



Acute cutaneous zygomycosis of the scalp: A case report and literature review



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KEYWORDS

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Summary Cutaneous zygomycosis is the third most common form of zygomycosis. However, scalp involvement is rare for this disease. In this study, we present a case of acute zygomycosis in a diabetic patient who was effectively treated with local debridement, amphotericin B lipid complex and posaconazole.

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Introduction

The incidence of invasive zygomycosis has been increasing over the past two decades [1–4]; this is most likely secondary to the increasing prevalence of diabetes mellitus and high risk immunocompromised patients [4]. Cutaneous zygomycosis is the third most common form of zygomycosis (19%) [5], and it can be superficial, locally invasive or disseminated primarily from the skin to other non-contiguous organs or, rarely, from other organs to the skin [5,6]. Upper and lower extremities are common sites of involvement, although any area of the skin can be affected by zygomycosis [4]. However, scalp involvement is rare [4,7–10].

In this study, we present a case of scalp mucormycosis linked to use of a local herbal treatment.

Case report

A 76-year-old Saudi male with a history of poorly controlled diabetes, hypertension and blindness presented with a 5-day history of a black scalp wound associated with localized pain and pruritus. He had previously applied an herbal medication to a small trauma-induced laceration on the scalp caused by a falling object at home. He had no history of fever, headache or change in level of consciousness and no new neurological symptoms.

On examination, he was afebrile with stable vital signs. Multiple erythematous indurated

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Figure 1 Day 0 at presentation.

plaques with overlying pustules were present on the scalp. Several well-demarcated ulcers with overlying black eschars, with the largest measuring $6\text{ cm} \times 4\text{ cm}$ and the smallest measuring $0.5\text{ cm} \times 0.5\text{ cm}$, were also presented (Fig. 1). The initial wound culture grew both gram-positive and gram-negative bacteria. His blood culture was negative for bacteria.

His white cell count was 17.7×10^9 per liter (L), with 79% neutrophils, 17 g/dL hemoglobin and 345×10^9 /L platelets. BUN was 5.6 mmol/L, creatinine was $61\ \mu\text{mol/L}$, CO_2 was 19 mmol/L and RBS was 16.8 mmol/L. The results of his liver function tests were normal. His last HbA1c was 13%.

His initial antibiotic treatment was 1 g IV cefepime Q12H. The AFB smear was negative. He did not improve clinically after 5 days (see Fig. 2). He had increased erythema and induration over his scalp wound but, otherwise, remained afebrile. A head CT did not show any signs of bone invasion or intracranial extension. Tissue culture and histopathology results confirmed a diagnosis of mucormycosis (*Rhizopus* species) (Figs. 2 and 3). He was treated with surgical debridement and 5 mg/kg IV lipid complex amphotericin B lipid complex daily for 1 month, followed by posaconazole for 3 months. The patient's lesions completely resolved.

Discussion

Zygomycosis was first described as a cause of human disease in 1885, and the first cutaneous case

was reported in 1929 [10]. Cutaneous zygomycosis is the third most common form of zygomycosis (11–19%) following rhinocerebral (39%) and pulmonary disease (24%) [4–6]. Unlike other presentations of mucormycosis, 40–50% of patients with cutaneous zygomycosis are immunocompetent [4,5,11]. Trauma is the most common predisposing factor for cutaneous zygomycosis, especially when associated with soiling.

Risk factors for cutaneous zygomycosis include uncontrolled diabetes, diabetic ketoacidosis, burns, chronic renal failure solid organ transplants, hematological malignancies, neutropenia, steroid use, prolonged use of voriconazole and deferoxamine and low birth weight [4,7,11–14].

Cutaneous zygomycosis can present as a localized, deep or disseminated disease [4]. Almost half of patients with cutaneous zygomycosis have their disease confined to cutaneous and subcutaneous tissues, while the disease may extend to deeper tissues, such as bones, tendons and muscles in 24% of cases. Disseminated disease is defined as hematogenous spread of zygomycetes from the skin to other noncontiguous organs (20%) or from other organs to the skin (3%) [4,5]. Fungal elements are isolated from multiple noncontiguous sites [5]. Blood cultures are rarely positive.

Direct inoculation of the skin after penetrating trauma, surgery, burns, motor vehicle accidents, falls and insect bites is the usual port of entry for this disease [6]. Contact with soils or vegetation containing zygomycetes increases the chance of acquiring the disease [15]. In our patient, it was not possible to determine if the primary trauma to the scalp or a secondary infection caused by the use of a contaminated herbal treatment caused the patient's disease. Contamination of such herbal products has been previously documented [16,17].

Cutaneous zygomycosis can also be hospital-acquired [18]. Risk factors in the hospital include contaminated venous access, types of adhesives used, occlusive dressings, burn wounds and post-operative wounds. Sites of cutaneous zygomycosis formation described in the literature include intramuscular injection, insulin injection and catheter insertion sites [19–22].

The onset of cutaneous zygomycosis can be gradual and slowly progressing or aggressive and fulminant [4,23], and its clinical presentation is determined by the immunity of the host, the virulence of the fungi and the timing of diagnosis and intervention. The skin lesion appears red and indurated and then progresses to a black eschar and large ulcers. It can progress to necrotizing fasciitis and extend to deeper tissues if left untreated [24,25]. In cases of disseminated

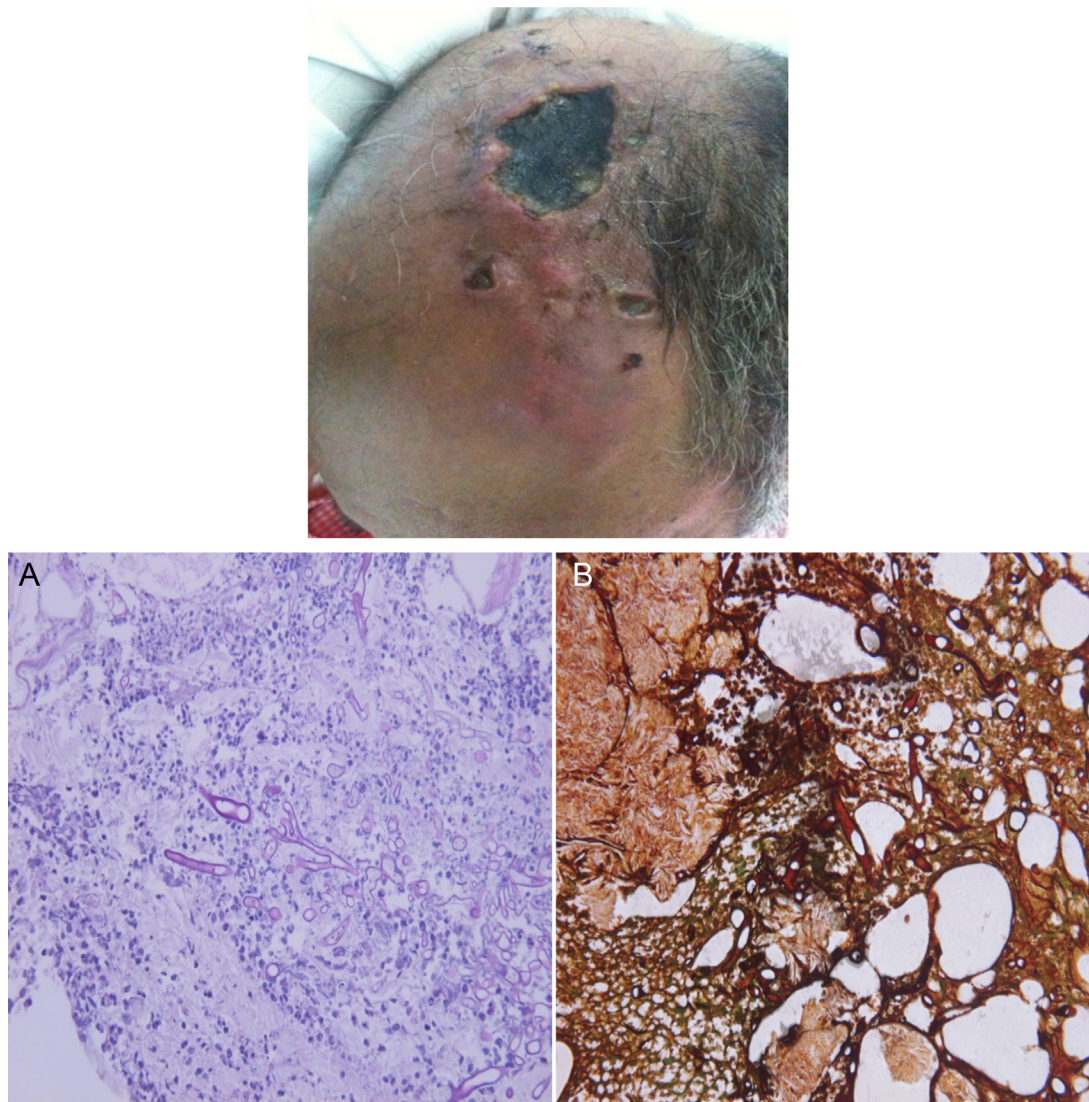


Figure 2 Day 5 treatment with cefipime. (A) H&E stain. (B) GMS (Gomori's methenamine silver stain). They showed classical nonseptated ribbon-like hyphae with wide-angle branching.

disease in an immunosuppressed host, skin lesions may present as a nonspecific erythematous macule [26]. While *Rhizopus* is the most commonly isolated genus of all zygomycosis infections across all sites, *Apophysomyces*, *Saksenaea* and *Mucor* genera are more common in cases of cutaneous or wound zygomycosis [27].

Mortality varies depending on the clinical form of zygomycosis; estimates range from 10% for localized disease to 94% for disseminated disease. Necrotizing fasciitis in cutaneous mucormycosis has high mortality [5,6].

Early diagnosis and treatment is important to improve patient outcomes. The two main methods of diagnosis are isolation of zygomycetes by culture and histopathological examination. Biopsies should be taken from the center of the lesion,

especially from the black eschar and subcutaneous fat because zygomycetes frequently invade blood vessels. In the histopathological analysis, focal areas of infection, such as nodules, extensive necrosis and hemorrhages with abscess formation are frequently observed. Peripheral tissue invasion by hyphal elements are easily identified, and this identification is necessary for diagnosis [27].

Treatment of cutaneous zygomycosis includes a combination of aggressive surgical debridement, effective antifungal therapy and resolution of underlying risk factors. Angioinvasion, thrombosis, and extensive tissue necrosis result in poor penetration of anti-infective agents to the site of the infection, unless effective, aggressive and early surgical debridement is performed. A mortality rate of less than 10% has been reported for

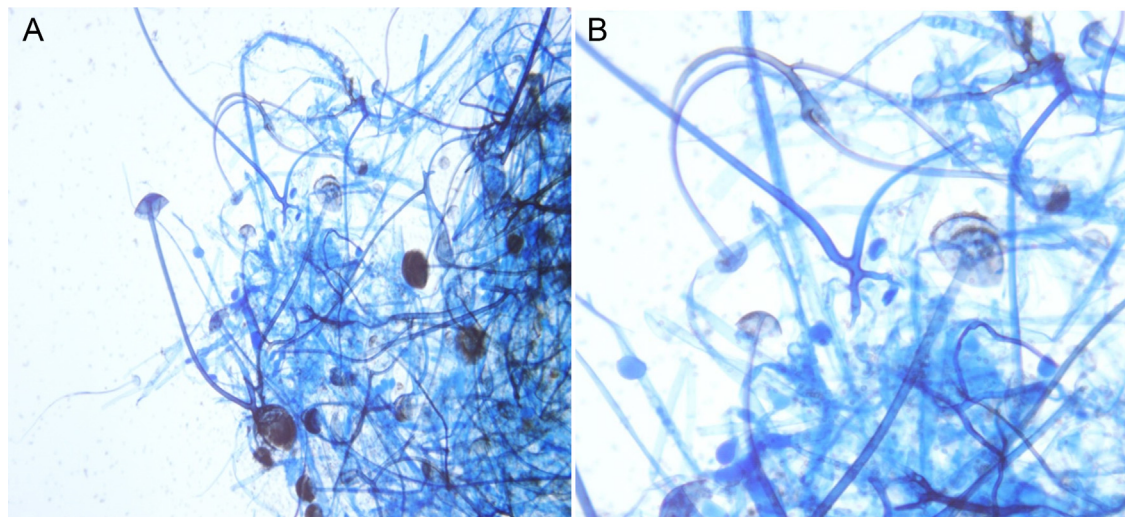


Figure 3 Photomicrograph of *Rhizopus* species. Note the rhizoid structure at the end, characterizing *Rhizopus* from the other zygomycosis.

patients with cutaneous mucormycosis after treatment with aggressive debridement and adjunct antifungal therapy [5].

The first-line antifungal agent for the treatment of all forms of mucormycosis is a high dose (10–15 mg/kg/day) of liposomal amphotericin B [6,28]. Treatment with liposomal amphotericin was associated with a 67% survival rate compared to a 39% survival with amphotericin B deoxycholate treatment [6]. However, the pharmacokinetics of amphotericin B lipid complex are different from those of liposomal amphotericin B and, thus, it cannot be considered an equal alternative treatment for mucormycosis, especially for central nervous system mucormycosis. Liposomal amphotericin B penetrates the brain parenchyma more efficiently. Even at a high dose of 30 mg/kg/day, amphotericin B lipid complex did not improve survival in a murine model of disseminated zygomycosis compared to liposomal amphotericin [6].

The pharmacological property differences between polyenes are less likely to be important in the treatment of non-disseminated cutaneous diseases and in cases with a non-immunocompromised host, when aggressive source control is performed [28]. Our patient was adequately treated with amphotericin B lipid complex, and this agent was used because it was available on our formulary list.

Among azoles, posaconazole and ravuconazole have in vitro activity against mucormycosis. Posaconazole has been used as a salvage therapy for refractory mucormycosis, including for cases that failed amphotericin treatment [29,30]. Micafungin, a recently introduced echinocandin, may

have a future role in the treatment of mucormycosis in combination with amphotericin and as a salvage treatment for a failing regimen [31].

Hyperbaric oxygen (HBO) has been used as an adjunctive therapeutic modality in rhinocerebral and soft tissue zygomycosis since 1970 [32]. HBO inhibits fungal growth, promotes the oxidative action of amphotericin B and improves tissue healing. In a review of 28 published cases of zygomycosis, adjunctive HBO therapy was more beneficial in patients with modifiable immune suppression, such as patients with zygomycosis due to diabetes and trauma, compared to patients with hematological malignancies [32].

Other adjunctive therapies that have been used in case reports include interferon gamma and colony-stimulating factor, which both increase the ability of phagocytes to kill agents of mucormycosis in vitro [6].

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Competing interests

None declared.

Ethical approval

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