Slowly Progressive Cutaneous, Rhinofacial, and Pulmonary Mucormycosis Caused by *Mucor irregularis* in an Immunocompetent Woman

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We herein report a case of slowly progressive cutaneous, rhinofacial, and pulmonary mucormycosis caused by *Mucor irregularis* in an immunocompetent woman who was successfully managed by combined surgical debridement and antifungal therapy. Slow progression, pulmonary involvement, occurrence in an immunocompetent patient, and good prognosis are unusual features of our case.

**Keywords.** mucormycosis; *Mucor irregularis*; cutaneous mucormycosis; rhinofacial mucormycosis; pulmonary mucormycosis.

Mucormycosis is a rare, life-threatening fungal infection that almost invariably occurs in immunocompromised patients [1]. On the basis of clinical presentation and anatomic site(s) involved, mucormycosis can be classified into at least 6 categories: rhinocerebral, pulmonary, cutaneous, gastrointestinal, disseminated, and miscellaneous [2]. Mucormycosis involving multiple anatomic sites is relatively rare. Generally, mucormycosis progresses rapidly and has a high mortality rate of approximately 31% [1, 3]. Many species belonging to Mucorales can cause mucormycosis, but mucormycosis caused by *Mucor irregularis* is extremely rare [2, 4]. Here we report a case of slowly progressive cutaneous, rhinofacial, and pulmonary mucormycosis caused by *M. irregularis* in an immunocompetent woman.

CASE REPORT

A 29-year-old woman was admitted to the General Hospital of Beijing Military Command (Beijing, China) for severe rhinofacial lesions. She developed a localized inflammatory lesion 14 years ago following the excision of a pea-sized red tubercle on the right paranasal area, and the lesion had been slowly expanding over the past years. She developed progressive destruction of the nasal sinus, nasal septum, soft and hard palates, and uvula. These symptoms were alleviated in summer and aggravated in winter. Three months ago, the paranasal erythema suddenly spread to most of her facial area, leading to acute necrosis, ulceration, and nasal bone cavitation, as well as fever, cough, sputum production, headache, dysphonia, and dysphagia.

Upon admission, the patient had a body temperature of 38.9°C and body weight of 45 kg. She suffered from malnutrition, fatigue, lack of energy, weight loss, and difficulty in speech. A dull percussion was noted in the right side of the chest, with a weak breath sound. Necrosis, ulcers, purulent secretion, and dark scabs were observed on her face (Figure 1A). The nasal bone was completely disfigured by cavitation. The soft and hard palates were fenestrated, whereas the nasal septum and paranasal sinus were dissolved and had developed into dark scabs. Nasal endoscopy and computed tomography (CT) revealed a largely damaged nasal structure, as evidenced by the dissolution of the nasal bone, collapsed nasal sinus, and disappearance of the sinus cavity. Craniocerebral nuclear magnetic resonance imaging demonstrated an increased density in the right temporal meninx region but showed no apparent pathological changes in the cerebrum. A CT scan of the chest detected a large high-density consolidation area in the right upper and middle lobes of the lung (Supplementary Figure 1A). Bronchoscopy revealed obvious abnormalities of the right bronchus, including bronchial stenosis, edema, and complete white obstructions. A lung biopsy was suggested, but the patient refused. Laboratory tests disclosed no abnormalities. Facial skin microscopy revealed a large amount of wide and nonseptate mycelia. Histopathological analysis showed epidermal necrosis and granuloma in the dermis. A large number of multinuclear giant cells and lymphocytes were mixed with epidermal cells and nonseptate mycelia (Supplementary Figure 1B). The presence of mycelia was confirmed by periodic acid-Schiff staining. A 5-day potato dextrose agar culture of facial tissues at 25°C produced white...
villous colonies and some were faint yellow. The colonies grew well at 25°C and 36°C, but could not grow at 37°C or 40°C. The same pathogen was also identified in bronchial lavage cultures.

The isolated pathogen was subjected to morphologic and genetic analyses. Under a microscope, the hyphae were broad, transparent and nonseptate, with chlamydospores and perpendicular sporangia (Figure 1B). The sporangia had a diameter of 70–85 μm, without receptaculum. The sporangiospores were ellipsoidal, smooth, and transparent, and had a diameter of 3–8 μm. These morphologic features were in agreement with those of Mucor species. A BLAST search of the GenBank database revealed that the internal transcribed spacer region of nuclear ribosomal DNA from the isolated pathogen had 96% homology with that from M. irregularis (GenBank accession number JN827387). Thus, the isolated pathogen was identified as M. irregularis.

An in vitro drug sensitivity assay was subsequently performed, which demonstrated that the isolate was sensitive to amphotericin B (minimum inhibitory concentration [MIC], 0.25 μg/mL) and slightly sensitive to itraconazole (MIC, 4.0 μg/mL), but resistant to fluconazole (MIC, >128 μg/mL), voriconazole (MIC, >16.0 μg/mL), and caspofungin (MIC, >32.0 μg/mL). On the basis of these results, the patient was treated by surgical debridement to remove necrotic tissue and intravenous injections of amphotericin B at 25 mg/day. After 1 week of treatment, the patient’s body temperature had returned to normal. Two weeks later, her cough and headache were alleviated, the ulcer dried, and scars formed. When the total dosage of amphotericin B reached 0.7 g, liposomal amphotericin B was administered at 50 mg/day. Three months later, the ulcer healed with scar formation, and the fungus was not detectable from multiple histopathological sites and in fungal cultures. Consolidation in the lung was diminished. Four and a half months after the initiation of treatment, all of the dermatologic symptoms had cleared (Figure 1C). Pulmonary inflammation had proceeded into inclusion bodies and pulmonary fibrosis (Supplementary Figure 1C). The treatment was terminated after the total dosage of liposomal amphotericin B reached 5.2 g. Cicatricial ectropion of both eyelids was further repaired by dermepenthesis. No recurrence or further development of pulmonary fibrosis was observed by pulmonary CT at 7 months after treatment.

DISCUSSION

Mucormycosis caused by M. irregularis is an extremely rare disease and, thus far, there have been only 16 reported cases (including our case) [5–7]. Here we describe a case of chronic mucormycosis caused by M. irregularis that involved multiple anatomic sites. Our case report highlights several unusual or previously unrecorded features of this disease.

Involvement of Multiple Anatomic Sites

In patients with M. irregularis infection, damage is mostly located in the nasal and facial areas and limbs, and can mimic the symptoms of lethal midline granuloma [7]. The majority of reported cases have been cutaneous mucormycosis [6], except for our case, which involved multiple anatomic sites. Pulmonary involvement was also only observed in our case. As mucormycosis caused by M. irregularis often causes superficial mycoses and facial mycoses can spread to the lungs via the respiratory tract, pulmonary mucormycosis in our case might have developed as a result of inhalation of the pathogenic fungus.

Slow Progression

Despite the rapidly progressive nature of mucormycosis, several chronic cases of mucormycosis caused by M. irregularis have been reported [8]. Interestingly, the isolated pathogen in
our case could not grow at 37°C, which is inconsistent with a previous report [6]. This may reasonably explain the observation that the patient’s symptoms subsided in summer and were aggravated in winter. Thus, it is speculated that different optimal temperatures for fungal growth may be responsible for the slow progression of mucormycosis in our case and a previously reported case [8].

**Occurrence in an Immunocompetent Patient**

Mucormycosis virtually always develops in patients with defects in their host defense [2]. Intriguingly, most patients diagnosed with mucormycosis due to *M. irregularis* have been immunocompetent and did not display apparent immunodeficiency, which is quite different from other fungal infections [6, 7]. These observations suggest that the pathogenesis of mucormycosis caused by *M. irregularis* might be unique and distinct from that of mucormycosis caused by other species; however, the underlying mechanisms remain unclear.

**Good Prognosis**

Most cases of mucormycosis are rapidly progressive and result in death without prompt treatment. Combination treatment with surgical debridement and antifungal therapy has been suggested to improve treatment outcomes [2]. Until recently, only members of the polyene class, including amphotericin B and its lipid derivatives, have been shown to be effective in treating mucormycosis. As the recommended dose of amphotericin B (1–1.5 mg/kg/day) has a very high toxicity [2], the dose of amphotericin B used in our case was much lower to minimize the side effects while maintaining the therapeutic effects. This strategy is utilized in several cases of mucormycosis with successful outcomes using either liposomal amphotericin B or amphotericin B lipid complex [9, 10]. Additionally, several novel therapeutic strategies have emerged, which include combinational therapy using lipid-based amphotericin with an echinocandin or an azole (largely itraconazole or posaconazole), or all 3 in combination [2, 11]. Of note, although our patient had a good prognosis, she could have been successfully managed by surgical excision of the local lesion before the small lesion progressed to destroy critical structures, which suggests the importance of early diagnosis.

In conclusion, we have described a very rare case of chronic mucormycosis caused by *M. irregularis* that was successfully managed by a combination of surgical debridement and antifungal therapy. Slow progression, pulmonary involvement, occurrence in an immunocompetent patient, and good prognosis are unusual features of our case. Owing to the extreme rarity of the disease, awareness and knowledge among physicians should be emphasized. Additionally, our case emphasizes the importance of early diagnosis.

**Supplementary Data**

Supplementary materials are available at *Clinical Infectious Diseases* online (http://cid.oxfordjournals.org/). Supplementary materials consist of data provided by the author that are published to benefit the reader. The posted materials are not copyedited. The contents of all supplementary data are the sole responsibility of the authors. Questions or messages regarding errors should be addressed to the author.

**Notes**

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