Mucormycosis as a Rare Infection in Lower Limb Necrotizing Fasciitis: A Case Report

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Abstract

Introduction: Necrotizing fasciitis is a severe, life-threatening infection that can be fatal and rapidly progressive. It is usually caused by polymicrobial infection, monomicrobial infection by group-B streptococci (GBS) or staphylococci, or by anaerobes like Clostridium difficile that presents as a gas gangrene or rarely by fungi. Fungal infections, though found in diabetic foot ulcers, remain extremely rare agents in necrotizing fasciitis, often causing severe morbidity and higher mortality than regular bacterial infections. Though severe, these infections are not often late to diagnose and very few reports exist citing their presence. With our case report, we present another rare manifestation of Mucormycosis in a foot wound.

Case Report: We present a 57-year-old diabetic male patient who presented with a rapidly progressing very painful right foot ulcer, with high-grade fever and fatigue that did not respond to surgical intervention and treatment with broad-spectrum antibiotics. Mucormycosis species were identified in wound cultures. The patient then underwent an amputation and was treated with liposomal Amphotericin B.

Conclusion: This report aims to further highlight that virulent fungal infections, especially mucormycosis, should be considered when suspecting or diagnosing necrotizing fasciitis. An extensive review of the literature with our newly added case would serve as an eye-opener on this pathogen in the setting of difficult-to-treat necrotizing fasciitis.

Keywords: case report, necrotizing fasciitis, mucormycosis, amputation, amphotericin
Introduction

Necrotizing fasciitis is a very severe disease, often fatal if not treated adequately [1]. Its presentation dates to the 5th century BC, when Hippocrates described it as a severe and fearsome complication of erysipelas [1]. Later, the term “flesh-eating bacteria” was given as a description of the severity of this infection. This term is rather misleading for two reasons. First, it has been found to be rarely caused by fungal species. And second, the organisms involved do not actively “eat the flesh” [1]. Their presentation is triggered by systemic and local inflammation, causing the destruction of tissues. In 1952, the term necrotizing fasciitis came into existence, described by U.S. Army Surgeon Wilson [1].

This infection is defined as a rapid inflammation that progresses over the course of hours, involving the fascia layers and sparing the muscles [1].

Therefore, necrotizing fasciitis is a rare presentation of cellulitis, that can be caused by a direct penetrating trauma or by hematogenous spread from another infection [2–4]. There are several risk factors for it, including, diabetes mellitus, intravenous (IV) drug usage, and intramuscular (IM) injections that might delay the symptoms until progression to this deadly phase [3,4].

Clinically, the patient presents with pain that is disproportionate to the site involvement, quickly progressing to hypoalgesia [5–7]. Patients also complain of tense edema and blistering. The paramount feature to present is a fast rate of necrosis spread [5].

The disease is often due to the release of superantigen exotoxins from the offending agents, triggering an inflammation that leads to necrosis [8]. The most commonly described toxins are the streptococcal and staphylococcal toxic shock syndrome toxins, or TSSTs [8].

Having it clogs small vessels, the involved areas of necrosis are naturally isolated from the anti-microbial the patient receives. The intervention should involve extensive removal of the involved tissue, as not doing so can be the cause of a new ongoing infection [9,10].

We present a patient with a non-healing rapidly progressing foot ulcer whose swab identified mucormycosis that would serve as an eye-opener to consider mucormycosis in necrotizing fasciitis, hence its importance.

Case Presentation

A 57-year-old Lebanese male presented to our emergency department (ED) for a rapidly progressive foot ulcer. He had a history of hypertension, diabetes mellitus, dyslipidemia, and peripheral vascular disease. The patient reported the lesion to appear first as a solitary ulcer, blackish in color, on the dorsum of the right foot. The ulcer was very painful and associated with chills but no reported fever. It was surrounded by a red, hot, and painful area.

He denied rash or itchiness and a full review of systems did not reveal abnormal findings. The patient’s ulcer was growing rapidly over the second day, and it was becoming less painful. On the day of presentation, the ulcer had involved the entire dorsal area of the right foot, with associated red, hot tissue areas involving the entire dorsal and plantar area of the left foot extending to the right ankle. The patient reported the center of the ulcer to be black in color and totally numb, not painful (Figure 1). He reported no wound oozing or liquid formation. The chills were getting worse, but the patient denied any episode of reported fever.

To note, the patient’s diabetes is uncontrolled, with the last HbA1C done 1 year prior to presentation that showed a result of 8%. There is no previous history of diabetic foot ulcers, diabetic neuropathy, or diabetic nephropathy. The patient takes no medication for his peripheral vascular disease.

He has a history of below-knee amputation of the right foot secondary to gangrene as a result of his diabetes. He is a 30-pack-year smoker who quit 3 years prior to this presentation. There is no family history of
chronic disease and he denied any exposure to pets or insect bites as well as any travel history. The patient is a resident of Beirut.

Upon presenting to the emergency department (ED), the patient had stable blood pressure and a heart rate of 95, but he had a fever of 38.5 degrees Celsius with a normal saturation on room air. He was well awake, alert, and oriented to person, time, and place. Head, neck, chest, cardiac, and abdominal physical exams were unremarkable. However, a lower limb examination showed a large, necrotic ulcer presenting as a large black lesion on the dorsal area of the right foot with extensive swelling and redness extending to the toes. The fourth toe was totally necrotic and stiff. The lesion was non-painful, and the remaining toes were extremely cold with very weak posterior tibial pulse. There was an area of extensive swelling and redness indicating inflammation spreading to the right ankle. A small round necrotic ulcer was also seen on the distal lateral plantar area of the foot. All the lesions described were dry and non-oozing. The left foot showed no lesions but very weak dorsal pedis and posterior tibial pulses. Laboratory workup showed a white count of 18,000/mm3 with 87% neutrophils, CRP of 15 mg/dL, creatinine of 1.5 mg/dL, sodium of 137 mg/dL, and a blood glucose level of 220 mg/dL. In the Emergency department, the patient was started on intravenous (IV) fluids, and infectious diseases were urgently consulted for the high probability of necrotizing fasciitis. Infectious diseases confirmed this high suspicion and recommended urgent IV antibiotics and surgical consults. The patient was immediately started on meropenem 1g intravenously (IV) every 8 hours and vancomycin 20mg/kg once followed by 15mg/kg every 12 hours. An urgent surgical consult was ordered with a recommendation of urgent below-the-knee amputation, above all areas of noted swelling and inflammation. The patient was examined by the surgical team and based on the patient’s wishes, he underwent an ankle-sparing excessive debridement with trans-metatarsal amputation and removal of all the necrotic tissue. Throughout the night, the patient continued to have low-grade fever spikes. The next day, upon dressing change, recurrence of the non-oozing, non-bleeding necrotic areas was noted. Wound cultures were taken, and another extensive debridement was performed, as the patient did not give consent for a below-knee amputation. On the third day, the wound dressing again showed a recurrence of the necrosis (Figure 2). The microbiology lab reported a positive culture that grew molds on Sabouraud Dextrose agar, with a slide preparation showing molds with wide caliber hyphae, large spores, and wide-angle branches, identified as mucormycosis (Figure 3).
The patient was then immediately started on Liposomal amphotericin B at a dose of 5mg/kg/day. Again, the patient was reluctant to the mentioned amputation, and another debridement was performed. At this point, the chills stopped but the wound dressing showed a recurrence of the necrosis again.

Eventually, the patient agreed to the amputation, and a below-knee amputation was performed above all areas of cellulitis and fasciitis (Figure 4). The patient tolerated the procedure well and did well post-op. Liposomal amphotericin was continued for a total of one week and the patient was discharged home without further antifungal treatment.

Discussion

Our case presentation is yet another rare documentation of the life-threatening condition known as type IV necrotizing fasciitis, or fungus-induced necrotizing fasciitis. This subcategory remains a rare entity that is seldom seen and often misdiagnosed initially. Type I is the polymicrobial entity, type II is the monomicrobial presentation and type III is the gas gangrene caused by clostridium perfrengens [4,5]. And despite the fact that this type IV has a similar clinical presentation as type II, caused by streptococcus group A or staphylococcus aureus species, it is far more deadly in terms of morbidity, mortality as well as treatment difficulty, and side effects [3,4].

Diabetes mellitus is one of the biggest risk factors for necrotizing fasciitis. Due to the vascular compromise and immunodeficient state, it causes in addition to the decreased sensation secondary to diabetic neuropathy, it makes it easier for the causative organisms to infect and invade tissues with little resistance and decreased sensation to pain [11]. For similar reasons, diabetes is an independent risk factor for mucormycosis infections [12].

For instance, and aside from the fact that it requires antifungal treatment, type IV has a mortality rate as high as 47% if not treated emergently, and such a rate rises to 90% if not treated at all [10,13]. The literature suggests going for urgent surgery once necrotizing fasciitis is clinically suspected, as antimicrobial treatment showed no benefit in curing the condition without surgically excising the necrotic tissue [1,9]. It is worth noting that in the case of mucormycosis, fungal hyphae invasion of the blood vessels clogs them, causing wide areas of ischemia and necrosis, where the fungus can grow freely without being affected by antifungals [10,14].

However, when not sure whether the
presentation is that of necrotizing fasciitis, doctors are to calculate the “Lab Risk Indicator for NECrotizing fasciitis”, or the LRINEC score, in which a score of more than 7 indicates a high-risk, necessitating surgery, while a score of 6 or 7 indicates an intermediate risk, where imaging by ultrasound, X-Ray, Computed Tomography (CT) or Magnetic Resonance Imaging (MRI) is warranted, in addition to frozen section pathology to aid in the diagnosis. Once confirmed, surgery is, again, of utmost importance [3,6,15].

That being said, the LRINEC score is calculated to be 7 (Table 1), but the clinical suspicion was very high, indicating an urgent surgery.

As for the surgery, areas of fasciitis that are visible on physical exam are to be excised. As our patient had that area extending to above the ankle, a below-knee amputation was advised by the infectious diseases department [13]. During the operation, frozen sections are to be performed to rule out any microscopic positive borders of the removed tissue, to ensure a clean-border amputation that is free of the invading fungus [9].

In addition to surgery, patients with such a diagnosis should be treated with antifungals as soon as possible [9]. Usually, liposomal amphotericin B 5mg/kg once daily, Isavuconazole 200 mg three times daily for two days then once daily, or Posaconazole IV 200 mg twice daily for one day then once daily are the recommended treatment agents [13,14]. The doses then can be increased or changed whether no response or toxicity is noted [13,14].

Our case adds one again a rare case that is often mistaken for a bacterial infection at the time of diagnosis, sometimes delaying treatment, which poses great risks to the lives of our patients. It is crucial to consider type IV necrotizing fasciitis in any patient who presents with the risk factors for fungal systemic infection, especially diabetic patients, who are well known for growing fungi in their diabetic feet such as our patient, patients on chronic steroids and all other immun-compromised states [8]. This diagnosis indeed does not only necessitate treatment by an anti-fungal rather than an antibacterial but also requires extensive surgery guided by frozen sections to make sure the fungus is microscopically removed as well, as it has high mortality if under-diagnosed or under-treated. Though fungal necrotizing fasciitis is a rare entity, it should always be suspected when risk factors are present.

Table 1: LRINEC score and patient results

<table>
<thead>
<tr>
<th>Parameter</th>
<th>LRINEC Points</th>
<th>Patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRP (mg/L)</td>
<td>&lt;150 (none)</td>
<td>150</td>
</tr>
<tr>
<td></td>
<td>150+ (4 points)</td>
<td>4 points</td>
</tr>
<tr>
<td>WBC count (/cubic millimeter)</td>
<td>&lt;15k (none)</td>
<td>18000</td>
</tr>
<tr>
<td></td>
<td>15-25k (1 point)</td>
<td>(1 point)</td>
</tr>
<tr>
<td></td>
<td>25k+ (2 points)</td>
<td></td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>&gt;13.6 (none)</td>
<td>12.1</td>
</tr>
<tr>
<td></td>
<td>11-13.5 (1 point)</td>
<td>(1 point)</td>
</tr>
<tr>
<td></td>
<td>&lt;10.9 (2 points)</td>
<td></td>
</tr>
<tr>
<td>Serum Sodium (mmol/L)</td>
<td>&lt;135 (none)</td>
<td>137</td>
</tr>
<tr>
<td></td>
<td>&lt;135 (2 points)</td>
<td></td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>1.6 or less (none)</td>
<td>1.5</td>
</tr>
<tr>
<td></td>
<td>&gt;1.6 (2 points)</td>
<td>(none)</td>
</tr>
<tr>
<td>Glucose (mg/dL)</td>
<td>&lt;180 (none)</td>
<td>220</td>
</tr>
<tr>
<td></td>
<td>180+ (1 point)</td>
<td>(1 point)</td>
</tr>
<tr>
<td>Total</td>
<td>5 or less (low risk)</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>6-7 (intermediate risk)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>8+ (high risk)</td>
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</tbody>
</table>

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In addition to surgery, patients with such a
yet deadly condition, requiring a different management than the other types. This, as well as the few other case reports issued on such a condition, might in the near future, provide data for a larger epidemiological study that would provide a better understanding of this illness and aim to help reduce its burden on the patients and the healthcare systems.

References


