CLINICAL CASE REPORT

Bilateral Endogenous Bacterial Panophthalmitis

Lina Krėpštė, Reda Žemaitienė, Valerijus Barzdžiukas, Arūnas Miliauskas
Department of Ophthalmology, Medical Academy, Lithuanian University of Health Sciences, Lithuania

Key Words: endogenous endophthalmitis; bacterial panophthalmitis; Streptococcus pneumoniae; intravitreal antibiotic; meningitis.

Summary. We present a case of meningitis with bilateral endogenous bacterial panophthalmitis in a previously healthy individual. The management of this ocular condition is unclear, and the prognosis is poor. The patient was admitted to the Clinic of Eye Diseases after a 9-day treatment with systemic antibiotics with a complete systemic recovery but impaired vision of both eyes. Functional vision was restored in the better eye with intravitreal vancomycin and pars plana vitrectomy. Nevertheless, after the removal of silicone oil, phthisis bulbi began to develop. Better outcomes could be expected if bacteremic patients were examined routinely by an ophthalmologist and, in case of endogenous bacterial endophthalmitis, treated with intravitreal antibiotics.

Introduction

Infectious endophthalmitis is a potentially blinding eye condition when intraocular spaces with structures from the anterior and posterior segments are involved. Exogenous endophthalmitis is caused by microorganisms entering the intraocular space due to the eye wall defect after trauma, ocular surgery, or cornea ulcer. The rates of postoperative endophthalmitis are reported to be 0.05%–0.29% (1). Endogenous endophthalmitis (EE) occurs in approximately 5% of endophthalmitis cases (2) and indicates the hematogenous spread of an infective agent to an eye from another site in the body. The incidence of EE in bacteremic patients is 0.06%–0.44% (3). The final visual outcome is worse than counting fingers in 69% (4), and the mortality rate due to this condition is 30%–50% since it usually develops in chronically ill patients (4, 5). Despite the severity and miserable outcomes of the condition, the best management is still unclear.

We present a case of severe meningitis and concurrent bilateral endogenous panophthalmitis – the most advanced form of EE – in a young, previously healthy individual.

Case Report

A 41-year-old Caucasian man presented to the Clinic of Eye Diseases, Hospital of Lithuanian University of Health Sciences, following a 9-day treatment in the Clinic of Infectious Diseases, Kaunas Clinical Hospital, including 3 days in the Inten-

sive Care Unit due to cerebral edema, meningitis, and bilateral vision loss. He received ceftriaxone at a dosage of 2 g twice a day intravenously and 0.3% tobramycin drops 3 times a day to both eyes. A cerebral spinal fluid (CSF) specimen was taken on the first hospitalization day in the Clinic of Infectious Diseases, and the CSF culture was positive for *Streptococcus pneumoniae* sensitive to penicillin, erythromycin, cefotaxime, and trimethoprim with sulbactam. Despite a systemic recovery without a neurologic deficit, bilateral vision loss and ocular pain remained severe.

On admission to the Clinic of Eye Diseases, the right eye showed the visual acuity of no light perception, and the left eye, visual acuity of light perception with incorrect projection. The proptoses were considerable, more significant in the right eye. Ocular hypertension was present in both eyes (4+ by palpation). The eyelids of both the eyes were swollen with marked ptosis and significant conjunctival hyperemia and chemosis. The right eye was immobile, and there was no adduction in the left eye. The slit-lamp examination of the right eye revealed the infiltrated, melting cornea with total hypopyon (Fig. 1). There was hypopyon (0.5 mm), exudative pupillary membrane, iris hyperemia at the pupillary border, *seclusio pupillae,* and no red reflex or view of the fundus in the LE, but the cornea was clear (Fig. 2). Ultrasound sonography of this eye showed numerous membranous vitreous opacities and the thickened retina, choroid, sclera, and optic nerve (Fig. 3) but no vitreous or retinal detachment.

Computed tomography of the head revealed inflammatory changes of the eyeballs (more significant in the right eye) involving the walls, moderate

Correspondence to L. Krėpštė, Department of Ophthalmology, Medical Academy, Lithuanian University of Health Sciences, Eivenių 2, 50028 Kaunas, Lithuania
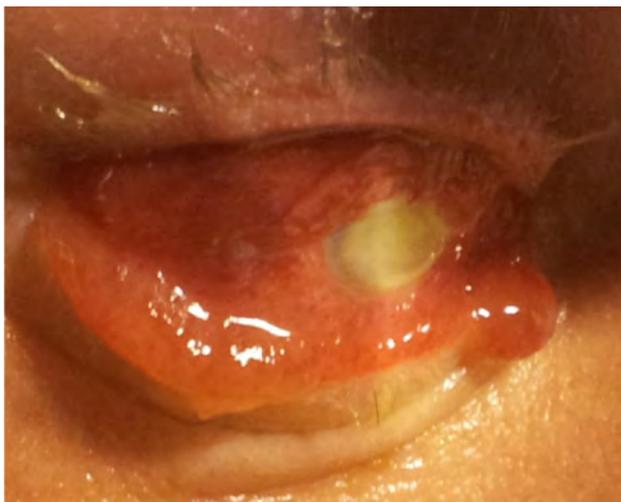E-mail: krepste@gmail.com

Fig. 1. The right eye at presentation: significant conjunctival hyperemia and chemosis, infiltrated, melting cornea, and total hypopyon
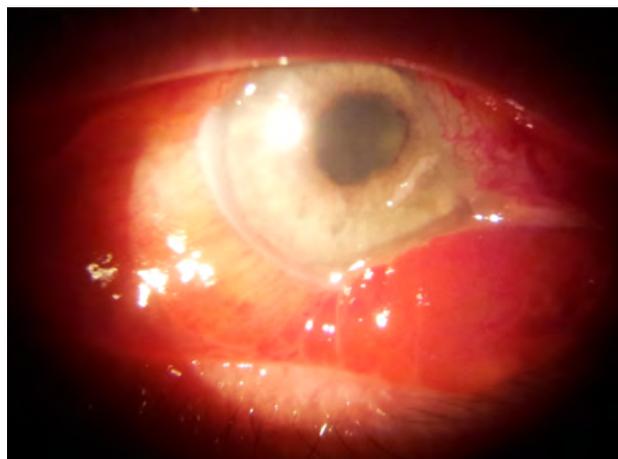

Fig. 2. The left eye at presentation: conjunctival hyperemia and chemosis, clear cornea, exudative pupillary membrane, iris hyperemia at the pupillary border, and *seclusio pupillae*
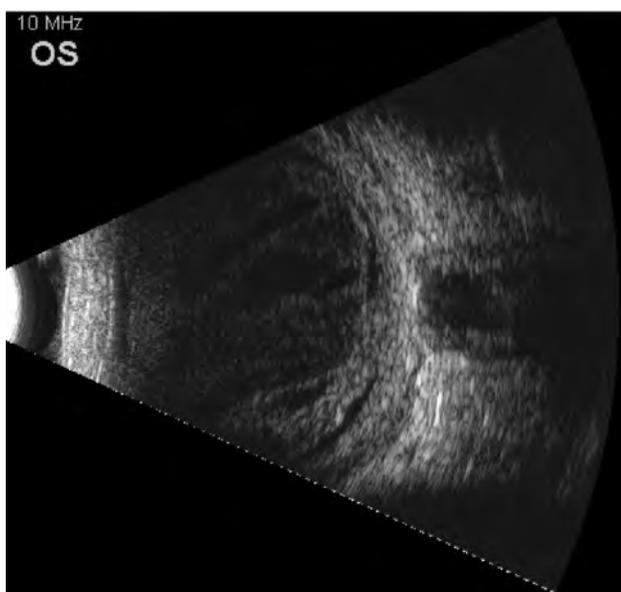

Fig. 3. Ultrasound sonography of the left eye: membranous opacities in the undetached vitreous with edema of the retina, the choroid, the sclera, and the optic nerve

Fig. 4. Computed tomography: inflammatory changes in the preseptal and retrobulbar spaces and both eyeballs

signs of retrobulbar cellulitis, and shaded but not enlarged contours of the optic nerves (Fig. 4).

On the first day at our clinic (the ninth day of illness), the findings from the CSF examination were normal, and a complete blood count test showed leukocytosis (15.4×10^9/L) with polymorphonuclear leukocytes accounting for 70.9%. The C-reactive protein level was 45.37 mg/L, which was substantially decreased compared with that on the first day of the illness (238 mg/L). The results of other labo-

ratory tests and electrocardiography were normal.

The diagnosis of endogenous bilateral panophthalmitis was made on the first day of arrival to the clinic after the abovementioned tests, and a prompt treatment was started. Before the intravitreal injections of vancomycin, the specimens from the anterior chamber, the vitreous, and the conjunctivas were cultured, which were negative to bacteria. The treatment is outlined in Table.

Despite the treatment, vision in the right eye did

Table. Conservative Treatment of Bilateral Panophthalmitis

Medications	Doses/Regimens	Notes
Intravitreal		
Vancomycin 1 mg/0.1 mL	0.1 mL on alternate days	Possible after paracentesis due to ocular hypertension
Intravenous		
Ceftriaxone	2 g × 2/d	
Metronidazole	500 mg × 3/d	
Vancomycin	1 g × 2/d	
Per os		
Acetazolamide	500 mg × 2/d	
KCl	750 mg × 20/d	
Intracameral		
Epinephrine	Once	Posterior synechiae were immediately broken
Subconjunctival		
Dexamethasone 0.1%	×1/d	
Vancomycin	×1/d	
Epinephrine	×1/d	
Topical		
Ciprofloxacin drops 0.3%	×5/d	
Tobramycin ointment 0.3%	×2/d	
Diclofenac drops 0.1%	×3/d	
Cyclopentolate 1%	×2/d	
Timolol 0.5%	×2/d	
Dorzolamide 2%	×2/d	

not recover, and pain in the eye intensified. After the 5-day treatment, intermittent left bundle branch block was observed in the electrocardiogram, and infectious vegetations of the aortic valve were suspected, which hastened the enucleation of the right eye. The histological examination of the enucleated eye revealed vast neutrophilic infiltration of all the ocular structures, including the fibers of the extraocular muscles and a purulent exudate in all the intraocular spaces.

The left eye responded immediately to intravitreal vancomycin. On the next day, pain in the eye, hyperemia, and chemosis of the conjunctiva decreased and hypopyon disappeared. Two days later, vision acuity of hand movements was documented, but adduction was still limited.

Pars plana vitrectomy (PPV) and lensectomy were performed, when the left eye stopped improving, and the intraocular pressure normalized. The vitreous was white, organized with no signs of active disease, and undetached. After core vitrectomy, necrosis of the retina at 2- to 7-o'clock position reaching the macula was found, and the fovea looked altered. Retinectomy at 2- to 7-o'clock position sparing the macula was performed (the necrotized retina did not bleed); the retina was fixed by cryocoagulation. At the end of the operation, an intravitreal injection of vancomycin and tamponade with silicone oil (Oculentis 5000) were made. An intraocular lens was not implanted.

On the next day, the patient was transferred to the Clinic of Cardiac, Thoracic, and Vascular Surgery for prosthesis of the aortic valve.

After 13 weeks following PPV, best-corrected visual acuity (BCVA) of the left eye was 0.07, and the adduction was incomplete; there were slight signs of band keratopathy and no signs of inflammation, and the retina was attached with a grayish change in the macula inferonasally from the fovea (Fig. 5). BCVA was the same after the next 4 weeks, but keratopathy was developing further, and the silicone oil had to be removed. Two weeks after the removal of silicone oil, visual acuity decreased to light perception due to hypotony and significant swelling of the retina and the choroid, which were suggestive of developing phthisis bulbi. A 5-month follow-up

Fig. 5. Fundus of the left eye after 13 weeks following pars plana vitrectomy: remaining retina attached, green–grayish macula parafoveal and nearby chorioretinal scars from cryocoagulation

showed the same visual acuity, but eyeball shrinkage was observed.

Discussion

Endogenous bacterial endophthalmitis (EBE) is the result of bacterial multiplication within the eye after bacteria cross the blood-ocular barrier during bacteremia. Associated conditions are related to an immune-compromised state, such as chronic diseases, especially diabetes mellitus, malignancies, therapy, long-term catheters, intravenous drug abuse, or invasive surgery. Predisposing factors for the condition were indicated in 40%–100% of EBE cases (3, 4, 6).

The source and the most frequent causative agents of the infection vary greatly comparing the Asian and Caucasian populations. In the latter, gram-positive bacteria dominate (60.7% of EBE cases with *Staphylococcus aureus* and *Streptococcus pneumoniae* being the most common); in the Asians, gram-negative microorganisms dominate with *Klebsiella species* in 77.4% of cases (4). Pyogenic metastases besides endophthalmitis include arthritis, endocarditis, pneumonia, meningitis, infection of the hepatobiliary (common for *Klebsiella*), renal, or urinary tracts, and skin infection, which all could be a primary focus of bacteremia (3–5, 7). Microorganisms are cultured from intraocular fluids, blood, or relevant sites. A negative blood or vitreous culture does not exclude EBE as a positive blood culture is observed in 33%–75% and a positive vitreous culture in 56% of EBE cases (3).

The period from systemic to ocular signs in EBE is short. The reported range is from a simultaneous presentation to 35 days with the mean varying from 4.4 to 6.7 days (3, 4, 7). The rapid manifestation of ophthalmic symptoms from the onset of sepsis is associated with a poorer prognosis (4) and may serve as a marker of a high virulence of the bacteria. In our case, the virulence of the microorganisms was also the foremost factor for concurrent severe bilateral endophthalmitis and meningitis since the individual without any possible predisposing condition was suddenly affected.

According to the literature sources, 53.1%–63.6% of EBE cases result in no light perception, phthisis bulbi, and evisceration or enucleation, and in 69%, the final visual acuity is worse than counting fingers (3, 4, 7). The suggested prognostic factors for poorer outcomes are different and contradictory. The possible factors include a delay in diagnosis, time to ocular symptoms, use of inappropriate antibiotics, infection with virulent organisms, namely gram-negative bacteria and group B *Streptococcus pneumoniae*, diffuse infection/panophthalmitis, hypopyon, and opaque media (3,4, 7).

Our patient was severely ill from the onset of the disease as it is in many septic patients. Meningitis could have been just another pyogenic metastasis as *Streptococcus pneumoniae* is capable of spreading rapidly. Still we consider it as a primary focus due to the fact that bacterial meningitis is mainly caused by *Streptococcus pneumoniae* (8), and no other infectious focus was found except endocarditis 2 weeks after the onset of the disease. Theoretically, the bacteria could have spread to the eyes through the meningeal layer, but bacteremia and hematogenous spread were proven by the presence of endocarditis.

The ocular presentation of EE in the present case was typical and met all the criteria for panophthalmitis according to the classification proposed by Greenwald et al. (9). The prognosis of EBE of such a grade is very poor. For instance, all the bacterial panophthalmitis cases observed by Greenwald et al. resulted in blindness and phthisis bulbi or were enucleated (9). Bilateral cases are more commonly caused by EE of fungal than bacterial origin, i.e., 33%–45% vs. 13%–25% (6, 9).

Delay in recognizing EBE occurs mainly for 2 reasons: a severe systemic state deterring early detection or diagnostic errors. The most frequently (37.5%) reported misdiagnosis was noninfectious uveitis as an acutely inflamed eye with hypopyon mimics Behcet's disease and involvement of multiple joints suggests the diagnosis of Reiter's syndrome (3, 5). The diagnosis is facilitated by septic appearance and panophthalmitis. Extreme eyelid swelling, as in the case of our patient, may suggest cavernous sinus thrombosis or orbital cellulitis (3).

Despite the rapid systemic improvement due to treatment with intravenous antibiotics, the condition of our patient was deteriorating, and the left eye improved only after the administration of intravitreal vancomycin. Such a case suggests that the therapeutic levels of systemic antibiotics were not reached within the vitreous regardless of the damaged blood-ocular barrier. The administration of systemic antibiotics may be insufficient for the treatment of EBE despite their good ocular penetration (penicillin or cephalosporins). Data show an improvement in visual outcomes and a reduction in evisceration/enucleation rates with intravitreal antibiotics (3). The time from the onset to the efficacious treatment (intravitreal vancomycin) in our case was 9 days, which is consistent with the reported mean of a 9.5-day delay in misdiagnosed EBE cases (3). We did not treat with intravitreal steroids since they are associated with a worse visual outcome (10).

The role in saving the vision function and the timing of PPV in EBE are not as clear as it is in

cases of postoperative endophthalmitis after the Endophthalmitis Vitrectomy Study. Some reviews show an unrelated visual outcome to the use of PPV (4, 5); others suggest that eyes after PPV are more likely to retain useful vision and less likely to be eviscerated/enucleated (3). The general rationale for a procedure is obtaining vitreous samples, clearing the vitreous, and reducing the amount of infective organisms, toxins, or inflammatory substances in order to prevent retinal necrosis. Nevertheless, an inflammatory response and exotoxins may irreversibly damage photoreceptors within 24 hours of inoculation (3); so, in case of a virulent organism, only early PPV could hinder necrosis. There was no reason for prompt PPV in our case since the patient was admitted to the Clinic of Eye Diseases after 9 days; the bacteria were cultured from the CSF, and above all, intravitreal vancomycin was effective. We proceeded with vitrectomy only when no improvement was observed in the left eye.

Conclusions

Though initially functional vision in the better eye was restored, phthisis bulbi began to develop after the removal of the silicone oil, proving many factors of a bad prognosis in EBE: a delay in diagnosis, an infection with a virulent organism, simultaneous systemic and ocular symptoms, panophthalmitis, opaque media at presentation, and hypopyon. Better outcomes of EBE could be expected if bacteremic, especially unconscious, patients were examined routinely by an ophthalmologist and, in case of EBE, prompt intravitreal antibiotics were administered.

Statement of Conflict of Interest
The authors state no conflict of interest.

References

1. Nagaki Y, Hayasaka S, Kadoci C, Matsumoto M, Yanagisawa S, Watanabe K, et al. Bacterial endophthalmitis after small-incision cataract surgery. J Cataract Refract Surg 2003;29:20-6.
2. Chee SP, Jap A. Endogenous endophthalmitis. Curr Opin Ophthalmol 2001;12:464-70.
3. Jackson TL, Eykyn SJ, Graham EM, Stanford RM. Endogenous bacterial endophthalmitis: a 17-year prospective series and review of 267 reported cases. Surv Ophthalmol 2003; 48:403-23.
4. Wong JS, Chan TK, Lee HM, Chee SP. Endogenous bacterial endophthalmitis: an east Asian experience and a reappraisal of a severe ocular affliction. Ophthalmology 2000; 107:1483-91.
5. Lee SH, Chee SP. Group B streptococcus endogenous endophthalmitis: case reports and review of the literature. Ophthalmology 2002;109:1879-86.
6. Schiedler V, Scott IU, Flynn HW, Davis JL, Benz MS, Miller D. Culture-proven endogenous endophthalmitis: clinical features and visual acuity outcomes. Am J Ophthalmol 2004;137:725-31.
7. Ang M, Jap A, Chee SP. Prognostic factors and outcomes in endogenous Klebsiella pneumoniae endophthalmitis. Am J Ophthalmol 2011;151:338-44.
8. Koedel U, Scheld WM, Pfister HW. Pathogenesis and pathophysiology of pneumococcal meningitis. Lancet Infect Dis 2002;2:721-36.
9. Greenwald MJ, Wohl LG, Sell CH. Metastatic bacterial endophthalmitis: a contemporary reappraisal. Surv Ophthalmol 1986;31:81-101.
10. Shah GK, Stein JD, Sharma S, Sivalingam A, Benson WE, Regillo CD, et al. Visual outcomes following the use of intravitreal steroids in the treatment of postoperative endophthalmitis. Ophthalmology 2000;107:486-9.