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Endophthalmitis : The current perspective

KEYWORDS

Endophthalmitis; postoperative, cataract surgery, broad spectrum antibiotics

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ABSTRACT Endophthalmitis is a dreaded complication following intraocular surgeries. Trauma, spread of infection from other body organs (endogenous) and intravitreal injections are the other causes of endophthalmitis. Due to improvement in the surgical technologies, better understanding of the disease and availability of broad spectrum antibiotics the incidence of postoperative endophthalmitis has reduced. In this article we have given a brief overview of clinical features, diagnostic modalities and management of this condition so that the vision and affected eye can be saved.

Introduction:

Endophthalmitis is an inflammation of internal coats of the eye along with inflammation of the intraocular cavities i.e. aqueous and vitreous humour with involvement of retina and uvea1. This dreaded complication has to be kept in mind while performing any intraocular procedure, particularly cataract surgery2. Infection is the most common cause of endophthalmitis and causative agents are bacteria and fungi but parasites and viruses can also cause Endophthalmitis. Based on the time of onset, the disease may be acute, sub acute, or chronic. If the Infection develops within six weeks of intraocular surgery, it is termed acute post operative endophthalmitis and chronic infection can manifest weeks to months after surgery. The incidence of infective Endophthalmitis (Fig.-1) sharply declined over the last two to three decades because of variations in surgical technique, scrupulous asepsis and use of preoperative and post operative broad spectrum antibiotics. The present estimated incidence of postoperative bacterial endophthalmitis is 0.03 to 0.204 percent[3].

Endophthalmitis can be classified based on

1 Mode of entry: Endogenous, Exogenous

2 Etiology: Infective, Non infective

Mode of entry:

Endogenous Endophthalmitis (2-15%): It is from haematogenous spread of organism from distant source of infection. Breech in structural integrity of the eye is not necessary. Common predisposing factors are immuno- compromised status, transplant recipients, septicemia or IV drug abuse. Mainly fungal etiology is seen in these cases[4].

Exogenous Endophthalmitis: Exogenous infection can result from direct inoculation of an organism from outside as a complication of ocular surgery (49-76%), foreign bodies, blunt or penetrating ocular trauma (16-23%).

Type of etiological agents

Bacterial, Fungal, Parasites

Organisms Responsible for Endophthalmitis

- Gram positive bacteria (75% to 85% of culture positive cases). Most common organisms causing bacterial endophthalmitis are coagulase- negative Staphylococci and Staphylococcus aureus, Streptococci, Propionibacterium acnes and Bacillus.
- Gram Negative organisms (10-15%) are Pseudomonas Aeruginosa, Haemophilus influenzae, Acinectobacter spp and Enterobacteriaceae
- Fungal Endophthalmitis although rare, can be caused by Candida, Aspergillus, Histoplasma capsulatum and Blastomyces species (seen from the irrigating solutions).
- Helminths are Onchocerca, Taenia solium and Toxocara
- Protozoa : Toxoplasma gondii

Endophthalmitis due to bacteria are due to usage of infected phacoemulsifier tubing, contamination of the irrigating fluid, or viscoelastic material. Cluster endophthalmitis, defined as five or more cases of endophthalmitis occurring on a particular operating day in a single operating room in one center is usually caused by Pseudomonas or by Bacillus spp. 25% to 35% of endophthalmitis account for culture negative cases.

Postoperative Infection:

Post operative infection constitutes two- thirds of all causes of endophthalmitis. Any surgical procedure that disrupts the integrity of the globe can lead to exogenous endophthalmitis (e.g. after intraocular surgery – commonly seen after cataract surgery. But may occur after glaucoma filtration surgery, vitreoretinal surgery, intraocular injections, strabismus surgery, corneal transplantation, Nd: YAG capsulotomy) and is usually bacterial in origin.

Causes of Post operative Endophthalmitis

- Periocular flora
- Because of surgical complications (wound dehiscence, suture abscess, vitreous loss and wound site infection)
- Contaminated surgical supply (Irrigating fluid, viscoelastics, IOLs, solution used for storing IOLs)
- Secondary IOL implantation
- Faulty sterilization of operation theatre, operative field and surgical instrument.
- Patient himself is common source of infection, patient's personal hygiene, and living conditions.

Diff**erential Diagnosis:**

TASS, Uveitis, Retained lens matter should be kept in mind while dealing these condition.

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Table: 1 Clinical Features:-

Acute Post Operative	Organism	Time of onset	Clinical Features
Severe	S aureus Streptococcus G-ve Bacilli	1-7 days	Rapid progression VA<20/400 Hypopyon Severe vitritis
Mild	S epidermidis Sterile	7-14 days	Slow progression VA>20/400 Hypopyon ± Mild vitritis
Chronic	P acne, S epidermidis, Fungi	> 2wks	KPs, Capsular plaque, Chronic Uveitis

Clinical Features:

Patient presents with symptoms most commonly on day 2 to 7 after surgery. The commonest symptoms are reduced vision, lid edema, red eye and pain. Examination of these patients reveal conjunctival chemosis, lid edema, increased congestion, yellowish exudates in the conjunctiva, corneal edema, increased number of cells in anterior chamber, hypopyon, exudates in the pupillary area and on the IOL, presence of vitreous exudates and vitritis (Fig.- 2). On distant direct ophthalmoscopy fundal glow will be diminished or absent, exudates and active retinitis patches may be seen on retina along with, retinal haemorrhages and periphebitis. Signs of penetrating intraocular foreign body and wound dehiscence should be looked for while examining these cases[5]. Bacterial endophthalmitis progresses rapidly and may destroy eye within 24 to 72 hours of onset of symptoms[6]. Fungal endophthalmitis is characteristically indolent course and may show little change for days to weeks from the onset of symptoms. Progression of disease within two to four hours of recognizing symptoms is highly indicative of bacterial endophthalmitis.

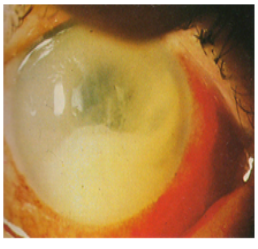


Fig.-2 Endophthalmitis with Hypopyon

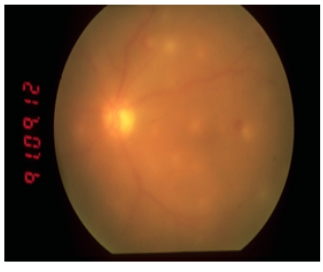


Fig-3 Vitritis

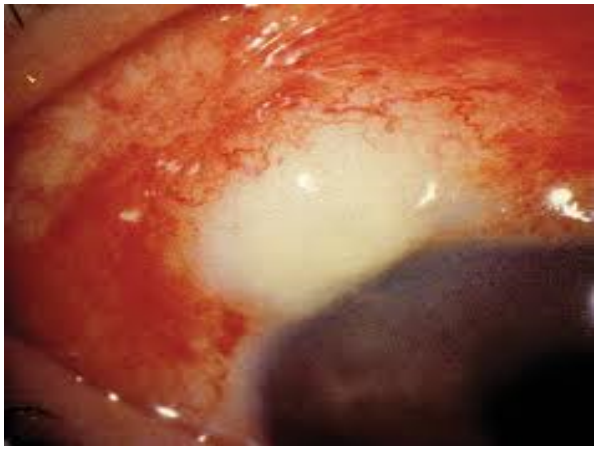


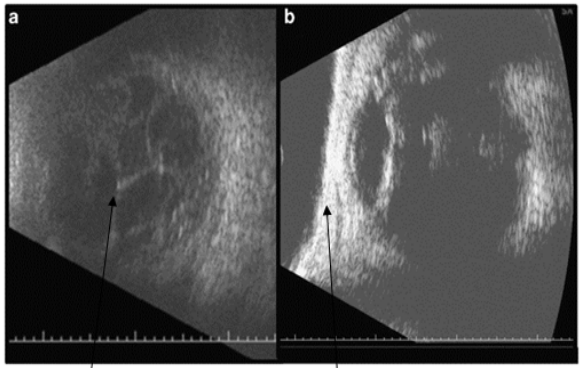
Fig-4 Blebitis

Investigations: diagnosis is based on clinical features, lab investigations and PCR. Clinical picture can be confirmed by isolating the organism by culture. The microbiological diagnosis of endophthalmitis is based on the microscopy and culture of the microorganisms. The samples of investigations are the anterior chamber (collected during paracentesis), vitreous fluid (by vitreous tap or biopsy), and the cassette fluid in cases where vitrectomy is done.

– Smears of exudates from infected area are placed on glass slides for Gram stain, Giemsa staining,KOH and Calcofluor white preparation for Bacterial and Fungal examination respectively.

– Samples from anterior chamber and vitreous (tap or biopsy) are taken for culture. Possibility of isolating an organism from aqueous is 30 to 40% while from vitreous it is around 60 to 70% (media include both solid blood agar, chocolate agar, Sabouraud dextrose agar) and liquid media (thioglycollate broth, brain heart infusion). Positive culture is characterized by growth of the same organism in more than one medium or a confluent growth on one or more solid media at inoculation site.

Ultrasonography in cases endophthalmitis shows vitreous membranes and opacities, extent of inflammation, posterior vitreous detachment, retinal detachment, retained lens matter, choroidal detachment, presence of IOFB and its location and any associated retinochoroidal thickening.



Vitreous strands and membranes capsular hyper reflectivity

Computed Tomographic Scan in endophthalmitis shows scleral thickening, with or without preseptal inflammation, proptosis and IOFB.

Management of Post operative Endophthalmitis

Endophthalmitis must be treated very aggressively because of the rapid progression of the condition. The classic triad of acute postoperative endophthalmitis is diagnosis, intravitreal drug therapy and vitrectomy. Treatment goals are control or minimize the infection, manage the complications, symptomatic relief and retention of useful vision. Time duration between onset of symptoms and diagnosis of endophthalmitis, virulence of the organism and spectrum of antibiotics are the key factors which determines the final outcome.

Antibiotics have poor penetration in vitreous by means of systemic, subconjunctival and topical route. Systemic antibiotics are required in metastatic endophthalmitis. Intravitreal injection is superior to all other routes of administration in halting the progress of Endophthalmitis7. In case of Postoperative endophthalmitis intravitreal injection of antibiotics is the mainstay of treatment. One antibiotic directed against gram positive organism and other against gram negative, based on antimicrobial activity and safety profile should be used.

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Table 2: Commonly used Intravitreal Drugs

S. No.	Antibiotic	Intravitreal Dose	Toxicity	Vitreous Therapeutic level / hr.
1.	Ceftazidime	2.25 mg/ 0.1ml	Commonly used, Almost nontoxic	48
2.	Cephazolin	2.25mg/ml	Non toxic	12 hrs
2.	Vancomycin	1 mg. / 0.1 ml	Almost Nontoxic	72-96
3.	Gentamycin	0.2mg/0.1ml	Retinal Toxicity(9)	24-36
4.	Amikacin	400 g /0.1 ml	Macular Toxicity, less Retinal Toxicity then gentamycin	24-36
5.	Dexamethasone	400g./0.1ml	Not recommended in fungal endophthalmitis	

Table 3:

S. No.	Antifungal	Intravitreal Dose
1.	Amphotericin-B	5-10 g.
2.	Voriconazole	50-100g.

A nontoxic intravitreal antibiotic drug can produce sustained bactericidal and fungicidal intraocular concentrations.

Usually combination of two antibiotics are [vancomycin (1mg/0.1ml) and Ceftazidime (2.25 mg in 0.1 ml)] are given intravitreally to give cover for both Gram positive and Gram negative infection8. While Amikacin (400 ug/0.1ml) could be used in place of ceftazidime, it poses a higher risk of macular toxicity and should be avoided. Some people favour intravitreal injection of steroid (Dexamethasone 400 ug/0.1ml) to limit damage due to inflammation and it's consequences. An intravitreal injection of 0.2 to 0.4 mg of Dexamethasone is recommended within first 10 hrs after inoculation except in case of fungal endophthalmitis.

EVS demonstrated that systemic antibiotics do not benefit much, though some studies justify use of systemic antibiotics like fluoroquinolones. Because most cases are caused by gram positive organisms, vancomycin (broad spectrum activity against most gram positive species) has become an agent of choice, and studies have proven that intravitreal vancomycin is the most effective drug for treating endophthalmitis. Administration of single intravitreal vancomycin dose results in adequate antibiotic concentration for 72 to 96 hours. Ceftazidime has emerged as an alternative to Amikacin, and found to be more effective than aminoglycosides. Vancomycin combined with Amikacin or Ceftazidime appears to be best combination in treatment of post operative endophthalmitis.

Intravitreal Injection Technique:
Intravitreal injection should be given in operation theatre under full aseptic precautions after vitreous tap, biopsy or vitrectomy. Topical anesthesia should be given. If patient is not cooperative than peribulbar block is required. Site for intravitreal injection is 3mm from limbus in aphakic eye and 3.5 mm in Pseudophakic eye preferably in the inferotemporal quadrant. Each drug is prepared separately and labelled. 0.2 to 0.5cc cc vitreous should be aspirated with a 23 guage needle / or with a butterfly needle. Then antibiotics are injected sequentially into vitreous cavity, preferably with a 30 gauge needle. Antibiotics solution is slowly injected into the mid-vitreous cavity with the bevel of the needle pointing towards the pupil through pars plana.

E-Kit

Surgical management:
Vitrectomy : Vitrectomy debulks the vitreous cavity, reduces load of bacteria and toxins and makes place for intravitreal drugs. It is required when
1. lack of improvement or worsening of the condition clinically after 48 hrs of conservative treatment

2. moderate to advanced stage of infection on initial presentation/ vision hand motion or less

3. suspected fungal infection

4. filtering bleb or trauma related cases with or without IOFB, endogenous endophthalmitis

5. chronic endophthalmitis.

Vitrectomy can be performed under peribulbar anesthesia in majority of patients, but some uncooperative patient requires general anesthesia. 3 port pars plana vitrectomy is carried out in all cases of post operative endophthalmitis. The choroid is thickened in endophthalmitis. Hence use 6mm infusion cannula. Remove anterior chamber exudates and deposits over IOL. The infusion bottle should not be kept 24 inches higher from patients eye. Vitreous exudates usually not present beyond anterior vitreous during vitrectomy. A high cutting rate and low suction should be kept for this procedure. A core vitrectomy is required to ensure a successful result in majority of cases. For fear of causing retinal detachment in inflamed and necrotic retina manipulation of vitreous close to retina should be avoided.
Procedure is completed by closing all incision in a water tight manner and injecting intravitreal antibiotics. There is increasing evidence that some cases may benefit with silicone oil injections. Mechanism may include increased concentration of intravitrel antibiotics, innate bactericidal properties of silicone oil, and stabilization of atrophic retina and minimizing occurrence of retinal detachment[10].

ENDOPHTHALMITIS VITRECTOMY STUDY[11]:
Multicenter Randomized controlled trail conducted at 25 centres in US (1990-1994)

Purpose: To determine the role of IV antibiotics, Role of immediate vitrectomy in management of in POE.

Total 420 patients with features of POE, within 6 wks of surgery.
Treatment assignment: GP VIT - IV. initial virectomy (VIT) and intravenous (IV) antibiotics, GP VIT- No IV. Initial vitrectomy & no IV antibiotic, Gp TAP-IV. initial vitreous tap (TAP) &IV antibiotics, Gp TAP-NoIV. No IV antibiotic

Results: No difference in visual outcome in PPV followed by intravitreal group compared to vitreous tap and intavitreal if vision is better than light perception. No difference in final visual acuity or media clarity whether or not systemic antibiotic was used. Vision

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with light perception or worse, much better results with immediate vitrectomy.

Limitation : Only studied postoperative endophthalmitis after cataract surgry, doesn't mention effects of vitrectomy in other forms of endophthalmitis.

the EVS recommends immediate vitrectomy for eyes with LP only and it observed that routine vitrectomy was not advantageous in eyes with hand motions or better vision.

Prophylaxis: Use of preoperative antibiotic, povidone iodine5% for 3 min, meticulus draping,single use of instruments (12)

Complications of endophthalmitis: Retinal necrosis, Retinal detachment, raised IOP, retinal vascular occlusion, optic neuropathy, panophtahlmitis, hypotony.

Conclusion:

Post operative endophthalmitis is devastating complication of intraocular surgery. Adequate precautions to be taken pre operatively, so that the risk of post operative endophthalmitis can be reduced. Primary use of topical broad spectrum antibiotic eye drop is beneficial. Newer broad spectrum antibiotic eye drop provide efficacy and may help control resistance.

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