

Comments by: Nathan Radcliffe, MD and Eytan Blumenthal, MD

Late-onset Bleb Leakage

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CASE REPORT

A 75-year-old man presents for routine follow-up examination 6 years after uncomplicated primary trabeculectomy with a 2-minute intraoperative application of mitomycin C (MMC, 0.4 mm/mL). Although progression had occurred when the intraocular pressure (IOP) was in the mid teens, the visual fields have remained stable since filtration surgery was performed. The IOP is 8 mm Hg and a large, thin-walled avascular filtration bleb is present at the superior limbus. A conjunctival epithelial hole is visible in the center of the bleb overlying the scleral flap and leakage is noted when fluorescein is applied (positive Seidel test). No infiltrate is observed within the bleb, and there is no evidence of intraocular inflammation, choroidal effusion, or chorioretinal folds in the macula. The visual acuity is 20/40 due to an early nuclear cataract.

QUESTIONS

1. In which patients do you routinely perform Seidel testing?
2. What are the indications for bleb leak repair? What is the role, if any, of observation with prophylactic antimicrobial therapy?
3. What are the surgical options for this patient? How would you approach the management?

COMMENTS

Comments by Nathan Radcliffe, MD, Assistant Professor of Ophthalmology, Weill Cornell Medical College, New York-Presbyterian Hospital, New York, NY

This asymptomatic man presents with a late-onset (at least 3 mo postoperatively) bleb leak after trabeculectomy associated with low IOP, a thin and avascular conjunctival filtering bleb, a focal leak, and prior application of antifibrosis chemotherapy with MMC. Blebs remodel over time and some proceed to progressive thinning and avascularity, particularly after MMC use, which confers a

higher risk of leak than does 5-fluorouracil.¹ The patient does not currently have complications associated with ocular hypotony. He will likely require cataract extraction in the future and his disease progressed with IOPs in the mid teens, so treatment for this leak will have to maintain a low IOP to be considered successful.

A bleb may be tested for a leak by applying a moistened 2% fluorescein strip to the filtering bleb. This should be performed under direct, slit-lamp visualization and the bleb observed using cobalt blue illumination for 30 seconds to allow for detection of a stream of aqueous within the fluorescein. Bleb leaks should be differentiated by diffuse bleb “sweat,” which is present in many patients with successful blebs and has not been reported to be associated with late infection. Blebs associated with epiphora, hypotony, shallow anterior chamber depth, or with thin walls or prior known history of bleb leak should be tested in this manner. While low IOPs often accompany bleb leaks, bleb leaks may occur in eyes with normal IOPs and therefore IOP alone should not determine the need for surveillance.

My primary goal in treating this patient is to avoid a potentially devastating bleb-related ocular infection and to a lesser extent to circumvent the potential sequelae of ocular hypotony. Many eyes with bleb-related ocular infection have had known preexisting bleb leak or a leak at the time of presentation. The prior use of antifibrosis agents also increases the risk of infection, and may be higher in eyes treated with MMC. Complications related to hypotony include decreased visual acuity from folds in the macula or cornea, persistent choroidal effusion, or shallow anterior chamber.

Initially, I would educate the patient with respect to signs and symptoms of bleb-related infection and hypotony and instruct him or her to seek immediate medical attention if problems arise. I would treat any preexisting blepharitis, another risk factor for infection (often due to streptococcus and staphylococcus species) in this setting.

Treatment options range from observation to a more definitive surgical revision. Conservative treatment usually consists of lubrication, eye shield, aqueous suppression, and bandage contact lens or pressure patch placement along with prophylactic antibiotics. This approach takes time to work and is successful in less than half of cases. Meanwhile, the risks of complications persist until the leak is gone. Recurrence (or a second occurrence in an adjacent area) is likely because the underlying conjunctiva is thin. Office-based procedures offer the hope of stopping the leak without jeopardizing the bleb, but their efficacy is lacking. These methods include application of trichloroacetic acid or autologous blood injection to promote inflammation and leak closure, cyanoacrylate glue, argon laser photocoagulation, or autologous fibrin tissue glue to directly close the

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leak, and bleb needling to redirect flow away from the leak and reduce tension at the site of the leak. Despite reports that the aforementioned techniques may be successful upon occasion, it has been our experience that even when successful, leaks treated with these maneuvers usually recur.

The definitive approach to treatment of bleb leaks, particularly if they are recurrent or have been associated with infection, is conjunctival advancement. Budenz et al² reviewed 26 patients treated with this technique and found the intervention to be successful in stopping the leak and in controlling IOP in 92%. However, 50% later required hypotensive medications and 8% required additional filtration surgery.

For this patient, I would immediately begin conservative measures, including a topical fourth generation fluoroquinolone antibiotic, aqueous suppressants to slow the leak, and an eye shield while sleeping to reduce the risk of inadvertent pressure on the bleb and exacerbation of the leak. The patient should be engaged in the decision-making process and the various risks, benefits, and alternatives should be reviewed and indications and timelines for more aggressive interventions established. In this patient with cataract, I would strongly consider cataract surgery to improve visual function and hope that the leak closes due to postoperative inflammation. If the leak persists, I would schedule the patient for a conjunctival advancement procedure with excision of the thinned conjunctiva with frequent monitoring until that time. If the leak stops with conservative intervention, I would continue observation, but would proceed to excision of the leaking bleb with conjunctival advancement for persistent leak, particularly if it is associated with complications associated with hypotony or infection. If filtration fails after the leak is closed, tube-shunt surgery should be considered to control IOP without antifibrosis chemotherapy and its attendant risks of creating a new thin-walled bleb and a new cycle of leak and treatment.

Comments by Eytan Blumenthal, MD, Senior Lecturer, Hadassah-Hebrew University Medical Center, Jerusalem, Israel

Bleb leaks may be easily missed by the clinician. It is important to inspect the bleb with fluorescein and cobalt blue illumination before measuring the IOP in eyes postfiltration surgery, especially when the IOP is unexpectedly low, or when the patient complains of tearing, or "wetness" in the corner of the eye. When searching for late leakage, one should focus on the region of transparent bleb tissue, in contrast to eyes with early leakage where the conjunctival incision site should be carefully inspected.

Tips for identifying bleb leaks include applying a generous amount of fluorescein stain, and observing the bleb using blue light for an extended period of time (often 20 to 30 s) with an occasional sliding of the upper lid very (very) gently over the bleb surface to apply a fresh layer of fluorescein-stained tear film. Another approach to achieve a fluorescein-saturated tear film is to ask the patient to look down, manually elevate the upper lid, and gently apply a moistened fluorescein strip to the anesthetized conjunctiva above the region of the bleb. Note that in the setting of very low IOP, it is possible to entirely miss a bleb leak due to the absence of a pressure gradient across the 2 sides of the hole. Thus, it is a good habit to apply very gentle pressure to the globe through the lower lid (far from the surgical site) in

eyes with suspected leakage and no sign of a spontaneous leak.

Bleb leaks, often thought to be an incidental micro-hole in an ischemic, thin conjunctiva, might be better perceived as a manifestation of a failing trabeculectomy bleb. The formation of a "ring-of-steel" scar surrounding a localized bleb creates an unstable situation where free communication exists between the anterior chamber and the localized bleb, with absent filtration from the bleb base. The elevated pressure within this localized bleb pocket and resulting tightness of the overlying bleb wall exposes it to further thinning, ischemia, and erosion by the upper lid, and eventually the emergence of a late bleb leak.

Managing a late bleb leak is one of the more difficult dilemmas of the glaucoma surgeon. Initial observation using a prophylactic antibiotic is a reasonable first-line approach, in the hope that the leak will self-seal. The size and location of the hole, amount of leakage, and response to therapy will all determine how quickly the patient may need to be brought to surgery.

Surgical closure of the bleb leak may raise the IOP above the target goal, noted in this patient to be below the mid teens. One aspect of the surgical approach, therefore, may be to attempt to fully dissect the ring-of-steel (scarred Tenon's firmly adherent to the episclera along the posterior aspect of the bleb) during surgery to reestablish flow from the base of the new bleb. This maneuver should also assist in mobilizing conjunctiva for closure. However, it should be recognized that scarred areas, even if fully dissected, have a strong tendency to rescar, perhaps due to the abundance of fibroblasts in that location. The possibility of subsequent filtration surgery at a different site should be kept in mind when planning the extent of the revision. Lastly, the success of bleb leak repair surgery may depend on whether the conjunctival sutures hold or "cheese-wire" through the conjunctival bites due to posteriorly directed forces retracting the stretched conjunctiva back to its original location. In some eyes, postoperative steroids should be reduced in the early postoperative period, and nonabsorbable suture materials are recommended.

Late-onset bleb leakage is a common complication after filtration surgery. Successful management is crucial for vision preservation. Appropriate use of antifibrosis therapy, careful intraoperative tissue manipulation and dissection of the bleb pocket, postoperative corticosteroid therapy, and interventions such as suture lysis or needle revision contribute to glaucoma filtering surgery success.

DISCUSSION

Donald L. Budenz, MD, MPH

Drs Blumenthal and Radcliffe have nicely outlined the salient issues that apply to this patient. Late-onset bleb leaks are not uncommon in these days of aggressive use of antifibrotic agents.¹ The thinner and more successful the bleb, the greater the risk of late-onset bleb leaks. This particular patient is elderly and white, 2 factors that have probably increased the likelihood of this complication. Glaucoma subspecialists differ in their approach for assessment of a bleb for possible leakage. Some, as Dr Blumenthal implies, advocate always inspecting a bleb for possible leakage; others inspect the bleb with Seidel testing only when a specific symptom or sign, such as hypotony or infection, is identified. They also differ in terms of whether to pursue closure of the leak. The patient under discussion

has no complications related to the leak and, in fact, has an excellent IOP that is most likely slowing or preventing further glaucomatous damage. One could, therefore, argue that the patient should be left alone and given a list of the early warning signs of bleb-related infection as outlined by Dr Radcliffe. We use the convenient mnemonic “RSVP” or Redness, Sensitivity to light, Vision loss, or Pain, and tell our patients with bleb leaks to seek immediate medical attention should they develop. Others may argue that any patient with a bleb leak is at very high risk for developing a bleb-related infection, which may be vision threatening, and therefore closure of the leak should be uniformly recommended. There have been several papers that suggest that bleb leakage is a major risk factor for bleb-related infection.^{3,4} The conjunctiva and sclera are the primary barriers for entry of bacteria into the eye and a hole in the conjunctiva, coupled with a sclerostomy, render the eye vulnerable to infection.

Various treatment strategies have been described to close late-onset bleb leaks ranging from conservative measures (patching, contact lens, ocular hypotensive medications), to more aggressive therapies including cryotherapy, fibrin glue, trichloroacetic acid, argon laser shrinkage, and autologous blood injection. As indicated by Dr Radcliffe, such interventions often fail. A retrospective comparative case series found that the success rate of nonsurgical treatment is only 50%, considerably lower than with surgical management.⁵ In our experience, if the hole through which aqueous humor is leaking can be seen at the slit lamp, it is unlikely to close without surgical intervention. Surgical options include conjunctival advancement with or without bleb preservation, free conjunctival autograft, or amniotic membrane graft, which we reserve for patients without enough native conjunctiva for grafting. In this particular patient, as the hole is visible, I would proceed to conjunctival advancement directly. However, Dr Radcliffe’s approach of performing cataract surgery with the hope of inducing sufficient postoperative inflammation to close the leak could be considered, assuming the cataract is symptomatic and has interfered with activities of daily living.

Conjunctival advancement is a simple and effective procedure for reconstructing a filtering bleb. A large conjunctival peritomy is performed that extends beyond the preexisting filtering bleb by approximately 2 clock hours on either side. Extensive blunt dissection of the conjunctiva and Tenon’s layers is performed using blunt Westcott scissors posteriorly and on both sides of the old filtering bleb to allow one to advance or slide these layers over the filtration area. Oftentimes one encounters a thick ring of scar tissue delineating the old filtering bleb that must be incised. The prior ischemic bleb may be excised at this point. To facilitate adherence between the conjunctival tissue and cornea, one may denude the peripheral corneal epithelium using a blade or cautery. Conjunctiva and Tenon’s layers are then pulled down past the limbus and closed using 2 polyglactin “wing” sutures at either end of the wound, and a horizontal mattress suture using 10-0 nylon anterior to the trabeculectomy site. Inflating the anterior chamber with balanced salt solution through a paracentesis site and inspecting the bleb for leakage using a Seidel test should be performed. Lastly, a subconjunctival injection of corticosteroid and antibiotic is administered 180 degrees from the bleb.

REFERENCES

1. Greenfield DS, Liebmann JM, Jee J, et al. Late-onset bleb leaks after glaucoma filtering surgery. *Arch Ophthalmol*. 1998;116:443–447.
2. Budenz D, Chen P, Weaver Y. Conjunctival advancement for late-onset filtering bleb leaks: indications and outcomes. *Arch Ophthalmol*. 1999;117:1014–1019.
3. Soltau JB, Rothman RF, Budenz DL, et al. Risk factors for glaucoma filtering bleb infections. *Arch Ophthalmol*. 2000;118:338–342.
4. Jampel HD, Quigley HA, Kerrigan-Baumrind LA, et al, the Glaucoma Surgical Outcomes Study Group. Risk factors for late-onset infection following glaucoma filtering surgery. *Arch Ophthalmol*. 2001;119:1001–1008.
5. Burnstein AL, WuDunn D, Knotts L, et al. Conjunctival advancement versus nonincisional treatment for late-onset glaucoma filtering bleb leaks. *Ophthalmology*. 2002;109:71–75.