Infective Gangrene in Extremity Trauma—Are We Targeting the Right Organisms?

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Abstract Mucormycosis is a rare and fatal infection that is known to occur in immunocompromised and diabetic patients. The infection is caused by a fungus of the class Zygomycetes. It has been associated with open fractures in patients at risk. We report a case of cutaneous mucormycosis leading to gangrene after a closed fracture. We recommend considering mucormycosis as a differential for wound infections not responding to antibiotics, even in closed injuries. Tissue from surgical debridement should be sent for histopathological and microbiological examination to diagnose the condition early. Early recognition, surgical management, and parenteral antifungal therapy are the mainstay of management of this illness.

Keywords Mucormycosis · Trauma · Fungus · Gangrene

Introduction

Wound infections are the most common type of infection dealt by a hospital with trauma services [1]. Bacterial infections are the most common type of wound infection.

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Sometimes, fungi may be responsible for wound infection as a part of monomicrobial or polymicrobial infection [2]. Mucormycosis is the third most common invasive fungal infection after Aspergillosis and Candidiasis [3] and have the highest mortality [4]. It is a fatal infection, which usually occurs in immunocompromised and diabetic patients [4]. It is caused by fungi of class Zygomycetes and order Mucorales [4]. Generally, *Mucor*, *Rhizopus*, and *Lichtheimia* genera are most often implicated species [3]. *Rhizomucor*, *Saksinae*, *Cunninghamella*, and *Apophysomyces* are less commonly implicated [3]. Mucorales are vasotropic fungi, and they cause tissue infarction of the tissue [3]; this can be visualized in the histopathology as well.

Case Report

A 71-year-old lady presented to surgical emergency with progressively worsening pain of right upper limb following a closed reduction and immobilization of closed right olecranon fracture 8 days back. The patient was a known case of type II diabetes mellitus (apparently controlled on insulin), and controlled hypertension. At the time of presentation, local examination revealed a necrotic patch of 2×2 cm on the posterolateral aspect of the elbow with erythema extending up to the right arm and forearm with few blebs containing serous fluid. Her baseline investigations revealed anemia, leucocytosis, and normal blood sugar. The patient was started on parenteral antibiotics (co-amoxycylav), and the wound was debrided. Gram stain and blood culture did not show any organism. As the infection progressed, antibiotics were changed to piperacillin/tazobactam and linezolid. However, the condition of the limb did not improve and signs of wet gangrene developed over forearm and lower one third of the arm (Fig. 1). Patient

Fig. 1 Limb showing gangrene

underwent an above-elbow Guillotine amputation, and the amputated limb was sent for histopathological examination. The patient's general condition continued to deteriorate. On post operative day four, the patient died, due to septicemia with multi organ failure.

The histopathological examination of the amputated limb showed a focal foreign body giant cell reaction and broad aseptate hypha, suggestive of *Rhizopus* family (Fig. 2). Based on this histopathology report, we concluded that the soft tissue infection of upper limb being treated as bacterial with routine anti bacterial agents was in fact fungal in origin (cutaneous mucormycosis with gangrene) and the patient may have died of fungal septicemia (although no laboratory or autopsy evidence of disseminated fungal infection or fungal septicemia was available).

Fig. 2 Section from resected margin showing degenerating and necrotic skeletal muscle fibers with numerous broad aseptate hyphae in between. (Inset shows a vessel infiltrated by similar hyphae.) (Silver methenamine staining $\times 100$)

Discussion

Mucormycosis is an emerging angioinvasive infection caused by filamentous fungi of the Mucorales order of class Zygomycetes [3]. These fungi are found in decaying matter all over the world [3]. In developed countries, it is found more often in diabetic patients and patients undergoing chemotherapy for hematological malignancies [3]. In developing countries like India, uncontrolled diabetes and trauma are the most common causes [5]. A study by the European Confederation of Medical Mycology Working Group reported 230 cases between 2005 and 2007, out of which 44 % were because of hematological malignancies, 15 % were due to trauma, 9 % because of stem cell transplant and 9 % due to diabetes mellitus [6]. Other predisposing conditions include neutropenia, iron overload, corticosteroid use, illicit IV drug use, and malnourishment [3]. Based on its clinical presentation and anatomic site, invasive mucormycosis is classified as one of the following major clinical forms: rhinocerebral, pulmonary, cutaneous, gastrointestinal, disseminated, and uncommon rare forms, such as endocarditis, osteomyelitis, peritonitis, and renal infection.

Cutaneous mucormycosis constitutes 10–16 % of all cases and is the second most common form of the disease [7]. It occurs after a break in the integrity of the skin as may occur due to surgery, burns, motor vehicle accidents, bone fractures, intravenous lines, insect bites, etc [5]. A typical presentation of cutaneous mucormycosis is a necrotic eschar accompanied by surrounding erythema and induration [3]. The disease has a gradual onset and is slowly progressive, leading to gangrene and hematological dissemination. The brain, liver, spleen, and heart are the most common sites of dissemination [3]. Symptoms vary widely reflecting vascular invasion and tissue infarction of affected organ. High index of suspicion is necessary for diagnosis [3].

Several different techniques (e.g. treatment with 20 % potassium hydroxide, Gomori's methenamine silver staining, haematoxylin and eosin staining, and periodic acid–Schiff (PAS staining)) can be used for direct microscopic detection of Mucorales. Microscopy of frozen section or potassium hydroxide (KOH) mount shows broad aseptate hyphae, branching at irregular intervals. Early tissue biopsy is the gold standard for diagnosis, but a frozen section may be performed if a rapid diagnosis is required [4].

Successful treatment includes early diagnosis and prompt initiation of polyenes antifungals (Amphotericin B). Oral posaconazole is used as step-down therapy for patients who have responded to amphotericin B and rarely as salvage therapy for patients who do not respond to or cannot tolerate amphotericin B. Other antifungal agents, including voriconazole, fluconazole, and flucytosine, are not effective against the Mucorales. Reversal of predisposing factors is also essential along with antifungal treatment [8]. Surgical

debridement or even amputation maybe necessary in some cases [5]. Debridement is known to give a better outcome because drugs have poor penetration in the infected tissue because of vessel thrombosis and tissue necrosis. Anti-fungal therapy with liposomal Amphotericin B is less nephrotoxic and also increases survival in comparison to Amphotericin B [8].

In our case, the patient may have developed mucormycosis due to abrasion over a closed fracture. Predisposing factors for this condition specifically include diabetes, leukemia, and organ transplantation. Patients with uncontrolled hyperglycemia or ketoacidosis are the most susceptible to such infections [3]. In our patient, the diabetes was apparently controlled on insulin; still, the patient developed this infection. The association of open wounds and mucormycosis has been established and reported previously in multiple reports, but it is very rare in closed wounds. Thus, we recommend considering mucormycosis as a differential for wound infections not responding to antibiotics, even in closed injuries. The clinicians should be extra vigilant and consider this condition in patients with normal serum glucose. Tissue from surgical debridement should be sent for histopathological and microbiological examination to diagnose the condition early. It is not only helpful in diagnosis but is also therapeutic.

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