Hospital Construction–associated Outbreak of Ocular Aspergillosis after Cataract Surgery

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Objective: This study aimed to report an outbreak of Aspergillus endophthalmitis after cataract extraction during hospital construction.

Design: The study design is a case series of an outbreak of Aspergillus endophthalmitis.

Participants: Five patients in whom Aspergillus endophthalmitis developed during a period of hospital construction in Jeddah, Saudi Arabia, participated. Severe postoperative uveitis occurred in all five patients and failed to subside with topical steroid therapy. The patients were referred to the King Khaled Eye Specialist Hospital for treatment. The causative organism was identified as Aspergillus fumigatus in each case.

Intervention: All five patients were subjected to aqueous or vitreous tap. Three patients had vitrectomy. Patients were given systemic, periocular, and intravitreous antifungal agents.

Main Outcome: The final outcome in each patient was evisceration or enucleation, despite an intensive course of antifungal therapy.

Results: There were five patients, three females and two males, ranging in age from 51 to 65 years. Postoperative signs of infection developed in the patients 4 to 15 days after surgery. In all five cases, cultures of aqueous or vitreous grew A. fumigatus.

Conclusion: Aspergillus endophthalmitis is a serious and devastating complication of ocular surgery. The outbreak, herewith, may have been related to hospital construction. The infection can be prevented, notably, by proper maintenance of old, "sick" buildings and by following certain procedures during hospital construction.

Invasive aspergillosis is a well-recognized complication among patients who are immunocompromised.1–12 In many of the intraocular cases, invasive aspergillosis appears to be a nosocomial disease.11,13–15 Aspergillus endophthalmitis has been reported after sutureless surgery.16 Fungal scleritis may occur after cataract surgery17 or radial keratotomy.18 Postoperative fungal endophthalmitis is a devastating complication of intraocular surgery. The combination of trauma and the exposure of ocular tissues to an inoculum of Aspergillus spore may set the stage for infectious endophthalmitis. Old hospitals with “sick” buildings may harbor spores of fungi, including Aspergillus. The problem is worldwide, and construction within such sick buildings may expose patients to high inocula of Aspergillus species spores. Construction-associated nosocomial aspergillosis has been reported in several hospitals.14,15,18

We report, herewith, five patients with Aspergillus endophthalmitis after cataract surgery. All five cases occurred in a 3-week period coinciding with hospital construction at El Maghraby Hospital in Jeddah, Saudi Arabia. Patients were referred to the King Khaled Eye Specialist Hospital in Riyadh, Saudi Arabia, for treatment. The eye in each patient was enucleated or eviscerated because of the patient’s pain and poor response to treatment (Table 1).

Case Reports

Case 1. A 51-year-old woman arrived reporting pain and decrease in vision in her right eye over a 2-week period. She had undergone uneventful extracapsular cataract extraction with posterior chamber intraocular lens implantation in the right eye under local anesthesia. At the conclusion of surgery, the patient had been given dexamethasone 4 mg and gentamicin 20 mg subconjunctivally. After surgery, the patient was given intravenous amphotericin B in 500 ml of 5% dextrose in water with 1000 units of heparin. Intravitreous amphotericin
Table 1. Clinical History, Findings, and Outcome in Five Cases of Ocular Aspergillosis

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs)/Sex</th>
<th>Preceding Surgery</th>
<th>Onset (postoperative days)</th>
<th>Clinical Findings</th>
<th>Management/Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>51/F</td>
<td>ECCE PC-IOL</td>
<td>9</td>
<td>Endophthalmitis</td>
<td>Antifungal therapy</td>
</tr>
<tr>
<td>2</td>
<td>65/F</td>
<td>ECCE PC-IOL</td>
<td>4</td>
<td>Endophthalmitis</td>
<td>Enucleation</td>
</tr>
<tr>
<td>3</td>
<td>50/M</td>
<td>ECCE PC-IOL</td>
<td>15</td>
<td>Endophthalmitis</td>
<td>Vitrectomy/amphotericin B Removal of IOL Evisceration</td>
</tr>
<tr>
<td>4</td>
<td>57/M</td>
<td>ECCE PC-IOL</td>
<td>9</td>
<td>Endophthalmitis</td>
<td>Enucleation</td>
</tr>
<tr>
<td>5</td>
<td>55/F</td>
<td>ECCE PC-IOL</td>
<td>7</td>
<td>Endophthalmitis</td>
<td>Pars plana vitrectomy Removal of IOL Evisceration</td>
</tr>
</tbody>
</table>

ECCE = extracapsular cataract extraction; PC = posterior chamber; IOL = intraocular lens.

B (5 μg) also was given. The patient had superior infiltration of the cornea and was referred to the King Khaled Eye Specialist Hospital for further treatment. At that time, the patient had hand motion vision in her right eye. Biomicroscopy of the right eye showed chemosis and hyperemia of the conjunctiva. The cornea showed diffuse edema with superior corneal infiltrate at the site of the cataract wound reaching the upper half of the cornea. The anterior chamber was filled with fibrinoid exudates, and the iris details were hazy. The vitreous cavity was not visualized, and ultrasonography showed echoes in the anterior vitreous consistent with cells and exudates. Systemic amphotericin B was continued, together with subconjunctival miconazole. In view of the increase in the creatinine, intravenous amphotericin B was discontinued. The vision of the patient deteriorated over the next 24 hours and became light perception with no projection. She was given 10 pg of amphotericin B intravitreally but showed poor response. The retina consultant thought that the patient would not benefit from a vitrectomy. Because of the pain and lack of response to antifungal therapy, the patient's right eye was enucleated.

Histopathology of the globe stained for Gomori methenamine-silver nitrate stain showed septated hyphae in the cornea, sclera, and intraocular structures (Fig 1). Necrosis was noted in the sclera and cornea, which were infiltrated heavily by neutrophils, plasma cells, and lymphocytes. Chronic inflammatory cells also were seen in the iris. Segments of the lens capsule were surrounded by fibrinous exudates and neutrophils. The vitreous cavity contained fibrin and neutrophils. The optic disc was infiltrated by lymphocytes and neutrophils but showed no evidence of fungal elements.

Case 2. Four days after uneventful extracapsular cataract extraction with posterior chamber intraocular lens implantation, a 65-year-old Saudi woman started reporting pain and redness in her left eye associated with a decrease in vision. The patient underwent anterior chamber paracentesis and vitreous tap and was given intravitreous injections of cefazolin and amikacin. The patient started receiving intravenous amphotericin B and subconjunctival miconazole. She had pars plana vitrectomy with removal of her intraocular lens and was given injections of vancomycin, amphotericin B, and amikacin intravitreally. Cultures of the aqueous and vitreous cultures grew A. fumigatus. The retina consultant thought that the patient would not benefit from a vitrectomy. Because of the pain and lack of response to antifungal therapy, the patient's left eye was enucleated.

Histopathology showed necrosis with fibrin formation and diffuse infiltration with polymorphonuclear cells, lymphocytes, and macrophages. The cornea showed polymorphonuclear cell infiltrates and numerous branching hyphal elements.

Case 3. A 50-year-old man had undergone uneventful extracapsular cataract extraction with posterior chamber intraocular lens implantation and peripheral iridectomy on his right eye. After surgery, the patient received topical Maxitrol eyedrops (dexamethasone 0.1%, neomycin, polymyxin B; Alcon Laboratories, Ft. Worth, TX) four times daily. He was seen at 1 week and was found to have no significant inflammatory reaction in
the anterior chamber. Two weeks after the procedure, the patient started reporting a decrease in vision, burning sensation, tearing, and pain in his right eye. He started receiving fortified gentamicin drops (14 μg/ml) and was given prednisolone acetate 1% eyedrops and gentamicin 80 mg intravenously every 8 hours. The patient showed little improvement, then his vision started to deteriorate. He was referred for further treatment.

On examination, the patient was found to have hand motion vision in his right eye. Tension was 8 mmHg by applanation, and the right eye showed mucoid discharge with swelling of the eyelids and conjunctival hyperemia. The cornea was clear. The anterior chamber showed + cells and hypopyon inferiorly reaching 10% of the anterior chamber. The pupil was mid-dilated, and fibrin was seen over the intraocular lens. There was vitreous haze and whitish fibrinous exudates. Vitreous and anterior chamber taps were obtained. The patient underwent therapeutic vitrectomy with intravitreous injection of amphotericin B 10 μg and 35 μg miconazole. Despite treatment, the patient's vision continued to deteriorate. Ultrasonography showed an increase in the vitreous exudates. The patient underwent enucleation because of pain and lack of light perception.

Culture from the aqueous, vitreous, and ocular contents grew Aspergillus fumigatus. Histopathology of the globe showed evidence of necrosis with extensive infiltration by polymorphonuclear cells, lymphocytes, plasma cells, and macrophages. Descemet membrane was disrupted at several places where fungal hyphae covered the endothelial surface. The retina showed disorganization with evidence of necrosis and infiltration with polymorphonuclear cells, lymphocytes, and plasma cells.

Case 4. A 57-year-old man had undergone uneventful extracapsular cataract extraction with posterior chamber intraocular lens implantation on his right eye under local anesthesia. The patient received topical Maxitrol eyedrops (Alcon Laboratories) four times daily. He was seen at 1 week and had 2+ cells and 2+ flare in the anterior chamber. The administration of topical Maxitrol eyedrops was increased to five times daily. Two days later, the patient had an increase in the ocular pain and redness of the eye develop. He was found to have fibrin in the anterior chamber and 4+ cells with chemosis of the conjunctiva. An anterior chamber tap grew A. fumigatus. The patient started receiving topical antifungal agents and then was referred for further treatment at the King Khaled Eye Specialist Hospital.

On examination, the patient was found to have light perception and poor projection in the right eye. There was evidence of swelling of the eyelids with chemosis of the conjunctiva. Necrosis of the conjunctiva and sclera and peripheral corneal melting were noted at the site of the cataract wound superiorly (Fig 2). The 10–0 continuous suture that was used previously was loose on the wound. The cornea showed diffuse edema. The anterior chamber was filled with fibrinous exudates, and the pupillary area was covered with fibrin. The intraocular lens could not be seen. His cultures again showed A. fumigatus from the wound edge superiorly. The patient was given intravitreous 10 μg of amphotericin B daily for 3 days. Because the patient had no light perception and was in pain, enucleation was performed.

Cultures taken from the vitreous and anterior chamber showed A. fumigatus. Histopathology of the globe showed extensive necrosis of the sclera and cornea, which was infiltrated with neutrophils. The iris was covered by fibrinous exudation and infiltrated by polymorphonuclear cells, plasma cells, and macrophages. Descemet membrane was disrupted at several places where fungal hyphae covered the endothelial surface (Fig 3). Gomori methenamine-silver nitrate staining showed numerous septate hyphae in the anterior scleral tissue just behind the ciliary body. The hyphae showed dichotomy. The retina was disorganized with evidence of necrosis and infiltration with polymorphonuclear cells, lymphocytes, and plasma cells.

Case 5. A 55-year-old Saudi woman had redness, pain, and a decrease in vision develop 15 days after an uneventful extracapsular cataract extraction with posterior chamber intraocular lens implantation on her right eye. The patient had an uneventful immediate postoperative course. She was maintained by receiving topical Maxitrol eyedrops four times daily. At 1 week, the patient was found to have an increase in the anterior chamber inflammation. She started receiving high-dose topical and systemic steroids in the form of prednisolone acetate 1% eyedrops once every hour and prednisone 60 mg orally per day. The patient's condition deteriorated, corticosteroids were stopped, and subconjunctival amikacin and vancomycin were given. Despite this treatment, the patient's vision continued to deteriorate and her pain increased. She was referred to the King Khaled Eye Specialist Hospital. On examination, the patient was found to have hand motion vision in her right eye. The intraocular pressure was 15 mmHg. The right conjunctiva showed hyperemia. The cornea was clear. The anterior chamber showed fibrinous exudates with a retrocorneal membrane superiorly at the site of the cataract wound (Fig 4). The pupil was...
covered with fibrinous exudates. The vitreous cavity showed exudates and was hazy. The fundus could not be visualized. Ultrasonography showed diffuse thickening of the retinochoroidal layer with posterior vitreous detachment and increased vitreous echoes suggestive of inflammatory reaction. The patient underwent anterior chamber tap and resuturing of the wound superiorly with intracameral injection of 5 μg amphotericin B. Vitrectomy was performed, and an intravitreous injection of amphotericin B 10 μg was administered. The injections were repeated, but the patient’s vision continued to deteriorate despite intravitreous and intracameral injections of amphotericin B. At that time, resection of the infiltrated cornea and sclera was done, and sclerocorneal patch was placed and sutured to healthy cornea and sclera. The patient was given another injection of micanozole 25 μg and amphotericin B 10 μg into the anterior chamber. In addition, 10 mg of micanozole was administered subconjunctivally superiorly. The patient was given another injection of amphotericin B 10 μg into the vitreous. Despite aggressive antifungal treatment, the patient’s vision continued to deteriorate. Histopathology of corneal and scleral tissues showed diffuse infiltration by polymorphonuclear cells, plasma cells, and lymphocytes. Culture grew A. fumigatus. The patient underwent pars plana vitrectomy, removal of the intraocular lens, and was given another intravitreous injection of amphotericin B (10 μg). Despite this treatment, the patient’s vision deteriorated to no light perception coupled with persistent pain, and she underwent enucleation.

Histopathology of the eye showed necrosis and infiltration of the cornea and sclera with lymphocytes, plasma cells, and polymorphonuclear cells. In addition, hyphae stained positively with Gomori methenamine-silver nitrate stain were seen in the corneal and scleral tissue.

**Discussion**

Aspergillus species are ubiquitous in nature and frequently are isolated from soil and vegetation. Aspergillus belongs to the Ascomycetes class of fungi and produces tiny spores (conidia) that are disseminated easily by wind. The organism can grow anywhere, including on grains, bread, and decaying vegetation, and because it is thermophilic, it can grow under a wide range of environmental conditions. The atmospheric temperature and humidity in Saudi Arabia from January to March are optimal for the growth and multiplication of A. fumigatus. All five patients described here came from one hospital in January and February during a period of hospital construction.

We did not carry out microbiologic studies on the construction site, but reports from the hospital showed isolation of A. fumigatus from the patients’ wards. All patients had undergone cataract surgery and posterior chamber intraocular lens implantation with lenses from different batches. In all five patients, unequivocal signs of infection developed 4 to 15 days after surgery. In two of the five eyes, A. fumigatus was isolated from the corneal wound; there was evidence of melting of the cornea and sclera superiorly in both cases. A. fumigatus has the ability to produce proteolytic enzymes that may lead to melting of the collagen fibers of the cornea and sclera.

Aspergillus endophthalmitis can be endogenous or exogenous. Endogenous Aspergillus endophthalmitis has been reported in association with drug abuse, periodontitis, orthoptopic liver transplant, and corticosteroid therapy. It is of rare occurrence in immunocompetent individuals. Exogenous Aspergillus endophthalmitis may occur in normal and immunosuppressed animals.

The organism can cause serious and devastating complications after cataract surgery. Aspergillus spores are light and disseminated easily. Therefore, once they have contaminated an operating theater, the area should be isolated and fumigated. It is extremely difficult to sterilize air conditioning ductwork. Thus, it may have to be replaced. A major step toward preventing the disease, therefore, is to ensure ongoing proper maintenance of air conditioning ducts and filters in hospital buildings and operating facilities.

Hospitals throughout the world are becoming old, and many may be contaminated with spores of fungi. Several reports of invasive aspergillosis have occurred throughout the United States during the past 2 years. This situation may present a serious problem for ocular surgery in the future, especially when surgical procedures are performed in older buildings or those undergoing construction. Patterson and associates monitored the epidemiology of invasive aspergillosis at Yale University Hospital during a period of hospital construction. They compared the efficacy of active epidemiologic surveillance for invasive aspergillosis using Aspergillus cultures and Aspergillus antigen detection. They found that of 24 cases identified over a 12-month period, 7 were nosocomial and 17 were community acquired. During hospital construction, it is advisable to do an aerobiologic evaluation for fungal spores. This can be done by prospective air sampling for molds using the gravity air settling plate method. The outbreak of Aspergillus endophthalmitis in this study coincided with a period of hospital construction. All patients contracted their infection within this 4-week period.

During hospital construction, special preventive measures should be taken. These include installation of wall-mounted portable high-efficiency particulate air-filter pu-
rififers, application of copper-8-quinolinolate-formulated paint, and replacement of perforated ceiling tiles with nonperforated types. Other measures include sealing windows, replacing horizontal dust-accumulating blinds with opaque vinyl roller shades, and regularly and systematically cleaning surfaces. In addition, the air conditioning systems should be checked routinely for spores. Loo and associates studied 36 cases of nosocomial aspergillosis during a period of hospital construction. The incidence density in the preconstruction period was 3.18 per 1000 days at risk. During the construction activity and before implementing the control strategy, the incidence density increased dramatically to 9.88 per 1000 at risk. After implementation of infection control measures and completion of construction work, the incidence density decreased to 2.91 per 1000 days at risk, a figure comparable to the preconstruction baseline rate.

The current study stresses the importance of implementing environmental control strategies that incorporate widely available technology as a means of controlling outbreaks of construction associated invasive aspergillosis endophthalmitis.

References