



Case report

Invasive cutaneous mucormycosis: A case report on a deadly complication of a severe burn

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ABSTRACT

A 38 year old woman presented with burns totaling 45 % total body surface area, following an explosion resulting from manufacturing cannabis wax. Initial debridement, was delayed to hospital day 7 due to hemodynamic instability. Over the course of her hospitalization, she required multiple debridements and grafting to her lower extremities; grafted tissue never survived longer than 72 h. Her bilateral lower extremities began to exhibit visible mold growth. She underwent repeated debridements down to vitalized tissue only for recurrent necrosis and mold growth to occur. She underwent serial amputations eventually reaching the level of her mid thigh. At this point her clinical condition deteriorated further resulting in multiorgan failure. Ultimately family made the decision to remove her from life support, and she expired, within a few hours. Postmortem analysis identified *Rhizopus* spp, *Fusarium* spp, and *Geotrichum candidum*. Mucormycosis species are a frequent infector of Cannabis, sativa, which our patient was working with in the inciting explosion. Cutaneous mucormycosis is a documented but rare manifestation. We propose that the patient's, relatively young age, severity of burns, and exposure to cannabis plants resulted in this, unusual presentation

The patient

A 38-year-old woman with a past medical history of morbid obesity, presented with burns totaling 45 % of her total body surface area (TBSA) following an explosion while cooking cannabis wax. She suffered full thickness burns to the bilateral lower extremities, feet, breasts, buttocks, and abdomen with additional concern for inhalational injury.

Hospital course

Aggressive fluid resuscitation using a modified Brooke formula based on the patient's adjusted ideal body weight was given. She was taken emergently to the operating room for escharotomies to release circumferential third-degree burns extending from her bilateral thighs down to her feet. Postoperatively, she remained intubated and was severely hypotensive. Fluid resuscitation was uptitrated to match urine output and she was started on norepinephrine. Her clinical status continued to decline rapidly as she began to have increasing oxygenation demands, renal failure, and metabolic acidosis requiring continuous renal

replacement therapy. Unfortunately, she developed ventilator-associated pneumonia with rapid progression to acute respiratory distress syndrome. Low tidal volume ventilation strategies and scheduled proning were used. Early surgical debridement was delayed due to rapidly declining clinical status including hemodynamic instability to reduce the risk for intraoperative complications.

On hospital day seven, the patient had sufficiently stabilized and was taken to the operating room for her first debridement. Tangential excision and wound bed preparation of her bilateral lower extremities and feet with cadaver allograft placement was performed. Her surgical wounds were placed in Vashe-soaked gauze and dressed with standard burn dressings. Over the next two weeks she underwent an additional five tangential debridements, including her abdomen and torso. On hospital day 20, the patient demonstrated significant medial foot necrosis down to bone and underwent a left below-the-knee guillotine amputation. On hospital day 24, she underwent placement of a percutaneous tracheostomy, due to chronic ventilator dependence, and placement of split thickness skin graft to her torso. Dressing takedown revealed healthy uptake of the autograft. Despite the patient's

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encouraging torso grafts, her bilateral lower extremity grafts repeatedly failed. Deep tissue cultures of her bilateral lower extremities grew vancomycin-resistant *Enterococcus faecium* and a yeast. Bone biopsy of the exposed left tibia was obtained intraoperatively and also grew a fungus.

The patient's hospitalization was complicated by numerous nosocomial infections. Three weeks into her stay, she developed fever and worsening leukocytosis. Blood and respiratory cultures were obtained. Blood cultures grew *Enterococcus casseliflavus* from the arterial line and *Lactobacillus* species from peripheral blood cultures. Simultaneously, respiratory cultures grew methicillin-sensitive *Staphylococcus aureus* (MSSA), Group B streptococcus, and *Stenotrophomonas*. Due to clinical deterioration, the isolates were considered pathogenic and were treated with targeted antimicrobials.

The patient's tissue devitalized rapidly after every thorough debridement of her lower extremities, and her cadaver grafts never succeeded. Due to the recurrent allograft failure on day 34, she was taken for fascial excision and wound bed preparation of the bilateral lower extremities, with a right guillotine below-the-knee amputation. Her surgical wounds appeared clean and healthy the following day. Two days later, a visible growth of mold was found across the entire wound bed. Thus, she was taken back to the operating room for a repeat debridement. Operative tissue cultures were obtained. Local wound care was switched to full-strength Dakin's solution. Infectious Disease was updated and the patient was started on liposomal amphotericin B and isavuconazonium. Twenty-four hours later, her wounds demonstrated visible mold again. She continued to deteriorate—developing renal failure and requiring multiple vasopressors. The following day, her wounds developed a thin coating of black tissue, the cause of which was unclear if it was fungal involvement or it was secondary to necrosis. Again, an aggressive debridement was repeated with bilateral guillotine above-the-knee amputations. Within 72 h her wounds became malodorous and showed recurrent fungal growth. At hospital day 43, she was taken back emergently for an aggressive debridement of her bilateral lower extremities. Local wound care was transitioned to acetic acid to enhance inhibition of fungal growth.

On hospital day 45, the patient's bilateral lower extremities again showed fungal growth. The option of bilateral hip disarticulation was discussed with her family. Based on what the family believed to be her wishes and in the setting of relentlessly invasive fungal growth, despite aggressive debridements and antifungal therapy, the decision was made to cease further operative intervention. She showed no promise of improvement. The fungal infection appeared to spread past the level of the hip and up to the lower portion of the back within a few days. Palliative care was consulted and her family was allowed to visit. She was placed on comfort care measures and expired within a few hours.

The post-mortem report of the fungal culture from the left tibia bone biopsy showed *Geotrichum candidum*. Fungal culture and mold identification from intraoperative tissue taken after the first identification of clinical mold grew *Rhizopus* species and *Fusarium* species. All subsequent cultures obtained during her debridement grew fungi.

Discussion

Geotrichum candidum is a common yeast found worldwide. This yeast is frequently isolated from soils, fruits and vegetables; it also plays an important role in cheese fermentation [1]. Although often found in skin flora, there are few documented cases of invasive skin infections from *G. candidum*, instead the pulmonary system is the most frequent site of infection [2]. Reported cases of systemic geotrichosis have been shown to have a strong correlation with poorly-controlled diabetes, malignancy or other causes of immunosuppression [3]. In this example, geotrichosis occurred due to skin loss following multiple aggressive debridements of extensive surface area burns, which allowed this low-virulence yeast the opportunity for infection.

Mucormycosis is a condition in which patients are infected in some

capacity by fungi of the order Mucorales, which includes the genus *Rhizopus*. *Rhizopus* species are among the common fungi found infecting the root systems of *Cannabis sativa*, the strain of cannabis with which our patient worked [4]. *Rhizopus* is also commonly found in soil, and many cases of cutaneous mucormycosis have been reported in soil-contaminated burn wounds [5,6]. Importantly, our patient's extensive wounds were covered in soil when she was found by EMS. Cutaneous mucormycosis is relatively rare in the general population. However, patients suffering large TBSA burns (approximately 40–60 %) are at an increased risk for cutaneous mucormycosis [7]. Mucormycosis is commonly associated with poorly-controlled diabetes and is a frequent cause of mortality in diabetic ketoacidosis. Systemic mucormycosis is caused by angioinvasion leading to direct seeding of end organs and tissue necrosis [8].

Fusarium species are likewise a common saprophyte found in soils. Human infection from this species is rare and is most commonly seen in people receiving treatment for hematologic malignancies; however, rare cases of fusariosis has been reported in burn and trauma patients. The spectrum of disease burden with fusariosis ranges from keratitis and onychomycosis to pneumonia, fungemia, and mycetoma [9].

One of the many challenges in this case was the difficulty not just in diagnosing fungal infection, but in identifying the specific fungi involved. Initially, concern for fungal infection was lower given that the initial set of operative cultures did not grow any fungal species. On hospital day 24, the patient was taken to the operating room for one of her numerous debridements, and the culture obtained at that time grew yeast. This was the first clinical indication of fungal disease. Empiric coverage with fluconazole was started in response to this new information. Later in the hospital course, nursing staff visualized fuzzy mold during a wound dressing change. In addition to more debridement, at this time antifungal therapy was escalated to liposomal amphotericin B and isavuconazonium. Yet, it was still unknown which specific fungal species was present and requiring treatment. Proper and rapid fungal species identification provides a challenge to microbiology testing. While microbiology labs are frequently well-equipped for rapid identification of bacteria, especially given the emergence of matrix assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF), fungal identification is most often done by visual inspection performed by a technician trained in mycology, which also carries a significant rate of practitioner error [9]. Since MALDI-TOF assays specific for fungi are an emerging technology, many laboratory facilities do not yet have access to this technology. Due to the limitations of our facility, the requested fungal identification studies required samples to be shipped across the country. The identification of *G. candidum* was only made available a few days prior to the patient's death, and the identification of *Rhizopus* and *Fusarium* were only available post-mortem.

Despite the initial isolation of *G. candidum*, we propose that the patient's extensive tissue invasion was due to zygomyces, including *Rhizopus* spp, and due to the presence of *Fusarium* spp.

We suspect that the patient was infected with *Rhizopus* on initial presentation either from the cannabis plant or from the soil covering her wounds. Of note, the isolated fungal pathogens all show a predisposition for poorly-controlled diabetes; however, our patient had achieved strict glycemic control while admitted due to aggressive insulin therapy. Although the significant loss of skin tissue allowed the fungus to flourish, her intact cellular immune system and well-controlled glycemia slowed fungal growth resulting in delayed diagnosis. Her age was likely another protective factor as the median age of patients with cutaneous mucormycosis has been documented to be 42–45 years old [7]. This hypothesis proposes that older patients are often unable to survive invasive mucormycosis long enough to develop cutaneous manifestations. Unfortunately, in this case there was no clinical concern for fungal infection until nearly one month past the initial presentation when the bone culture was found to have a yeast. Determining the pathogenicity of the yeast was clinically difficult, because the patient had no clinical signs of invasion or visible fungal growth early in

presentation. The delay in targeted antifungal therapy may have allowed for angioinvasion of *Rhizopus* to occur. In addition, this patient was not taken to the operating room for initial debridement until post-burn day seven due to hemodynamic instability. This delay in first debridement likely increased her risk of angioinvasion of the mucormycosis. Early debridement is crucial to a burn patient's outcome, with the optimal goal being 24–48 h to allow time for hemodynamic stabilization of the patient, as well as for nonviable tissue to show visual signs of necrosis [10]. Thus optimal source control was impossible to achieve despite numerous futile aggressive debridements as necrosis would quickly develop post-operatively. In retrospect, early initiation of broad-spectrum empiric antifungal coverage in this patient, as well as reduction in the time from burn to debridement may have prevented further tissue invasion, which may have increased the likelihood of a successful outcome. It is important to note that routine prophylaxis against mucormycosis is not currently recommended due to its relative rarity [9]. However, it is important to consider the possibility of invasive fungal infections in the critically-ill burn patient due to the high morbidity and mortality these infections may represent, and it is possible that select patients may benefit from earlier empiric antifungal therapy.

CRedit authorship contribution statement

Geoffrey Welch: lead author. **Andrew Sabour:** co-author. **Kushal Patel:** revision. **Kimberly Leuthener:** Writing – review & editing, expert opinion. **Syed Saquib:** expert opinion. **Luis Medina-Garcia:** expert opinion, Writing – review & editing.

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Ethical approval

N/A.

Consent

The patient in this case report expired. Written consent was obtained from the patient's next-of-kin and was documented in the patient's medical record. This study as a case report did not require approval by an ethic committee.

Conflicts of Interest

The authors have no conflict of interest to report.

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