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CASE PRESENTATION

A 56-year-old man with a history of acute myelogenous leukemia (category M1) is admitted to the hospital for a temperature of 102°F and diarrhea for the previous 24 hours. He is found to be neutropenic and is started on cefepime and vancomycin empirically. Four days after hospital admission, he develops a small painful erythematous lesion on his right chest. Within 24 hours, the lesion rapidly enlarges to a 3 × 3-cm tender, indurated round lesion with central necrosis and surrounding erythema (**Figure 1**). No history of trauma exists. The patient's leukocyte count is 200/mm³ with 30% segments and 2% bands. Blood culture drawn on admission from his Hickman catheter grows two strains of *Bacillus* species, and a peripheral blood culture grows *Micrococcus* species.

WHAT IS YOUR DIAGNOSIS?

- A) Pyoderma gangrenosum
- B) Ecthyma gangrenosum
- C) Mucormycosis
- D) Aspergillosis

WHAT IS THE APPROPRIATE TREATMENT?

- A) Surgical débridement
- B) Intravenous (IV) amphotericin B with surgical débridement
- C) Ceftazidime and gentamicin
- D) IV amphotericin B only

ANSWERS

The correct answers are mucormycosis (C) and IV amphotericin B with surgical débridement (B).

DISCUSSION

Mucormycosis is a fungal disease that is generally limited to patients who have severe immunocompromise, diabetes mellitus, or trauma¹, although this disease has also been reported in immunocompetent individuals without underlying pathology.² Mucormycosis is caused by members of the class Zygomycetes, order Mucorales, and genera *Mucor*, *Rhizopus*, and *Absidia*. *Mucor* species are ubiquitous in distribution, grow as



Figure 1. Photograph of a patient with a black, indurated, round lesion with central necrosis and surrounding erythema on the right side of the chest.

hyphae (mold) in tissues and the environment, and have low virulence potential in human hosts.

Pathogenesis

Most of the current understanding about the pathogenesis of mucormycosis is derived from animal studies. Important defense mechanisms against *Mucor* are neutrophils. In contrast, free iron and iron siderophores such as deferoxamine may augment fungal growth. The mode of entry of the *Mucor* organism is through the respiratory tract or by direct inoculation of abraded skin. However, *Mucor* has been reported in association with sterile adhesive dressings,³ cloth tape,⁴ and donor leukocyte infusions.⁵ After inhalation or

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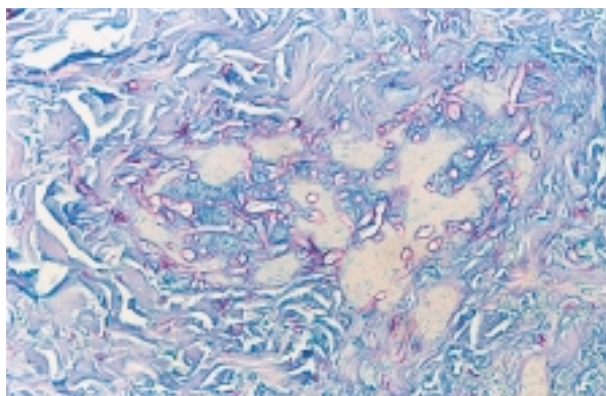


Figure 2. Periodic acid-Schiff stain of a pathologic specimen showing *Mucor* with broad, nonseptate hyphae branching at right angles. Original magnification $\times 400$.

inoculation, the spores germinate and grow in situations of impaired immunity. The hyphae invade tissues and have a special affinity for blood vessels; the hyphae can also disseminate to peripheral tissues.

Clinical Manifestations

Mucormycosis can present with different manifestations depending on the site of infection. The various presentations of mucormycosis include rhinocerebral, pulmonary, cutaneous, gastrointestinal, and central nervous system manifestations. Predilection for one of these types of presentation depends on the underlying or predisposing conditions. In neutropenic patients, the most common clinical presentation is rhinocerebral or pulmonary mucormycosis.¹ Disseminated or cutaneous mucormycosis can present with black skin lesions, as in this case patient.

Differential Diagnosis

The differential diagnoses of mucormycosis include pyoderma gangrenosum, ecthyma gangrenosum, and aspergillosis, which all present in a clinically similar manner. Ecthyma gangrenosum is a bacterial disease caused by *Pseudomonas aeruginosa*, whereas pyoderma gangrenosum is a skin condition associated with inflammatory bowel disease. Aspergillosis is a fungal disease caused by *Aspergillus* species and can present clinically as mucormycosis.

Diagnosis

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

slide preparations, and Gomori's methenamine silver or periodic acid-Schiff staining also demonstrate the fungal elements in fixed tissues. Typically, the fungi appear as broad, nonseptate hyphae with branches occurring at right angles (**Figure 2**). Identification of genus and species requires culture of the organism.

Treatment

Optimal treatment of mucormycosis involves a medical-surgical approach. Administration of amphotericin B (1 to 1.5 mg/kg/day) and extensive surgical débridement of necrotic tissue represent the most important therapies. Repeated operations may be required for satisfactory removal of necrotic tissue. Once the patient is stabilized, alternate-day amphotericin B can be considered.¹ 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.

A retrospective study by Pagano et al⁶ involving 37 patients with hematologic malignancy and histologically documented mucormycosis demonstrated that resolution of chemotherapy-induced neutropenia, in addition to prolonged treatment with amphotericin B and (if feasible) radical surgical débridement, was significantly correlated with recovery from infection. A few adjunctive therapies have been reported but are not proven to be effective; these therapies include hyperbaric oxygen,⁷ granulocyte colony-stimulating factor,⁸ and topical hydrogen peroxide soaks.⁹

SUMMARY

In the setting of immunocompromise, diabetes mellitus, or trauma, infection may be caused by a variety of pathogens. The finding of necrotic skin lesions should raise the suspicion for fungal disease, particularly mucormycosis. A skin biopsy should be performed to confirm the diagnosis. Therapy using a combined medical-surgical approach offers the best chance of cure. HP

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