

Endophthalmitis following open-globe injuries

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Abstract

The incidence of traumatic endophthalmitis may be decreasing due to earlier wound closure and prompt initiation of antibiotics. Risk factors for endophthalmitis include retained intraocular foreign body, rural setting of injury, disruption of the crystalline lens, and a delay in primary wound closure. The microbiology in the post-traumatic setting includes a higher frequency of virulent organisms such as *Bacillus species*. Recognizing early clinical signs of endophthalmitis, including pain, hypopyon, vitritis, or retinal periphlebitis may prompt early treatment with intravitreal antibiotics. Prophylaxis of endophthalmitis in high-risk open-globe injuries may include systemic broad-spectrum antibiotics, topical antibiotics, and intravitreal antibiotics to cover both Gram-positive and Gram-negative bacteria. For clinically diagnosed post-traumatic endophthalmitis, intravitreal vancomycin, and ceftazidime are routinely used. Concurrent retinal detachment with endophthalmitis can be successfully managed with vitrectomy and use of intravitreal antibiotics along with a long acting gas or silicone oil tamponade. Endophthalmitis is a visually significant complication of open-globe injuries but early wound closure as well as comprehensive prophylactic antibiotic treatment at the time of injury repair may improve visual acuity outcomes.

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Introduction

Endophthalmitis is a potentially devastating complication of open-globe injury. There is a higher reported rate of infection after

open-globe injuries (~1 in 100) when compared with intraocular surgery (~1 in 1000).^{1,2} Post-traumatic endophthalmitis is typically associated with worse visual acuity outcomes compared with postoperative endophthalmitis due to a variety of factors including associated co-morbidities, more virulent organisms, and possible delayed diagnosis and initiation of treatment (Tables 1 and 2).^{1–28}

Previously published data regarding epidemiology, risk factors, diagnostic considerations, microbiology, and management are reviewed. Prevention strategies for post-traumatic endophthalmitis are discussed.

Method of literature search

The literature search was performed using the online electronic Medline PubMed search from January 1950 to August 2011. The keywords searched included: Penetrating eye injuries, perforating eye injuries, open-globe injuries, ruptured globe, traumatic endophthalmitis, intraocular foreign body, endophthalmitis, retinal detachment, microorganisms, prophylaxis, treatment, antibiotics, and vitrectomy. Combinations of these terms were used as well. Relevant articles were obtained and a further search was conducted through references.

Incidence and risk factors

Among patients with infectious endophthalmitis, post-traumatic endophthalmitis comprises ~25–31% of cases.^{5,14} The reported incidence rate of endophthalmitis following open-globe injury ranges from 0 to 16.5% (Table 1), with evidence of a general decline over the past 70 years.^{4,6,12,14–24} Prophylactic factors in the setting of trauma include primary wound repair within 24 h, lack of tissue prolapse into wounds and self-sealing wounds.²⁰ In a report from the American Trauma Registry, the incidence of

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endophthalmitis did not significantly differ among various types of foreign bodies.⁶ However, some reviews have reported higher incidences of traumatic endophthalmitis associated with non-metallic intraocular foreign body (IOFB).^{19,26,28}

Factors associated with increased risk of endophthalmitis following penetrating trauma include:

- (1) Retained IOFB—the incidence of endophthalmitis with retained IOFB varies from 6.9 to 16.5%.^{6,12,14–24}
- (2) Delay in wound closure of >24 h—there is a fourfold increase in the infection rate when there was a delay of >24 h.⁶
- (3) Injury in a rural setting—the incidence of endophthalmitis was reported to be higher when penetrating injury occurred in a rural setting, which was attributed to a higher incidence of soil contamination.¹²

Table 1 Reported incidence of endophthalmitis following open-globe injuries

Author	Years	No. of cases	Incidence %
Snell	(1935–1942)	26/172	15.1
Edmund ^a	(1958–1965)	32/263	12.0
Affeldt	(1969–1985)	27/369	7.3
Nirranen	(1970–1977)	8/285	2.8
Barr ^b	(1976–1980)	4/122	3.3
Boldt	(1979–1987)	47/284	16.5
Schrader	(1981–1999)	37/1026	3.6
Yang ^c	(1981–2002)	15/125	12.0
Thompson	(1987–1991)	13/258	5.0
Essex	(1998–2000)	17/250	6.8
Zhang	(2001–2005)	571/4795	11.9
Colyer ^d	(2003–2005)	0/79	0.0
Andreoli	(2000–2007)	5/558	0.9

^aExogenous intraocular inflammation.

^bExcluded IOFB.

^cOpen-globe injury with retained IOFB.

^dPerforating globe injuries associated with combat ocular trauma.

- (4) Ruptured lens capsule—disruption of the crystalline lens in the setting of an open-globe injury is a reported risk factor for endophthalmitis because it gives microorganisms direct access to the vitreous cavity as well as impedes their clearance by blocking the normal flow of aqueous. The ruptured lens may also serve as a source of nutrition and growth for the microorganisms.¹⁹

Diagnosis

Clinical features of post-traumatic endophthalmitis

Penetrating ocular trauma is typically associated with pain and decreased visual acuity (Table 2).^{3,5–11,18,19,22} Clinical signs of open globe include eyelid edema, hemorrhagic chemosis, abnormal anterior chamber depth, presence of corneal or scleral lacerations with/without uveal prolapse, intraocular hemorrhage, pupil peaking, cataract, and retinal detachment.¹ Useful clinical symptoms and signs in the diagnosis of endophthalmitis after open-globe injury include hypopyon, vitritis, worsening vision and pain, as well as corneal ring infiltrate (Table 3).^{1,4} The presence of one or more of these may justify diagnostic imaging.

Imaging

Diagnostic imaging in the setting of trauma helps in the detection of suspected IOFB or to rule out retinal and choroidal detachments.²⁹ Historically, plain film radiography was used to screen for the presence of an IOFB given the low cost and ease of interpretation. However, it may detect only about 40% of IOFBs.³⁰ Axial computed tomography (CT) scans with 0.5–1.0 mm fine cuts through the orbit and coronal reconstruction images are most useful for localization of metallic IOFBs 0.5 mm

Table 2 Final visual acuity in post-traumatic endophthalmitis

Author	Year	No. of cases	Visual acuity				
			<20/400	20/400–20/200	20/200–20/50	>20/50	Not reported
Peyman <i>et al</i>	1980	12	3	1	4	4	
Brinton <i>et al</i>	1984	19	11	1	2	5	
Affeldt <i>et al</i>	1987	27	21	3	2	1	
Thompson <i>et al</i>	1993	34	10	1	5	3	15
Alfaro <i>et al</i>	1994	36	27	3	2	4	
Verbraeken <i>et al</i>	1994	25	18	3	2	2	
Duch-Sampers <i>et al</i>	1997	17	16	1			
Abu el-Asrar <i>et al</i>	1999	18	10		7	1	
Lieb <i>et al</i>	2003	20	10	3	4	3	
Essex <i>et al</i>	2004	17	6	1	3	7	
Andreoli <i>et al</i>	2009	5	1 ^a		2	2	

^aNo light perception.

Table 3 Clinical features of endophthalmitis following open-globe injuries

Before primary repair of eye	After primary repair of eye
Pain out of proportion to the degree of injury	Increase in pain
Visual loss worse than media opacities might suggest	Further reduction in vision
Purulent exudation from the site of injury	Progressive inflammation
Hypopyon	Hypopyon
Vitritis	Vitritis
Retinitis	Retinitis
Periphlebitis	Periphlebitis
Corneal ring infiltrate (early)	Corneal ring infiltrate (advanced)

or larger. Less radiopaque materials can be visualized using soft-tissue windows. CT is relatively expensive but has limited ability to visualize materials such as wood, ceramics, and plastics. Magnetic resonance imaging (MRI) can be used to localize IOFBs that may be radiolucent on CT. However, given the strong magnetic fields used in MRIs, metallic IOFB must be excluded first.²⁹

Echography facilitates assessment of the degree of vitreous opacification, presence of IOFB, status of the posterior hyaloid face, as well as detection of either choroidal or retinal detachment. Its portability, low cost and dynamic capabilities with regard to the detection of foreign bodies of various compositions make it important in selected trauma evaluation.^{29,30} Of note, the diagnostic quality of the ultrasound is operator dependent and may be compromised by the need to image through closed lids with minimal pressure in the setting of an open-globe injury.

Microbiology

There is a high incidence of *Bacillus species* endophthalmitis following open-globe injuries, particularly in the setting of an IOFB or soil contamination.^{4-6,9} Endophthalmitis caused by *Bacillus* is characterized by a rapid onset (often <24 h) of severe pain and inflammation, hypopyon, chemosis, ring shaped corneal infiltrate, and rapid progression to panophthalmitis. Its severity is likely caused by an enterotoxin-mediated reaction.^{4,9}

Polymicrobial infection is more frequent in endophthalmitis following open-globe injuries (Table 4). The most common isolated organisms include Gram-positive *Staphylococcus epidermidis* and *Streptococcus species*, likely as they are a part of the normal skin flora and regularly contaminate open wounds.³¹

Table 4 Bacteria and Fungi commonly associated with endophthalmitis following open-globe injuries

Bacteria (species)	Fungi (species)
<i>Staphylococcus</i>	<i>Candida</i>
<i>Bacillus</i>	<i>Aspergillus</i>
<i>Streptococcus</i>	<i>Paecilomyces</i>
<i>Clostridium</i>	<i>Fusarium</i>
<i>Pseudomonas</i>	<i>Demataciuous fungi</i>

Organisms that can cause fulminant endophthalmitis include *Pseudomonas* and *Clostridium species*.^{7,32,33} Fungal endophthalmitis following open-globe injuries is less common than bacterial endophthalmitis, but should be suspected in the setting of vegetable matter injuries such as a tree branch or thorn injury. Causes of fungal endophthalmitis most commonly include *Candida species* but may also consist of molds such as *Aspergillus species*, *Paecilomyces species*, *Fusarium species*, and *Demataciuous fungi*.³⁴

Although traumatic endophthalmitis has a high yield for positive cultures, the intraocular specimen may remain culture-negative despite obvious signs of infection in certain cases.³² Culture positivity from a vitrectomy specimen or IOFB does not always equate to clinical infection and clinical course should be monitored carefully in this setting.

Treatment

The first step in management of endophthalmitis associated with an open-globe injury is closure of the wound and restoration of globe integrity. Patient's history of immunization against tetanus should be evaluated, especially if there is soil contamination of the injury. The timing of IOFB removal remains controversial. A number of studies have shown that removal of foreign bodies within 24 h of injury is associated with a reduced risk of endophthalmitis.^{6,19,20,28} In one series of 27 patients, there were no endophthalmitis cases with early closure, selective intraocular antibiotics, and immediate removal of the IOFB (<24 h).³⁵ However, other reports have demonstrated that early removal of IOFB may not be necessary. In a study from Operation Iraqi Freedom in 2007, no cases of endophthalmitis were reported among 79 soldiers who sustained ocular trauma and IOFB. These patients underwent early prophylaxis with systemic fluoroquinolone antibiotics and wound closure with delayed IOFB removal (median time: 21 days; Table 5).²¹

Vitrectomy is often indicated for post-traumatic endophthalmitis, traumatic retinal detachment,

Table 5 Rate of endophthalmitis with early or delayed removal of IOFB

	Mieler et al ⁵⁰ (1986–1989)	Colyer et al ²¹ (2003–2005)
No. of patients	27	79
Type of primary intervention	Early closure/ Early removal of IOFB	Early closure/ Delayed removal of IOFB
IOFB removal	Systemic antibiotics Selective IOAB <24 h Average 4.5 h	Systemic antibiotics No IOAB Median time: 21 Days (range 2–661 days)
Rate of endophthalmitis	None (7 with + cultures)	None

and perforating ocular injuries. The goals of vitrectomy in this setting include debulking vitreous toxins, microorganisms and inflammatory debris, obtaining intraocular fluid for microbiological analysis, as well as providing space for injection of intravitreal antibiotics.^{36,37} Repair of retinal detachment and removal of IOFBs are possible as needed.

Systemic broad-spectrum antibiotic therapy is a common approach to prophylaxis against endophthalmitis in the setting open-globe injury. Oral levofloxacin (500 mg once a day for 7–10 days) has good intravitreal penetration and covers the most common causative organisms with the exception of *Pseudomonas aeruginosa*. In high-risk cases, vancomycin (1 g) intravenous covers nearly all Gram-positive organisms including *Bacillus cereus* while ceftazidime (1 g) intravenous covers most Gram-negative organisms, including *P. aeruginosa* (Table 6), however, vitreous penetration remains questionable with these intravenous medications.^{38,39}

In patients with suspected fungal endophthalmitis, systemic antifungal agents can be considered. Systemic amphotericin B is rarely used as it requires monitoring of complete blood count, serum electrolytes, liver function tests, and renal function tests. The azoles, including oral voriconazole (200 mg) or fluconazole (200 mg) are more commonly used because they offer a better safety profile as well as good intravitreal penetration (Table 6).^{1,39,40}

Fortified topical antibiotics can be considered in conjunction with intravitreal antibiotics. They are generally started on first postoperative day and while awaiting culture results. A common regimen includes vancomycin (25 mg/ml) and ceftazidime (100 mg/ml) every hour, along with topical cycloplegics and steroids. Subconjunctival antibiotics can also be considered. A common subconjunctival regimen includes vancomycin (25 mg), ceftazidime (100 mg), and dexamethasone (12 mg; Table 6).¹

Table 6 Treatment for post-traumatic endophthalmitis

Route of delivery	Medication regimen
Topical medication	Vancomycin 50 mg/ml every hour Ceftazidime 50 mg/ml every hour Topical cycloplegics and steroids
Subconjunctival antibiotics	Vancomycin 25 mg Ceftazidime 100 mg Dexamethasone 12 mg
Systemic antibiotics	Oral Levofloxacin 500 mg once a day (OR) Vancomycin 1 g IV every 12 h and Ceftazidime 1 g IV every 12 h (OR) Voriconazole or Fluconazole 200 mg PO every 12 h (fungal endophthalmitis)
Intravitreal injection	Vancomycin 1 mg Ceftazidime 2.25 mg or Amikacin, 0.4 mg Optional: Amphotericin B 5 µg or Voriconazole 100 µg (in suspected fungal endophthalmitis) Optional: Dexamethasone 0.4 mg (contraindicated in fungal endophthalmitis)

The use of intravitreal antibiotics can be considered in eyes with a history of soil contamination, retinal periphlebitis, and exudation around a retained IOFB even in the absence of hypopyon or prominent vitreous opacities. In these high-risk cases, it is important to achieve high drug concentration in the vitreous, which only intravitreal injections can provide.^{1,41} Vancomycin (1 mg/0.1 ml) and ceftazidime (2.25 mg/0.1 ml) are generally used.

Fungal coverage with amphotericin B (5 µg) or voriconazole (100 µg) can be added in patients with the appropriate history.⁴² Dexamethasone (0.4 mg/1 ml) can be used for its anti-inflammatory effects but is contraindicated if a fungal etiology is suspected (Table 6).⁴³

Repeat intravitreal injections can be considered for eyes with persistent or worsening inflammation, eyes with persistent moderate inflammation with particularly virulent or resistant organisms such as *Bacillus species* or *Streptococcus species*, and eyes in which a fungal organism is suspected.^{1,44}

Concurrent retinal detachment and endophthalmitis

Patients with a retinal detachment in the setting of endophthalmitis can have poor visual outcomes, especially if associated with a virulent organism.^{3,45} Retinal detachment with associated endophthalmitis is

usually managed by pars plana vitrectomy with fluid air exchange, endolaser, followed by tamponade with either silicone oil or long acting gas such as C₃F₈. Silicone oil should be considered in most severe cases because it not only provides effective endotamponade but also it does not support microbial growth.^{46,47}

In a prospective randomized study of 24 consecutive patients with post-traumatic endophthalmitis, visual acuity was better than 20/200 in 7/12 patients who underwent vitrectomy with silicone oil endotamponade compared with 1/12 patient who underwent vitrectomy without silicone oil.⁴⁶ In an *in vitro* study, silicone oil was effective in the suppression of multiple endophthalmitis-causing organisms including *Staphylococcus aureus*, *S. epidermidis*, *P. aeruginosa*, *Candida albicans*, and *Aspergillus* species.⁴⁷

The routine concentration of intravitreal antibiotics can be considered if a 50% or less gas fill is used at the end of the surgery. When >50% gas fill is provided, a lower dose of intravitreal antibiotics should be used to prevent toxicity.^{3,48}

Endophthalmitis prophylaxis after open-globe injuries

The most important prophylactic method in the prevention of post-traumatic endophthalmitis is primary globe repair within 24 h. Cases in which high-risk factors are involved (gross contamination of the wound, organic IOFB, soil contamination, and lenticular disruption) may necessitate earlier vitrectomy. Although there is no level 1 evidence from a randomized controlled trial, systemic antimicrobial prophylaxis is generally used as discussed previously (Levofloxacin 500 mg q.d., or Vancomycin 1 g/Ceftazidime 1 g) while intravitreal antibiotic injections are used at the individual surgeons discretion. A large prospective randomized controlled trial of 346 eyes with penetrating eye injury showed development of endophthalmitis in 0.3% (1/179) of eyes in the group receiving intracameral or intravitreal antibiotic injection compared with 2.3% (8/167) of eyes in the control group.⁴⁹

Although there are no 'gold standard' guidelines for endophthalmitis prophylaxis, the most widely accepted regimen includes a combination of topical, systemic, and intravitreal antibiotics depending on the degree of clinical suspicion of subsequent infection (Table 6). Antifungal prophylaxis is generally not recommended in the absence of clinical or microbiological evidence of fungal infection.

Conclusions

Endophthalmitis is a serious complication of open-globe injury, which can lead to severe visual loss. Early wound

closure as well as comprehensive prophylactic antibiotic treatment at the time of injury repair may improve visual acuity outcomes following open-globe injuries.

Conflict of interest

Harry W Flynn Jr is the consultant for Alcon, Allergan, Pfizer, and Santen. The remaining authors declare no conflict of interest.

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