

CASE REPORTS

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

Philip A Bloom, D A H Laidlaw, D L Easty, D W Warnock

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 *Petridium 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.¹ In immunosuppressed patients infection may result in fatal disseminated pseudallescheriosis.

There have been at least 14 reported cases of *P boydii* keratitis² but none treated with itraconazole, a recently introduced orally adminis-

Bristol Eye Hospital,
Lower Maudlin Street,
Bristol BS1 2LX
P A Bloom
D A H Laidlaw
D L Easty

Regional Mycology
Laboratory, Department
of Microbiology, Bristol
Royal Infirmary, Maudlin
Street, Bristol BS2 8HW
D W Warnock

Correspondence to:
Philip A Bloom, FRCS Ed,
FCOphth.

Accepted for publication
14 November 1991

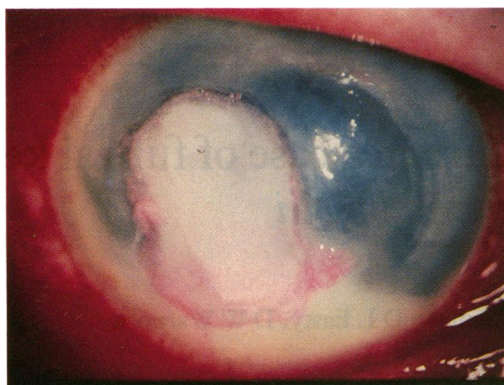


Figure 1 Corneal ulcer with hypopyon, due to *Pseudallescheria boydii*.

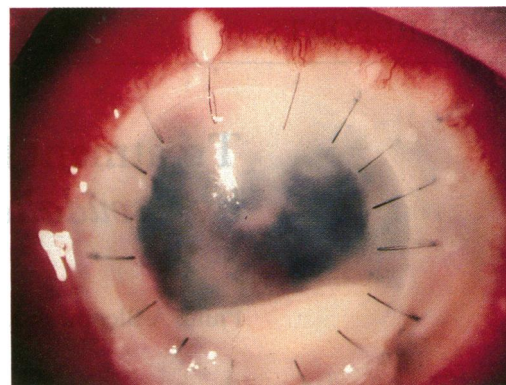


Figure 2 Reformed hypopyon after penetrating keratoplasty for *Pseudallescheria boydii* keratitis. A stitch abscess can be seen superiorly.

tered broad-spectrum triazole compound. In only five of these 14 cases was treatment successful, the remainder requiring evisceration. Although many isolates of *P. boydii* are resistant to amphotericin B,³ several cases of keratitis have been successfully treated with this drug alone, or in combination with nystatin or natamycin.⁴⁻⁶

Although many strains of *P. boydii* are sensitive to miconazole,^{3,7} 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 corticosteroids 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 endophthalmitis following cataract extraction⁸ the patient recovered after 3 months of topical treatment with amphotericin B, 4 mg/ml 2 hourly. Treatment success may have been due to the anterior location of this infection. In a second case³ 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 case⁹ occurred in a 15-year-old patient who developed aspiration pneumonia and died despite niconazole 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.^{10, 11} Nystatin and amphotericin B have been even less successful than natamycin, and both are irritating to the involved tissue.¹¹ Of the topical imidazoles, econazole has the broadest spectrum¹² and has been used successfully to treat mycotic keratitis due to *Aspergillus* spp and *Fusarium* spp. Miconazole has been used successfully in treating mycotic keratitis both topically¹³ 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, 16}

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 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 caution, if at all.

We thank Mrs G Bennerson for the photographs.

- 1 Warnock DW, Johnson EM. Clinical manifestations and management of hyalohyphomycosis, phaeohyphomycosis and other uncommon forms of fungal infection in the compromised patient. In: Warnock DW, Richardson MD, eds. *Fungal infection in the compromised patient*. 2nd ed. Chichester: Wiley, 1991: 247-310.
- 2 Rippon JW. Medical mycology. *The pathogenic fungi and the pathogenic actinomycetes*. 3rd ed. Philadelphia: Saunders, 1988.
- 3 Lutwick LI, Galgiani JN, Johnson RH, Stevens DA. Visceral fungal infections due to *Petridium boydii* (*Allescheria boydii*). In vitro drug sensitivity studies. *Am J Med* 1976; **61**: 632-40.
- 4 Gordon MA, Vallotton WW, Groffead GS. Corneal sclerosis. A case of keratomycosis treated successfully with nystatin and amphotericin B. *Arch Ophthalmol* 1959; **62**: 758-63.
- 5 Matsuzaki O. Ocular infection with a fungus from rice leaf. *Jpn J Med Mycol* 1969; **10**: 239.
- 6 Zapater RC, Albei EJ. Corneal monosporiosis. *Ophthalmologica* 1979; **178**: 142-7.
- 7 Galgiani JN, Stevens DA, Graybill JR, Stevens DL, Tillinghast AJ, Levin HB. *Pseudallescheria boydii* infections treated with ketoconazole: clinical evaluation of seven patients and in vitro susceptibility results. *Chest* 1984; **86**: 219-24.
- 8 Glassman MI, Henkind P, Altire-Werber E. *Monosporium apiospermum* endophthalmitis. *Am J Ophthalmol* 1973; **76**: 821-4.
- 9 Meadow WL, Tipple MA, Rippon JW. Endophthalmitis caused by *Petridium boydii*. *Am J Dis Child* 1981; **135**: 378-80.
- 10 Jones DB. Initial therapy of suspected microbial corneal ulcers. II. Specific antibiotic therapy based on corneal scrapings. *Surv Ophthalmol* 1979; **24**: 97.
- 11 Forster RK. Fungal diseases. In: Smolin G, Thoft RA, eds. *The cornea: scientific foundations and clinical practice*. Boston: Little, Brown, 1983: 168-77.
- 12 Jones BR, Clayton YM, Oji EO. Recognition and chemotherapy of oculomycosis. *Postgrad Med J* 1979; **55**: 625-8.
- 13 Foster CS. Miconazole therapy for keratomycosis. *Am J Ophthalmol* 1981; **91**: 622-9.
- 14 Ishibashi Y, Matsumoto Y, Takei K. The effects of intravenous miconazole on fungal keratitis. *Am J Ophthalmol* 1984; **98**: 433-7.
- 15 Thomas PA, Abraham DJ, Kalavathy CM, Rajasekaran J. Oral itraconazole therapy for mycotic keratitis. *Mycoses* 1988; **31**: 271-9.
- 16 Ragge NK, Dean Hart JC, Easty DL, Tyers AG. A case of fungal keratitis caused by *Scopulariopsis brevicaulis*: treatment with antifungal agents and penetrating keratoplasty. *Br J Ophthalmol* 1990; **74**: 561-2.