Surgical Approach to Sickle Cell Retinopathy

Recommendations for successful surgery in these challenging cases.

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Sickle cell disease (SCD), first described by James Herrick in 1910, is the most common inherited blood disorder in the United States and worldwide. It is caused by the inheritance of abnormal beta globin alleles carrying the sickle mutation on the hemoglobin gene. The mutations most frequently associated with ophthalmic changes are HbSS and HbSC disease, two of the most common types of SCD.

The ophthalmic manifestations of SCD range from nonproliferative to proliferative changes, but the major sight-threatening complication in SCD is proliferative sickle cell retinopathy (PSR). Large-scale population-based studies indicate that the prevalence of PSR is as high as 32% in HbSC and 6% in HbSS. More specifically, symptomatically decreased vision typically occurs only in the last two stages of PSR—Goldberg stage IV (presence of vitreous hemorrhage) and Goldberg stage V (presence of retinal detachment). The precise incidence and prevalence of severe vision loss in PSR is as yet unknown; reported numbers vary depending on the study. But, overall, severe vision loss in PSR is relatively uncommon.

Natural history studies demonstrate that PSR can regress, and sea-fan neovascular complexes can undergo autoinfarction, even without treatment, while the patient remains visually asymptomatic. When vision loss occurs, it is most commonly a result of vitreous hemorrhage or retinal detachment. Less commonly, it can occur due to vitreomacular interface abnormalities as a consequence of neovascularization, such as macular hole, or epiretinal membrane (ERM).

Rarely, selected cases will require vitreoretinal surgical management to improve or stabilize vision. Visually significant nonclearing vitreous hemorrhage, or vitreous hemorrhage occurring bilaterally or in a monocular patient, may be an indication for surgical intervention in PSR, as is retinal detachment.

Avoiding Surgery

In our anecdotal experience, intravitreal injection with an anti-VEGF agent may be useful in facilitating the involution of sea-fan neovascularization and clearing vitreous hemorrhage, potentially avoiding the need for surgery. It is known that SCD leads to peripheral retinal ischemia that can be easily seen on ultrawide-field fluorescein angiography (Figure 1). The peripheral ischemia leads to the release of proangiogenic factors such as VEGF and formation of the characteristic sea-fan neovascular complexes. Therefore, there is a biologic rationale for intravitreal injection of anti-VEGF agents such as bevacizumab (Avastin, Genentech) for the regression of sickle neovascularization. Other authors have reported this as well in case reports. Similar success has also been reported with ranibizumab (Lucentis, Genentech).

At a Glance

- Although severe vision loss in proliferative sickle cell retinopathy (PSR) is relatively uncommon, symptomatically decreased vision can occur in the last two stages of PSR.
- Despite medical management, a small number of eyes with PSR will require vitreoretinal surgical intervention.
- Visually significant nonclearing vitreous hemorrhage, or vitreous hemorrhage occurring bilaterally or in a monocular patient, and retinal detachment are indications for surgical intervention in PSR.
- Recommended practices for the surgical management of PSR include consideration of an injection of an anti-VEGF agent prior to surgery for eyes with stage IV and V PSR, blood transfusion or exchange transfusion per hematologist, general anesthesia or sub-Tenon block, and avoidance of high and broad scleral buckles.
These studies are limited by the length of follow-up. Additional evidence is needed to better define the role of anti-VEGF agents in clearing vitreous hemorrhage in PSR; however, our initial experience is encouraging as a possible way to clear vitreous hemorrhage.

Despite medical management, a small number of eyes with PSR will require vitreoretinal surgical intervention. In this article, we report our experience with the surgical approach to PSR.

**PREOPERATIVE PLANNING**

Because the characteristic vaso-occlusive episodes of SCD can affect every organ system, surgical intervention in these eyes presents a unique set of challenges that requires careful preoperative planning, incorporating a multidisciplinary approach, with discussion with other medical teams caring for the patient, including hematology and anesthesiology.

Preoperative planning should start with a detailed discussion with the patient and other members of the team regarding the need for exchange transfusion. Exchange transfusion in the setting of retinal surgery for SCD is controversial. There is no randomized controlled trial in the ophthalmic literature evaluating the efficacy of exchange transfusions. Some authors believe that partial exchange blood transfusion, increasing hemoglobin A to more than 60%, is protective against anterior segment ischemia. Others have argued against the use of preoperative exchange transfusion, citing risks of transmissible diseases. In a more recent surgical series, the authors propose that adequate intraoperative hydration, oxygenation, and intraocular pressure control can obviate the need for preoperative exchange transfusions.

There is no consensus in the hematology literature, either, for preoperative exchange transfusions. One randomized controlled clinical trial assessed transfusion 10 days before surgery but included only sickle cell patients with HbSS and HbS beta thalassemia undergoing abdominal and orthopedic surgeries. The authors reported that patients who received preoperative transfusions had fewer clinically important complications, but it is unclear how these results apply to ophthalmic surgery.

Given the lack of evidence, we recommend a tailored approach to exchange transfusion, involving the anesthesiologist and hematologist preoperatively to determine whether it is needed for each individual patient. Careful attention to postoperative analgesia and hydration for patients with SCD is also imperative. Severe postoperative pain, lack of hydration, and the overall stress of surgery can trigger a positive feedback loop of painful vaso-occlusive crises.

**SURGICAL CONSIDERATIONS**

Once the patient has been cleared for surgery, we recommend general anesthesia rather than local anesthesia. General anesthesia allows optimal intraoperative pain control. If it is contraindicated for some reason, then a sub-Tenon block is preferable to retrobulbar block. SCD patients can have orbital compression syndrome from sickling events in or around the orbit, and a retrobulbar block could theoretically increase this risk.

Once the decision for surgical intervention has been made in patients with stage IV or V PSR, intravitreal bevacizumab can be used as a presurgical adjunctive agent to decrease the likelihood of intraoperative bleeding and to facilitate dissection of sea-fan neovascular complexes, similar to the way anti-VEGF agents are used in surgery for proliferative diabetic retinopathy. We have previously reported that administration of bevacizumab 3 days before the surgical procedure leads to increased fibrosis of the sea-fan neovascularization and decreased intraoperative bleeding. There is a theoretical concern of anti-VEGF crunch—as seen in the setting of tractional retinal detachments in proliferative diabetic retinopathy—but we have not experienced this.

**SURGICAL TECHNIQUE**

When removal of neovascular fibrovascular tissue is needed to relieve traction, we recommend segmentation over delamination techniques, as have other surgeons. Segmentation involves the vertical cutting of the fibrovascular tissue into small segments to relieve circumferential traction, which allows removal of each small segment individually. Delamination describes the removal of the membranes through horizontal dissection in the plane between the retina and the fibrosis. The sea-fan neovascular complexes are usually located in the anterior retina where the tissue is ischemic, and thus very thin and prone to iatrogenic breaks. These peripheral neovascular complexes are also often strongly adherent, and removing them using delamination techniques can cause iatrogenic retinal tears. The same principles of segmentation apply to removal of ERMs in the setting of PSR. Use of a bimanual...
technique with a lighted pick or a chandelier as an additional light source can also facilitate dissection. Figure 2 shows a patient who presented with decreased vision as a result of an ERM. Flattening of the macula was achieved after use of segmentation techniques described above.

We recommend the use of a scleral buckle to support peripheral pathology if needed. Historically, encircling scleral buckles were implicated in high rates of anterior segment ischemia in SCD. More modern series do not demonstrate an increased risk for anterior ischemia with the use of an encircling buckle. This is possibly due to changes in surgical technique, as modern scleral buckles are no longer routinely used after surgical removal of the ERM demonstrates flattening of the macula and some restoration of foveal contour (C).

CONCLUSION

There have been numerous surgical advances since the first series describing the surgical management of PSR was published. In the contemporary era of vitreoretinal surgery, we recommend the following practices:

- Injection of bevacizumab 3 days before surgery in selected eyes with stage IV and V PSR;
- Transfusion exchange as recommended by hematology and anesthesiology;
- General anesthesia or sub-Tenon block over retrobulbar block;
- Segmentation techniques for dissection of peripheral neovascular fibrovascular tissue;
- Avoidance of high and broad scleral buckles; and
- Careful intraoperative and postoperative monitoring of analgesia, hydration, oxygenation, and intraocular pressure.