Invasive fungal wound infection in an otherwise healthy trauma patient (Mucor Trauma)

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Abstract

Background: Mucor fungi are found ubiquitously in the environment and rarely cause infections in humans. Mucormycosis is typically seen in immunocompromised patients, but has been increasingly documented in previously healthy trauma patients. Mortality due to these infections can be high due to delayed diagnosis from a subtle clinical presentation and spread of infection by angioinvasion. Early recognition and prompt treatment is critical for survival. We describe a case of invasive mucormycosis in a previously healthy trauma patient treated at a Level 1 trauma center.

Case report: A 22-year-old male presented to the hospital after being involved in a motor vehicle accident. He sustained multiple traumatic injuries and developed multi-system organ failure within 48 hours of admission. He developed invasive, soft tissue mucormycosis (Rhizopus sp) at the laparotomy site, requiring multiple surgical debridements and prompt antifungal therapy. The fungus was also cultured from respiratory secretions and likely associated with his abdominal infection. We suspect the patient was predisposed to an invasive fungal infection in the setting of multi-system organ failure and multiple blood transfusions. The patient ultimately did well and continued to improve on follow up in the outpatient setting.

Conclusions: Mucormycosis is a rare infection that has been increasingly documented in trauma patients. Early recognition together with prompt debridement and antifungal therapy is key to successful management. Understanding risk factors for post-traumatic mucormycosis should raise our index of suspicion and prompt early diagnosis and initiation of treatment. Aggressive debridement is a critical component of appropriate management due to the angioinvasive spread of the mucor fungi. This means frequent debridement beyond the demarcation of gangrenous tissue. The management of our patient demonstrates the importance of early recognition of the clinical presentation, prompt initiation of antifungal therapy, and aggressive debridement of the wound.

1. Introduction

Mucorales fungi of the Zygomycetes class are found ubiquitously in the environment. Mucormycosis is uncommon and typically associated with patients who are diabetic or otherwise immunocompromised [1]. However, mucormycosis has been increasingly...
documented in otherwise healthy trauma patients [2,3]. Post-traumatic mucormycosis is often the result of direct inoculation of the fungus into traumatic wounds. According to a review of 929 cases of zygomycosis, cutaneous infections can result in local invasion (24%) and hematogenous dissemination (20%) [4]. Hematogenous dissemination resulted in 94% mortality, which improved to 30% with aggressive debridement and antifungal therapy [4].

Given the significant morbidity and mortality of invasive mucormycosis, recognizing these infections in traumatic wounds is critical.

We present the case of a healthy patient who sustained severe traumatic injuries related to a motor vehicle accident. During his hospitalization, the patient developed invasive, cutaneous mucormycosis requiring multiple surgical debridements and antifungal therapy. We review the current diagnostic and treatment standards for managing post-traumatic mucormycosis. We also discuss risk factors in critically ill trauma patients that may promote the development of mucor infections. We demonstrate successful management of post-traumatic invasive mucormycosis through early recognition followed by aggressive surgical debridement and prompt antifungal therapy.

2. Case

A 22-year-old healthy male presented after a motor vehicle collision with a wall and then a tree. On admission, the patient was hypotensive and required multiple blood transfusions, including 18 units of packed red blood cells. He underwent a damage control laparotomy, which included a right hemicolectomy left in discontinuity. Two days later, he underwent a second look laparotomy and creation of an ileocolic anastomosis with fascial closure of the abdominal wall. Within 48 hours of admission, he developed coagulopathy, encephalopathy, myocardial infarction, rhabdomyolysis, acute renal failure requiring hemodialysis, and respiratory failure requiring ventilation. Other injuries included multiple orthopedic fractures, a vertebral fracture, pulmonary contusions, and small intracranial hemorrhages (Injury Severity Score 50). On hospital day six, he became febrile with increasing leukocytosis (19,300/mm³) and worsening pulmonary secretions. Bronchoalveolar lavage was performed and cultures grew *Klebsiella pneumoniae* and a “mold”. He was started on intravenous posaconazole and empiric antibiotics. The patient remained febrile with increasing leukocytosis despite antimicrobial therapy. On hospital day 12, the final respiratory cultures grew *Rhizopus* and his midline incision from the exploratory laparotomy was noted to be erythematous with necrotic edges. Because of the wound’s appearance (Fig. 1) and *Rhizopus* in his pulmonary secretions, there was immediate concern for an invasive fungal infection of his laparotomy wound. The patient was taken to the operating room that day for wide debridement of the abdominal wall down to fascia (Fig. 2). Histologic examination of the abdominal wall tissue showed non-septate fungal hyphae, which was subsequently identified as *Rhizopus* species. His antifungal was changed to intravenous liposomal amphotericin B (LAB), 5 mg/kg daily. The patient was taken to the operating room for another five abdominal wall debridements over the next week. Nine days after the initial debridement, a vicryl mesh was placed and the abdomen was closed primarily. The patient went on to develop superficial purulent drainage from the midline abdominal wound and the skin incision was opened. However, no further necrotic tissue was noted. He ultimately underwent split thickness skin grafting to his anterior abdominal wall (Fig. 3). The patient received 3 weeks of LAB, followed by 9 weeks of posaconazole. He continued to improve and did well on follow up as an outpatient post-discharge day 169.

3. Discussion

Cutaneous mucormycosis in healthy patients is frequently the result of trauma and occurs via direct inoculation of fungi into a traumatic wound. The wound infection in our patient was atypical in that there were no penetrating injuries or abrasions of the abdominal wall on presentation and none of his penetrating extremity injuries developed a fungal infection. However, he did have an emergency laparotomy on admission. The fungus *Rhizopus*, which is not normal respiratory flora, was initially isolated from his respiratory tract and likely contaminated his abdominal incision.

Cutaneous mucormycosis can be very challenging to identify and diagnose due to initially vague symptoms like fever, erythema, induration, or cellulitis. Once inoculated into a wound, Mucorales fungi invade the blood vessels of the soft tissue and obstruct blood flow to the wound. This process causes necrosis of the wound borders. Angioinvasion continues beyond the border of necrotic demarcation and is often insufficiently debrided. Wound cultures or biopsies are the definitive method for diagnosis, but specimen

![Fig. 1. Midline laparotomy incision on hospital day 12.](image)
processing often delays diagnosis and initiation of early treatment. Bedside tissue preparation with potassium hydroxide shows non-septate hyphae with right-angle branching that is diagnostic of mucor, providing an early indicator of mucor involvement. A high index of suspicion and early diagnosis is crucial for initiating early and aggressive therapy with antifungals and surgical debridement.

The standard of treatment is early and aggressive surgical debridement together with prompt initiation of antifungal therapy. Aggressive surgical debridement can practically be defined as debridement beyond the area of gangrenous demarcation every 24–48 hours in the operating room until no further necrosis is identified. Aggressive debridement is critical to 1) prevent the angioinvasive spread of infection and 2) to augment the poor antifungal penetration of ischemic tissue. The antifungal of choice for mucormycosis is intravenous liposomal amphotericin B (5–10 mg/kg daily) because of reduced nephrotoxicity. In patients who do not tolerate or respond to amphotericin B, an intravenous triazole antifungal (i.e. posaconazole or isavuconazole) can be used as alternative or salvage therapy. A recent Phase 3 clinical trial showed that isavuconazole was comparable to amphotericin B as a primary monotherapy option. There was no statistically significant difference in mortality, and isavuconazole had a better side effect profile [5].

Physiological changes in patients with multi-system organ failure may increase susceptibility to invasive fungal infections. Acidosis and blood transfusions, in particular, can promote the growth and pathogenicity of the mucorales fungi. Mucor fungi produce ketone reductase, which enables them to thrive in conditions of hyperglycemia and acidosis associated with diabetic ketoacidosis [6]. These conditions are associated with elevated serum iron levels, which contribute to mucor pathogenicity. A case report by Sharma et al. describes invasive mucormycosis in a patient with severe acidosis not associated with diabetes, suggesting that severe acidosis may independently elevate serum iron levels and predispose a patient to mucor infections [7]. Elevated serum iron can also result from multiple blood transfusions [8]. In addition, blood transfusions have been associated with a dose-dependent increase in the rate of infection in trauma patients [9]. Studies have estimated that the risk of infection increases 5% per unit of packed red blood cells [10]. In our patient, where the source of infection was suspected to be contamination, we suspect that multi-system organ failure and multiple blood transfusions contributed to the development of an invasive fungal infection of his abdominal wound.

Management of cutaneous mucormycosis in previously healthy trauma patients can be very challenging. Recognizing that trauma patients with multi-system organ failure may be at increased risk for developing invasive fungal infections should prompt a high index of suspicion when managing these patients. As traumatic injuries become increasingly common, following the basic principles of early recognition, aggressive surgical debridement, and prompt initiation of antifungal therapy will help reduce the morbidity and mortality of invasive fungal infections.
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