

Bleb-Related Infections

Diagnosis, risk factors, and the treatment of blebitis and bleb-related endophthalmitis.

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Blebitis, an infection limited to the bleb, must be approached with a high level of suspicion for bacterial infection and treated aggressively. The condition can rapidly spiral into a bleb-related endophthalmitis, which may lead to significant vision loss (as advanced as no light perception) or even the need for evisceration/enucleation.

SIGNS AND SYMPTOMS

The signs and symptoms of blebitis are similar to those of any ocular infection, and they can be mistaken for viral conjunctivitis. Patients typically describe pain or discomfort, redness, and blurred vision. Their eyelids may be hyperemic and edematous with subsequent ptosis. As blebitis evolves into endophthalmitis, these symptoms may become more severe. In a retrospective study from Duke University, a prodrome was documented in 35% of physician visits prior to the one at which the bleb-related infection was diagnosed; these early clinical symptoms included brow ache, headache, or external ocular inflammation.¹

Blebitis threatens a patient's vision, and it may develop years after surgery, when the patient may not correlate his or her symptoms directly to the trabeculectomy. Patients therefore must be frequently reminded to seek immediate ophthalmic attention upon experiencing the symptoms of redness, sensitivity, vision loss, and pain (the mnemonic device RSVP is useful). Otherwise, they may first seek a remedy for these symptoms in the ER or from their primary care provider. Physicians who do not specialize in eye care may diagnose viral conjunctivitis and discharge the patient without recognizing the true risk of endophthalmitis. For this reason, it is highly important to educate patients about their risk of losing all vision from an infection after glaucoma surgery so that they will know to insist that an ophthalmologist be called to see them.

The signs of blebitis include a whitened bleb surrounded by intense conjunctival injection (Figure 1). A mucopurulent infiltrate, precipitates similar to keratic precipitates, and/or a hypopyon may be visible within the bleb,



(Courtesy of Richard A. Lewis, MD.)

Figure 1. Example of early blebitis. Notice the whitened bleb and diffuse hyperemia of the conjunctiva. The anterior chamber at this point has a few cells present, but there is no vitreous cell.

which is often avascular with thin walls. These signs can be accompanied by a varying degree of anterior chamber reaction and/or a hypopyon, depending on the duration of the blebitis. Frequently, there is a bleb leak and consequent hypotony. If there are vitreous cells in the presence of a blebitis, the infection is classified as an endophthalmitis. Many vitreous cells make the diagnosis of endophthalmitis obvious. The presence of only a few cells can make differentiating between blebitis and endophthalmitis more difficult. A few cells can be spillover inflammation (especially if the eye is pseudophakic or aphakic). Given the rapidity and severity of a bleb-related endophthalmitis, however, it is best to err on the side of diagnosing endophthalmitis and to treat accordingly.

RISK FACTORS

Blebs that develop an infection frequently have been described as thin and avascular. A late-onset bleb leak is the most important risk factor for blebitis; such leaks increased

the risk of blebitis 26 times compared with intact blebs in a recent case-controlled study.² It is unknown, however, whether the leak allows bacteria to enter the eye or if an infection leads to a breakdown of the bleb wall and the subsequent leak. The antifibrotic agents 5-fluorouracil and mitomycin C both increase the risk of late-onset bleb leaks and blebitis.³⁻⁵ Histopathology has demonstrated that the walls of a bleb after trabeculectomy with adjunctive mitomycin C have epithelial irregularities, basement membrane breaks, and hypocellularity.^{6,7} One histopathological study of blebs with recurrent blebitis noted a loss of goblet cells; mucin is considered a physiological and biological barrier to infection.⁸

Location is important. Blebs placed inferiorly or nasally have some of the highest reported rates of blebitis.^{9,10} It is thought that their exposure to the inferior tear lake, where bacteria are concentrated, and a lack of protection by the lid are causative issues.

Blepharitis, which may impart a higher bacterial load around the eye, is an additional risk factor.³ The intermittent or chronic use of topical antibiotics beyond the immediate postoperative period is another factor associated with blebitis.³ In a study of recurrent infections of the bleb, 50% of the eyes were receiving topical, prophylactic antibiotics.¹¹

Other factors associated with an increased risk of blebitis are full-thickness versus guarded procedures, trabeculectomy without concurrent cataract extraction, and early complications (such as early wound leak, choroidal hemorrhage, and a flat chamber).³ Weaker associations include systemic corticosteroids, juvenile glaucoma, nasolacrimal duct obstruction, releasable sutures, contact lens wear, bleb revision surgery, and epinephrine drops. Many studies have shown a higher prevalence of blebitis in younger, male, and black patients.³

TREATMENT

Treatment should be tailored to the severity of the infection and to the infecting organism, if known. The onset of bleb-related infections may be early or late, although the former is relatively rare. The organisms in early-onset infections are similar to those seen with acute-onset endophthalmitis after cataract surgery. *Staphylococcus* species and *Propionibacterium acnes* are the most commonly cultured organisms.¹²

Bleb-related infections of late onset are most frequently caused by *Streptococcus* species and gram-negative bacteria such as *Haemophilus influenzae*.^{10,12-14} Many clinicians will treat a severe blebitis as an endophthalmitis because of the traditionally poor outcomes in bleb-related endophthalmitis. The tipping point to perform a tap and injection varies among clinicians and is probably influenced by their previous experience. No prospective randomized trial has stud-

ied this subject. If one decides to hold off on a tap and injection of antibiotics, it is probably a good idea to see the patient 3 to 8 hours later to observe the effects of topical treatment rather than to delay the assessment until the next day.

For patients who truly have an isolated blebitis without the involvement of vitreous or a hypopyon, intensive topical antibiotics alone are appropriate as initial therapy. Starting therapy should be broad spectrum against pathogens known to be associated with blebitis until the culture results become available. (Anterior chamber culture results have been found to yield fewer positive results than vitreous taps.^{15,16}) Some physicians advocate hourly topical fourth-generation fluoroquinolones with or without oral fluoroquinolones, whereas others prefer going straight to fortified topical agents. The most commonly used fortified antibiotic is vancomycin in combination with gentamicin, tobramycin, or ceftazidime.

If an endophthalmitis is obvious or highly suspected, a vitreous tap and injection are warranted that cover for *Streptococcus* and gram-negative organisms (the two most common infecting organisms in late-onset infections).^{10,12-14} For patients whose infections appear severe and who have poor visual acuity at the time of diagnosis, surgeons should strongly consider performing an immediate pars plana vitrectomy with the injection of intravitreal antibiotics. At many centers, the visual acuity that triggers the decision for a vitrectomy is better than the levels used in the Endophthalmitis Vitrectomy Study.¹⁶

PROGNOSIS

Eyes that have been successfully treated for a bleb-related infection remain at risk for recurrent infection. Researchers at the New York Eye and Ear Infirmary found that the infecting organisms in recurrent infections are not necessarily the same as those in the first infection. Also, the long-term use of antibiotics after the initial infection did not confer protection against subsequent infection in the study.¹¹

After a bleb-related infection, the IOP may increase from baseline levels due to additional scarring from inflammation. In these cases, the options (and their risks and benefits) to be discussed are revision, additional trabeculectomy, the placement of a tube shunt, or alternative glaucoma surgeries that do not create a bleb (eg, canaloplasty, goniotomy ab interno). If the pressure remains low due to a persistent leak, the leak should be fixed after the infection resolves. Conjunctival advancement has been shown to result in better outcomes than less conservative treatment for leaks.¹⁷

After an infection, a patient's vision may return to its previous levels if the problem was limited to the bleb and treated aggressively.¹² Bleb-related endophthalmitis may

cause significant vision loss despite aggressive treatment.¹²⁻¹⁴ Because the Endophthalmitis Vitrectomy Study enrolled subjects with a different type of endophthalmitis, its results cannot be applied directly to bleb-related infections.¹⁶ □

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1. Poulsen EJ, Allingham RR. Characteristics and risk factors of infections after glaucoma filtering surgery. *J Glaucoma*. 2000;9:438-443.
2. Soltau JB, Rothman RF, Budenz DL, et al. Risk factors for glaucoma filtering bleb infections. *Arch Ophthalmol*. 2000;118:338-342.
3. Jampel HD, Quigley HA, Kerrigan-Baumrind LA, et al. The Glaucoma Surgical Outcomes Study Group. Risk factors for late-onset infection following glaucoma filtration surgery. *Arch Ophthalmol*. 2001;119:1001-1008.
4. Liebmann JM, Ritch R, Marmor M, et al. Initial 5-fluorouracil trabeculectomy in uncomplicated glaucoma. *Ophthalmology*. 1991;98:1036-1041.
5. Skuta GL, Beeson CC, Higginbotham EJ. Intraoperative mitomycin versus postoperative 5-fluorouracil in high-risk glaucoma filtering surgery. *Ophthalmology*. 1992;99:438-444.
6. Mietz H, Brunner R, Addicks K, et al. Histopathology of an avascular filtering bleb after trabeculectomy with mitomycin-C. *J Glaucoma*. 1993;2:266-270.
7. Shields MB, Scroggs MW, Sloop MW, et al. Clinical and histopathologic observations concerning hypotony after trabeculectomy with adjunctive mitomycin-C. *Am J Ophthalmol*. 1993;116:673-683.
8. Matsuo H, Tomita, Araie M, et al. Histopathological findings in filtering blebs with recurrent blebitis. *Br J Ophthalmol*. 2002;86:827.
9. Caronia RM, Liebmann JM, Friedman R, et al. Trabeculectomy at the inferior limbus. *Arch Ophthalmol*. 1996;114:387-391.
10. Greenfield DS, Sulz LJ, Miller MP, et al. Endophthalmitis after filtering surgery with mitomycin. *Arch Ophthalmol*. 1996;114:943-949.
11. Waheed S, Liebmann JM, Greenfield DS, et al. Recurrent bleb infections. *Br J Ophthalmol*. 1998;82:926-929.
12. Ciulla TA, Beck AD, Topping TM, Baker AS. Blebitis, early endophthalmitis, and late endophthalmitis after glaucoma-filtering surgery. *Ophthalmology*. 1997;104:986-995.
13. Kangas TA, Greenfield DS, Flynn HW, et al. Delayed-onset endophthalmitis associated with conjunctival filtering blebs. *Ophthalmology*. 1997;104:746-752.
14. Song A, Scott IU, Flynn HW, Budenz DL. Delayed-onset bleb-associated endophthalmitis: clinical features and visual acuity outcomes. *Ophthalmology*. 2002;109:985-991.
15. Forster RK. Etiology and diagnosis of bacterial postoperative endophthalmitis. *Ophthalmology*. 1978;85:320-326.
16. Results of the Endophthalmitis Vitrectomy Study. A randomized trial of immediate vitrectomy and of intravenous antibiotics for the treatment of postoperative bacterial endophthalmitis. Endophthalmitis Vitrectomy Study Group. *Arch Ophthalmol*. 1995;113:1479-1496.
17. Burnstein AL, WuDunn D, Knotts SL, et al. Conjunctival advancement versus nonincisional treatment for late-onset glaucoma filtering bleb leaks. *Ophthalmology*. 2002;109:71-75.