CASE REPORTS

Treatment failure in a case of fungal keratitis caused by Pseudallescheria boydii

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Abstract
A case is presented of Pseudallescheria boydii fungal keratitis in an agricultural welder. Treatment with azole antifungal drugs (miconazole and itraconazole) and with penetrating keratoplasty was unsuccessful in eradicating the infection, and eventually the eye was eviscerated.

Case report
A 57-year-old man presented with a painful red eye. Ten days previously he had been welding in a pig slurry tank while wearing a face mask, but recalled no injury. An ulcer noted on the right cornea initially was thought to be herpetic and treated with 3% acyclovir ointment. Three days later 0·1% dexamethasone drops four times a day were added. One week later the ulcer had greatly extended and topical steroids were stopped.

Microscopy following extensive lamellar corneal debridement (biopsy) showed massive fungal infection. The organism was later identified as Pseudallescheria boydii, but sensitivity tests were not performed on this isolate. Treatment was instituted with 1% miconazole drops hourly and itraconazole 200 mg once a day orally, and a subconjunctival injection of miconazole 0·5 ml of 10 mg/ml was given. The ulcer did not improve, so 1 week later further corneal debridement was performed and the subconjunctival miconazole was repeated. Systemic antifungal treatment was changed to miconazole 600 mg three times a day intravenously, but the ulcer continued to enlarge. Ten days later the patient was transferred to Bristol Eye Hospital.

On admission the cornea was hazy and thickened with a deep central ulcer and marked stromal infiltrate (Fig 1). The anterior chamber was deep with an intense fibrinous exudate and a 2·5 mm hypopyon. Following deterioration, an 8 mm eccentric right penetrating keratoplasty and clearout of the anterior chamber exudate were performed 3 days after transfer (5 weeks after presentation). Pseudallescheria boydii was isolated from excised cornea and anterior chamber fibrin, but there was no bacterial growth from these specimens. Microscopy showed fungus up to the corneal resection margin.

Because of the patient’s clinical deterioration before surgery, postoperative antifungal treatment was changed from miconazole to itraconazole, initially 200 mg once a day orally. Topical 1% miconazole was continued.

Twelve hours postoperatively there was a marked fibrinous anterior uveitis and the donor corneal button was thickened and hazy. Over the next 2 days the graft cleared but the hypopyon reformed, so 0·1% dexamethasone drops four times a day were added. The fibrinous reaction progressed with lifting of the graft, and the dexamethasone was increased to 2 hourly. This failed to halt the progression to endophthalmitis (Fig 2).

Serum concentrations of itraconazole were low (0·2 mg/l at 4·5 hours), so the dose was increased to 200 mg twice a day. The results of sensitivity testing of the Bristol corneal isolate became available 4 days postoperatively. These showed that the organism was sensitive to miconazole (minimum inhibitory concentration [MIC]= 0·5 mg/l), but resistant to amphotericin B (MIC=5 mg/l) and itraconazole (MIC > 50 mg/l). Miconazole 600 mg intravenously three times a day was therefore recommenced. This was later increased to 1200 mg three times daily in combination with hourly topical miconazole 1% and two further subconjunctival injections of miconazole.

The endophthalmitis did not respond, however, and the patient became depressed and nauseated from systemic treatment. Because clinical success was deemed unlikely, the patient requested evisceration, which was performed 8 weeks after the original infection. Pseudallescheria boydii was isolated from evisceration specimens of cornea and anterior chamber fibrin but not from lens or vitreous.

Discussion
Fungal keratitis is most prevalent in agricultural workers in the rural populations of tropical areas, following traumatic implantation of fungal spores from soil or plant matter into the corneal stroma.

Pseudallescheria boydii (previously Petriellidium boydii, Allescheria boydii, Monosporium apiospermum) is a ubiquitous fungus that has been isolated from soil, polluted water, and sewage. It has been reported to cause keratitis, endophthalmitis, mycetoma, pneumonia, osteomyelitis, arthritis, sinusitis, endocarditis, meningitis, and brain abscess. In immuno-suppressed patients infection may result in fatal disseminated pseudallescheriosis.

There have been at least 14 reported cases of P boydii keratitis but none treated with itraconazole, a recently introduced orally adminis-
Although many forms of P. boydii are sensitive to miconazole, studies have shown that miconazole is not effective against all strains. In fact, some strains of P. boydii are resistant to miconazole, and it is ineffective in treating infections caused by this fungus. Miconazole has been used successfully in treating some cases of severe keratitis due to Aspergillus spp., but it has proved less successful in eradicating infections caused by Fusarium spp and other filamentous fungi.

Suspected mycotic keratitis, or mycotic keratitis in which the organism or its sensitivities have not yet been identified, should be treated empirically with a combination of antifungal agents. The broadest such ‘best guess’ combination treatment should probably include topical miconazole or econazole, subconjunctival miconazole, and either oral itraconazole or intravenous micafungin.

In any case of atypical or indolent keratitis the possibility of fungal infection should be borne in mind, and steroids should be used with great caution, if at all.

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10 Jones DB. Initial therapy of suspected microbial corneal ulcers. II. Specific antibiotic therapy based on corneal scrapings. Surv Ophthalmol 1979; 24: 97.