Bacillus-induced endophthalmitis: new series of 10 cases and review of the literature

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Abstract

We reviewed the charts of 10 patients who were admitted to the Massachusetts Eye and Ear Infirmary over a 10-year period with the diagnosis of *Bacillus* species endophthalmitis. To our knowledge this is the largest single series in the literature and includes the first two reported cases of *Bacillus* endophthalmitis following glaucoma filtering procedures. Seven cases developed following penetrating ocular trauma. One occurred in an intravenous drug abuser. Five eyes ultimately underwent enucleation; only the two eyes that developed endophthalmitis after elective surgery retained useful vision. Review of the literature indicates that parenteral and intravitreal antibiotic prophylaxis against endophthalmitis after penetrating ocular trauma should include gentamicin, in combination with vancomycin or clindamycin, to provide adequate coverage against infection with *Bacillus* spp., as prognosis is poor once infection is established. *Bacillus* spp. cultured from ocular tissues or fluids should not be dismissed as contaminants.

insights to the pathogenesis, and review strategies for prophylaxis and treatment.

Subjects and methods

The bacteriology log books of the Porter Bacteriology Laboratory of the Massachusetts Eye and Ear Infirmary were reviewed for *Bacillus*-induced endophthalmitis cases diagnosed between October 1978 and February 1989. Diagnosis was based on culture of *Bacillus* spp. from the ocular surface and/or intraocular fluids of patients with endophthalmitis. Eleven cases were identified. The charts of 10 were located. Follow-up information was obtained through questionnaires distributed to the patients' ophthalmologists.

Results

Data from the charts of the 10 patients are summarised in Tables I and II. All except patient eight (see below) were healthy males.

Only patients nine and 10 had had previous ocular disease. Patient nine had undergone a filtering procedure two months prior to the onset of endophthalmitis; patient 10 had undergone multiple ocular operations (see case two below). Neither of these patients had a history of ocular trauma. Visual outcome was good in both cases: patient nine achieved a visual acuity (VA) of 20/30, patient 10 achieved 20/50.

Patients 1-7 presented after penetrating ocular trauma. Five had an associated intraocular foreign body (IOFB), metallic in four cases and stone in one. The other two cases followed trauma with metallic objects without an associated IOFB on presentation.

All lacerations were sutured primarily and prophylactic antibiotics were given (Table II). In all cases following trauma the antibiotics were

Bacillus spp. are ubiquitous, Gram-positive organisms that can infect ocular and adnexal tissues leading to dacryocystitis, conjunctivitis, keratitis, and iridocyclitis.¹ *Bacillus cereus* can lead to endogenous^{2,3} or exogenous⁴⁻¹³ endophthalmitis. Intraocular infections with this and other *Bacillus* spp. rapidly progress to panophthalmitis necessitating enucleation.^{2-7,9-11,13}

A review of our cases and the literature indicates an increased incidence of *Bacillus*-induced endophthalmitis. We describe features of the trauma and the appearance of the eye that should alert the ophthalmologist to the possibility of infection with *Bacillus*, provide

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TABLE 1 Cases of *Bacillus*-induced endophthalmitis

Patient/age/sex	Eye	Route of infection	IOFB*	Culture site	Organisms cultured	VA†	Outcome
1/21/M	OS	Trauma	metal	vitreous	<i>Bacillus</i> spp.	LP‡	NLP§
2/27/M	OS	Trauma	metal	vitreous	<i>B. cereus</i>	LP	Enucleation
3/19/M	OD	Trauma	rock	aqueous	<i>Bacillus</i> spp.	LP	20/400
4/20/M	OD	Trauma	metal	vitreous	<i>Enterobacter</i>	HM	Enucleation
5/42/M	OS	Trauma	NO	vitreous	<i>B. cereus</i>	LP	LP
6/49/M	OS	Trauma	metal	wound	<i>Bacillus</i> spp.	LP	Enucleation
7/15/M	OS	Trauma	NO	conjunctiva	<i>Bacillus</i> spp.	20/50	Enucleation
8/40/M	OS	IV drug	NO	vitreous	<i>B. cereus</i>	NA¶	Enucleation
9/50/M	OS	Filter	NO	aqueous	<i>Bacillus</i> spp.	NA	20/30
10/80/M	OS	Filter	NO	aqueous	<i>S. epidermidis</i> <i>Bacillus</i> spp.	20/200	20/50

*Intraocular foreign body.

†Visual acuity on initial presentation.

‡Light perception.

§No light perception.

¶Not available.

TABLE II Cases of *Bacillus*-induced endophthalmitis

Patient	Initial antibiotics*				Time started after diagnosis (h)
	Intravenous	Subconjunctival	Topical	Intravitreal	
1	Cephalothin 4 g, gentamicin 240 mg	—	Chloroptic gentamicin	—	8 h
2	Cephalothin 4 g, gentamicin 240 mg	—	—	—	6 h
3	Cephalothin 12 g, gentamicin 240 mg	—	Erythromycin	—	6 h
4	Cephalothin 4 g, gentamicin 240 mg	Cephalothin, gentamicin	Tobramycin, polymyxin-B, polysporin	—	6 h
5	Cephalothin 4 g, gentamicin 240 mg	—	—	Clindamycin 1 g, gentamicin 400 mg	6 h
6	Cephalothin 4 g, gentamicin 180 mg	—	Cephazolin gentamicin, polymyxin-B, polysporin	—	10 h
7	Ampicillin 1 g, gentamicin 120 mg	—	—	—	6 h
8	Clindamycin 1.8 g, vancomycin 2.4 g, gentamicin 120 mg	Gentamicin	Cephazolin, tobramycin	Vancomycin 1 g, clindamycin 1 g, gentamicin 400 mg	6 h
9	Methicillin 6 g, gentamicin 240 mg	Methicillin, gentamicin	Bacitracin, neosporin	—	6 h
10	Cephalothin 4 g, gentamicin 180 mg	Cephalothin, gentamicin	Cephazolin, gentamicin	—	6 h

*On admission to the Massachusetts Eye and Ear Infirmary.

started within 11 hours of the trauma. None received clindamycin or vancomycin on admission. Clindamycin was added intravenously (IV) to the antibiotic regimen of patients two and seven 24 hours after the diagnosis of endophthalmitis; vancomycin was added topically to patient two 24 hours after diagnosis.

Patient five received intravitreal gentamicin and clindamycin on presentation, and vancomycin four days after admission; none of the other patients with ocular trauma received intravitreal antibiotics initially. Intravitreal cephazolin and gentamicin were administered to patients four and seven two days after admission.

The onset of the endophthalmitis occurred within 24 hours of the trauma in two patients, and within 48 hours in five.

Vision was lost in all cases following trauma (except patient three, who retained a VA of 20/400) regardless of the prophylactic and therapeutic measures.

Endophthalmitis developed in a 40-year-old man (patient eight), an IV drug abuser and alcoholic without a history of ocular trauma or ocular surgery. Presentation resembled that in the cases that followed trauma (see below). Despite early (four hours after onset of symptoms) and vigorous intravitreal and systemic combinations of clindamycin, vancomycin, and gentamicin, the condition of the eye deteriorated rapidly, and enucleation was performed one week later.

The onset of the endophthalmitis was explosive in all cases following trauma and in the IV drug abuser, with severe chemosis, pain, injection, proptosis, corneal ring abscess, and pus in the anterior chamber. The presentation was milder in the cases that followed intraocular surgery lacking the above signs. No patient developed fever or leucocytosis.

Bacillus spp. were cultured in all cases, and in cases two, four, five, seven and eight *B. cereus* was identified. Antibiotic susceptibilities were available for eight of the isolates (Table III).

CASE I

A 27-year-old white man (patient two) presented to another hospital on 12 April 1988 after a penetrating injury to the left eye. He had been striking steel against steel. A metallic IOFB was removed, the corneal laceration was repaired, and he was started on IV cephalothin and gentamicin. No cultures were taken and no intraocular antibiotics administered. On 13 April 1988 he was transferred to the Massachusetts Eye and Ear Infirmary. The right eye was normal. The left eye had light perception; the eyelids were swollen and red, and severe chemosis and conjunctival injection were present with a purulent discharge (Fig 1). The corneal laceration was dehiscent, with iris tissue prolapse. A corneal ring abscess was present (Fig 2). The anterior chamber had a fibrinous reaction. Proptosis was present. Ultrasound revealed panophthalmitis and retinal detachment but no IOFB. Two hours after presentation vitreous and anterior chamber taps were performed; 200 µg gentamicin and 450 µg clindamycin were injected into the vitreous, and topical tobramycin and cephazolin were started. Appropriate doses of IV tobramycin, and cephalothin were also started. On 14 April 1988 the cultures grew an abundant *Bacillus* sp., later determined to be *B. cereus*, and susceptibilities were determined (Table III). Topical cephazolin and systemic cephalothin were discontinued, topical vancomycin and IV clindamycin were added. The condition of the eye continued to deteriorate with increasing pain; intravitreal injections of clindamycin and gentamicin were repeated. On 16 April 1988 light perception failed and on 19 April the eye was enucleated.

CASE 2

An 80-year-old white man (patient 10) presented with tearing and redness of the left eye that had started a few days previously. He denied having suffered trauma. The eye had undergone trabeculectomy seven years earlier for medically

TABLE III Antibacterial susceptibilities of cultured *Bacillus*

Patient	Antibiotics								
	Bacitracin	Clindamycin	Erythromycin	Methicillin	Penicillin	Cephazolin	Chloromycetin	Gentamicin	Vancomycin
1	S	R	S	R	R	R	S	S	NT
2	R	S	S	R	R	R	R	S	S
3	R	R	S	R	R	R	S	S	NT
4	R	S	S	R	R	R	R	S	S
5	R	R	S	S	R	R	R	S	S
7	R	S	S	R	R	R	S	S	S
8	R	—	S	R	R	R	S	S	S
10	S	S	R	S	S	S	S	S	NT

S=sensitive.

R=resistant.

NT=not tested.

Figure 1: Infected eye of patient two on presentation, showing proptosis, periorbital swelling, and chemosis.

Figure 2: Eye of patient two showing purulent discharge, chemosis, and a corneal abscess.

uncontrollable glaucoma. Four years later a bleb revision had been performed, and two years after that an intracapsular cataract extraction had been performed. Two months prior to presentation the visual acuity OS was 20/60; the eye was quiet with a thin functioning bleb without a leak.

On presentation the VA was 20/200 OS. The conjunctiva was 2+ injected superiorly, with mucopurulent discharge. The filtering bleb, anterior chamber, and vitreous were filled with products of inflammation, and the cornea was without an abscess.

Inflammatory cells but no organisms were found in Gram-stained fluid from an anterior chamber tap. An unidentified *Bacillus* was cultured and susceptibilities determined. Subconjunctival, topical, and IV cephalothin and gentamicin were given. Topical prednisolone was added. No intraocular antibiotics were administered. Eight days later the VA was 20/200, eventually 20/50.

Discussion

Bacillus spp. are Gram-positive, facultative, and aerobic rods that are ubiquitous, especially in environments where soil, dust, or animal manure are common.¹¹ Spores produced by *Bacillus* spp. persist in soil for years.^{14,15} First recognised in 1891 by Poplawska⁴ and subsequently by others^{5,6,16} as a cause of destructive endophthalmitis, *Bacillus* spp. are now the second most common cause of endophthalmitis after *Staphylococcus epidermidis* following penetrating ocular trauma.^{8,10-13} Whether this reflects an increased incidence of *Bacillus*-induced endophthalmitis or improved reporting is uncertain. While *B. subtilis* dominated earlier reports of *Bacillus*-induced endophthalmitis, more recent reports have stressed the occurrence of *B. cereus*, with scattered case reports of endophthalmitis secondary to *B. licheniformis* and *B. laterosporus*.^{13,17,18} Five of our cultures were identified as *B. cereus*.

B. cereus produces a unique exotoxin in addition to enterotoxins, phospholipase C, haemolysins, proteolytic enzymes, and bacteriolytic enzymes, and is resistant to lysozymes.¹⁵ These might explain the ocular destruction caused by the organism. However, other factors must play a part in the pathogenicity of *Bacillus* spp. since the non-toxin producing *B. licheniformis* can also cause severe, vision-threatening endophthalmitis.¹⁷

The rapid progression and destructive nature of endophthalmitis caused by *Bacillus* pose a problem for the ophthalmologist. All series reported so far, including ours, show a consist-

ently poor outcome when treatment was begun after the identification of *Bacillus* as the cause. The only exceptions are our two cases that followed surgery and the case reported by Schemmer and Driebe in 1987,¹² where early, *Bacillus*-specific, vigorous treatment was successful in saving useful vision.

Endophthalmitis secondary to *B. cereus* after trauma or in IV drug abusers typically presents with the rapid onset of proptosis, severe injection, and chemosis. A corneal ring abscess is common,^{7,9,11} and hypopyon may be present. Patients may have fever and leucocytosis.^{11,17} An IOFB, present in four of our patients, is frequently found and may be contaminated with *Bacillus* spp., or may allow a *Bacillus* sp. that has colonised the conjunctiva (in environments such as farm work) to enter the eye.¹⁹

In 1901 Romer described one case of *Bacillus*-induced endophthalmitis after intraocular surgery.²⁰ In 1918 Greenspoon described two such cases occurring 24 hours after cataract surgery resulting in phthisis bulbi.¹⁶ The source of the *Bacillus* was the irrigating solution used during surgery. In contrast, our two postsurgical cases occurred two months and two years after the last surgery and were characterised by a milder onset and better outcome. This could be due to a smaller inoculum or infection with a less virulent *Bacillus* species.

B. cereus produces β -lactamases that render it resistant to penicillin-G and the cephalosporins.¹¹ Gentamicin has been shown to offer moderate to good activity against *B. cereus*,^{1,21} but alone is not sufficient for therapy of *Bacillus* spp. endophthalmitis. This is supported by our findings and by others.^{7,9,13} Most notably, O'Day *et al*^{7,9} reported that endophthalmitis developed despite the use of gentamicin for prophylaxis and/or therapy.

Clindamycin has moderate to good activity against *B. cereus*¹ and, when administered subconjunctivally or parenterally, reaches therapeutic levels in the iris, choroid, and vitreous.^{22,23}

O'Day *et al* found that control of *B. cereus*-induced endophthalmitis in rabbits was best when clindamycin and gentamicin were administered concomitantly; the action may have been synergistic.⁷ This was confirmed by the *in-vitro* work of Gigantelli and coworkers.²⁴

Because of the destructive nature of *Bacillus*-induced endophthalmitis and the variable to poor intraocular penetration of most systemically or periocularly administered antibiotics, intra-

vitreal administration is favoured.²⁵⁻²⁷ A combination of 200-400 µg of gentamicin and 450 µg of clindamycin is recommended.²⁵⁻³⁰ In addition, eight µg/ml gentamicin and nine µg/ml clindamycin can be added to the vitrectomy infusion fluid.³¹

Experimental results indicate that gentamicin and vancomycin are another effective antibiotic combination.³² *B. cereus* is highly sensitive to vancomycin,¹ which produces no significant ocular toxicity when injected into the vitreous of rabbit eyes in doses up to 2 g. Vancomycin may act additively or synergistically with aminoglycosides against Gram-positive organisms.³²

Topical and intravenous gentamicin, vancomycin, and clindamycin are also administered. Serum levels of the antibiotics and the appropriate haematological and urine parameters should be carefully monitored to prevent adverse effects.³³

Intravitreal dexamethasone (to control the destructive inflammation)^{26-29, 34} and early vitrectomy^{25-27, 30} have recently been recommended in the management of sight threatening endophthalmitis such as that induced by *B. cereus*.

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