Scedosporium apiospermum keratitis

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Summary A case of *Scedosporium apiospermum* keratitis is reported in a 65-year-old farmer referred for treatment of an extensive corneal ulcer in the left eye. Direct examination of scrapes revealed abundant filamentous septate hyphae; all cultures were consistently positive for the same fungus, identified later as *Scedosporium apiospermum*. The patient successfully responded to treatment with amphotericin B.

Key words *Scedosporium apiospermum*, Mycotic keratitis, Amphotericin B

Queratitis por *Scedosporium apiospermum*

Resumen Se presenta un caso de keratitis por *Scedosporium apiospermum* en un granjero de 65 años remitido para el tratamiento de una úlcera corneal extensa en el ojo izquierdo. El examen directo revela abundante hifas septadas y todos los cultivos fueron positivos para el mismo hongo que fue identificado posteriormente como *Scedosporium apiospermum*. El paciente respondió satisfactoriamente al tratamiento con anfotericina B.

Palabras clave *Scedosporium apiospermum*, Queratitis micotica, Anfotericina B

Mycotic keratitis is a devastating eye infection acquired after injury from plant matter. It occurred usually in rural environments, although it has been increasingly reported following eye-surgery procedures [1,2].

Over 60 fungal species have been reported to cause keratomycosis, the most frequent being *Fusarium solani, Fusarium oxyosporum, Aspergillus fumigatus, Aspergillus flavus, Acremonium, Penicillium, Paecilomyces* and *Curvularia* [3]. Fungal keratitis is associated with greater morbidity than its bacterial counterpart, since diagnosis is often delayed and available drugs are not always effective.

Scedosporium apiospermum, previously known as *Monosporium apiospermun* is the anamorph of *Pseudallescheria boydii,* a fungus known for some time as *Petriellidium boydii* and *Allescheria boydii* [4]. It is a ubiquitous, earth-borne fungus frequently isolated from soil and water, and has been identified in several cases of endophthalmitis and keratitis. Treatment of these pathologies usually proves ineffective due to the resistance of this fungus to the various antifungal agents currently marketed [5,6].

In the present report, we describe a case of fungal keratitis due to *S. apiospermum* in a farmer who successfully responded to treatment with amphotericin B.

Case report. A 65-year-old farmer was referred for treatment of an extensive corneal ulcer in the left eye (Figure 1). The ulcer was not associated with any known injury. A scraping was cultured on media for aerobic and anaerobic bacteria and fungi, and topical treatment was started with 1% cyclopentolate every 8 h, and cefazolin (50 µg/ml) and vancomycin (25 µg/ml) on an hourly basis. Culture results were negative. Lack of any improvement after five days' treatment gave rise to the suspicion of a possible mycotic infection. A new scraping was taken for direct examination and culturing; after debridement, topical treatment was commenced with hourly amphotericin B (2 µg/ml). From day 4 of treatment onwards, a slight but progressive improvement was observed; accordingly, on day seven treatment was expanded to include topical fluorometholone every 8 h, to interrupt corneal healing. Amphotericin B dose-rates were gradually lowered, and the drug was fully withdrawn after eight weeks, with no sign of corneal toxicity. Final biomicroscopic examination revealed mild inferior leukoma and a visual acuity of 0.5 Snellen with + 1.5 diopters.

Direct examination of a portion of scrape material using lactophenol blue revealed abundant hyaline septate hyphae. A further portion of scrape material was then cultured on solid media (Sabouraud dextrose agar plus chloramphenicol and blood agar). A number of colonies, apparently of the same fungus, grew up on all media and

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Figure 1. Corneal ulcer in the left eye.

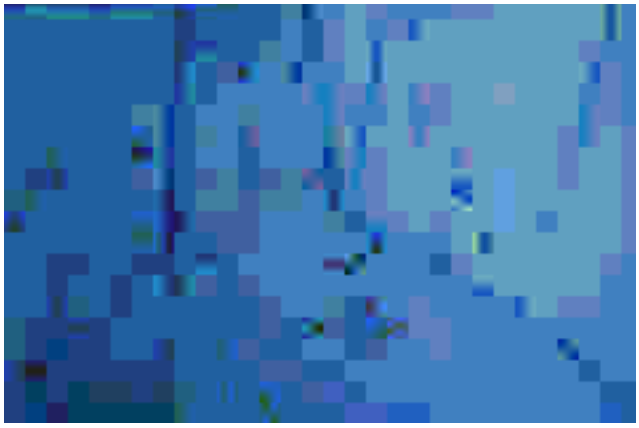

Figure 3. Annelloconidia and annellophores of *Scedosporium apiospermum* (lactophenol cotton blue, x400).

at various temperatures; the fungus was subsequently identified as S. apiospermum (Figures 2 and 3).

The susceptibility of this *S. apiospermum* isolate to five antifungal agents (amphotericin B, fluconazole, itraconazole, ketoconazole and 5 -fluorocytosine) was tested using a standardised microdilution in RPMI 1640 liquid medium. Broth microdilution MICs were determined by NCCLS method [7,8]. The isolate displayed *in vitro* resistance to all the antifungal agents studied, with MICs of over 16 µg/ml (amphotericin B, itraconazole and ketoconazole) and over 64 µg/ml (5FC) and 256 µg/ml (fluconazole) after 72 h.

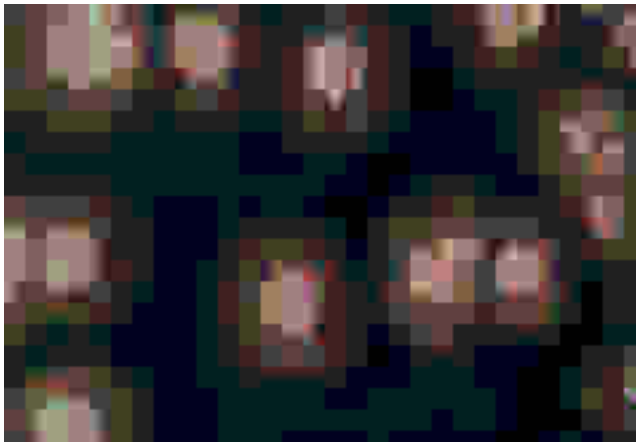

Figure 2. Seven-day-old fungal growth on Sabouraud dextrose agar plus chloramphenicol at 37 °C.

Mycotic keratitis is diagnosed by microbiological examination, although it is the clinical history that suggests the need for thorough mycological studies, giving positive results in 60% of cases.

S. apiospermum and its sexual form (*Pseudallescheria boydii*) are an uncommon cause of mycotic keratitis in humans. The species is commonly found in soil, which accounts for the fact that most cases are attributable to injury exacerbated by concomitant soil contamination. No such injury was reported by this patient, although it cannot be ruled out, given that he is engaged in agricultural activity.

Although direct microscopic examination of scrapes infected by *S. apiospermum* usually reveals a distinctive appearance (characteristic hyphae and ovoid conidia), in the present case only septate hyphae were visible, with no sign of conidia. Identification was subsequently made from typical colonies growing after three days' incubation at 37 °C, by gross (Figure 2) and microscopic examination and by microculture (Figure 3).

This isolate displayed *in vitro* resistance to all the antifungal agents tested, including amphotericin B. The good *in vivo* response to the latter confirms the view that for filamentous fungi there is little correlation between the results obtained *in vitro* and the efficacy observed *in vivo* [9]. *In vitro* sensitivity tests in filamentous fungi are thus of little value in predicting clinical response.

Although the ulcer was fairly extensive at the start of antimycotic therapy, it was not deep-seated (anterior stroma) and had not previously been treated with topical corticoids; both these factors were favorable to the eventual recovery of visual acuity.

Treatment was based on debridement, a good response to amphotericin B, and the rational use of topical corticoids to interrupt final corneal healing. Since there is currently no ideal antimycotic drug, (i.e., non-toxic, fungicidal and with good corneal penetration), the choice is often based on clinical response. *S. apiospermum* displays variable sensitivity to amphotericin B. Although most strains are resistant *in vitro*, there are occasional reports of a good *in vivo* response to amphotericin B, as the case recorded in this report [10]. Antifungal azoles are often cited as the agents of choice for infections due to *S. apiospermum* (and its teleomorph *P. boydii*) [11]. Voriconazole was reported to be less effective against another species of *Scedosporium, Scedosporium prolificans* [12], although apparently it has been used successfully to treat *S. apiospermum* [13,14]. The combination of amphotericin B and antifungal azoles, miconazole, fluconazole and itraconazole, may provide an important therapeutic option [15,16].

References

1. Bhermi G, Gillespie I, Mathalone B. *Scedosporium* (*Pseudallescheria*) fungal infection of a sponge explant. Eye 2000; 14: 247-249.
2. Surg Sridhar MS, Garg P, Bausal AK, Sharma S.Fungal keratitis after laser in situ keratomileusis. J Cataract Refract 2000; 26: 613-615.
3. Kwon Chung KJ, Bennett JE. Infections due to miscellaneous molds. In: Kwon Chung KJ, Bennett JE (Eds.) Medical Mycology. Philadelphia, Lea & Febiger, 1992: 743-753.
4. Guého E, De Hoog GS. Taxonomy of the medical species of *Pseudallescheria* and *Scedosporium.* J Mycol Med 1991; 118: 3-9.
5. Sterinert RF, McColgin AZ, White A, Horrsburgh GM. Diffuse interface keratitis after laser in situ keratomileusis (LASIK): a nonspecific syndrome. Am J Ophthalmol 2000; 129: 380-381.
6. Del Palacio A, Pérez-Blázquez E, Cuétara MS, García Bravo M, Criado-Gimeno C, Noriega AR. Keratomycosis due to *Scedosporium apiospermum*. Mycoses 1991; 34: 483-487.
7. National Committee for Clinical Laboratory Standards (NCCLS): Reference method for broth dilution antifungical susceptibility testing of conidium-forming filamentous fungi; Proposed standard NCCLS, document M38-P Wayne, Pa, NCCLS, 1998.
8. Espinel-Ingroff A, Bartleett M, Bowden R, *et al*. Multicenter evaluation of proposed standardized procedure for antifungical susceptibility testing of filamentous fungi. J Clin Microbiol 1997; 35: 139-143.
9. Kobayashi GS, Spiteer DE. Testing of organisms for susceptility to triazoles: is it justified? Eur J Clin Microbiol 1989; 8: 387-389
10. Cunningham R, Mitchell DC. Amphotericin B responsive *Scedosporium apiospermum* in a patient with acute myeloid leukaemia. J Clin Pathol 1996; 49: 93-94.
11. Dworzack DL, Clark RB, Borkowski Jr WJ, *et al*. *Pseudallescheria boydii* brain abscess: association with near drowning and efficacy of high-dose, prolonged miconazole therapy in patients with multiple abscesses. Medicine 1989; 68: 218-224.
12. Espinel-Ingroff A, Boyle K, Sheehan DJ. *In vitro* antifungal activities of voriconazole and reference agents as determined by NCCLS methods: Review of the literature. Mycopathologia 2001; 150: 101-115.
13. Hoffman HL, Rathbun RC. Review of the safety and efficacy of voriconazole. Expert Opin Investig Drugs 2002; 11: 409-429.
14. Girmenia C, Luzi G. Monaco M. Martínez P. Use of voriconazole intreatment of *Scedosporiumapiospermum* infection. J Clin Microbiol 1998; 36: 1436-1438
15. Walsh TJ, Peter J, McGough DA, Forthergill AW, Rinaldi MG, Pizzo PA. Activities of amphotericin B and antifungal azoles alone and in combination against *Pseudallescheria boydii*. Antimicrob Agents Chemother 1995; 39: 1361-1364.
16. Nulens E, Eggink C, Verweij PE. Combination therapy for keratitis by the fungus *Scedosporium*. Cornea 2003; 22: 92.