CASE REPORT

Delayed-onset postoperative endophthalmitis secondary to *Exophiala*

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SUMMARY

Exophiala is a genus of slow-growing, melanin-producing, saprophytic fungi most commonly found in soil, faeces and decaying plant matter. It is an unusual fungal pathogen capable of causing a variety of ophthalmic manifestations, including keratitis, scleritis and endophthalmitis. In this report, we present a rare case of delayed-onset postoperative endophthalmitis confined to the anterior segment, secondary to *Exophiala* species. Previous reported cases of delayed-onset postoperative endophthalmitis have been treated medically, with suboptimal outcomes. Our experience supports the use of anterior segment surgery to clear the nidus of disease combined with intravitreal voriconazole to prevent recurrence of the infection.

BACKGROUND

We strongly believe that this manuscript contributes to existing medical literature by first describing a successful treatment approach to a rare condition.

CASE PRESENTATION

A 65-year-old woman with a history of diabetes mellitus underwent bilateral phacoemulsification with intraocular lens (IOL) placement outside the USA. A single surgeon performed both surgeries within a 1-week period, 2.5 years prior to presentation at our institution. The patient reported a history of postoperative uveitis in her left eye, diagnosed 8 months after cataract extraction and treated with topical and systemic steroids. Two years following her initial surgery, the patient developed a corneal melt with IOL expulsion in the left eye, for which evisceration was performed. Two months later, the patient was diagnosed with idiopathic ocular inflammation of the right eye for which methotrexate, 15 mg orally weekly, was prescribed.

The patient presented to the Bascom Palmer Eye Institute with pain and decreased vision in her right eye. In the right eye, visual acuity was light perception, with temporal greater than nasal light projection on confrontation field testing. Intraocular pressure was 9 mm Hg. The pupil was not visualised. The patient's left eye had no light perception (status postevisceration). On slit lamp examination of the right eye, there was minimal conjunctival injection, significant oedema and neovascularisation of the corneal stroma, brown pigment staining the corneal endothelium, and consolidated yellow material occupying the anterior chamber (figure 1). High-resolution ultrasonography of the right eye

Figure 1 Preoperative slit lamp photograph of the patient's right eye. Pigmented fungal elements are visible on the corneal endothelium centrally. A yellow coagulum occupying the anterior chamber prohibits visualisation of the rest of the eye.

showed a formed anterior chamber filled with moderately dense opacities surrounding the iris and IOL. B-scan ultrasound of the posterior segment showed no evidence of vitreous involvement or retinal complications (figure 2).

The patient was observed for a period of 8 weeks, during which time the examination remained stable. All topical and systemic immunosuppression was discontinued. The patient then underwent penetrating keratoplasty (PKP), removal of the IOL and capsular bag, and anterior vitrectomy of the right eye. The host corneal button was divided and submitted to pathology and microbiology. The yellow coagulum from anterior chamber and IOL was cultured on chocolate agar and thio-glycolate broth. No extension of this material into the vitreous cavity was evident intraoperatively; notably, the vitreous appeared clear and free of inflammatory cells or membranes. The anterior chamber was irrigated thoroughly and the patient was left aphakic. No intraoperative steroids were given due to a suspicion for fungal infection. On postoperative day 4, the microbiology laboratory reported fungal elements from the anterior chamber and IOL cultures. Histopathological analysis of the host cornea and associated inflammatory material confirmed the presence of a chronic lymphocytic infiltrate, acellular debris and pigmented fungal elements (figure 3). The patient received intravitreal voriconazole 50 µg/0.1 mL and was started on fluconazole 150 mg orally twice daily, cyclosporine-A (0.5%) drops four times a day and voriconazole (1%) drops every 3 h. The microbiology results were revised to 'slow-growing black

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Figure 2 Preoperative ultrasonography of the patient's right eye. The anterior chamber is formed with moderately dense opacities surrounding the iris and intraocular lens. In the posterior segment, the retina is attached and there are no significant vitreous opacities or membranes.

yeast' on postoperative day 16. An additional dose of intravitreal voriconazole 50 µg/0.1 mL was given and the topical voriconazole drops were tapered to four times a day at this time. Final microbiology results disclosed an *Exophiala* species sensitive to voriconazole and amphotericin B. Microbiology was unable to elucidate the specific pathogen.

OUTCOME AND FOLLOW-UP

The patient was seen in postoperative week 7 with a best corrected visual acuity (BCVA) of 20/80 and a clear graft centrally. Neovascularisation at the graft host junction and new keratic precipitates were noted (figure 4), however there was no hypopyon. Prednisolone drops were started six times daily, given concern for early graft rejection. Aggressive treatment with topical steroids controlled the inflammation caused by the graft rejection but 3 months after the cornea became oedematous. The eye remained quiet with no signs of fungal involvement. Consultation with a vitreoretinal surgeon found no fundoscopic evidence of vitreous involvement. The patient was regrafted and the pathology of the corneal specimen demonstrated no fungal infection.

DISCUSSION

Exophiala is a genus of slow-growing, melanin-producing, saprophytic fungi most commonly found in soil, faeces and

Figure 3 Histopathological examination of the patient's corneal button. On periodic acid-Schiff (PAS) staining (×4), there is attenuation of the corneal endothelium and Descemet's membrane. Amorphous inflammatory debris is present in the anterior chamber containing lymphocytes, acellular debris and pigmented PAS-positive fungal elements. On Gomori methenamine silver (GMS) staining (inset, upper right, ×20), the presence of GMS-positive fungal hyphae and budding yeasts is confirmed. Gram and acid-fast staining were negative (not shown).

Figure 4 Slit lamp photograph at postoperative week 7. The penetrating keratoplasty graft is clear centrally with evidence of peripheral neovascularisation at the graft host junction. There are a few keratic precipitates consistent with early graft rejection, but no hypopyon or other signs of infection.

decaying plant matter. Its typical spectrum of disease in humans includes 'saxophone lung' (hypersensitivity pneumonitis), tinea nigra and maduromycosis (eg, Madura foot). Ophthalmic manifestations include subconjunctival mycetoma,¹ necrotising scleritis,¹ post-LASIK interface keratitis,^{2 3} corneal ulcer^{4 5} and endophthalmitis.^{6 7} It has been reported to colonise municipal drinking water, saunas, steam baths, as well as dental unit water lines.⁷ We do not know for certain the aetiology of the intractable postoperative uveitis that lead to evisceration of the patient's left eye. One possible explanation is that she developed bilateral *Exophiala* endophthalmitis secondary to contamination of the irrigation/aspiration system used during phacoemulsification of her cataracts.

There are a total of three case reports of *Exophiala* species endophthalmitis after cataract extraction in the literature. One was a case of acute postoperative endophthalmitis secondary to *Exophiala werneckii*, which responded to treatment with intravitreal amphotericin B followed by a 3-week course of systemic fluconazole, 200 mg orally twice a day, and topical natamycin every 2 h.⁶ Two other cases of delayed onset postoperative endophthalmitis secondary to *E. jeanselmei* presented at 8 and 9 months following cataract extraction.⁷ These delayed-onset cases were more resistant to treatment; despite an initial response to intraocular amphotericin B, the infections recurred and lead to permanent loss of vision and phthisis bulbi.

In our patient, a more intensive surgical approach was pursued including PKP, removal of the IOL-capsular bag complex, and anterior vitrectomy. Two doses of intravitreal voriconazole were administered at 4 days and 2 weeks postoperatively. The patient's aphakic visual acuity improved to a BCVA of 20/80. Of note, no topical steroids were given for prophylaxis of graft rejection, due to concerns about recurrent fungal infection in the setting of steroid use. Unfortunately, the patient developed an aggressive graft rejection and required a secondary transplant.

Some unique aspects of this case included corneal involvement and the patient's monocular status at presentation, both which were taken into consideration in choosing a more aggressive approach. In comparison to other cases of delayed-onset postoperative *Exophiala* endophthalmitis treated medically,⁷ our patient fared relatively well and retained a functioning eye with ambulatory vision. Surgical evacuation of the infectious contents may more effectively clear the inoculum than antimicrobial

therapy, particularly in the case of slow-growing organisms like *Exophiala*. While previous cases of *Exophiala* endophthalmitis have been treated with intravitreal amphotericin B,^{6 7} our experience supports the use of intravitreal voriconazole, which has a more favourable ocular toxicity profile.

Most cases of postoperative endophthalmitis present with bicameral involvement. An interesting observation is that this case of *Exophiala* endophthalmitis was confined to the anterior segment, with no evidence of vitreous involvement. Furthermore, experiments in an animal model have shown that injection of *Exophiala* organisms into the vitreous cavity fails to produce endophthalmitis.⁸ Perhaps nutritional or other trophic features of the vitreous cavity are inhospitable to the growth of this fastidious organism.

Exophiala is an unusual opportunistic pathogen capable of producing an unusual delayed-onset postoperative endophthalmitis confined to the anterior segment. Our experience supports the use of anterior segment surgery to clear the nidus of disease combined with intravitreal voriconazole to prevent recurrence of the infection.

Learning points

- ▶ *Exophiala* is an opportunistic pathogen capable of producing an unusual delayed-onset postoperative endophthalmitis confined to the anterior segment.
- ▶ Previous reported cases of delayed-onset postoperative endophthalmitis have been treated medically, with suboptimal outcomes.
- ▶ Our experience supports the use of anterior segment surgery to clear the nidus of disease combined with intravitreal voriconazole to prevent recurrence of the infection.

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Contributors JAQ-E contributed to case conception and design, acquisition, analysis and interpretation of data, formatting and writing the first draft, conducting literature searches, coordinating and managing case progress and submission of the manuscript. SW contributed significantly to case research and manuscript revision, including case conception and design, acquisition, analysis and interpretation of data, and critical revision of the manuscript for important intellectual content. FV contributed to case conception and design, acquisition, analysis and interpretation of data, reviewing and commenting on first draft, conducting literature searches, and further revision of manuscript. GA contributed to conceiving the idea for the case, case design, reviewing and commenting on first draft, coordinating and managing case progress, submission of the manuscript and critical revision of first and final drafts for important intellectual content. SW and GA were directly involved in patient management.

Competing interests None.

Patient consent Obtained.

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