

Chapter 2

Management of Endophthalmitis

Vivek P. Dave and Taraprasad Das

Infectious endophthalmitis is initially a clinical diagnosis made on the constellation of signs and symptoms discussed before. The commonest test beyond clinical examination by slit lamp and indirect ophthalmoscopy is the ultrasonography.

B-scan ultrasound usually shows low- to medium-amplitude vitreous echogenicity and variable amount of choroidal thickening. It can also pick up associated features like retinal detachment, choroidal detachment, or retained intraocular foreign body. In cases with opaque cornea or significant cataract, serial B-scan ultrasound examination is helpful in documenting improvement or worsening by assessing the intensity of the echoes. Though no correlation is seen between the baseline echographic features in endophthalmitis and the infecting organism, the presence of advanced echographic features like dense vitreous opacities, marked vitreous membranes, retinal detachment and choroidal detachment is associated with a relatively poor visual outcome [1, 2] (Figs. 2.1, 2.2, 2.3, 2.4, and 2.5).

Prior to deciding the treatment plan and discussing with the patient (and the family), one must know the following details because it could impact in decision-making:

1. What is the duration between the event (surgery/trauma/systemic disease) and the manifestation? Usually virulent organisms manifest faster than less virulent infection. A chronic infection could be due to a slow-growing organism or even a fungus.
2. In event of trauma, what was the scene of injury? A metal foreign body is different than a vegetative one, and a road traffic injury is different than injury in a relatively clean work place. This helps in suspecting infective organism.
3. Is this bilateral? This could be endogenous in nature.

V.P. Dave, M.D., F.R.C.S (✉) • T. Das, M.D.
LV Prasad Eye Institute, Hyderabad, India
e-mail: vivekoperates@yahoo.co.in

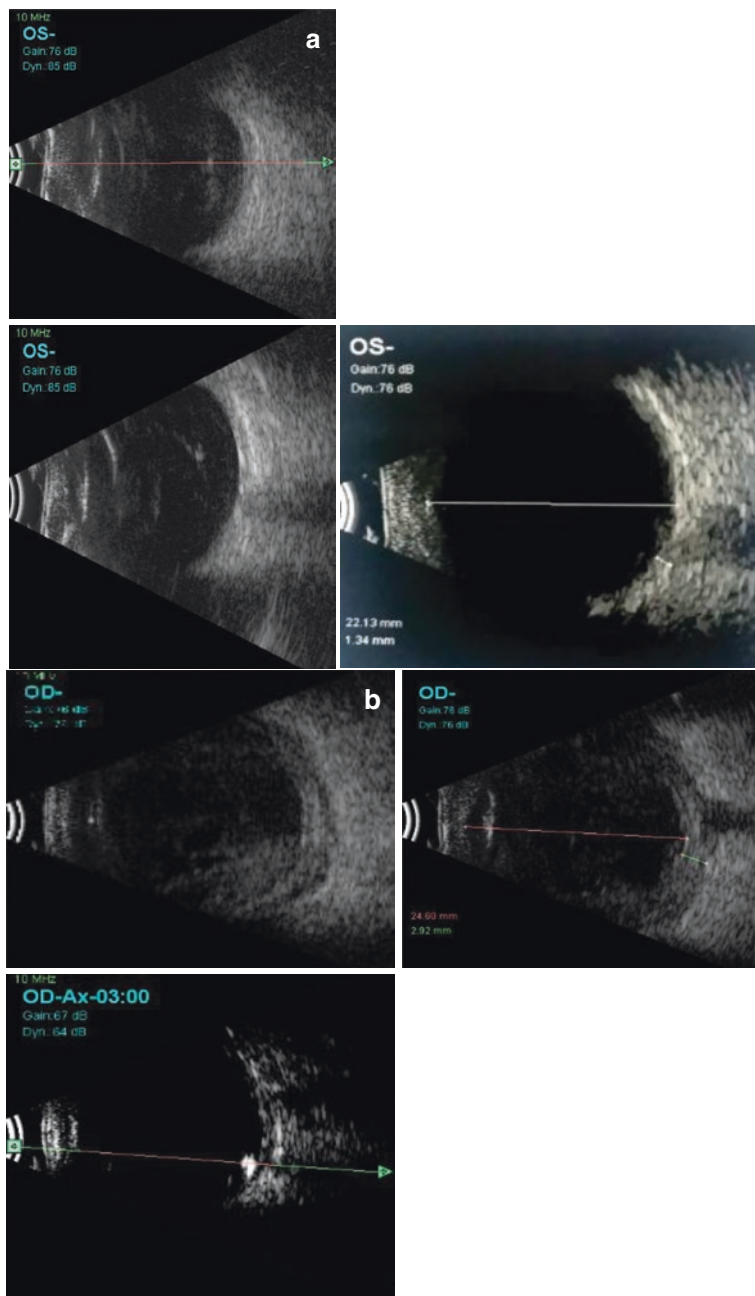


Fig. 2.1 (a) *Top*: B-scan in endophthalmitis showing multiple low to medium reflective echoes in the vitreous cavity. *Bottom-left*: B-scan in endophthalmitis showing membrane-like echoes in the vitreous cavity. *Bottom-right*: minimal echoes on B-scan in a case of resolved endophthalmitis. (b) *Top*: endophthalmitis progressed to panophthalmitis with vitreous echoes and T-sign suggestive of sub-Tenon's fluid. *Bottom*: endophthalmitis following open-globe injury showing a high reflective echo with posterior shadowing suggestive of a retained intraocular foreign body

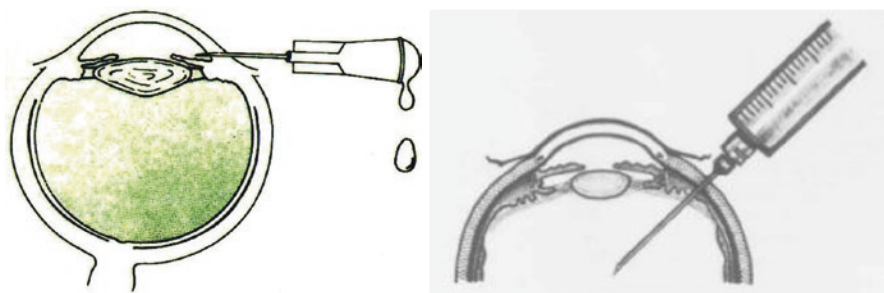


Fig. 2.2 Ocular fluid collection. *Left*—aqueous humor collection; *right*: vitreous humor collection

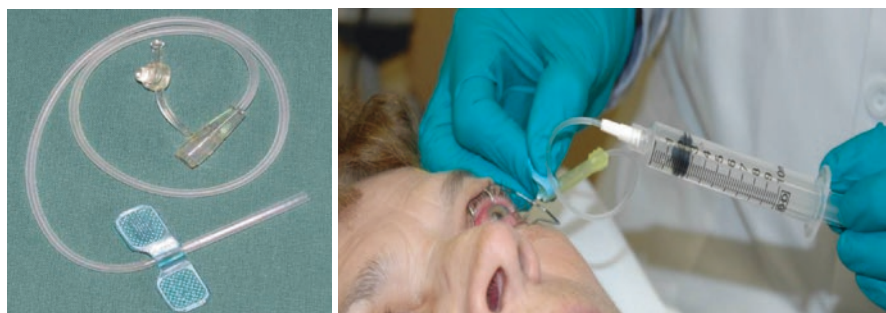


Fig. 2.3 *Left*: butterfly needle. *Right*—vitreous humor collection using a butterfly needle and 10 ml syringe (Courtesy: Harry W. Flynn Jr., MD)

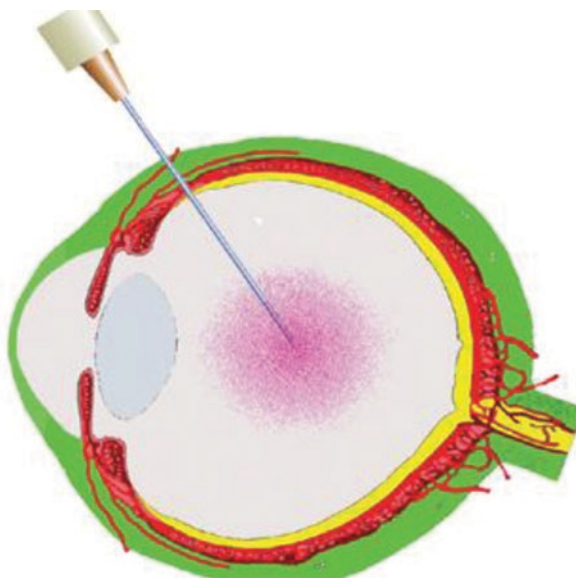


Fig. 2.4 Injection of intravitreal antibiotic into the mid-vitreous cavity

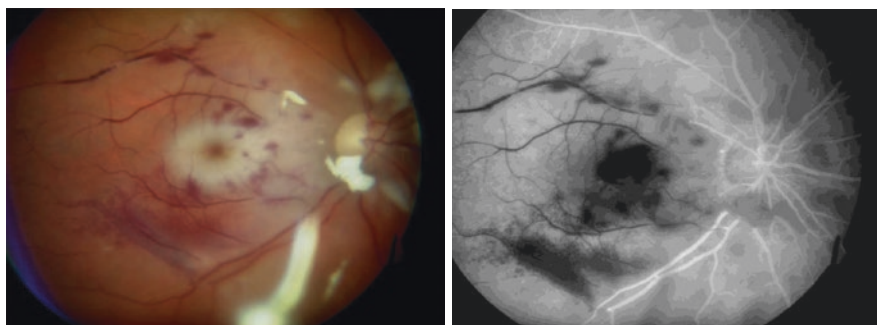


Fig. 2.5 Macular infarction after intravitreal amikacin 0.4 mg in *Staphylococcus epidermidis* endophthalmitis. *Left*—color photo shows attenuated vessels and edema of the posterior pole; *right*: fluorescein angiography shows nonfilling of the posterior pole arteries even in the late phase (Courtesy: Avinash Pathengay, MD)

The First Management Steps

The five essential management principles in management of infectious endophthalmitis are (1) collection of ocular fluid (aqueous/vitreous) specimen for microbiological study; (2) injection of intravitreal antibiotics; (3) intravitreal corticosteroid, when required; (4) vitrectomy, when required; and (5) care of all associated eye injuries.

Collection of Ocular Fluid Specimen

The aqueous humor collection is similar to a paracentesis (Fig. 2.2 left). Following appropriate anesthesia of the eye (usually topical anesthesia) and eye surface sterilized (typically with 5% povidone-iodine), the eye is stabilized with a pair of forceps, and the sample is taken with a small gauge (23–27 gauge) needle attached to a tuberculin syringe. The needle is kept over the iris to avoid trauma to the crystalline lens. It is not ideal to disturb the hypopyon, for fear of creating a tract. A 0.2 ml of fluid is ideal and is processed for microbiology (see the microbiology section of the book).

The mid-vitreous is the ideal location for vitreous humor collection, and when not possible, it is collected from the anterior vitreous. A 0.5 ml undiluted vitreous is ideal. This can be collected manually using a 2 ml syringe or using a vitreous cutter. The eye is anesthetized (usually a peribulbar block), the ocular surface is sterilized (typically, with 5% povidone-iodine), the instrument (needle mounted on a syringe or the vitreous cutter) is inserted in the pars plana region (3.5–4 mm from the limbus), and the required sample is withdrawn for microbiological study. When vitreous surgery is a part of the management, the vitreous fluid is collected using a vitreous cutter. In this case, the vitrector is placed in the mid-vitreous

cavity, and a manual suction could be applied over the aspiration port of the vitrector. In either case, it is necessary that the needle/vitrector tip is visible to the surgeon (Fig. 2.3 right).

A safe vitreous aspiration method has been described using a butterfly needle [3]. In this case the 23 gauge butterfly needle is inserted in the pars plana region to the mid-vitreous cavity, and using a manual suction with a 10 ml syringe, vitreous fluid is collected in the silicone tubing of the butterfly needle system (Fig. 2.3). The collected vitreous sample is sent directly for microbiological processing. This could be safely used for aqueous humor collection.

Intravitreal Antibiotic Injection

Intravitreal antibiotics are given after withdrawal of intraocular fluid, preferably vitreous, or at least aqueous humor, and after vitrectomy, when this is done. The preparation of the antibiotic is described in another chapter (Chap. 22). They are taken in individual syringe and injected slowly in the mid-vitreous cavity with the beveled of the needle pointed to the pupillary area (Fig. 2.4). It is necessary to inject the correct dose of antibiotic, and hence a correct preparation is imperative. Some antibiotics are known to be retina toxic, especially the aminoglycosides, and hence one must not inject the incorrect dose, inject in the mid-vitreous cavity, and take precaution that the drug does not settle on the macula. Two antibiotics are injected, typically one against gram-positive bacteria and one against gram-negative bacteria. In case of fungal infection, only one antifungal antibiotic is injected. The volume of each antibiotic is 0.1 ml, and when required, they could be repeated 36–72 h after the first injection.

Macular infarction is not uncommon with wrong dosage or incorrect method of injection (Fig. 2.5). So as to reduce the dilution error for the commonly used antibiotics (vancomycin, ceftazidime, and voriconazole), the recently introduced E-Kit (Aurolab, Madurai, India; available in India currently) has made the dilution steps easier—add 10 ml of BSS to the antibacterial antibiotic and add 1 ml for the antifungal antibiotic to withdraw 0.1 ml for intravitreal injection [4] (Table 2.1). The current E-Kit contains only four standard intravitreal drugs—two antibacterial antibiotics (ceftazidime and vancomycin), one antifungal antibiotic (voriconazole), and one corticosteroid (dexamethasone) (Fig. 2.6).

Intravitreal Corticosteroid Injection

Dexamethasone is the commonest intravitreal corticosteroid used in endophthalmitis. The intravitreal dose is 0.4 mg in 0.1 ml; it is directly withdrawn from the vial that contains 4 mg dexamethasone phosphate. The details of dexamethasone and other corticosteroid injection are described in another chapter (Chap. 23). Intravitreal

Table 2.1 Traditional and E-Kit dilution steps of three common antibiotics

Antibiotic		Traditional	E-Kit
Vancomycin	Vial size	500 mg	100 mg
	Dilution steps	1. Add 10 ml BSS 2. Withdraw 0.2 ml 3. Add 0.8 ml to make it to 1 ml 4. Keep 0.1 ml	1. Add 10 ml BSS 2. Withdraw 0.1 ml
	Final dose	1 mg in 0.1 ml	
Ceftazidime	Vial size	500 mg	250 mg
	Dilution steps	1. Add 2.2 ml BSS 2. Withdraw 0.1 ml 3. Add 0.9 ml to make it to 1 ml Keep 0.1 ml	1. Add 10 ml BSS 2. Keep 0.1 ml
	Final dose	2.25 mg in 0.1 ml	
Voriconazole	Vial size	200 mg	1 mg
	Dilution steps	1. Add 20 ml BSS 2. Withdraw 0.1 ml 3. Add 0.9 ml to make it to 1 ml 4. Keep 0.1 ml	1. Add 1 ml BSS 2. Keep 0.1 ml
	Final dose	0.1 mg in 0.1 ml	



Fig. 2.6 E-Kit

dexamethasone helps reduce the inflammation element in endophthalmitis without compromising the final visual acuity irrespective of the culture positivity [5] (Fig. 2.7).

Vitrectomy

Vitrectomy (Fig. 2.8) is the second key to management of endophthalmitis after intravitreal antibiotics. A three-port vitrectomy is an ideal method of vitrectomy. A longer infusion cannula, such as 6 mm cannula, or use of anterior chamber

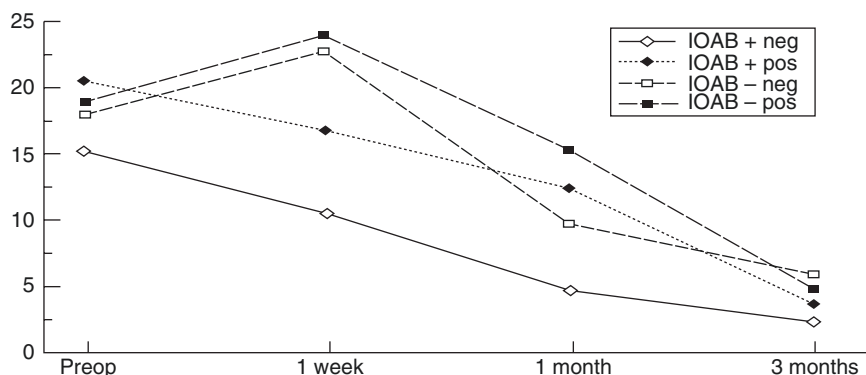
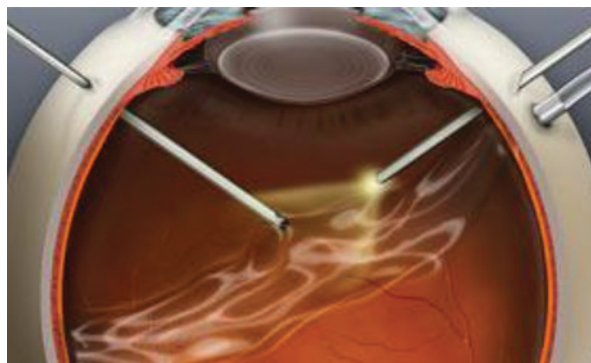


Fig. 2.7 Inflammation is reduced faster in eyes that received intravitreal dexamethasone irrespective of culture positivity, and at end of 3 months, the regained vision was similar to eyes that did not receive intravitreal dexamethasone (Courtesy: Taraprasad Das, MD; reproduced with permission from Br J Ophthalmology 1999; 83: 1050–55)

Fig. 2.8 Pars plana vitrectomy in endophthalmitis



maintainer is the safer way to avoid suprachoroidal infusion. Vitreous is collected before the infusion begins, and the tip of infusion cannula must be visualized before the infusion is started. The EVS recommended removal of 50% of vitreous and not to induce posterior vitreous detachment for fear of causing retinal detachment. But with the greater safety of vitreous surgery technique and technology, such as smaller gauge vitrector, more distal position of the cutter port, faster cutting rates, and superior fluidics management have made a complete vitreous surgery in endophthalmitis a distinct possibility.

The Complete and Early Vitrectomy in Endophthalmitis (CEVE) study proposed that if the eye with good red reflex or with some retinal visibility does not benefit from intravitreal antibiotics and intravitreal corticosteroid in 24 h, it should receive a complete vitrectomy regardless of visual acuity [6]. A complete vitrectomy includes separation of posterior hyaloid in the posterior pole, but staying short of the periphery. The rationales of complete vitrectomy are the following: (1)

Table 2.2 Decisions of post-cataract surgery endophthalmitis in China [7]

Period	Tap-inject (%)	Vitrectomy-inject (%)	No intervention (%)
1995–1999	47.0	47.0	6.0
2000–2004	27.5	66.4	6.1
2005–2009	17.8	78.0	4.2

vitrectomy reduces dramatically the inflammatory debris in the vitreous cavity; and (2) vitrectomy reduces the incidence and severity of macular complications. Since the publications of the Endophthalmitis Vitrectomy Study (EVS) over two decades ago, more often the decision is made for vitrectomy-inject than tap-inject. Table 2.2 shows the increasing decisions for vitrectomy over “tap” only in a Chinese study [7].

Adjunctive Systemic Therapy

The EVS used intravenous amikacin and oral ciprofloxacin in people with penicillin allergy, for 5–10 days [8]. But the study did not find any specific advantage and hence did not recommend systemic antibiotics in acute postoperative bacterial endophthalmitis. The good bioavailability of oral moxifloxacin (400 mg twice daily for 5 days) that obtains intravitreal drug concentrations exceeding the minimum inhibitory concentration MIC 90 of most bacteria responsible for endophthalmitis, would merit revisiting the decision of systemic antibacterial therapy [9, 10]. The EVS recommendations do not hold true for other forms of endophthalmitis, such as acute purulent, bleb-associated, posttraumatic, and endogenous endophthalmitis. We recommend systemic fluoroquinolone (typically, oral ciprofloxacin 750 mg twice daily in adults) for 7–10 days in all cases of endophthalmitis.

Repair of Associated Ocular Injury

The repair of associated ocular injury must be done at priority basis. All obvious open-globe injuries should be assessed for the extent of corneal and scleral tear and should be repaired at first intervention. In cases with no obvious tear but evident clinical signs of globe rupture, limbus should be carefully examined for subtle globe rupture. Globe exploration should be done by 360° peritomy to search for an occult scleral tear with meticulous examination including under the insertion of the rectus muscles. An attempt can be made to repair any associated retinal detachment in the same sitting provided visualization permits and the surgeon has adequate clinical experience in the same.

Treatment Options

All cases of suspected or proven endophthalmitis are treated by one of the two methods—(1) tap and inject intravitreal antibiotics and (2) vitrectomy and inject intravitreal antibiotics. The decision to “tap” or perform “vitrectomy” as the first choice depends on the severity of the cases. The EVS recommended “tap-inject” for eyes presenting with hand motions (perception of hand motions at 60 cm) or more and “vitrectomy-inject” for eyes presenting with light perception (LP) or less [8]. Immediate vitrectomy was also advised for patients with diabetes mellitus irrespective of the status of presenting vision. With refinement of vitreous surgery instrumentation, specifically decreased instrument diameter and the safety of working close to the retinal surface, many consider vitrectomy as the first choice in all cases of endophthalmitis irrespective of the presenting vision [6]. Also the modern safety features in vitrectomy system allow one to perform near-complete vitrectomy as opposed to “core vitrectomy” suggested by the EVS. The newest evolution in vitreous surgery is endoscopic vitreous surgery that could obviate the corneal opacity [11].

Explantation an intraocular lens (IOL) is a surgeon-based decision. There are indeed a very few occasions where it is rather mandatory to explant an IOL. Some of these indications include a chronic endophthalmitis not responding to treatment and severe fungal endophthalmitis where the infection has spread anteriorly and involves the IOL.

The standard of care is to inject two intravitreal antibiotics at the conclusion of “tap” or “vitrectomy.” This decision is always empirical and is given before the microbiology reports are available. The current recommendations are vancomycin (1 mg in 0.1 ml) that works against gram-positive organisms and ceftazidime (2.25 mg in 0.1 ml) that works against gram-negative organisms. A repeat injection is considered when the culture-antibiotic sensitivity reports are different or there is clinical worsening. The repeat injections can be done safely 48–72 h after the first injection. Antifungal antibiotics are not injected as the primary intravitreal injection unless there is a strong clinical suspicion. Injection of antibiotics into the capsular bag of the crystalline lens is made in cases of chronic endophthalmitis where the infecting microorganisms are suspected to be “sequestered” in the capsular bag.

We recommend intravitreal dexamethasone injection along with the antibiotics as the primary event. This is of course withheld in cases of fungal endophthalmitis.

Associated ocular repair is necessary in bleb-associated endophthalmitis (bleb revision, described in detail in Chap. 8) and in cases of eye trauma. All attempts are made to preserve the crystalline lens in all phakic eyes but must be sacrificed when already injured. IOL implantation is not recommended when the crystalline lens is removed; it is deferred to another time after the infection clears. The treatment algorithm as followed by us in a typical post-cataract surgery acute endophthalmitis is shown in Fig. 2.9 [12].

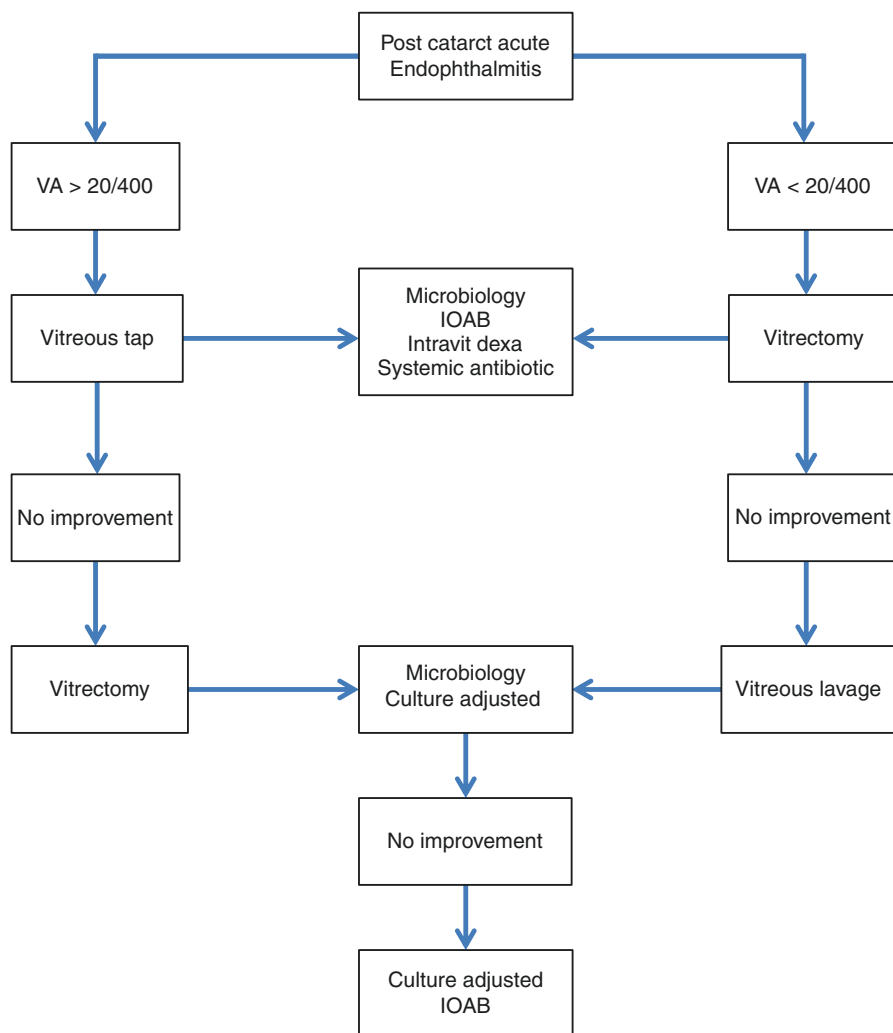


Fig. 2.9 Post-cataract acute endophthalmitis treatment algorithm [12]

Outcomes

The outcome of endophthalmitis care is both anatomical and functional. Many studies have documented outcome after cataract surgery endophthalmitis. We compared our results with the results of the EVS. The settings were not similar. The EVS included only “mild” forms; our cohort included all cases of endophthalmitis. The treatment regimen in our cases included more liberal decisions for vitrectomy contrary to the EVS recommendations for vitrectomy. In the EVS, over 50% eyes

Table 2.3 Visual acuity outcome following treatment for post-cataract surgery endophthalmitis

Visual acuity	EVS (8)	LVPEI [2]
≥20/40	53%	20%
≥20/60	NA	27%
≥20/100	74%	48%
≥20/200	NA	59%
<5/200	15%	NA
No LP	5%	

EVS Endophthalmitis Vitrectomy Study; LVPEI LV Prasad Eye Institute, Hyderabad, India

Table 2.4 Visual outcome following post-cataract surgery in China [7]

Period	>20/40	>20/400	No LP
1995–1999	11.2%	40.3%	26.8%
2000–2004	20.2%	57.7%	13.1%
2005–2009	19.2%	71.2%	9.6%

No LP no light perception

regained 20/40 or better, and 5% eyes reduced to no light perception. In contrast, only 20% regained 20/40 or more vision in our study (Table 2.3).

There is also better visual recovery in successive years even in similar setting as shown in a Chinese study [7] (Table 2.4).

Future Challenges

Though over the years the diagnoses and treatment outcomes of infectious endophthalmitis have improved, some inherent hurdles prove a challenge even today. The biggest challenge is the current culture negativity rate, which, in spite of prompt microbiological evaluation, can be as low as 35–40%. Culture negativity causes an inability to get antibiotic sensitivity patterns that usually guide treatment. Secondary sequelae following endophthalmitis like retinal necrosis and retinal detachment are very difficult to manage and invariably lead to loss of functional vision and often phthisis.

The change in the spectrum of microorganisms causing the infections and emerging antibiotic resistance is a great challenge. The Western countries report coagulase-negative staphylococci as the commonest organisms in post-cataract surgery endophthalmitis, minimal gram-negative infection, and almost unknown fungal etiology. In contrast, the Asian and Indian literature reports a high incidence of gram-negative and fungal etiology causing endophthalmitis. These cases have poorer prognosis due to high virulence of the organisms and relatively complicated presentations with corneal involvement that is often a poor prognostic factor.

Frequently Asked Questions

1. *I had an endophthalmitis which was appropriately managed. Now the media is completely clear, and optic disk does not show gross pallor, but the vision is still very poor on final refraction. What to do?*

A: Assess the fovea on slit lamp biomicroscopy and with an optical coherence tomography. Most such cases which do not improve optimally have a chronic cystoid macular edema. An accompanying fundus fluorescein angiography to assess macular perfusion adds to the information. In an ischemic macular edema, the guarded visual prognosis should be explained. In case the macula is well perfused, intravitreal anti-VEGF or steroids can be attempted with due discussion with the patient about the pros and cons.

2. *Is there a way to suspect microorganism-specific infection?*

A: There is no foolproof clinical examination modality to identify a specific microorganism in endophthalmitis. Certain clinical features and demographics may suggest a particular organism. Acute post-cataract surgery endophthalmitis is usually caused by coagulase-negative staphylococci. In post-surgical cases following corneal tissue transplants or fulminant host corneal infiltrates, a gram-negative etiology is suspected. Associated nasolacrimal duct blockade often suggests infection with pneumococci. *Bacillus* species especially *Bacillus cereus* is a common etiology following open-globe injuries. In a filtering bleb-associated endophthalmitis, the etiology of acute endophthalmitis is coagulase-negative staphylococci, whereas in a delayed presentation, *Streptococcus* spp. and *Haemophilus influenzae* are commonly seen. Organisms commonly seen in chronic low-grade endophthalmitis include coagulase-negative staphylococci, *Propionibacterium*, and fungi. Fungus species especially *Candida* are the commonest isolates seen in endogenous endophthalmitis especially in immunocompromised and systemically ill patients.

3. *How long should one wait for a second intervention?*

A: The second intervention is guided by the half-life of the antibiotics injected at the first intervention. The most commonly used empirical antibiotics have a vitreous half-life of about 48 h. Hence a repeat intervention is merited at 48 h. For intravitreal voriconazole, as the half-life is lesser, a repeat intervention is required every 24 h.

4. *What do we infer when the injected antibiotics are not sensitive to the identified microorganism, but the patient is doing well clinically?*

A: The laboratory reports in endophthalmitis management are a guideline to initiate treatment. The final decision of the treatment is based on the clinical impression. Occasionally, it's possible that the culture plate has picked up a contaminant preferentially which outgrows the actual organism from the biopsy sample. This could also indicate that the organism from the sample is not virulent. The culture sensitivity report in this case may reflect that of the contaminant and not of the one in the sample. Alternately, there could be the same organism with multiple strains of resistance patterns in the same infection. The culture may have grown the resistant ones preferentially, while the vitreous may be harboring the sensitive ones. So continuation of the same treatment is warranted.

5. *What do we infer when the injected antibiotics are sensitive to the identified microorganism, but the patient is not doing well clinically?*

A: Similar to the previous situation, a possibility of a contaminant should be kept in mind. This situation would warrant a repeat vitreous sampling preferably along with the cassette fluid. One may also consider changing the laboratory to get a correct yield of organisms. In spite of the above if no suitable culture sensitivity patterns are obtained, change the empirical antibiotic combination. One can consider also taking an expert second opinion and a possibility of a noninfectious masquerade.

6. *How do I approach a patient for the fellow eye intraocular surgery where the other eye was successfully treated for culture-positive endophthalmitis?*

A: Revisit the history and postinfection surveillance report to identify causative factors if any for the previous endophthalmitis. Take adequate precautions to ensure all protocols are adhered to and the deficiencies are corrected. Before taking up the other eye for surgery, ensure patent sac syringing in both eyes, and allow adequate time interval between surgeries to settle the inflammation in the eye treated for endophthalmitis.

References

1. Rachitskaya AV, Flynn HW Jr, Fisher YL, Ayres B. Correlation between baseline echographic features of endophthalmitis, microbiological isolates and visual outcomes. *Clin Ophthalmol*. 2013;7:779–85.
2. Das T, Kunimoto DY, Sharma S, Jalali S, et al. Relationship between clinical presentation and visual outcome in postoperative and posttraumatic endophthalmitis in south central India. *Indian J Ophthalmol*. 2005;53:5–16.
3. Raju B, Das TP, The Hyderabad Endophthalmitis Research Group. Simple and stable technique of vitreous tap. *Retina*. 2004;24:803–5.
4. Das TP, Ravilla RD, Ravilla SD, Venkatesh K. The endophthalmitis kit. *Asia Pac J Ophthalmol*. 2013;2:362–4.
5. Das T, Jalali S, Gothwal VK, et al. Intravitreal dexamethasone in exogenous bacterial endophthalmitis. Results of a prospective randomized study. *Br J Ophthalmol*. 1999;83:1050–5.
6. Kuhn F, Gianpaolo G. Complete and early vitrectomy for endophthalmitis (CEVE) as today's alternative to endophthalmitis vitrectomy study. In: *Vitreous retinal surgery, Essentials in ophthalmology*. New York, NY: Springer; 2007. p. 3–68.
7. Sheng Y, Sun W, Gu Y, Lou J, Liu W. Endophthalmitis after cataract surgery in China 1995–2009. *J Cataract Refract Surg*. 2011;37:1715–22.
8. Endophthalmitis Vitrectomy Study Group. Results of the Endophthalmitis Vitrectomy Study. A randomized trial of immediate vitrectomy and intravenous antibiotics for the treatment of postoperative bacterial endophthalmitis. *Arch Ophthalmol*. 1995;113:1479–96.
9. Kampougeris G, Antoniadou A, Kavouklis E, et al. Penetration of moxifloxacin into the human aqueous humor after oral administration. *Br J Ophthalmol*. 2005;89:628–31.
10. Lott MN, Fuller JJ, Hancock HA, et al. Vitreal penetration of oral moxifloxacin. *Retina*. 2008;28:473–6.
11. Martiano D, L'helgoualc'h G, Cochener B. Endoscopy-guided 20-G vitrectomy in severe endophthalmitis: report of 18 cases and literature review. *J Fr Ophtalmol*. 2015;38:941–9.
12. Das T, Sharma S. Current management strategies of acute postoperative endophthalmitis. *Semin Ophthalmol*. 2003;18:109–15.

Endophthalmitis

A Guide to Diagnosis and Management

Das, T. (Ed.)

2018, XVII, 409 p. 96 illus., 88 illus. in color., Hardcover

ISBN: 978-981-10-5259-0