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, Monoспорium 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 immunosuppressed patients infection may result in fatal disseminated pseudallescherosis.

There have been at least 14 reported cases of P boydii keratitis' but none treated with itraconazole, a recently introduced orally adminis-
tered broad-spectrum triazole compound. In
only five of these 14 cases was treatment success-
ful, the remainder requiring evisceration.
Although many isolates of P. boydii are resistant
to amphotericin B, several cases of keratitis have
been successfully treated with this drug alone, or
in combination with nystatin or natamycin. **

Although many strains of P. boydii are sensitive
to miconazole, there have been no published
reports of Pseudallescheria keratitis successfully
treated with this drug. The reasons for the failure
of high dose miconazole treatment in this case are
unclear, but the administration of topical corti-
sosteroids and lack of drug penetration to the
infection site may have contributed.

Only three cases of endophthalmitis due to
P. boydii have been previously reported, none
associated with keratitis. In one case of endop-
thalmitis following cataract extraction the
patient recovered after 3 months of topical treat-
ment with amphotericin B, 4 mg/ml 2 hourly.
Treatment success may have been due to the
anterior location of this infection. In a second
case the infection was haematogenous in origin
in a woman receiving corticosteroid treatment
for lupus nephritis. Parenteral therapy with
miconazole was unsuccessful despite the fact that
the drug was detected in the vitreous. The third
case occurred in a 15-year-old patient who
developed aspiration pneumonia and died
despite miconazole therapy.

The treatment of mycotic keratitis remains a
difficult problem, because none of the available
antifungal drugs is ideal. Natamycin has been
used successfully to treat filamentous fungal
infections, but its tissue penetration is limited and
it is ineffective subconjunctivally. (11) Nystatin and
amphotericin B have been even less successful
than natamycin, and both are irritat-
ing to the involved tissue. (11) Of the topical
imidazoles, econazole has the broadest
spectrum (12) and has been used successfully
to treat mycotic keratitis due to Aspergillus spp and
Fusarium spp. Miconazole has been used success-
fully in treating mycotic keratitis both topically
and intravenously. (14) Itraconazole has been shown
to be useful treating some cases of severe keratitis
due to Aspergillus spp, (15) but it has proved less
successful in eradicating infections caused by
Fusarium spp and other filamentous fungi. (15) 

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’ combina-
tion treatment should probably include topical
miconazole or econazole, subconjunctival
miconazole, and either oral itraconazole or intra-
venous miconazole.

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
care, if at all.

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