

## Case Report

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# Cutaneous Mucormycosis Resulting from Hematogenous Dissemination of *Rhizomucor pusillus* in an Immunocompromised Patient

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## Keywords

Mucormycosis · Opportunistic infection · Diabetes mellitus · Immunocompromised patients

## Abstract

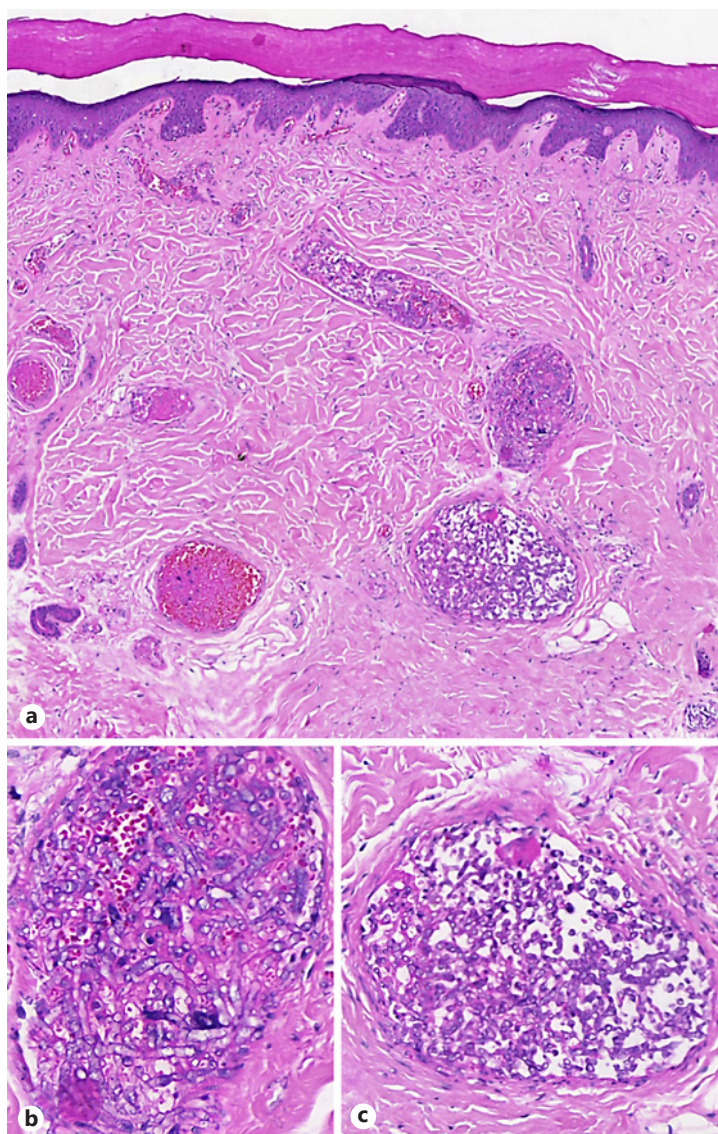
*Rhizomucor pusillus* is an opportunistic fungus that causes infections (mucormycosis) in patients with a predisposing disease, such as diabetes mellitus and immunodeficiency. Classic manifestations are sinus, pulmonary, and skin infections. Skin lesions consist of tender, erythematous, indurated, and necrotic plaques. The diagnosis is made by identification of the organisms by histopathological analysis of the lesion, showing nonseptate fungal hyphae in the dermis and invasion of the vessel walls, or by means of cultures. Amphotericin B and surgery are the treatments of choice.

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## Case Report

A 27-year-old woman with acute myelomonocytic leukemia was admitted to the hospital for a conditioning treatment for hematopoietic stem cell transplantation. The conditioning treatment consisted of cyclophosphamide, antilymphocytic serum, and total body irradiation. After the allogeneic transplantation, cyclosporine and mycophenolate mofetil treatment was introduced. Approximately 1 month after the beginning of the immunosuppressive therapy, the patient developed a nodular necrotic and painful lesion on the palm of the left hand but no other clinical manifestations.

Histopathological analysis of the lesion revealed numerous fungal hyphae in the dermis within the vessels, sometimes leading to vascular occlusions, confirmed by periodic acid



**Fig. 1.** **a** Numerous vascular occlusions in the dermis. HE.  $\times 40$ . **b, c** The dermis contains many fungal hyphae within the vessels, forming thrombosis. HE.  $\times 200$  (**b**).  $\times 100$  (**c**).

Schiff (PAS) staining (Fig. 1). A CT scan showed 3 nodular infiltrates in the right lung, consistent with a pulmonary fungal infection, but no other visceral involvement was detected. The skin culture revealed the presence of *Rhizomucor pusillus*. These findings led to the diagnosis of cutaneous mucormycosis, most likely resulting from hematogenous dissemination because the fungal hyphae were only found in the lumen and wall of the blood vessels (septic emboli).

### Discussion

Mucormycosis refers to opportunistic infections by fungi such as *R. pusillus*, that belong to the family Mucoraceae, in the order Mucorales. These fungi have been classified into 6 families. The most common species causing infection in humans is *Rhizopus arrhizus* [1]. These organisms are ubiquitous in nature and are present in the soil, animal matter, and decaying organic material such as vegetation, fruit, and bread. They may be contaminants in microbi-

ology [2]. Humans are frequently exposed to these organisms, but infection is very rare. Almost all infection due to these fungi occurs in the presence of a predisposing disease. It represents the third-most common opportunistic fungal infection in immunosuppressed hosts. Primary cutaneous mucormycosis resulting from direct inoculation of fungi into the skin is rare and is usually only seen in diabetics, in patients with thermal burns, and in immunocompromised patients. Secondary cutaneous mucormycosis is caused by hematogenous dissemination from a lesion located elsewhere in the body in patients with underlying diabetes, hematologic malignancy, or immunodeficiency (e.g., AIDS patients and drug addicts). Other known predisposing factors are iron overload, treatment with deferoxamine [3], and malnutrition. Diabetes mellitus is the most common risk factor, with or without diabetic ketoacidosis, followed by hematologic malignancies. It seems that fungal proliferation in mucormycosis is enhanced by an acidic and glucose-rich environment as well as a high level of unbound iron [4].

Mucormycosis causes necrosis of the tissues because of the invasion of the vessels by the hyphae. Skin lesions usually consist of tender, erythematous, indurated, and necrotic plaques. The most common sites for infection are the sinuses, lungs, and skin [5]. Sinus and pulmonary infections are probably due to the inhalation of spores. Symptoms and signs of sinus infection include fever, nasal congestion, purulent discharge, and headache. Symptoms of pulmonary infection include cough, dyspnea, fever, and hemoptysis. The infection can spread to contiguous structures such as the brain, mediastinum, or heart, and it can spread hematogenously. Renal and gastrointestinal manifestations have also been reported.

The diagnosis of mucormycosis is made by identifying organisms by means of histopathology and culture. Histological analysis shows broad and usually nonseptate fungal hyphae in the dermis, often invading the vessel walls; there is subsequent thrombosis and infarction of arterioles and tissue hemorrhage of venules. The inflammatory reaction is variable, and hyphal fragments are often engulfed by multinucleated giant cells [2].

Liposomal amphotericin B is the first-line drug of choice. The initial dose is 5 mg/kg/day, but this can be increased to as much as 10 mg/kg/day. Posaconazole and isavuconazole are alternatives for patients who cannot tolerate amphotericin B, or for a step-down therapy. Surgical debridement of the necrotic tissue is required for skin infections. Early surgical excision can also be helpful in rhinocerebral infection or monolobar pulmonary infection.

For our patient, we introduced amphotericin B at high doses (7 mg/kg), in combination with posaconazole and topical amphotericin B on the left hand. Forty-eight hours after the beginning of therapy, we performed a control CT scan. It showed a slight increase in nodule size and the presence of a fourth nodule in the left lung, despite the introduction of antifungal therapy. We finally interrupted the treatment because of impaired hepatic function. Unfortunately, the evolution for our patient was fatal.

## Conclusion

A necrotic skin lesion present in an immunocompromised patient should suggest a cutaneous mucormycosis, which needs to be confirmed by microscopic examination and fungal culture due to the aggressive clinical behavior of the disease.

## Statement of Ethics

The subject could not give a written informed consent (deceased). The director of the ethics committee at our institution approved the publication of this case with histological images only.

### Disclosure Statement

The authors have no conflicts of interest to declare.

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### Author Contributions

All the authors contributed equally.

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