Necrotizing cutaneous mucormycosis

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INTRODUCTION

Mucormycosis is generally an acute and rapidly developing fungal infection caused by fungi of the *Zygomycetes* class. In healthy hosts, these organisms seldom cause infections, but in debilitated or immunocompromised hosts, they produce a fulminant opportunistic infection, resulting in marked tissue destruction (Chun and Stevens, 2000). The infection is most commonly seen in acidotic patients, especially those in diabetic ketoacidosis. Prolonged treatment with antibiotics, corticosteroids and cytotoxic drugs; use of deferoxamine; haematological malignancies; severe malnutrition; trauma and extensive burns have been associated with this aggressive infection (Sugar, 2000).

Rhinocerebral mucormycosis is the most common presentation, accounting for over 75% of cases in the literature (Chun and Stevens, 2000; Sugar, 2000); approximately 10% have pulmonary, cutaneous or disseminated disease; and 2% have kidney or gastrointestinal involvement (Sugar, 2000). Isolated CNS mucormycosis is seen primarily in intravenous drug addicts (Chun and Stevens, 2000). This article describes an elderly diabetic woman with myelodysplasia who developed necrotizing cutaneous mucormycosis and highlights the difficulty of managing this condition.

DISCUSSION

Mucor species are ubiquitous in distribution, grow as hyphae (mould) in tissues and the environment, and have low virulence potential in human hosts. Neutrophils are important defense mechanisms against *Mucor*. Free iron and iron siderophores, such as deferoxamine, may augment fungal growth (Sugar, 2000). The mode of entry of the *Mucor* organism is through the respiratory tract or by direct inoculation of abraded skin. After inhalation or inoculation, the spores germinate and grow in cases of impaired immunity.

The hyphae invade tissues and have a special affinity for blood vessels; hyphae can also disseminate to peripheral tissues (Chun and Stevens, 2000). Mucormycosis can present with different manifestations depending on the site of infection. The various presentations of mucormycosis include rhinocerebral, pulmonary, cutaneous, gastrointestinal and CNS manifestations (Sugar, 2000). Predilection for one of these types of presentation depends on the underlying or predisposing condition. In neutropenic patients, the most common clinical presentation is rhinocerebral or pulmonary mucormycosis (Sugar, 2000).

Cutaneous mucormycosis is rare and is primarily a nosocomial infection in burn and blunt trauma victims (Chun and Stevens, 2000). Local infection has resulted from using contaminated elastic bandages, adhesive dressings and cloth tape (Mead et al, 1979; Wirth et al, 1997). Reports also have noted inoculation from trauma during gardening, tick implantation and automobile accidents (Johnson et al, 1987; Sugar, 2000). Primary cutaneous mucormycosis can develop rapidly in burn wounds, indwelling catheter sites, intravenous access sites, diabetic ulcers, surgical wounds, biopsy sites and following intramuscular corticosteroid injections (Jain et al, 1978; Tomford et al, 1980; Sugar, 2000).

Chronic obstructive pulmonary disease with respiratory acidosis, haemolytic anaemia, myelodysplastic syndromes and iatrogenic diabetes as a result of corticosteroid therapy may predispose to primary cutaneous mucormycosis (Garcia-Bustinduy et al, 1999). Patients with pulmonary or other forms of mucormycosis can develop skin lesions distant from the site of primary pathology. This secondary cutaneous involvement of the skin is a result of fungaemia, which is almost never documented with positive blood cultures and reflects the presence of widely disseminated disease (Meyer et al, 1973). The involved area is erythematous and painful, with varying degrees of central necrosis.

Cutaneous mucormycosis predominantly involves the epidermis and der-

CASE REPORT

A 75-year-old woman with a history of type 1 diabetes mellitus and myelodysplasia (refractory anaemia with excess blasts treated with monthly blood transfusions) presented with a temperature of 37.8 °C for the previous 48 hours. Clinical examination revealed a small, painful erythematous lesion on her thigh (*Figure 1*). There was no history of trauma to the area or use of adhesive dressings. She was found to be neutropenic and was started on ceftazidime and vancomycin empirically. Within 4 days, the lesion rapidly enlarged and became a black indurated necrotic ulceration with surrounding erythema (*Figure 2*). Histological examination of a skin biopsy specimen revealed invasive non-septate hyphal fungal forms consistent with the presence of an agent of zygomycosis (*Figures 3* and *4*); a culture grew *Rhizopus oryzae*. The patient was treated with intravenous amphotericin B and surgical debridement of the necrotic tissue. The patient's leukocyte count remained low (1.2x10^9/litre with 30% segments and 3% bands), and low grade fever persisted. Two weeks later, the patient developed gram-negative sepsis, her condition deteriorated and she died of complications of septic shock despite supportive inotropic therapy and the administration of broad-spectrum antibiotics.

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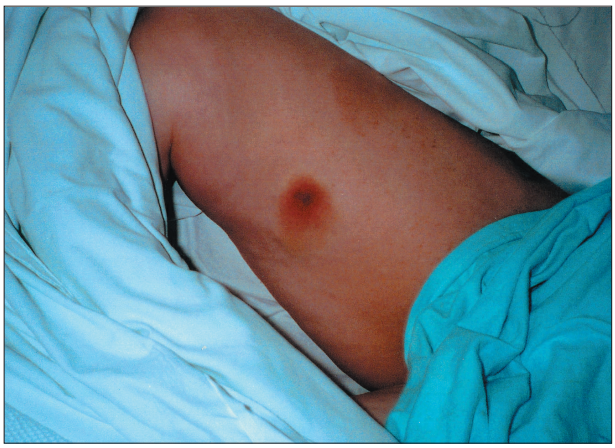


Figure 1. The initial painful erythematous lesion on the patient's thigh.

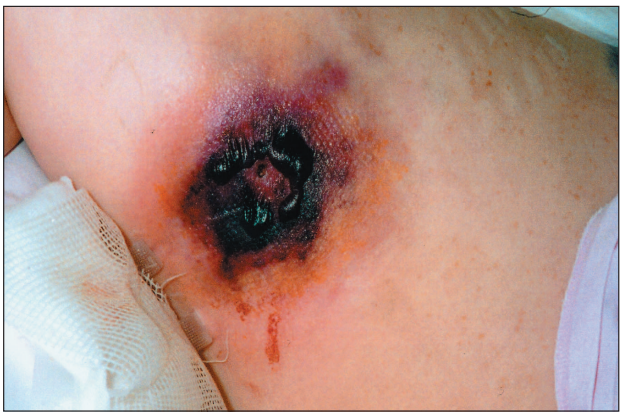


Figure 2. Development of a black necrotic ulceration with surrounding erythema several days later.

mis, and necrosis develops secondary to vascular invasion and ischaemic infarction, resulting in painful erythematous nodules and plaques that rapidly ulcerate and form central black eschars (Adam et al, 1994). Cultures have yielded *Rhizopus oryzae* or *Rhizopus rhizopodiformis* in most cases (Sugar, 2000).

The differential diagnosis of cutaneous mucormycosis includes ecthyma gangrenosum, pyoderma gangrenosum and aspergillosis, which all present in a clinically similar manner. History and physical findings lead to the suspicion of mucormycosis, but demonstration of the organism in tissue biopsy is necessary to establish a definitive diagnosis. Fungal hyphae can be seen on potassium hydroxide preparations of touch slides prepared from the biopsy specimen (Sugar, 2000). Fixed tissue can be stained with haematoxylin and eosin, and fungal hyphae can be seen with this routine histological stain. Grocott methenamine-silver or periodic acid–Schiff staining also demarcates fungal elements in tissue in most cases (Sugar, 2000). Typically, the fungi appear as broad, non-septate hyphae with branches occurring at right angles. Identification of genus and species requires the organism to be cultured.

Optimal treatment of mucormycosis involves a medical and surgical approach and control of the underlying disease. Administration of amphotericin B (1–1.5 mg/kg/day) and extensive surgical debridement of necrotic tissue represent the most important therapies. Repeated operations may be required for satisfactory removal of necrotic tissue. Once the patient is stabilized, administration of amphotericin B on alternate days can be considered (Sugar, 2000). In patients with primary cutaneous involvement, local debridement and topical administration of amphotericin B are satisfactory (Sugar, 2000). However, with any evidence of progression of the disease beyond the skin into the subcutaneous tissue and muscle, or development of signs and symptoms distant to the focus of infection, systemically administered amphotericin B is advised. Duration of antifungal therapy depends on the response of the infection to treatment and the success in resolving the underlying predisposing condition. Reversal of immunosuppression, if possible, may be beneficial to the outcome. HM

Figure 3. Hyphae in the deep dermis and subcutaneous fat with vessel wall invasion (haematoxylin and eosin, magnification x200 at width of 18.5 cm).

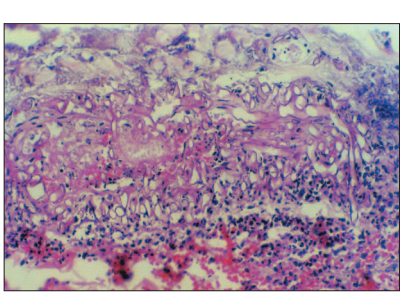
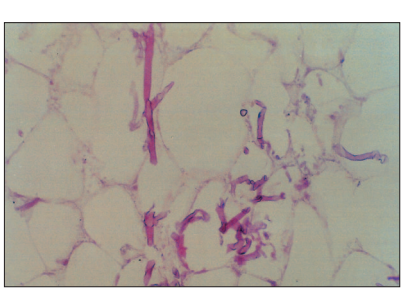


Figure 4. Large, broad aseptate hyphae with right angle branching, characteristic of the Mucorales (periodic acid-Schiff, magnification x200 at width of 18.5 cm).



Adam RD, Hunter G, DiTomaso J, Comerci G (1994) Mucormycosis: emerging prominence of cutaneous infections. *Clin Infect Dis* **19:** 67–76

Chun SF, Stevens DA (2000) Mucormycosis. In: Goldman L, Bennet JC, eds. *Cecil Textbook of Medicine.* 21st edn. W.B. Saunders Company, Philadelphia: 1883–5

Garcia-Bustinduy M, Guimera-Martin-Neda F, Noda A et al (1999) Primary cutaneous mucormycosis: a diagnosis to consider. *J Eur Acad Dermatol Venereol* **12:** 258–62

Jain JK, Markowitz A, Khilanani PV, Lauter CB (1978) Localized mucormycosis following intramuscular corticosteroid. Case report and review of the literature. *Am J Med Sci* **275:** 209–16

Johnson PC, Satter White RK, Monheit JE, Parks D (1987) Primary cutaneous mucormycosis in trauma patients. *J Trauma* **27:** 437–41

Mead JH, Lupton GP, Dillavou CL, Odom RB (1979) Cutaneous Rhizopus infection: occurrence as a postoperative complication associated with an elasticized adhesive dressing. *JAMA* **242:** 272–4

Meyer RD, Kaplan MH, Ong M, Armstrong D (1973) Cutaneous lesions in disseminated mucormycosis. *JAMA* **225:** 737–8

Sugar AM (2000) Agents of mucormycosis and related species. In: Mandell GL, Bennett JE, Dolin R, eds. *Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases.* 5th edn. Churchill Livingstone, Philadelphia: 2685–95

Tomford JW, Whittlesey D, Ellner JJ, Tomashefski JR (1980) Invasive primary cutaneous phycomycosis in diabetic leg ulcers. *Arch Surg* **115:** 770–1

Wirth F, Perry R, Eskenazi A, Schwable R, Kao G (1997) Cutaneous mucormycosis with subsequent visceral dissemination in a child with neutropenia: a case report and review of the pediatric literature. *J Am Acad Dermatol* **36:** 336–41