Chapter 8
Blebitis and Bleb Related Endophthalmitis

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Glaucoma is a chronic progressive optic neuropathy and is the leading cause of irreversible blindness worldwide [1]. The goal of glaucoma treatment is to control the intraocular pressure (IOP), which is most often achieved with antiglaucoma medications. When glaucoma is refractory to medical treatment, filtering surgery is performed. Described by Cairns in 1968 [2], trabeculectomy is considered the gold standard for glaucoma surgery. It is a partial-thickness guarded filtration procedure that allows aqueous to filter to the subconjunctival space forming a bleb, thereby decreasing the IOP. The conventional trabeculectomy has undergone various surgical modifications over half a century to improve the safety and efficacy of the procedure. Adjunctive antimetabolites have significantly improved the long-term survival of trabeculectomy, but at the expense of increased bleb-related complications [3, 4]. Infections after glaucoma-filtering surgery are infrequent but potentially devastating and mostly occur in the late postoperative period. Late leaking blebs and thin cystic blebs predispose these eyes to serious complications like blebitis and bleb-related endophthalmitis. Early identification and appropriate management is very crucial in salvaging these eyes and preventing loss of vision.

Epidemiology

The overall incidence of endophthalmitis after any intraocular surgery is reported to be 0.093% [5]. The incidence of endophthalmitis is much higher after glaucoma-filtering surgery [6] and is estimated to be 0.2–1.5% with non-augmented trabeculectomy [7–9] that increases with antimetabolite usage to 0.3–13.8% [3, 8, 10–13].

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Jampel et al. reported that risk ratio between the intraoperative use of antimetabolite agents and subsequent development of late-onset bleb-related infection (BRI) was around 2.48 with the use of mitomycin C (MMC) and 1.31 with 5-fluorouracil (5-FU) [11].

The incidence of early postoperative infection is estimated to be 0.12–0.19%, and the incidence of late-onset infections with partial-thickness filtering procedures is estimated to be 0.2–2.2% [10, 12–14] and that of blebitis is 0.08–0.55% [12, 15]. Surgical modifications like wide area application of MMC and suturing techniques have greatly improved the bleb morphology and have significantly reduced the incidence of bleb-related infections in the recent times from 5.2% (with longer duration and localized MMC application) to 1.2–1.3% (with shorter duration, wider area, and posterior subconjunctival MMC application) [15, 16].

Bleb-related infections can be localized involving only the bleb area called blebitis or could be associated with intraocular extension leading to bleb-related endophthalmitis (BRE). The progression of blebitis into endophthalmitis is probably a continuum of infection [6, 17, 18]. The prognosis of blebitis is usually good, unless infection has progressed to endophthalmitis. Despite prompt and intensive treatment of patients with bleb-related endophthalmitis, the outcomes remain unsatisfactory especially with virulent organisms and low initial visual acuity [19, 20].

Classification of Bleb-Related Infection by Greenfield and Katz [7, 10]

BRI is classified as:

Stage I: where bleb involvement is apparent.
Stage II: stage 1 + anterior chamber involvement, cells, flare, and hypopyon.
Stage III: stage II + vitreous involvement.
Stage III was further subdivided by Yamamoto [14, 21] into:
Stage IIIa: mild vitreous involvement
Stage IIIb: marked vitreous involvement

Blebitis: The term blebitis coined by Brown et al. in 1994 [21] describes a presumed infection in or around the filtering bleb, with surrounding congestion and mucopurulent infiltrate in the bleb. This may be associated with mild to moderate anterior chamber activity.

Bleb-related endophthalmitis: Bleb related endophthalmitis is more serious and is associated with hypopyon, vitreous involvement and severe visual loss. Bleb-related infections occurring within 1 month after the surgery are categorized as acute or early onset, and those developing later than 1 month are categorized as late onset [22].

It is important to differentiate between an early-onset infection from late-onset infection as they differ in terms of pathogenesis, causative agents, and prognosis.

Table 8.1 Risk factors for bleb-related infection [11, 23–25]

Association	Ocular	General
Strong	Thin and cystic bleb with late-onset bleb leak	
Midrange	Inferior or nasal bleb, intraoperative MMC usage, conjunctivitis, blepharitis, trabeculectomy alone compared to combined procedure, chronic antibiotic use, aphakia and pseudophakia, punctal plugs	Upper respiratory infection
Low-range	Juvenile glaucoma, nasolacrimal duct obstruction, releasable sutures, contact lens wear, bleb revision surgery: postoperative complications, history of prior bleb infection, high axial myopia	Young subjects, black race, presence of systemic diseases such as diabetes

Risk Factors for Bleb-related Infections

The eyes with a thin and cystic bleb with late-onset bleb leak are at increased risk of developing bleb-related infections [11, 23–25]. The odds of an eye with a bleb-related infection seen with a concomitant late-onset bleb leak is reportedly 25.8 times the odds of a noninfected eye having a late-onset bleb leak [24, 25].

Other risk factors are shown in the Table 8.1.

Yamamoto et al. described a significant association of aphakia or pseudophakia with the development of stage IIIa or stage IIIb bleb-related infection [14]. Thin cystic blebs are associated with intraoperative use of antimetabolites particularly MMC. The histopathology of these blebs shows very thin epithelium with breaks in the Bowman's membrane. The underlying stroma is relatively avascular and hypocellular. There is loss of goblet cells and absent mucin, which predisposes these blebs to infection either with the ocular commensals or with pathogens [26]. Peter DeBry et al. estimated that 5-year probability of developing bleb leaks was 18%, and bleb-related infection was 8% in patients when antimetabolites were used [3].

Microbiology

Causative organisms for blebitis: *Staphylococcus epidermidis* (more common) and *Staphylococcus aureus* are the commonest organisms to cause blebitis.

Causative organisms for bleb-related endophthalmitis (BRE): The most common causative organism associated with early-onset BRE is *Staphylococcus epidermidis* similar to that of acute endophthalmitis after cataract surgery. In contrast, the most common organisms causing late-onset endophthalmitis belong to *Streptococcus* species and *Haemophilus influenzae*.

Ramakrishnan et al. [27] reported early-onset blebitis (less than 36 months after trabeculectomy) to be associated with *Streptococcus* infection. These eyes had severe ocular surface disease and were associated with nasolacrimal duct obstruction.

The causative organism was coagulase-positive staphylococci in eyes with thin cystic bleb and blebitis; coagulase-negative staphylococci were associated with blebitis when there was associated bleb leak. *Corynebacterium* was isolated when blebitis was associated with blepharitis and *Streptococcus* was associated with releasable sutures [27]. Ohtomo et al. reported that BRE with highly pathogenic bacteria (*Streptococcus* species, *Enterococcus faecalis*, *Pseudomonas aeruginosa*, and *Haemophilus influenzae*) was associated with severe visual loss and carried poor prognosis even when intervened within 24 h [19].

Clinical Presentations

Typically the patients of blebitis and BRE report sudden onset of redness followed by pain in the eye, photophobia, discharge, and decreased vision. Many of these patients have prodromal symptoms like brow ache, headache, or external eye infections. The prodrome is longer in blebitis; it is accelerated in endophthalmitis with rapidly worsening ocular pain, reduced visual acuity, and redness within a few hours.

On clinical examination the area of the bleb is congested; there is loss of translucency of the bleb wall with milky content replacing the clear bleb and associated with mild to moderate anterior chamber reaction (Fig. 8.1a). Additionally, anterior chamber inflammation with hypopyon and vitritis may be noted in bleb-related endophthalmitis. (Fig. 8.2a). Ultrasound B-scan may be needed to evaluate the extent of posterior segment involvement.

Management: It is very important to examine these patients as soon as possible probably within an hour [20]. A thorough clinical examination including dilated fundus examination is mandatory to rule out endophthalmitis. One must also rule out blepharitis, nasolacrimal duct obstruction, and other risk factors. Workup must include conjunctival swabs under aseptic precautions, anterior chamber tap, and vitreous biopsy for microbiology investigation. Frequent instillation of appropriate antimicrobial therapy is the management of choice. Treatment could be with broad-spectrum antibiotics with activity preferably against gram-positive organisms. In addition to the spectrum of microorganism coverage, other considerations in choosing the most appropriate antibiotics include better kill kinetics and higher intraocular penetration of the topical antibiotics.

Fourth-generation fluoroquinolones such as moxifloxacin 0.5% or gatifloxacin 0.5% have broad-spectrum coverage and have better intraocular penetration and are widely used in the treatment of blebitis. In cases with severe blebitis, broad-spectrum fortified antibiotic combinations such as fortified cefazolin 5.0% and fortified gentamicin 1.4% are useful. At the initiation of treatment, the frequency of topical antibiotics should be every half to 1 h so as to attain adequate therapeutic concentration of the drug. To ensure close monitoring of compliance and response to therapy, admission and intensive medical care may be required. Subconjunctival injection of antibiotics or systemic therapy is not recommended unless the condition is severe and/or the compliance to topical therapy is

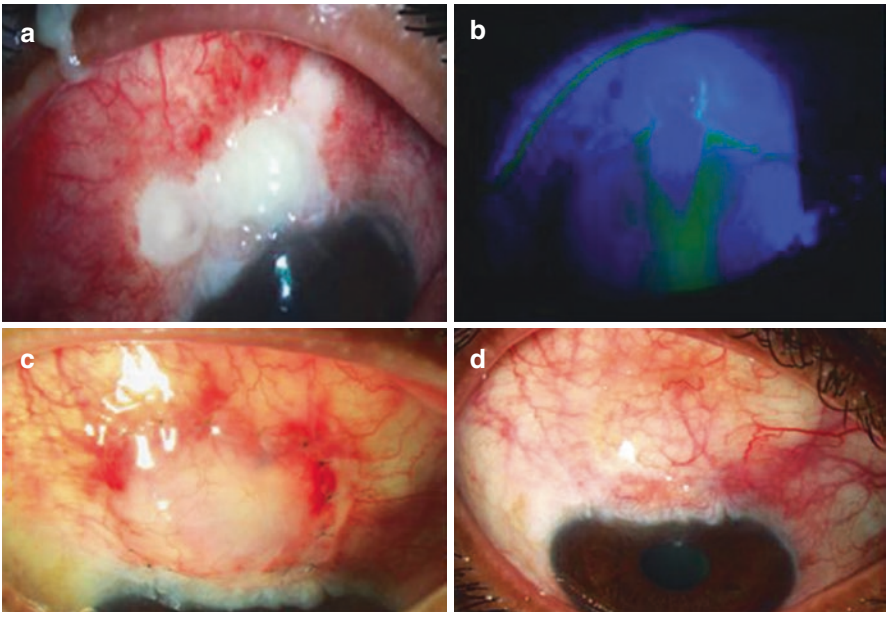

Fig. 8.1 Culture positive blebitis: A 27-year-old man presented with severe pain and redness with excess watering in his right eye for 2 days. He had mitomycin C augmented trabeculectomy for steroid-induced glaucoma 10 years ago. (**a**) The right eye showed severe superior conjunctival congestion; the bleb was avascular and necrotic, excess discharge with loss of bleb translucency suggestive of blebitis. Conjunctival swab showed gram-positive cocci; blebitis resolved in 3 weeks time with intense topical antibiotics (Moxifloxacin). *Staphylococcus aureus*, was grown in culture taken from conjunctival swabs and scrapings over the bleb area. The organism was sensitive to vancomycin, moxifloxacin, chloramphenicol, and cefuroxime. (**b**) Bleb leak was noted after resolution of blebitis. (**c**) The eye was treated surgically by conjunctival autograft harvested from the inferior conjunctiva. (**d**) Two months post-bleb repair, there was well-integrated conjunctival autograft with diffuse bleb; IOP was 10 mm Hg

questionable. Additional therapy includes topical cycloplegic agents and systemic analgesics. The intensive therapy should be continued for 48–72 h. Response to therapy could be measured by improvement in symptoms, reduction of congestion, and reduction in anterior chamber reaction. Once there is response to initial therapy, the frequency of antibiotic instillation can be reduced to two hourly administrations.

Once the blebitis resolves, the topical antibiotics should be stopped and never be tapered, and chronic use of antibiotics should be avoided, both of which could result in colonization of resistant microorganisms on the ocular surface. The empirical treatment should be initiated at the earliest and should not be delayed for microbiology workup and results. However, the subsequent microbiology results would guide in continuation of treatment or choosing alternative medications based on the sensitivity reports.

In the presence of AC involvement (stage II) or vitreous involvement (stage III), vitreoretinal surgeon's opinion and help with management would be required. It is

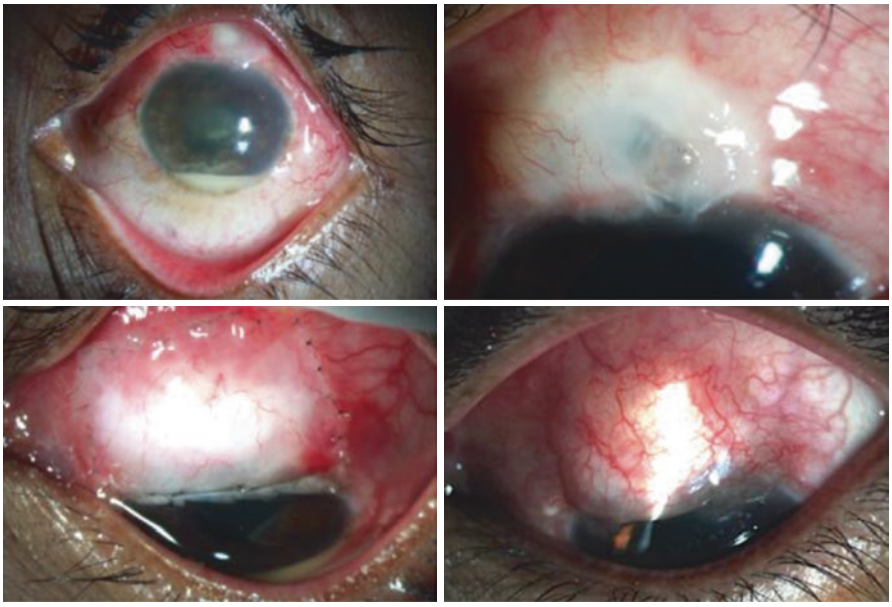

Fig. 8.2 Culture-negative bleb-related endophthalmitis. A 32-year-old man presented with severe pain and sudden decrease in vision for 1 day in his left eye, 3 years after trabeculectomy. *Top Left.* Blebitis with anterior chamber inflammation, hypopyon and few echoes in the anterior vitreous cavity on B-scan suggestive of endophthalmitis. He was treated with intensive topical and intravenous antibiotics, pars plana vitrectomy, and intraocular antibiotics. Both microscopy and culture were negative; hence, he was treated with broad-spectrum antibiotics covering gram-positive and gram-negative bacteria. *Top Right.* Endophthalmitis resolved and there was a thin cystic bleb, but no bleb leak. *Bottom Left.* Conjunctival autograft was performed 1 month after blebitis. *Bottom Right.* Two months later there was a well-healed autograft with diffuse bleb

prudent to begin intensive topical treatment similar to the treatment of blebitis before the referral.

One must remember that the management pearls of the Endophthalmitis Vitrectomy Study (EVS) for post-cataract surgery endophthalmitis cannot be applied to patients of endophthalmitis after glaucoma filtration surgery, more so in late-onset disease. A pars plana vitrectomy (PPV) and intravitreal antibiotic injection is more definitive treatment than a vitreous biopsy with intravitreal antibiotics. Studies have shown that more often poorer visual results (eyes with no light perception) are associated with the vitreous tap group compared to vitrectomy group [7, 28, 29]. Following vitrectomy one should continue treatment with frequent instillation of fortified antibiotic covering both gram- positive and gram-negative organisms till microbiology results are available. In addition, systemic antibiotics must be used. Topical and/or oral corticosteroids can be started after 24–48 h to decrease inflammation and scarring and to preserve the bleb function [7].

Once the infection is brought under control, one must reevaluate to identify the risk factors and treat them appropriately to prevent recurrent bleb infections [28]. Thin cystic blebs with late bleb leak need to be repaired. The technique of bleb

repair would depend on the site of leak and the health of the surrounding conjunctiva [29]. Both conjunctival advancement and conjunctival autograft have been successful in managing these thin cystic and leaky blebs [30, 31].

Summary

Blebitis and bleb-related endophthalmitis are serious and potentially vision threatening complications following glaucoma-filtering surgery. It is very important to diagnose the condition early and institute treatment at the earliest to salvage these eyes. All patients of glaucoma-filtering surgery must be clearly explained about the warning signals like brow ache, headache, associated light sensitivity, and decrease of vision. They should be asked to report to ophthalmologists immediately without any delay in appearance of these symptoms and signs. Early treatment carries better prognosis. Prognosis also depends on the type of organism and extent of intraocular involvement with blebitis and early-onset bleb-related endophthalmitis. Eyes infected with less virulent and/or less-resistant organisms enjoy better prognosis [28, 29, 32].

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