16 Endophthalmitis

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16.1 Introduction

Endophthalmitis is a devastating ocular inflammatory process that can lead to blindness. In endophthalmitis, there is inflammation of the vitreous cavity along with the retinal and uveal components of the eye. Endophthalmitis may be infectious or noninfectious, and the infectious cases may be a result of endogenous or exogenous sources. Endogenous endophthalmitis occurs secondary to a hematogenous dissemination and spread from a distant infective source in the body. Most cases of endophthalmitis are exogenous and occur after ocular surgery. Each type of infectious endophthalmitis differs in its microbial profile, symptoms, and clinical course as described herein.

16.2 Endogenous Endophthalmitis

Endogenous endophthalmitis as a result of hematogenous spread from other parts of the body makes up less than 2–8 % of cases [1]. Risk factors include a chronic disease state, invasive surgery, indwelling catheters, intravenous drug use, septicemia, and immunodeficiency. This type of endophthalmitis is rare in healthy individuals and is an indication for systemic investigations [2].

The presentation normally is acute and may be bilateral in 12 % of cases [3]. In one series, diabetes, intravenous drug abuse, and HIV/AIDS infection were the most influential risk factors, and liver abscesses, pneumonia, and endocarditis were the three most common sources of infection [3].

Both bacteria and fungi can cause endogenous endophthalmitis. The profile of bacteria that cause endogenous endophthalmitis differs according to geographical region. Gram-negative organisms, especially *Klebsiella*, predominate in East Asia [4]. *K. pneumoniae* genotype K1 is an emerging pathogen capable of causing catastrophic septic ocular or central nervous system complications from pyogenic liver abscess. Diabetes is a significant risk factor for the development of endogenous endophthalmitis and poor visual outcome in patients with *K. pneumoniae* liver abscess. Endogenous *K. pneumoniae* usually causes poor visual outcomes. Cases in Europe and North America are dominated by gram-positive organisms such as *Staphylococcus aureus*, *Staphylococcus epidermidis*, group B streptococci, *Streptococcus pneumoniae*, and *Listeria monocytogenes* [3, 5]. The most common cause of fungal endogenous endophthalmitis is *Candida* species, particularly *Candida albicans*,

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followed by *Aspergillus*. The presentation usually is subacute and is associated with long-term intravenous catheters. Intravenous drug abusers with endocarditis are also at risk for endogenous fungal endophthalmitis.

16.3 Endophthalmitis After Cataract Surgery

Endophthalmitis, an infection of the vitreous compartment and the retinal and uveal coats of the eye, is a problematic complication associated with intraocular surgery. Because cataract surgery is the most frequently performed intraocular surgery, 90 % of postoperative endophthalmitis occurs following this procedure [6]. Post-cataract surgery endophthalmitis is divided into two types: acute-onset and chronic or delayed-onset endophthalmitis.

16.3.1 Acute-Onset Endophthalmitis

In this entity, the patient typically presents within the first week after cataract surgery. Patients presenting within 6 weeks of the surgery with reduced visual acuity and symptoms and signs of endophthalmitis should be managed as for acute endophthalmitis. The overall incidence of endophthalmitis after cataract operations has been estimated to be in the range of 0.04–0.2 % [7].

Improvements in modern cataract surgery have mainly involved a series of technical refinements. Most have concerned the evolution in the type of surgical incision being performed, beginning with the implementation of intracapsular cataract extraction, followed by extracapsular cataract extraction (ECCE), then small-incision scleral tunnel phacoemulsification, and, finally, clear corneal incision (CCI) phacoemulsification. The implementation of these technical refinements has resulted in simplified postoperative care and faster visual recovery and has been promoted from a safety standpoint. However, retrospective studies have recently suggested an association between an increased incidence of endophthalmitis following cataract surgery and the use of CCIs for cataract extraction [6–15].

Al-Mezaine et al. [15] showed that over a 10-year period, the incidence of acute-onset nosocomial endophthalmitis following cataract surgery was 0.068 % and that the risk of endophthalmitis was 1.73-fold higher for CCI phacoemulsification than ECCE. In their meta-analysis of studies addressing endophthalmitis following cataract surgery, Taban et al. [6] found that the incidence of endophthalmitis has varied over time—that is, from 0.087 % in the 1990s to 0.265 % in 2000/2003. For the time period between 1992 and 2003, they also determined that CCI phacoemulsification was a risk factor for endophthalmitis, with an increased rate of 0.189 % compared with 0.074 % for scleral tunnel incisions. Moreover, Cooper et al. determined that clear corneal incision was associated with a threefold greater risk of endophthalmitis than was scleral tunnel incision [11].

16.3.2 Clinical Features

Patients with acute endophthalmitis typically present with blurred vision (94.3 %), red eye (82.1 %), pain (74 %), and swollen lid (34.5 %) as it has been shown by the Endophthalmitis Vitrectomy Study (EVS) [9]. Other clinical signs might include conjunctival discharge; conjunctival and corneal edema; turbidity in the anterior chamber with cells, hypopyon, or fibrin clot; and/or vitritis that precludes a view of the posterior segment. Acute endophthalmitis is diagnosed by clinical means. Ocular echography is a valuable adjunctive tool in this type of clinical evaluation particularly in eyes with opaque media [16].

16.3.3 Etiology

The normal flora of the ocular surface comprises an array of bacteria that are believed to be a primary source of infection in endophthalmitis. Gram-positive bacteria are the most common cause of postoperative endophthalmitis [9, 17–19]. In the EVS [9], researchers found that 94.2 % of culture-positive endophthalmitis cases involved gram-positive bacteria: 70 % of isolates were gram-positive coagulase-negative staphylococci, 9.9 % were *Staphylococcus aureus*, 9.0 % were *Streptococcus* species, 2.2 % were *Enterococcus* species, and 3.0 % were other gram-positive species. Gram-negative species were involved in 5.9 % of cases.

16.3.4 Risk Factors

An increased intraocular exposure to the patient's own normal adnexal and ocular surface flora that occurs during cataract surgery might be the main risk factor for endophthalmitis. Intraoperative complications such as posterior capsular rupture and vitreous loss also increase the risk for endophthalmitis by tenfold [20]. In addition, several studies have suggested that the performance of CCIs is a risk factor for endophthalmitis [21–24]. Moreover, it has been shown that the use of silicone IOL optic material increased the risk of endophthalmitis by 3.3-fold compared to acrylic lenses [21]. Other factors that increase the risk for endophthalmitis include failure of sterile technique during intraocular surgery [25], preexisting periocular infections, advancing age (>85 years), and immunosuppressed status such as diabetes [26, 27].

16.3.5 Management

As put forth in the EVS [9], the initial treatment of endophthalmitis following cataract surgery involves a two-pronged approach: specimen collection and the administration of broad-spectrum antibiotics (such as a combination of vancomycin and ceftazidime). The diagnostic yield of vitreous specimen is roughly doubled that of an aqueous specimen (54.9 % vs 22.5 %, respectively) [28]. Polymerase chain reaction (PCR) amplification produces yields for aqueous and vitreous sampling that are the same [29], thus allowing the diagnosis to be made with the faster and more easily performed aqueous tap [30].

According to the EVS, the presenting visual acuity should form the basis of the decision between a vitreous tap and vitrectomy for patients, with the exception of those with diabetes [9]. For patients with a visual acuity better than light perception, either method can be used without affecting the final outcome. Whereas for patients with light perception vision, pars plana vitrectomy (PPV) should be performed because a threefold increase in the likelihood of achieving 20/40 final visual acuity occurs when this procedure is carried out [28]. The situation differs for patients with diabetes. Regardless of the presenting visual acuity, patients with diabetes have a greater likelihood of obtaining 20/40 acuity with PPV (57 %) compared with a simple tap (40 %) [31].

It has been demonstrated by the EVS group that poor visual outcome was associated with a presenting visual acuity of light perception, presence of afferent pupillary defect, corneal infiltrate or ring ulcer, hypopyon, abnormal IOP (<5 or >25 mmHg), rubeosis iridis, small pupil size after maximal dilatation, absent red reflex, and inability to see any retinal vessels by indirect ophthalmoscopy [9].

16.3.6 Prevention

Preoperative sterile preparation of the surgical site is one of the most common practice patterns employed to prevent postoperative endophthalmitis. This practice most often entails the instillation of povidone-iodine 5 % into the conjunctival sac, which, according to research studies, effectively decreases the bacterial load [32, 33]. A recent European survey by Ang and Barras [34] determined that 99.5 % of surgeons use povidone-iodine irrigation for prophylaxis. In their prospective study, Halachimi-Eyal et al. [35] compared the effects of the preoperative administration of topical moxifloxacin 0.5 % and povidone-iodine 5 % and that of povidone-iodine 5 % alone on conjunctival bacterial colonization. They found that the decrease in conjunctival bacterial colonization achieved with topical moxifloxacin 0.5 % and povidone-iodine 5 % did not exceed the effect of povidone-iodine 5 % alone.

Proper surgical draping is also critical. This practice involves using overhanging wraparound flaps from the drape (held securely in place by the speculum) to sequester the lashes and lid margins completely [36, 37].

Although topical perioperative antibiotic prophylaxis is generally performed, controversy surrounds this practice because its effectiveness is there [25]. Of these types of drugs, fourth-generation fluoroquinolones have become the most commonly prescribed owing to their broad-spectrum activity and enhanced ocular penetration [38, 39].

Of the various methods of antibiotic prophylaxis, the strongest support in the literature is for direct intracameral bolus injection at the conclusion of surgery. In their retrospective study, Montan et al. [40] found that the administration of a direct intracameral cefuroxime injection in more than 32,000 cases in Sweden resulted in an endophthalmitis rate of 0.06 %, which was significantly lower than those previously determined. (However, they also reported that 12 of the 13 culture-positive endophthalmitis organisms were cefuroxime resistant.) In addition, a lower rate of endophthalmitis was associated with the administration of intracameral cefuroxime compared with topical antibiotic use alone in a 3-year prospective, nonrandomized study of more than 225,000 cases in Sweden [41]. Furthermore, the value of intracameral antibiotic prophylaxis is underscored by the finding of a multicenter, prospective, randomized study by the European Society of Cataract and Refractive Surgeons (ESCRS) [21] showing that direct intracameral cefuroxime injections resulted in a 5.86-fold decreased (95 % confidence interval, 1.72–20.0) risk for culture-positive endophthalmitis [21, 42]. Although support exists in the literature regarding the safety of using intracameral preparations of vancomycin and cephalosporin [43–49], there are several risks associated with compounding medications for intraocular administration, including toxic anterior segment syndrome, retinal toxicity, ocular contamination, and dosing errors [50]. However, the need for the compounding of medications is eliminated when moxifloxacin is administered. In their study on the use of moxifloxacin for intracameral prophylaxis, O'Brien et al. [38] noted its potency and bacterial activity and described how the self-preserved commercial formulation negated the need for compounding. Although no prospective randomized studies have been conducted to support the use of subconjunctival antibiotic prophylaxis, research has indicated that it has a protective benefit [7].

16.4 Chronic (Delayed-Onset) Endophthalmitis

Chronic endophthalmitis is defined as an infection that occurs 6 weeks or more after cataract surgery and frequently persists, with recurrent low-grade inflammation, for months thereafter [51].

16.4.1 Incidence

Data regarding the incidence of chronic endophthalmitis following cataract surgery are scarce. Rogers et al. [52] estimated the ratio of acute to chronic postoperative endophthalmitis cases to be between 5:1 and 2:1, indicating that the incidence rate can be five cases per 10,000 individuals. Al-Mezaine et al. [53] determined the incidence of chronic endophthalmitis following cataract surgery in a tertiary care eye center to be 1.7 cases per 10,000 individuals. However, determining the real incidence of chronic endophthalmitis might be difficult because of the nature of the disease and its indolent course [53].

16.4.2 Etiology

In 1986, Meisler et al. [54] reported a syndrome of chronic indolent granulomatous uveitis that manifests weeks to months after cataract surgery. This uveitis improves initially with topical corticosteroid therapy but flares up whenever the administration of steroids is tapered or stopped. According to electron microscopy findings and its identification in anaerobic cultures, *Propionibacterium acnes* was determined to be a cause of this syndrome.

In addition to *P. acnes* [53, 55–58], which has been implicated in the majority of cases of chronic endophthalmitis (41–63 %), various

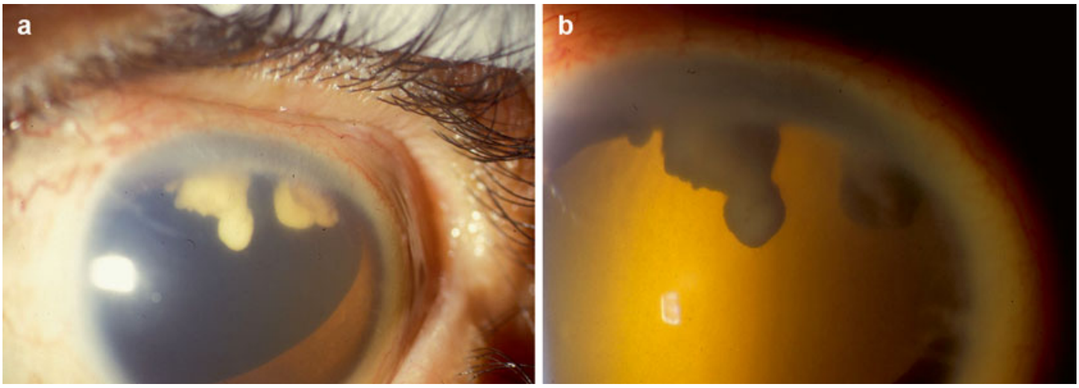

Fig. 16.1 Slit-lamp photograph showing (**a**) white plaque extending from the capsule equator "fluff balls" caused by *Aspergillus terreus*; (**b**) retroillumination (Adapted from Al-Mezaine et al. [53])

organisms have been associated with chronic endophthalmitis, including *Staphylococci* [59–61] (more frequently *S. epidermidis* but occasionally *S. aureus*), fungal organisms [62, 63], *Achromobacter* species [61], *Corynebacterium* species [61], *Mycobacterium chelonae* [64], *Cephalosporium* species [65], gram-negative bacteria (*Alcaligenes xylosoxidans*) [66, 67], and *Actinomyces* species [68], and polymicrobial or mixed infections [67, 69] have also been reported.

16.4.3 Clinical Presentation

Patients with chronic endophthalmitis usually present with low-grade and recurrent uveitis months or even years after cataract surgery. The inflammation starts at the anterior chamber and then progresses to the vitreous. Patients most frequently complain of decreased visual acuity and, to a lesser degree, mild pain, discomfort, and/or redness.

Clinical signs of chronic endophthalmitis might include the presence of cells and flare in the anterior chamber and granulomatous uveitis with precipitates on the cornea and intraocular lens. An infection is generally suspected when a white capsular plaque, representing retained lens particles and sequestered organisms, is present [70]. The endophthalmitis can develop or worsen following Nd-YAG laser posterior capsulotomy, presumably due to liberation of previously loculated organisms [71]. Although the plaque is indicative of *P. acnes* infiltrate, it is also observed with other bacterial and fungal infections [53, 72–74]. Vitritis is usually mild in cases of chronic endophthalmitis. The presence of "fluff balls" or "pearls on a string" in cases of chronic endophthalmitis is seen with fungal infections (Fig. 16.1). Moreover, sectoral iris infiltration by fungal element can occur before the infection developed into fulminant fungal endophthalmitis (Fig. 16.2) [53, 56, 70].

16.4.4 Diagnosis

Diagnosing chronic endophthalmitis poses a challenge. Any intraocular inflammation occurring at any time within several months of a breach of ocular integrity should prompt suspicion of the diagnosis. Anaerobic cultures of intraocular specimens should therefore be monitored for a period of 14 days. However, even after 14 days, these cultures are often negative because most of the organisms are usually sequestered within the capsular bag. Another challenge is the increased likelihood of false-negative culture results owing to the small number of microorganisms in the sample, the physiological requirements of fastidious organisms, and low pathogenicity [75]. Research has shown that PCR is more sensitive than culturing in the detection of chronic endophthalmitis caused by *P. acnes* [76].

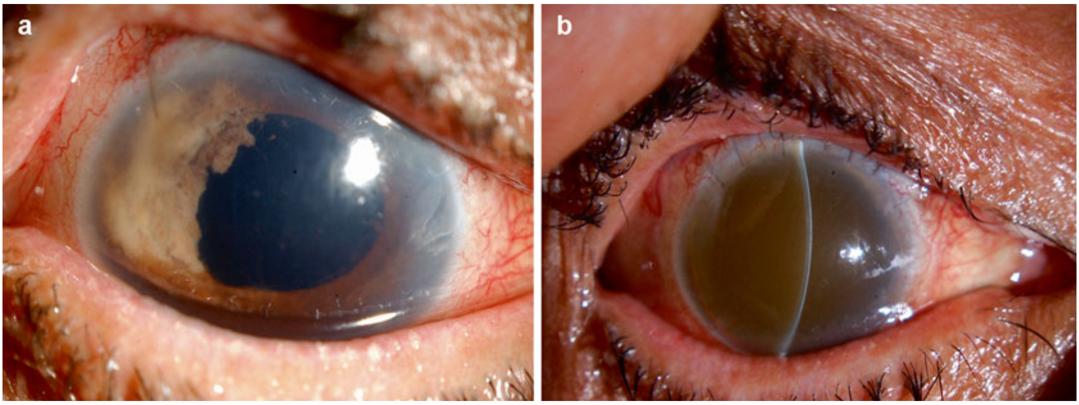

Fig. 16.2 Slit-lamp photograph showing (**a**) sectoral iris infiltration with *Aspergillus niger*; (**b**) fulminant fungal endophthalmitis 2 months later (Adapted from Al-Mezaine et al. [53])

16.4.5 Management

The indolent nature of the organisms and their sequestration within the capsule protects them from host defenses and their different virulence factors make it hard to define a treatment protocol for chronic postoperative endophthalmitis or extrapolate the guidelines set for acute endophthalmitis [70]. Clark et al. [57] and Aldare et al. [58] have proposed several management recommendations: the injection of intravitreal antibiotics alone, followed by PPV with partial capsulectomy, and, lastly, vitrectomy with total capsulotomy and intraocular lens (IOL) removal or exchange.

A cross-sectional review of the biggest case series [53, 57, 59, 77] on chronic endophthalmitis revealed varying results. Differences in causative organism, the type of initial therapeutic method performed, and the extent of the intervention [78] contribute to these varying results. From these series, a total of 98 patients with chronic endophthalmitis were studied. The overall visual outcome was 20/40 or better in about 46 % of the cases, whereas 54 % had varying degrees of visual impairment. An infection caused by *P. acnes* or gram-positive organisms was associated with a better visual outcome (better than 20/40 in more than 50 % of cases) than an infection caused by other types of bacteria. A fungal infection was associated with a more unfavorable prognosis. Those cases in which the initial treatment involved intravitreal injection alone had the highest rate of recurrence (90 %). The performance of PPV and the administration of intravitreal injections were associated with a decreased rate of recurrence in all series. The inclusion of partial capsulotomy to PPV and the administration of antibiotic injections further decreased the rate of recurrence to 42 % [78]. However, in all series, the overall calculated rate decreased to as low as 50 % when treatment involved PPV, intravitreal antibiotic injections, total capsulotomy, and removal or exchange of the IOL, whereas the rate of recurrence was 68 % when PPV was combined with only intravitreal antibiotic injection [78].

16.5 Posttraumatic Endophthalmitis

Infectious endophthalmitis is a devastating complication of open-globe injuries. It comprises approximately 25–30 % of all cases of infectious endophthalmitis. The incidence of culture-positive endophthalmitis after open-globe injuries varies between 0.5 and 17 % [79–93]. Previous reports have demonstrated that delayed primary repair, dirty wound, breach of lens capsule, retained intraocular foreign body (IOFB), grade 4 injury (presenting visual acuity of worse than 5/200 to light perception), placement of primary intraocular lens, needle injuries, and rural setting are associated with an increased risk of posttraumatic endophthalmitis [79, 81–84, 87, 88, 90–93]. Posttraumatic endophthalmitis is associated with its own microbiologic spectrum which is distinct from other subgroups of exogenous endophthalmitis. Gram-positive organisms such as *Bacillus*, *Staphylococci*, and *Streptococci* are frequently isolated pathogens [79–82, 94–101]. Posttraumatic endophthalmitis still carries a poor prognosis. When pooling data from previously reported studies of posttraumatic endophthalmitis, visual acuities of 20/40 or better were preserved only in 37 % of patients. Reasons for guarded prognosis include polymicrobial infection, the virulence of the infecting microorganisms, and possible delayed diagnosis and initiation of treatment. In addition, concomitant injuries may directly result in ocular damage that limits ultimate visual recovery [79–98, 101].

Useful clinical symptoms and signs in the diagnosis of endophthalmitis after open-globe injury include worsening vision and pain, hypopyon, vitritis, retinitis, periphlebitis, as well as corneal ring infiltrate. Diagnostic imaging in the setting of trauma helps in the detection of suspected IOFB or to rule out retinal and choroidal detachments. Axial computed tomography (CT) scans are most useful for localization of metallic IOFBs. Echography facilitates assessment of the degree of vitreous opacification, presence of IOFB, status of the posterior hyaloids face, as well as detection of either choroidal or retinal detachments.

Because of the substantial incidence of endophthalmitis after open-globe injuries, careful consideration should be given to the use of prophylactic antimicrobial therapy. The purpose of prophylaxis is to provide effective antibiotic level as rapidly as possible against a broad range of organisms. The use of systemic antibiotics in the prophylactic treatment of posttraumatic endophthalmitis has become the standard of care in patients with open-globe injuries, on the basis of clinical experience, but there is little experimental evidence that supports the efficacy of such therapy [79, 82, 95]. Ariyasu et al. [102] demonstrated microbial contamination of the anterior chamber at the time of repair in one-third of their eyes with open-globe injuries. None of these eyes developed clinical endophthalmitis. The incidence of positive anterior chamber culture was significantly lower in patients receiving intravenous antibiotics before wound repair compared with patients not receiving such therapy. These data support the prophylactic use of broad-spectrum intravenous antibiotics against the development of posttraumatic endophthalmitis by reducing the incidence of intraocular microbial contamination. Good coverage for most organisms is obtained with intravenous vancomycin coupled with a third-generation cephalosporin, such as ceftazidime, which can penetrate the vitreous cavity in effective levels in inflamed aphakic experimental eyes [103, 104]. Ceftazidime provides effective coverage for gram-negative intraocular infections [103, 105], and vancomycin provides coverage for gram-positive organisms [104, 105]. The beneficial role of prophylactic intravenous vancomycin coupled with ceftazidime was suggested [90, 92].

Animal models have demonstrated the efficacy of intravitreal antibiotics for prophylaxis of posttraumatic endophthalmitis [106, 107]. A small randomized trial showed that prophylactic intravitreal injection of vancomycin (1 mg) and ceftazidime (2.25 mg) decreases the risk of posttraumatic endophthalmitis [108]. Recently, a multicenter study provided strong evidence supporting the role of adjunct intraocular antibiotic injection at the time of primary repair in reducing the rate of posttraumatic endophthalmitis in open-globe injuries with retained IOFB [109]. Some authors recommended prophylactic intravitreal antibiotic administration in high-risk cases [81, 98, 110]. Therefore, it is crucial to identify these high-risk cases. Essex et al. [88] found that cases with ≥2 of the three risk factors (delay in primary repair of ≥24 h, dirty wound, and lens breach) had a relative risk of 5.1 for developing endophthalmitis. They therefore recommended intravitreal antibiotic injection for these cases at the time of primary repair. In a previous study, we identified clinical risk factors for the development of endophthalmitis after repair of open-globe injuries. Our logistic regression analysis indicated that dirty wound was an independent risk factor for the development of endophthalmitis with a relative risk of 11.6. In addition, the presence of retained IOFB in association with rural address or dirty wound was associated with a high risk for the development of posttraumatic endophthalmitis after primary repair. The relative risks were estimated to be 11.0 and 9.2, respectively, for developing endophthalmitis over those with none of these combinations. We therefore would consider prophylactic intravitreal administration of antibiotics in these high-risk groups at the time of primary repair [92]. The combination of vancomycin (1 mg/0.1 ml) and ceftazidime (2.25 mg/0.1 ml) can be considered in these cases.

Initial treatment of posttraumatic endophthalmitis includes intravitreal antibiotic injection. Directly injecting antibiotics into the globe affords highest drug concentration in the vitreous humor. One must cover gram-positive and gram-negative organisms when treating posttraumatic endophthalmitis. For initial therapy, we recommend intravitreal vancomycin (1 mg/0.1 ml) and ceftazidime (2.25 mg/0.1 ml). In addition to appropriate antibiotic treatment, early therapeutic vitrectomy is often indicated. The use of silicone oil tamponade in vitrectomy for posttraumatic endophthalmitis has been shown to be useful [111, 112].

16.6 Bleb-Associated Endophthalmitis

Bleb-associated infections are infrequent but potentially devastating complication after glaucoma-filtering surgery. The spectrum of disease severity ranges from infection limited to the filtering bleb to intraocular extension leading to endophthalmitis. Blebitis is defined as presumed infection in or around the filtering bleb without vitreous involvement. It may be associated with mild to moderate anterior chamber inflammation.

Bleb-associated endophthalmitis is a devastating complication of glaucoma-filtering surgery. It denotes bleb infection with involvement of the vitreous. The presence of inflammatory cells in the vitreous is a key for differentiating endophthalmitis from blebitis. It usually develops months or years after glaucoma-filtering surgery. Risk factors for its development include the use of an antifibrotic agent, an inferior bleb location, thin bleb, bleb leak, chronic use of antibiotics, blepharitis, prior conjunctivitis and upper respiratory infection, and a history of bleb infection.

The widespread introduction of antiproliferative agents such as 5-fluorouracil and mitomycin-C as an adjunct use in trabeculectomy has remarkably improved the success rate of filtration surgery. However, their use results in formation of thin, avascular blebs, increased risk of late bleb leaks, and a higher incidence of endophthalmitis. Lehmann et al. [113] reported the odds of endophthalmitis to be three times higher in patients who receive antiproliferatives versus those who do not. The reported incidence of bleb-associated endophthalmitis, after glaucoma-filtering procedures with adjunctive mitomycin-C, ranges from 2.1 to 3.2 %. This incidence is higher than the reported rate in eyes undergoing filtering surgery without the use of antifibrotic agents [114–116].

A different microbiological spectrum distinguishes this group from endophthalmitis observed in other clinical settings [114, 117–125]. Unlike acute postoperative endophthalmitis, which results from direct intraoperative inoculation of microorganisms, bleb-associated endophthalmitis follows transconjunctival migration of bacteria into the eye [117]. The poor visual outcome in bleb-associated endophthalmitis could be because of its association with the virulent *Streptococcus* species and gram-negative bacteria such as *Haemophilus influenzae*. Exotoxins produced by *Streptococcus* species might aid the organism in penetrating through intact conjunctiva overlying the bleb. Bleb-associated endophthalmitis is associated with its own microbiologic spectrum which is distinct from that of acute-onset endophthalmitis after cataract surgery. In acute-onset endophthalmitis after cataract surgery, the less virulent coagulase-negative staphylococci, predominantly *Staphylococcus epidermidis*, was the most common organism, accounting for 70 % of the isolates [105]. On the other hand, the more virulent streptococcal species and gram-negative bacteria such as *Haemophilus influenzae* are more common causes of delayed-onset bleb-associated endophthalmitis [114, 117–125]. Streptococcal species produce exotoxins and are capable of penetrating the intact conjunctiva overlying the bleb with rapid spread into the anterior chamber and vitreous. The most common isolates are *Streptococcus* species and gram-negative bacteria, predominantly *Haemophilus influenzae*, followed by *Staphylococcus epidermidis* [114, 117–125]. The rate of isolation of *Streptococcus* species in bleb-associated endophthalmitis is higher than the 9.0 % rate found in endophthalmitis after cataract surgery [105]. Endophthalmitis caused by *Streptococcus* species was reported to be associated with an aggressive clinical course and a correspondingly poor visual prognosis [126, 127]. Series of bleb-associated endophthalmitis reported that *Streptococcus* species was the organism most frequently associated with poor visual prognosis [114, 117–122, 124]. These findings are consistent with the results of the Endophthalmitis Vitrectomy Study showing that patients with growth of coagulase-negative *Staphylococci* achieved the best visual outcome and that *Streptococci* were associated with the poorest visual outcome [128]. Therefore, the favorable overall visual outcome in patients with endophthalmitis after cataract-related surgery relative to patients with bleb-associated endophthalmitis might be related to the high frequency of infection with coagulase-negative *Staphylococci* in endophthalmitis after cataract-related surgery [105].

Bleb-associated endophthalmitis still carries a poor prognosis. In combining previously reported studies, visual acuities of 20/400 or better were preserved in only 43 % of patients, and 24 % of patients had final visual acuity of no light perception. Reasons for guarded prognosis include the virulence of infecting organisms [114, 117–122, 124] and ocular comorbidities, such as the advanced stage of glaucoma in many of these patients. However, the poor outcome may also suggest the lack of an effective treatment regimen. In our series we identified a significant association between good visual outcome and better presenting visual acuity, shorter interval from onset of symptoms to treatment, and clear cornea at presentation in the univariate analysis. Shorter interval from onset of symptoms to treatment retained statistical significance in the multivariate analysis. In addition, univariate and multivariate analyses identified diabetes mellitus to be a negative predictor of good visual outcome [124].

Early diagnosis and prompt intensive treatment of blebitis are critical in view of rapid deterioration and potential risk of progression to endophthalmitis, which has relatively devastating outcome. In early stage, conjunctival injection localized to the region of filtering bleb may be noted. Later bleb appears milky, with loss of translucency. Turbid fluid inside bleb may be visible, possibly with frank purulent material in or leaking from the bleb. Inflammatory cells may spill over into the anterior chamber. Hypopyon in the presence of signs of external bleb infection indicates endophthalmitis until proven otherwise. The presence of inflammatory cells within the vitreous is key for differentiating endophthalmitis from blebitis. Slit-lamp biomicroscopy examination of the bleb and Seidel test to detect any bleb leak should be performed. Ultrasound examination of vitreous should be performed if fundus examination is obscured due to inflammation. A swab of conjunctiva over the bleb and an anterior chamber tap should be performed for Gram stain and culture sensitivity before starting antibiotic therapy. Vitreous tap also should be performed if a hypopyon is present or there is any indication of involvement of the vitreous.

Intensive topical broad-spectrum antibiotic regimen alone is appropriate for patients with blebitis, without evidence of vitreous involvement. After the antibiotics have been used for about 24 h and signs of improvement of blebitis become evident, topical steroid should be initiated to prevent scarring and preserve the filtration site. The EVS guidelines for the treatment of post-cataract surgery endophthalmitis [129] cannot be applied to bleb-associated endophthalmitis because it is different in its presentation, infective organisms, and prognosis. Bleb-associated endophthalmitis needs more aggressive treatment. Recent retrospective studies demonstrated that patients treated with initial vitrectomy had better visual outcome and a lower incidence of no light perception vision than those treated with tap and injection [122, 124]. On the other hand, other studies [121, 125] reported worse visual outcome with vitrectomy. In these studies, the patients who underwent initial vitrectomy had a more severe infection and poorer visual acuity at time of endophthalmitis diagnosis. Because of this selection bias, final visual outcomes would be expected to be worse in the vitrectomy group.

Compliance with Ethical Requirements

Conflict of Interest The authors declare that they have no conflict of interest.

Informed Consent No human studies were carried out by the authors for this article.

Animal Studies No animal studies were carried out by the authors for this article.

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