is on anticoagulation medicine, how would you approach the issue of stopping or modifying therapy, if at all?

Dr. Kaiser: I ask the patient to confirm with his or her doctor the necessity of taking the anticoagulant. A decent number of patients were put on warfarin sodium years ago—maybe because there was an episode of atrial fibrillation 10 years prior—and their prescribing doctors just never took them off. Every now and then, you will come across a patient who can safely be taken off the medication, but I never want to make that medical decision for the patient. That is up to the prescribing doctor. I would rather have to deal with a problem like this than to have to deal with a death or a stroke.

Dr. Sivalingam: You may want to check the prothrombin time-partial thromboplastin time (PT-PTT). I ask patients who are on anticoagulants the last time they had their PT-PTT checked and what the level was. If it is too high, and this happened, then I would say go back to the medical doctor to titrate it, but I do not say stop it.

Dr. Chiang: I have spoken with some cardiologists, and they appreciate me sending a patient back after a hemorrhage. They want to know because, in some of instances, they will decide to stop treatment. The prescribing physician wants to be aware of any type of systemic bleed, intraocular or otherwise.

Dr. Ho: I agree that it is our responsibility to report that hemorrhage as an event, but not necessarily to
manage that event. From the patients’ point of view, they want to know whether being on an anticoagulant increases their risk for a hemorrhage in the second eye after the first hemorrhage occurs. Unfortunately, there is a lack of quality data on which to formulate an answer to that question. Retrospectively, it seems that being on an anticoagulant does not increase the incidence of a hemorrhage, but it does appear to increase the severity of the hemorrhage when one does occur.

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