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INCIDENCE AND RISK FACTORS OF POSTOPERATIVE ENDOPHTHALMITIS AFTER PRIMARY SURGICAL REPAIR COMBINED WITH INTRAOCULAR FOREIGN BODY REMOVAL

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Purpose: To analyze the incidence and risk factors of postoperative endophthalmitis after primary surgical repair and intraocular foreign body (IOFB) removal within 24 hours of injury.

Methods: The records of all patients treated surgically for open globe injury and IOFB removal at the Eye Hospital of Shandong First Medical University between January 1, 2015, and June 30, 2020, were retrospectively reviewed. Variables included time from injury to operation, cause of injury, details of surgical repair, and follow-up. The incidence and risk factors of endophthalmitis after IOFB removal were studied.

Results: During 5 years, 99 patients with IOFB were reviewed. Of these, 19 patients were diagnosed with endophthalmitis on admission, and 5 were suspected of having endophthalmitis during operation. Fifty-four cases had no clinical signs of endophthalmitis on admission and during operation and were treated with operation within 24 hours after the injury. Two patients (2 of 54; 3.70%) developed endophthalmitis after IOFB removal, and the causative agent in both cases was *Bacillus cereus*.

Conclusion: The incidence of infectious endophthalmitis after primary surgical repair combined with IOFB removal (≤24 hours) was 3.70% in patients who received a series of standard treatments, and *B. cereus* infection might be a risk factor.

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Injuries caused by intraocular foreign bodies (IOFBs) account for 16%–41% of ocular trauma cases, leading to a wide range of ocular abnormalities and visual outcomes.[1,2] One of IOFBs' potential complications, endophthalmitis, is of particular concern owing to its tendency to cause rapid vision loss and even blindness. It has been reported to occur in approximately 6.9%–30% of patients with injuries caused by IOFBs.[3] Additionally, IOFBs are reported to be present in 43% of eyes diagnosed with traumatic endophthalmitis.[4] Therefore, prevention of IOFB-related endophthalmitis is of paramount importance.

Risk factors for posttraumatic endophthalmitis caused by IOFBs include delayed IOFB removal (>24 hours), IOFB material and location, dirty wounds, and old age.[5–7] Early surgical interventions to remove IOFBs (within 24 hours) can reduce the incidence of infectious endophthalmitis.[8–10] Based on this observation, a standardized protocol is followed for treating all cases of injuries caused by IOFBs at the Eye Hospital of Shandong First Medical University, a tertiary eye hospital. This protocol includes prompt administration of prophylactic systemic antibiotics and IOFB removal as soon as possible after admission to the hospital but does not include the use of prophylactic intravitreal antibiotics.

Maneschg et al[11] reported that the incidence of infectious endophthalmitis after IOFB extraction is 3.22% (1/31) and that their case might be associated with delayed IOFB removal (>24 hours). A standardized protocol in our hospital was administered to reduce the incidence of endophthalmitis. The rate of infectious endophthalmitis after IOFB removal is expected to decline when a standardized protocol is followed. However, the incidence and risk factors of infectious endophthalmitis after IOFB removal (≤24

hours) in patients who had accepted a standardized protocol have not been reported; therefore, this study aimed to analyze the incidence and risk factors of postoperative endophthalmitis after primary surgical repair and IOFB removal within 24 hours of injury in our hospital.

METHODS

A detailed retrospective review was conducted on all patients with penetrating ocular trauma and IOFBs who underwent primary surgical repair combined with IOFB removal at the Eye Hospital of Shandong First Medical University from January 1, 2015, to June 30, 2020. The study adhered to the principles of the Declaration of Helsinki and was approved by the Eye Hospital of Shandong First Medical University, Jinan, China (protocol number: SDSYKYY201501). The medical charts of the patients were collected through a retrospective hospital database search that included the cause of injury, time from injury to operation, location and nature of the IOFB, and surgical method, as well as the occurrence and risk factors of infectious endophthalmitis.

The exclusion criteria were as follows: (1) patients who underwent primary surgical repair and IOFB removal at other institutions, (2) patients who did not undergo primary surgical repair combined with IOFB removal within 24 hours of injury, (3) patients for whom infectious endophthalmitis was diagnosed or suspected at the time of admission or during operation, and (4) patients who were followed up for <30 days.

The diagnosis of infectious endophthalmitis was based on the patient's clinical symptoms and signs, including the presence of visual acuity reduction, worsening inflammation or hypopyon, a marked vitreous cellular reaction or vitreous opacification on B-scan ultrasonography, and retinal vasculitis.[12] Endophthalmitis was also suspected when vitreous purulent opacity or retinal vasculitis around the IOFB was found during operation.

During the 5-year study period, a standard management protocol was used (see **Table** and **Supplemental Digital Content 1**, http://links.lww.com/IAE/B650). The standard protocol included intravenous antibiotic treatment and surgical treatment (sclerocorneal laceration suture and IOFB removal) that was performed as soon as possible after admission to our hospital, but it did not include the use of prophylactic intravitreal antibiotics. Based on the IOFB position and characteristics, three different surgical methods were selected: pars plana vitrectomy (PPV), anterior chamber foreign body removal, and magnetic suction through a scleral incision. Intravenous administration of cefazolin sodium (1 g every 8 hours) or clindamycin (0.5 g every 8 hours) was performed in patients with normal renal function. The dose was reduced in patients with an impaired renal status or advanced age. Clindamycin was used instead of cefazolin sodium in patients with a history of significant penicillin allergy. Intravenous prophylaxis was continued for 48 hours. All surgeries were performed under the supervision of a surgeon whose designation was Deputy Director or above in the Department of Fundus Surgery, a full-time position rotating monthly, who is required to be on call for all patients with open globe trauma.

After IOFB removal, topical antibiotics (levofloxacin or moxifloxacin was administered 4 times daily for 2 weeks or until any epithelial defects had healed), topical corticosteroids (prednisolone acetate was administered 4 times daily to every 2 hours, followed by dose tapering over the subsequent 1 week, and tobramycin dexamethasone eye ointment was administered once per night for 2 weeks or as needed), and topical nonsteroidal anti-inflammatory drugs (diclofenac sodium administered four times daily for 6 weeks) were administered; additionally, antibiotics were administered intravenously for at least 48 hours. Patients were discharged after 48 hours of intravenous antibiotic treatment and prescribed topical therapy only when endophthalmitis was not suspected after operation. Visual acuity was graded in accordance with the published visual acuity grade set up by the Ocular Trauma Classification Group.[13] We defined

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effective visual acuity as a visual acuity of 20/200 or better.

The hospital database was searched for the prevalence of risk factors, such as IOFB location and nature, the surgical method, cultures of vitreous samples or extracted IOFBs, and rural residency. All records pertaining to cases of open globe injuries, including those excluded from the statistical analysis, were reviewed comprehensively.

RESULTS

During the 5-year study, 99 patients (99 eyes) with IOFBs were treated in our hospital and followed up for at least 30 days. Of these, 19 patients (19.19%) had infectious endophthalmitis at admission, 5 patients (5.05%) were diagnosed with endophthalmitis during operation, and 21 patients (21.21%) who underwent primary surgical repair combined with IOFB removal more than 24 hours after the injury were excluded. Finally, 54 patients (54 eyes) with IOFBs were included in the study; their average age was 42.0 ± 15.3 years. The baseline clinical characteristics are listed in Table 1. Among 54 eyes with IOFB injury, 2 eyes (3.70%) developed endophthalmitis after IOFB extraction. Both injured eyes were treated with IOFB extraction as soon as possible after admission of the patient to the hospital, and they developed clinical signs of endophthalmitis 24 hours after IOFB removal. In both cases, the IOFB was located in the vitreous body, and the infection was caused by *Bacillus cereus*.

Of the 2 patients with endophthalmitis, 1 patient (patient 1) was a 5-year-old child who was injured by a firecracker explosion and underwent surgical treatment with PPV combined with IOFB removal and cataract extraction 10 hours after the injury caused by an IOFB (Figure 1). The patient was uncooperative for the vision test upon admission. Hypopyon and vitreous purulent opacity were not observed during the operation. After operation, the operated eyes were covered with sterile gauze for 1 day. Clinical symptoms of infectious endophthalmitis, including corneal edema, severe fibrin exudates in the anterior chamber, and marked vitreous opacification on B-scan ultrasonography, occurred 24 hours after IOFB extraction when the sterile gauze was removed. The culture of the extracted IOFB was positive for *B. cereus*, and the patient was immediately treated with vitreous cavity lavage with sensitive antibiotics (5 mg vancomycin/500 mL of balanced salt solution) combined with intravitreal antibiotic injection of vancomycin (1 mg/0.1 mL). The infection was gradually controlled after 3 repeated intravitreal injections of vancomycin at 48-hour intervals.

Table 1. Demographics and Epidemiologic Features of Patients With an IOFB

Total number of IOFB removals	99
Excluded	45 (45.45%)
Infectious endophthalmitis	
Diagnosed at admission	19 (19.19%)
Suspected during operation	5 (5.05%)
Time from injury to operation (>24 hours)	21 (21.21%)
Included	
Time from injury to operation(≤24 hours)	54 (54.55%)
Average follow-up (months)	35.0 (1–69)
Average age (years)	42.0 ± 15.3 (3–73)
Men	50 (92.59%)
Women	4 (7.41%)
IOFB location	
Anterior segment	14 (25.93%)
Vitreous cavity	40 (74.07%)
IOFB nature	
Nonmetal	13 (24.07%)
Metal	41 (72.22%)
Cause of injury	
Fireworks	4 (7.41%)
Traffic	1 (1.85%)
Glass	2 (3.70%)
Stone	2 (3.70%)
Porcelain	2 (3.70%)
Metal splatter	41 (75.93%)
Uncertain	2 (3.70%)
Surgical method (IOFB removal)	
No vitrectomy	19 (35.19%)
Anterior chamber foreign body removal	14
Magnetic suction through a scleral incision	5
Vitrectomy	35 (64.81%)

The other patient (Patient 2) was a 61-year-old man with a metallic foreign body in an eye who underwent IOFB extraction with magnetic suction through a sclerotomy combined with corneal laceration repair 20 hours after the injury (Figure 2). His visual acuity was 20/80 on admission. Mild anterior chamber and vitreous cellular reactions were observed during the operation. After operation, the operated eyes were covered with sterile gauze for 1 day. Hypopyon and severe vitreous opacity were noted 24 hours after the operation when the sterile gauze was removed, and his visual acuity had dropped to hand motion. The patient underwent emergency PPV and intravitreal injections of vancomycin, and the infection was controlled after 3 repeated intravitreal injections of vancomycin at 48-hour intervals. Cultures of the vitreous samples were positive for *B. cereus*.

The two patients underwent retinal detachment repair and silicone oil tamponade after the infections

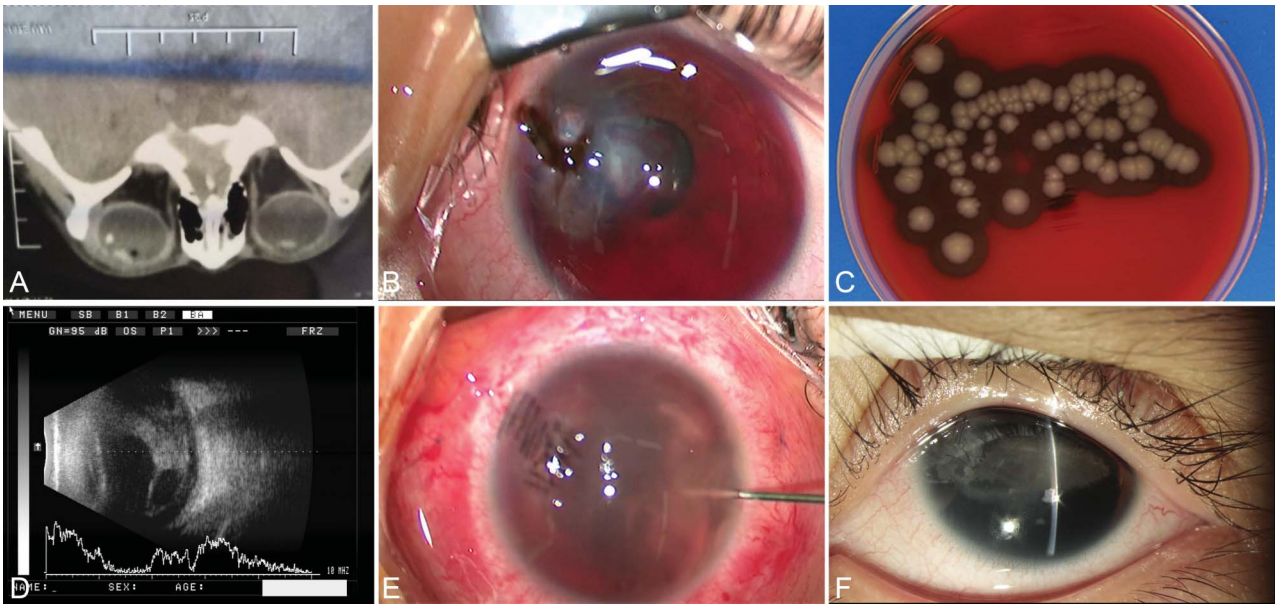

Fig. 1. A 5-year-old child who presented with an intraocular foreign body (IOFB) caused by firecracker explosion developed endophthalmitis after IOFB extraction. **A.** Head computed tomography (CT) image showing the presence of an IOFB in the posterior segment of the eye. **B.** Screenshot of the video of the first operation showing corneal lacerations, edema, and hyphema. **C.** Result of the bacterial culture of the removed IOFB: *Bacillus cereus* colonies with characteristics of double zones of hemolysis. **D.** B-scan ultrasonography revealing vitreous opacity 24 hours after the first operation. **E.** Screenshot of the video of the second operation showing corneal edema, hypopyon, and hyphema. **F.** Slit-lamp photographs showing band-shaped degeneration 6 months after operation.

were controlled. The retina was severely damaged by the disease, and little retinal tissue remained. The final visual acuity was light perception in Patient 1, and it ranged from 20/80 to hand motion in Patient 2 at the 8-month follow-up. Finally, effective visual acuity could not be achieved in the two eyes, and the eyes were classified as silicone oil-dependent eyes.

However, among the five cases of endophthalmitis suspected during operation in our study, one was a case of infection with *B. cereus*, and this case had a

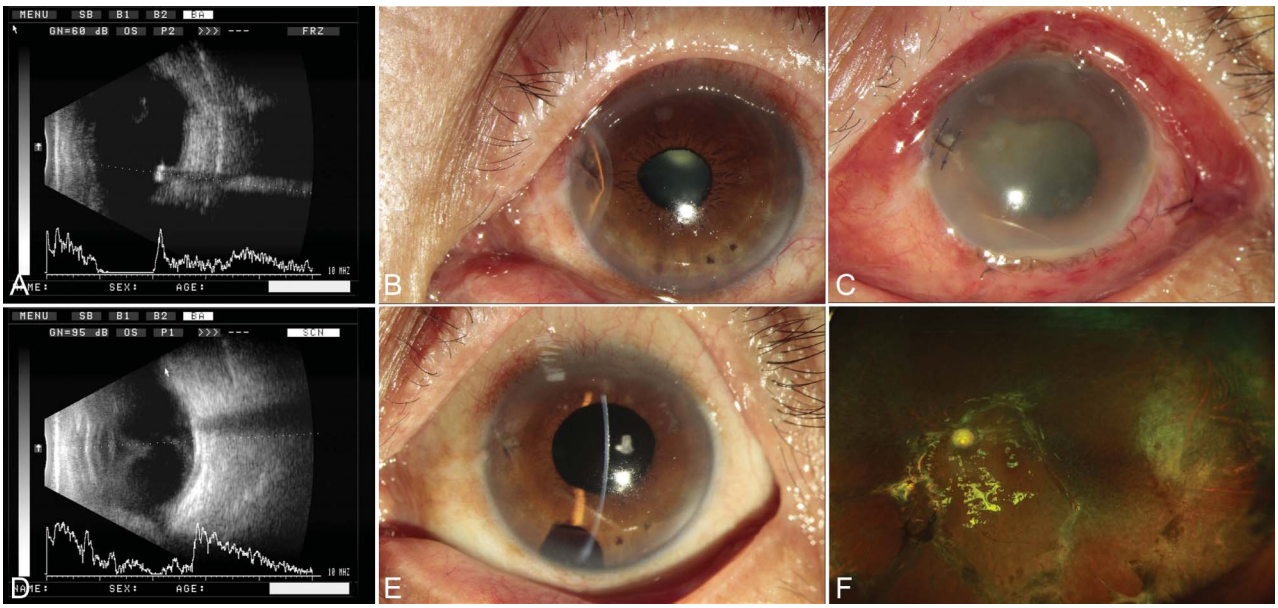

Fig. 2. A 61-year-old man with a penetrating injury caused by a metallic foreign body developed endophthalmitis after IOFB extraction. **A.** B-scan ultrasonography revealing an IOFB in the posterior segment at admission. **B.** Slit-lamp photograph showing corneal lacerations at admission. **C.** Slit-lamp photograph showing hypopyon on the first postoperative day. **D.** B-scan ultrasonography revealing vitreous opacity on the first postoperative day. **E.** Slit-lamp photograph showing corneal scar secondary to the penetrating trauma with the rest of the transparent cornea and the absence of the lens at the end of 6 months. **F.** Fundus photograph at the last visit (6 months) showed an attached retina, and little retinal tissue remained.

good visual outcome. A 6-year-old child injured by a firecracker explosion was diagnosed with infectious endophthalmitis during operation, and the patient had vitreous purulent opacity and retinal vasculitis around the IOFB during the operation and underwent PPV combined with injection of intravitreal antibiotics (vancomycin and ceftazidime) at the end of the procedure. The bacterial cultures of the removed IOFBs and vitreous were all positive for *B. cereus*. The infection was controlled, and the patient underwent retinal detachment repair and silicone oil tamponade 2 days after the first operation, and the patient's visual acuity improved to 20/25 after silicone oil removal (Figure 3).

Discussion

Intraocular foreign body has been identified as a risk factor for posttraumatic endophthalmitis by numerous studies.[3,6,14] Studies have shown that IOFB removal performed within 24 hours from the time of trauma significantly reduces the risk of endophthalmitis.[10,14] However, there are few reports on infectious endophthalmitis after IOFB removal performed within 24 hours. The present series consisted of 99 patients with IOFBs, including 75 patients without clinical signs of infectious endophthalmitis at the time of admission and during operation, who were followed up for at least 1 month. Of these patients, 54 patients underwent primary surgical repair combined with IOFB removal within 24 hours of the injury, and 2 patients developed infectious endophthalmitis after IOFB removal; the incidence of endophthalmitis after the standard treatment was 3.70% (2 of 54).

The inclusion criteria were strict in this study. To ensure that there was no clinical infectious endophthalmitis at the time of admission and during operation, all patients with hypopyon and vitreous inflammatory opacity around the IOFB were excluded. Those who underwent primary surgical repair combined with IOFB removal at >24 hours after injury were also excluded. To exclude late cases of endophthalmitis, the patients were followed up for at least 1 month.

There are very few reports of cases of infectious endophthalmitis after IOFB removal in the literature. A case of a young patient who developed endophthalmitis half a month after IOFB removal, showing moderate intracameral and intravitreous purulent inflammation with a best-corrected vision of counting fingers, has been reported; in this case, 16S ribosomal RNA gene sequencing confirmed the presence of *Gordonia sputi* infection. Five days later, a complete PPV combined with lensectomy and silicone oil tamponade was performed. Finally, the patient's visual acuity returned to 0.1.[15] Toride et al reported that infectious endophthalmitis developed 1 day after IOFB removal

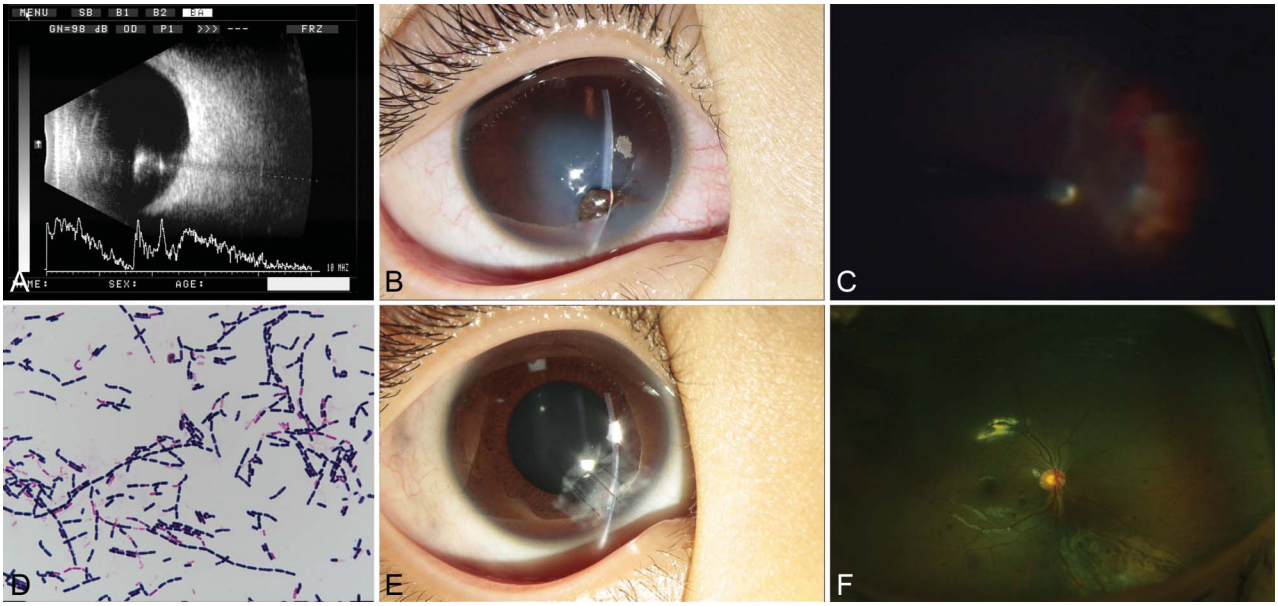

Fig. 3. A 6-year-old child injured by a firecracker explosion was also diagnosed as having *B. cereus* endophthalmitis during operation. **A.** B-scan ultrasonography revealing an IOFB in the posterior segment at admission. **B.** Slit-lamp photograph showing corneal lacerations, edema, and iris prolapse at admission. **C.** Screenshot of the video of the first operation showing vitreous purulent opacity around the IOFB. **D.** Result of the bacterial culture of the removed IOFBs: Gram staining of *B. cereus*. Magnification, 1,000× (**E**) Slit-lamp photograph showing a full-thickness corneal scar and suture with rest of the cornea and an otherwise normal anterior segment at the 6-month follow-up. **F.** Fundus photograph showing an attached retina at the 6-month follow-up.

and suturing for a sclerocorneal laceration in 1 eye of a 61-year-old man and that the incidence of infectious endophthalmitis after IOFB removal in patients with open globe eye injury is 2.5% (1 of 40).[16] Maneschg et al[11] mentioned that the incidence of infectious endophthalmitis after IOFB extraction is 3.22% (1 of 31) and that a risk factor may be delayed IOFB removal (>24 hours). In our study, we found two patients with infectious endophthalmitis after IOFB removal (≤24 hours). The bacterial cultures of the removed IOFBs were all positive for *B. cereus*. The incidence of infectious endophthalmitis after primary surgical repair combined with IOFB removal (≤24 hours) was 3.70% (2 of 54) in patients without clinical signs of infectious endophthalmitis preoperatively and during operation who received a series of standard treatments. These findings suggest that *B. cereus* infection may be a risk factor.

Bacillus cereus is an aerobic gram-positive bacillus found in soil, is normally found in the conjunctival sac, and is a rare cause of serious human infection; paradoxically, it causes one of the most severe posttraumatic or endogenous infections of the eye, endophthalmitis, which frequently results in blindness. Although intraocular infections caused by *B. cereus* are rare, they are the second most frequent cause of posttraumatic bacterial endophthalmitis.[17,18] In injuries caused by IOFBs that occurred in a rural or agricultural setting, there is a high incidence of endophthalmitis caused by *Bacillus* species.[19,20] In our study, the two cases of *B. cereus* endophthalmitis were also caused by IOFBs in rural settings.

Bacillus cereus endophthalmitis progresses rapidly, and delays in treatment result in permanent vision loss. Onset of symptoms (eye pain, red eye, and decreased vision) usually occurs within 12 to 24 hours of the injury and typically occurs within 48 hours.[21] In our study, the two patients had no symptoms or clinical signs of infectious endophthalmitis during the early stage of injury and developed endophthalmitis caused by *B. cereus* 24 hours after IOFB extraction. This might have been caused by the continued growth of residual bacteria after operation. After operation, the operated eyes of all patients were covered with sterile gauze for 1 day, and therefore, we could not assess for a visual acuity decline in time. Evolving clinical signs of *B. cereus* endophthalmitis may include severe ocular pain, chemosis of the conjunctiva, periorbital swelling, cells and flares in the aqueous humor, a hypopyon in the anterior chamber, and proptosis of the globe.[22] Development of a corneal ring abscess is a classic clinical sign of *B. cereus* endophthalmitis.[21] Systemic symptoms, such as fever, polymorphonuclear leukocytosis, and malaise, are also associated with *Bacillus* endophthalmitis.[10] The production of virulence factors such as proteases, lipases, enterotoxins, and hemolysins by *B. cereus* causes endophthalmitis, retinal layer folding, and detachment within 12 hours and complete central visual loss or even entire eye loss, which often occurs within 2 days.[23,24] It has been reported that in posttraumatic *B. cereus* endophthalmitis, more than 70% of patients lost some degree of vision in the infected eye, as few as 9% of those retained a visual acuity of 20/70 or better, and 48% of patients had eyeball enucleation, making it one of the most severe forms of bacterial endophthalmitis.[10,20,25] In our study, a 6-year-old child injured by a firecracker explosion was also diagnosed with *B. cereus* endophthalmitis during the operation and underwent vitrectomy combined with intravitreal antibiotic (vancomycin) injection 16 hours after the injury, and finally, the visual acuity improved to 20/25. However, two patients with *B. cereus* endophthalmitis who had no symptoms at admission and during the primary operation were treated with operation immediately after the development of endophthalmitis, but they failed to obtain effective visual acuity (≥20/200).

Bacillus cereus is susceptible to commonly used antibiotics, such as aminoglycosides, fluoroquinolones, and vancomycin. The most important component of treatment is intravitreal injection of antibiotics, along with vitrectomy in severe cases. In a rabbit model of endophthalmitis caused by intravitreal injection of *B. cereus*, Callegan et al[26] demonstrated that eyes treated with combined vitrectomy and intraocular vancomycin during the early stage of infection resulted in significantly better retinal function compared with eyes treated with intraocular antibiotics. Prophylactic intravenous and topical antibiotics have been administered at least 48 hours in all cases in our study. However, two patients with B. *cereus* endophthalmitis who had no symptoms at admission and during the primary operation (2/54; 3.70%) developed endophthalmitis after IOFB removal. Several studies reported the value of prophylactic intravitreal antibiotics in lowering the risk of posttraumatic endophthalmitis, especially in the high-risk cases identified based on the presence of 1 or more of the following risk factors: dirty wound, retained IOFB, rural setting, delayed primary repair of >24 hours and ruptured lens capsule.[27–29] The benefit of intraocular antibiotics use was only observed in eyes with IOFB.[28–30] Using ceftazidime and vancomycin provides a good coverage against both gram-negative and gram-positive organisms, including methicillin-resistant *Staphylococcus aureus*.[27] Among the five cases of endophthalmitis suspected during operation in our study, one was a case of infection with *B. cereus*, and this case had a

good visual outcome because intravitreal antibiotics were used at the time of initial treatment. Therefore, we recommended the use of prophylactic intravitreal antibiotics in cases of IOFB to reduce the risk of endophthalmitis after IOFB removal.

We learned many lessons from our investigations. Therefore, we also recommend the use of bacterial and fungal cultures of IOFBs to guide the application of antibiotics, especially when endophthalmitis occurs. Meanwhile, the patients' eyes should not be covered with sterile gauze after IOFB removal to be able to detect postoperative infectious endophthalmitis promptly. The present study has several limitations. First, there are a small number of patients who developed infectious endophthalmitis after IOFB removal, and statistical analysis of the data was not carried out. Further research is needed to elucidate the risk factors using correlational analysis. Second, a well-designed clinical trial is needed to establish the role of intravitreal antibiotics administration for IOFB-related endophthalmitis prophylaxis. In summary, we should be vigilant regarding the occurrence of infectious endophthalmitis after IOFB removal. Prompt diagnostic and therapeutic management are vital to prevent the occurrence of infectious endophthalmitis in patients with IOFBs.

Key words: Bacillus cereus, endophthalmitis, intraocular foreign body, surgery.

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