Chapter 10
Endogenous Endophthalmitis

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Endogenous endophthalmitis refers to the infection of the intraocular cavities that result from haematogenous dissemination of pathogens to the eye [1]. These pathogens typically reach the choroid or retina and then cross the blood retinal barrier to infect the vitreous cavity [2]. Unlike exogenous forms such as post-operative or post-traumatic endophthalmitis, the endogenous endophthalmitis is relatively rare and has been shown to account for 2–8% of all endophthalmitis cases in different studies [3, 4].

Causative Organisms

Endogenous endophthalmitis can be caused by a wide range of bacteria, gram-positive and gram-negative, and fungi, yeast and filamentous fungi. The microbiological spectrum is different from exogenous endophthalmitis, even for a given geographic region. In the Asian countries, bacteria, especially gram negative, are more common [5, 6], while in the Western populations, fungi are the predominant cause of endogenous endophthalmitis [3, 4]. This is in sharp contrast to exogenous endophthalmitis, which is commonly caused by gram-positive bacteria such as *Staphylococci* in the West and fungi, at least in some Asian populations, say in north India.

Risk Factors

Endogenous endophthalmitis can be associated with underlying systemic disease in up to 90% of cases [7]. These include diabetes mellitus, recent hospitalisation, sepsis, respiratory or urinary tract infection, intravenous drug abuse, indwelling catheters, various causes of immunosuppression such as malignancy, and acquired

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immunodeficiency syndrome (AIDS) [3–7]. The presence of infective foci/abscesses, elsewhere in the body, or surgical procedures, such as colonoscopy that can induce transient bacteraemia, are also important risk factors for endogenous endophthalmitis. There are reports of liver and lung abscess causing endogenous endophthalmitis with *Klebsiella* and *Aspergillus* infection [8]. However, a variable but significant proportion of patients may not have any obvious infective focus or risk factor for endogenous endophthalmitis. Such patients usually have a transient bacteremia from an occult systemic focus that needs a thorough investigation.

Clinical Features

Endogenous endophthalmitis can have a variable clinical presentation depending on the patient's systemic condition and virulence of the organism [1, 3, 4]. Most patients present with decrease in vision of sudden onset. Various symptoms and signs of anterior segment inflammation such as pain, photophobia, lid oedema, conjunctival and circumcorneal congestion, hypopyon and pupillary membranes may be present. It is important to examine carefully for signs of occult trauma, especially in children where the history may be unreliable. Anterior segment signs are more common in endogenous endophthalmitis with bacterial infection.

In general, endogenous endophthalmitis presents predominantly with posterior segment inflammation such as vitreous exudates, since the infection originates at the back of the eye (Fig. 10.1, top). *Aspergillus* may present with yellowish white subretinal lesions at the posterior pole, while *Candida* presents with white fluffy lesions projecting from the retina into the vitreous cavity (Fig. 10.1, bottom). Bacterial endogenous endophthalmitis is usually associated with greater vitreous inflammation and sometimes subretinal or choroidal abscess. Rarely, non-specific findings such as flame-shaped haemorrhages, Roth's spots and cotton wool spots may be seen. While some patients may present with obvious systemic disease, in other apparently healthy individuals, it is important to rule out recent fever, organ-specific infections and intravenous drug abuse.

Neonatal endophthalmitis is a special form of endogenous endophthalmitis seen in newborns with sepsis, very low birth weight and retinopathy of prematurity. It has two distinct clinical presentations [9]. Focal retinal infections generally have good visual prognosis, while fulminant nosocomial infections have poor outcomes. Clinical suspicion is crucial for early diagnosis, and vitreous aspiration and intravitreal antibiotic administration can be considered under topical anaesthesia, when general anaesthesia is contraindicated.

Diagnosis

Endogenous endophthalmitis is essentially a clinical diagnosis, based on the presence of characteristic ocular signs and often systemic risk factors. The diagnosis may be aided by B-scan ultrasonography that, besides showing vitreous exudates, may also reveal

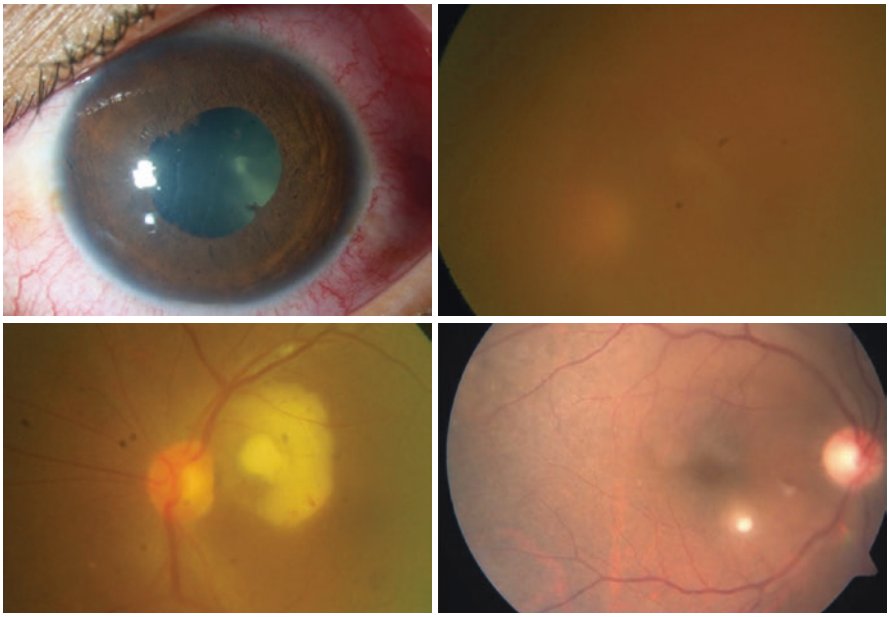

Fig. 10.1 Constellation signs of endogenous endophthalmitis. (*Top left*) Minimal anterior segment inflammation in a patient with dense vitreous exudates due to endogenous endophthalmitis; (*Top right*) dense vitritis with hazy view of the disc; (*Bottom left*) *Candida* endophthalmitis of the left eye, showing subretinal exudates with a preretinal projection into the vitreous cavity. (*Bottom right*) Another case of *Candida* endophthalmitis with a preretinal exudate but minimal subretinal involvement

choroidal abscesses that appear as dome-shaped choroidal lesions, underneath the vitreous exudates (Fig. 10.2, left). Rarely, optical coherence tomography may help delineate intra-retinal, subretinal or subretinal pigment epithelium location of infective foci.

The key test for confirmation of diagnosis is diagnostic vitrectomy. Since the infection originates at the back of the eye, sampling the vitreous near the infective focus greatly increases the diagnostic yield of the procedure. Rarely, subretinal biopsy of the subretinal exudates can help in identifying the causative organism (Fig. 10.2, right). Vitreous samples are subjected to standard microbiological examination (microscopy and culture) protocols for bacteria and fungi. Recently, quantitative real-time polymerase chain reaction (rt-PCR) has shown excellent sensitivity in diagnosis of bacterial and fungal infections, as compared to culture. Sugita et al. described a procedure that can be performed as quickly as 90 min [10]. Despite these advantages, current molecular techniques lack the ability to test for the entire range of antibiotic susceptibility and are prone to false-positive results, especially if care is not taken to prevent contamination of test samples.

Additional tests are required to rule out presence of systemic infection that may have been missed during clinical evaluation. The most effective method is blood culture using blood drawn on three consecutive days under sterile precautions. It is also useful to sample other extraocular sites of infection such as urine or pus from skin or other abscesses. A thorough internist evaluation can help in identifying occult infections (Table 10.1).

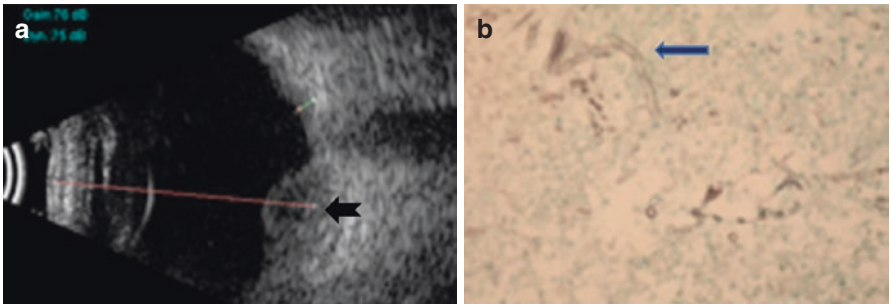

Fig. 10.2 A 41-year-old man presented with decreased vision in right eye, 1 day following percutaneous transluminal coronary angioplasty. The affected eye right eye had anterior chamber hypopyon with dense vitreous exudates. Ultrasound B-scan revealed dome-shaped elevation arising from the choroid (*notched arrow*, **a**) (*left*). Three consecutive vitreous biopsies did not grow any organism. However, a subretinal biopsy, 1 month after initial presentation, revealed presence of fungal filaments (*arrow*, **b**). (*Right*) The patient was treated with intravitreal and oral voriconazole, but vision could not be salvaged (Courtesy: Rajeev K. Reddy, MD)

Table 10.1 Etiological agents of bacterial and fungal endogenous endophthalmitis

Gram-positive bacteria	Gram-negative bacteria	Filamentous fungi	Yeast and yeast-like fungi	Other organisms
Streptococcus pneumonia	*Listeria monocytogenes*	*Aspergillus fumigatus*	*Candida albicans*	*Toxoplasma gondii*
α-Hemolytic streptococci	*Neisseria meningitidis*	*Aspergillus glaucus*	*Candida tropicalis*	*Toxocara canis*
β-Hemolytic streptococci (group A, B, G)	*Escherichia coli*	*Aspergillus terreus*	*Candida stellatoidea*	*Pneumocystis carinii*
Staphylococcus aureus	*Klebsiella pneumoniae*	*Fusarium* spp.	*Candida parapsilosis*	
Corynebacterium spp.	*Haemophilus influenzae*	*Sporotrichum* spp.	*Candida krusei*	
Cellulosimicrobium cellulans	*Serratia* spp.	*Coccidioides* spp.	*Cryptococcus* spp.	
Bacillus spp.	*Pseudomonas aeruginosa*	*Mucor* spp.	*Torulopsis* spp.	
Clostridium spp.				
Nocardia asteroids				
Mycobacterium tuberculosis				
Actinomyces spp.				

Differential Diagnosis

The diagnosis of endogenous endophthalmitis could be tricky, particularly in individuals who do not have obvious systemic risk factors. It is important to rule out different forms of endogenous uveitis that present with dense vitreous

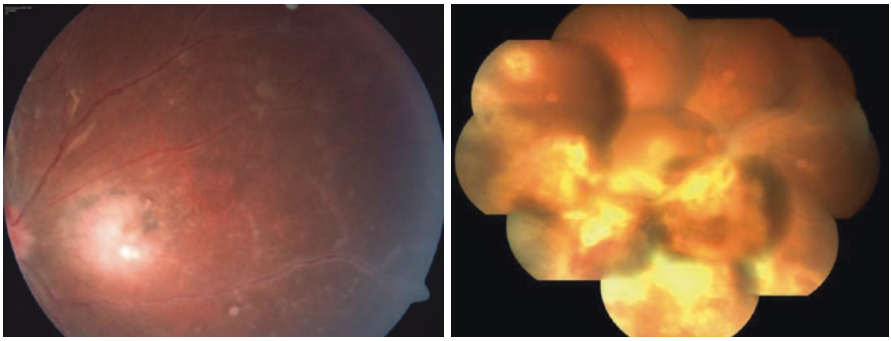

Fig. 10.3 (*Left*) Ocular toxoplasmosis. Colour fundus photograph of the nasal quadrants of right eye showing a focus of active retinitis, associated with pigmented scars, suggestive of recurrent ocular toxoplasmosis. It is crucial to identify such clinical patterns through the vitreous haze, to make an accurate etiologic diagnosis and initiate appropriate antibiotic therapy. (*Right*) Acute retinal necrosis. Colour fundus photograph of the right eye showing large areas of confluent necrosis in inferior fundus, extending from the periphery to the posterior pole and associated with mild vitritis and areas of scarring. In eyes, with dense vitreous reaction, and smaller areas of necrosis, the diagnosis may be missed at initial examination

inflammation. Most important are two common causes of infectious retinitis—acute retinal necrosis and ocular toxoplasmosis. It is useful to look through the vitreous exudates for bright retinitis lesions at the posterior pole (toxoplasmosis, in association with pigmented scar; Fig. 10.3, left) or at the periphery (acute retinal necrosis; Fig. 10.3, right). Tell-tale signs of active or healed retinitis in the other eye may also help in confirming the diagnosis. Rarely, a patient with a first episode of HLA-B27-associated uveitis, presenting with anterior chamber hypopyon and significant vitreous reaction, may also be mistaken for endogenous endophthalmitis. This may be differentiated by systemic history and identifying predominantly anterior segment inflammation.

Treatment

Treatment of endogenous endophthalmitis depends on the severity of ocular inflammation, including media clarity, presence of systemic risk factors and identification of causative organism.

Local Therapy

Although vitreous samples can be obtained by aspiration, it is advisable to perform a ‘more-than-core’ pars plana vitrectomy in these patients, if the patient can tolerate surgery, and adequate visualisation of the posterior segment is possible [11, 12]. This procedure not only helps in retrieving adequate sample for microbiological

evaluation but also significantly reduces the infectious load within the vitreous cavity. In eyes where a focal lesion (intra- or subretinal or choroidal abscess) is visible during initial evaluation, it is useful to begin sampling near the lesion under direct visualisation, to obtain greater diagnostic yield. This is followed by empirical intravitreal antibiotic therapy, usually vancomycin and ceftazidime/amikacin, in standard doses to cover both gram-positive and gram-negative organisms, respectively. The decision for repeat injections depends on response to initial treatment and microbiological results.

For fungal endogenous endophthalmitis, suspected on basis of clinical signs described earlier, or diagnosed after microbiological evaluation, intravitreal voriconazole or amphotericin B, can cover both yeast and filamentous fungi, though amphotericin B has a poorer intraocular safety profile.

Systemic Therapy

Since endogenous endophthalmitis results from haematogenous dissemination of pathogens to the eye, systemic antibiotic therapy to treat the underlying source of bacteraemia/fungemia is a vital adjunct to local treatment. However, it should be initiated after a series of blood cultures have been obtained. Fluoroquinolones are typically used for broad-spectrum anti-bacterial therapy unless antibiotic sensitivity reports show resistance in isolated organisms. Fluconazole, 400–800 mg daily for a minimum duration of 6 weeks, is recommended for *Candida* infection, while intravenous Amphotericin B is most useful for *Aspergillus* infection. The role of corticosteroids, systemic or intraocular, remains controversial in management of endogenous endophthalmitis.

Prognosis

The overall visual and anatomical prognosis of endogenous endophthalmitis is generally unfavourable compared to exogenous endophthalmitis. Important prognostic factors include timing of diagnosis and treatment, presentation of visual acuity, virulence of organisms, location of infective foci at the posterior pole and presence of underlying systemic disease such as diabetes mellitus. Early diagnosis and treatment is crucial particularly when systemic clues are absent. *Aspergillus* and other filamentous fungi and methicillin-resistant *Staphylococcus aureus* (MRSA) and gram-negative bacteria such as *Klebsiella* are known to have worse prognosis.

Conclusions

Successful management of endogenous endophthalmitis depends on prompt diagnosis and treatment. The key is to identify the causative organism and its systemic focus and any underlying risk factors. Early pars plana vitrectomy can significantly improve the chances of favourable treatment outcomes.

References

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