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An unusual ulcer: A case of cutaneous mucormycosis caused by *Rhizopus oryzae*

Bradley J. Gardiner [a,*], Ian Simpson [b], Mai H. Khuu [c], Sarah E. Kidd [d], Cheng H. Lo [e], Grant A. Jenkin [a,f]

[a] Monash Infectious Diseases, Monash Health, Clayton, Victoria, Australia
[b] Department of Anatomical Pathology, Monash Health, Clayton, Victoria, Australia
[c] Department of Microbiology, Monash Health, Clayton, Victoria, Australia
[d] National Mycology Reference Centre, SA Pathology, Adelaide, South Australia, Australia
[e] Department of Plastic & Reconstructive Surgery, Monash Health (Dandenong Hospital), Dandenong, Victoria, Australia
[f] Department of Microbiology, Monash University, Clayton, Victoria, Australia

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ABSTRACT

Mucormycoses are high-mortality infections feared by clinicians worldwide. They predominantly affect immunocompromised hosts and are associated with a spectrum of disease. We describe a case of cutaneous mucormycosis caused by *Rhizopus oryzae* in a patient with multiple risk factors cured with complete surgical excision and a short course of antifungal therapy.

1. Introduction

The diverse agents of mucormycosis (members of the subphylum Mucormycotina) are ubiquitous fungi found in environmental reservoirs associated with decaying matter worldwide. They have a broader, more heterogenous population of human hosts than other opportunistic molds but tend to affect the immunocompromised. Risk factors have been well described and include diabetes mellitus, malignancy, solid organ transplantation, iron overload, neutropenia and prednisolone use [1,2]. Classification of these fungi has changed over the years, leading to some confusion with nomenclature – the term zygomycosis, which was previously applied to these fungi, is now obsolete. *Rhizopus oryzae* is the most common agent, found in approximately half of reported culture positive cases. Mucormycosis is associated with a spectrum of disease of which the rhinocerebral form is the best characterized – however pulmonary, gastrointestinal, central nervous system, cutaneous and disseminated forms are also recognized [3].

The European Society for Clinical Microbiology and Infectious Diseases (ESCMID) and European Confederation of Medical Mycology (ECMM) have recently released comprehensive guidelines for the diagnosis and management of mucormycosis [4]. However even with optimal diagnostic and therapeutic strategies, mortality remains as high as 40% [1].

We describe a case of cutaneous mucormycosis secondary to *R. oryzae* in a patient with irreversible risk factors cured by surgery and a short course of antifungal therapy that illustrates the difficulties in managing this complex condition.

2. Case

A 69-year-old man presented (day 0) with a 4-day history of a skin lesion on his right lower leg which was initially erythematous, became black and necrotic, then broke down into an ulcer. He had no systemic symptoms, and could not recall any trauma or injury to the leg. His past history included poorly controlled type 2 diabetes mellitus, metastatic non-small cell lung cancer for which he had received chemotherapy and radiotherapy, chronic obstructive pulmonary disease, recurrent pulmonary emboli, peripheral vascular disease, and chronic renal impairment. He had received large doses of prednisolone for radiation pneumonitis and exacerbations of his airways disease, and had previously been a heavy smoker.

Physical examination revealed reduced pulses on his right lower leg but was otherwise unremarkable. The ulcer is shown in Fig. 1. When there was no improvement with empiric broad-spectrum antibiotics, biopsy of the ulcer was performed (day 4) and H&E stains (Fig. 2) revealed extensive dermal necrosis with a

* Corresponding author. Tel.: +61 395944564; fax: +61 395944533
E-mail address: bradgardiner@gmail.com (B.J. Gardiner).

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heavy neutrophilic infiltrate, with narrow-angled branching fungal hyphae with occasional septae seen under high-power magnification. Cultures were positive within 24 h for a cotton-like, white–gray fungus without reverse pigment growing at 28°, 37° and 40° but not 42 °C. Microscopically (Fig. 3) the isolate had broad aseptate hyphae, a white to gray–brown thallus formed from stolons with long unbranched sporangiophores which were sub-globose to ellipsoidal with longitudinal striations, up to 1500 μm. Simple rhizoids were positioned opposite the sporangiophores. It was later confirmed to be *R. oryzae* with DNA sequencing of the ITS1-5.8S-ITS2 region (100% sequence identity in both Genbank and CBS databases).

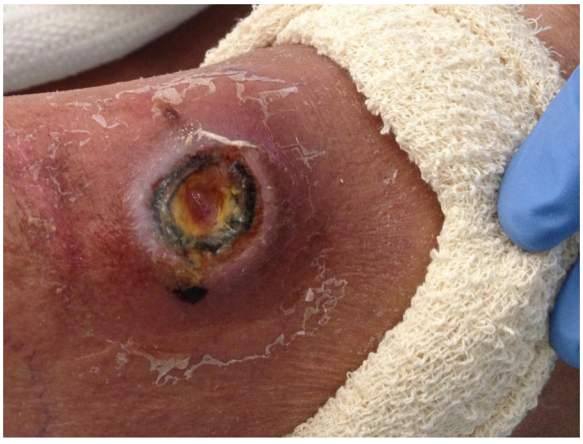

Fig. 1. Appearance of the ulcer on hospital admission (day 1).

Subsequent broth microdilution antifungal susceptibility testing revealed minimum inhibitory concentrations (MICs) of amphotericin 0.25 mg/L, 5-flucystosine >64 mg/L, fluconazole >256 mg/L, itraconazole 1.0 mg/L, voriconazole >8.0 mg/L, posaconazole 1.0 mg/L, caspofungin >8 mg/L, anidulafungin >8 mg/L, micafungin >8 mg/L [5].

Because of concern about pre-existing renal impairment, empiric therapy with posaconazole was commenced on day 15 and excision of the ulcer was performed on day 21. Liposomal amphotericin B (5 mg/kg) was added on day 20 due to concerns about posaconazole absorption but ceased when renal function deteriorated on day 24. As fungal hyphae were seen histologically out to the margins of the initial specimen, a second wide local excision was performed on day 24 with subsequent skin grafting (Fig. 4). Therapy also consisted of a right femoro-popliteal bypass to restore vascular supply to the limb, temporary cessation of prednisolone, and optimization of blood glucose control with insulin. There was no evidence of disseminated disease elsewhere on clinical assessment or on positron emission tomography (PET) imaging.

Despite 200 mg qid dosing with meals, cessation of pantoprazole and high fat intake, posaconazole levels >0.5 mg/mL could not be achieved. Antifungal therapy was ceased two weeks following the second excision given histologic margins were clear of fungal hyphae, and the wound progressively healed over several months (Fig. 5). The patient's malignancy however continued to progress despite treatment that included prednisolone and he died as a consequence of metastatic disease 9-months later, at which time there was no evidence of mucormycosis at the excision site or elsewhere. No post-mortem examination was performed.

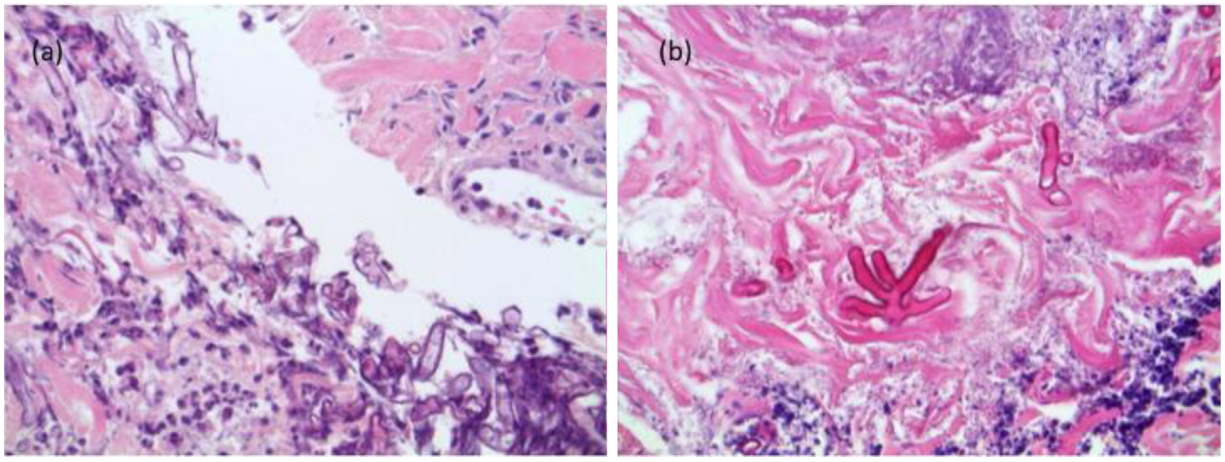

Fig. 2. Biopsy of ulcer performed on day 4: H&E stain, 400× (a) and PAS stain, 400× (b) showing narrow-angled branching fungal hyphae invading into necrotic dermis.

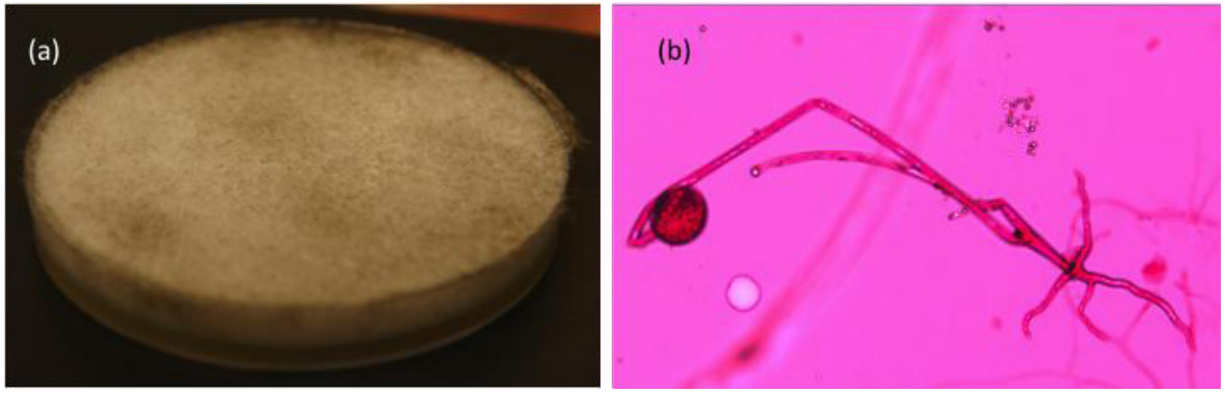

Fig. 3. Sabouraud agar plate following 24 h incubation (a) and view from slide culture (40×) showing the presence and orientation of rhizoids (b).