Absract

Invasive fungal infections are typically associated with immunosuppression and critical illness and occur often as the result of *Candida albicans*. Immunocompetent individuals are rarely susceptible to these often deadly infections. We report the case of invasive fungal necrotizing soft tissue infection secondary to *Candida dubliniensis* in a healthy, young patient after undergoing an elective laparoscopic operation. This rare emerging infectious entity produced a unique constellation of findings not previously reported. The importance of a high index of suspicion in concordance to wide, aggressive surgical debridement and early, empiric amphotericin B is highlighted.

Keywords

necrotizing soft tissue infection; fungal; surgery; postoperative; Candida dubliniensis

Introduction

Necrotizing soft tissue infections have the propensity to be physiologically devastating. Frequently associated with open wounds or immunosuppression, these rapidly advancing infections are associated with high mortality rates [1]. Incidence among immunocompetent patients is rare, however reports are on the rise. Polymicrobial infections are often encountered, with *Streptococcus* and *Staphylococcus* species emerging as the most common tissue isolates. Fungal organisms are rarely encountered, and when present are almost always associated with immunosuppression or immunocompromised states, such as poorly controlled diabetes or cancer [2]. Fungal soft tissue infections are almost exclusively caused by *Candida*, most of which are secondary to *C. albicans*. Other candidal species, such as *glabrata* and *tropicalis*, also have shown the ability to invade tissue, but the incidence of these are quite rare [3].

Invasive fungal infections have been described with several recent natural disasters, such as the 2011 Joplin, Missouri Fujita 5 tornado and the 2004 Indian Ocean tsunami. These events resulted in multiple cases of necrotizing fungal infections secondary to direct inoculation from wet, airborne debris [4]. Only a few reports, of spontaneous or post-surgical invasive fungal infections exist in the literature. We present an unusual case of a fungal necrotizing soft tissue infection in an immunocompetent patient following elective operation caused by *Candida dubliniensis*. 
Case Presentation

A 35-year-old male with no significant past medical history other than hypertension and gastroesophageal reflux, underwent an elective laparoscopic Nissen fundoplication at an outside hospital. The following day, he was tachycardic with peritonitis and bilious drainage from the periumbilical port site. He underwent emergent laparoscopic re-exploration with the finding of an enterotomy that was subsequently repaired. In the immediate post-operative period, the patient required reintubation secondary to hypoxia and experienced rapid clinical deterioration. The patient was subsequently transferred to our facility for respiratory distress and hemodynamic instability.

Upon arrival he was tachycardic and hypoxic. Physical exam revealed bawdy left abdominal and flank edema, extending from the axilla to the anterior left thigh. No crepitus was identified, however cloudy drainage was noted from one of the port sites. Due to suspicion of a necrotizing soft tissue infection, bedside wound exploration was performed via extension of the periumbilical port site. Characteristic cloudy, “dish water” fluid was identified, along with necrosis of the underlying soft tissue. He was then taken immediately to the operating room for debridement. Meropenem, gentamicin and clindamycin were all initiated simultaneously, as the patient had a penicillin allergy.

The peritoneal cavity was reopened to ensure no ongoing enteric leak. No contamination was noted, and the limited fascial incision subsequently closed. The patient then underwent wide excisional debridement of skin and soft tissue measuring over 4000 cm². Debridement extended from the left axillary vein to the anterior left thigh, including much of the left abdominal wall and flank. Several unique findings prompted suspicion for a necrotizing fungal infection. First, necrotic areas were noted to be a distinct black color, with a tar-like texture. Second, contrary to typical bacterial necrotizing infections, there was minimal thrombosis of blood vessels within the necrotic segments of tissue. Third, the infection appeared to skip over layers within tissue. In the axilla for example, necrosis involved the latissimus fascia, spared the muscle and then continued in the areolar and connective tissue beneath the muscle layer. Conversely, the abdominal muscular was necrotic with fascial sparing. (Figure 1) Our prior experience with necrotizing fungal infections during the 2011 Joplin, Missouri tornado prompted empiric intraoperative treatment with amphotericin B. Tissue cultures were sent both for microbiology and frozen section to speed return of results and to identify the presence of hyphae, which were noted on frozen section. Following wide surgical debridement, wounds were dressed with Dakin’s solution and gauze. He subsequently underwent two additional debridements and extensive skin grafting to the abdomen, groin and left lower extremity over a period of three weeks.

Initial tissue cultures grew heavy *Candida dubliniensis*, moderate *Enterococcus* and scant *Streptococcus viridans*. *Candida dubliniensis* was susceptible to caspofungin, as well as fluconazole. Despite apparent *ex vivo* susceptibility to fluconazole, we continued antifungal treatment with an echinocandin, given the high probability of fluconazole resistance developing *en vivo*. Pan-sensitivity was identified for both *Enterococcus* and *Streptococcus*. Subsequent pathologic specimens harvested during the following debridements did not demonstrate the presence of *Candida dubliniensis*. With the finding of a rare *Candida* species, we initiated an immunologic workup, including testing for hepatitis, diabetes and HIV. All were negative.
Invasive fungal infections have increased more than 200% in recent years [5]. Many of these infections are caused by *Candida albicans*, although several other species are known to be pathogenic, including *C. tropicalis*, *C. glabrata* and *C. parapsilosis*. *Candida dubliniensis*, first categorized in 1995 in isolates from HIV-positive patients, is an emerging species of clinical relevance. Reports of patients infected with *C. dubliniensis* have increased steadily since its discovery, partially owing to more advanced microbiological detection methods allowing for targeted identification of less common *Candida* species, specifically *C. dubliniensis* [6,7]. Clinical focus on *Candida dubliniensis* has subsequently grown, not only due to its ability to infect a wide variety of tissues, but also because of its ability to readily develop resistance to fluconazole, a commonly utilized antifungal medication [8]. The immunocompromised predilection of *C. dubliniensis* noted in recent literature, with several case reports and case series demonstrating virulence within immunocompromised hosts [3,8,9]. Despite the rise in detection, the overall incidence of *C. dubliniensis* in patients with fungal infections remains low, and ranges from 0.05-12% [8-11].

Immunocompetent patients also appear at risk to develop infection with *C. dubliniensis*. Case reports and case series highlighting infectious consequences related to *C. dubliniensis* have increased in recent years [12-19]. Although many of these infections in otherwise healthy patients involve oral candidiasis, cases of more serious entities, such as meningitis, discitis, osteomyelitis and systemic candidiasis, exist [15-19]. While other *Candida* species have been known to appear in necrotizing soft tissue infections, *C. dubliniensis*, however, has not been previously reported [1,20,21]. In our case, we saw a polymicrobial milieu with *C. dubliniensis*, *Enterococcus* and *Streptococcus*.

In the presented case, several interesting findings prompted surgeons to suspect a rare mycotic infection. While the characteristic “dishwater” fluid associated with many necrotizing infections was present upon our initial incision, we then encountered a tar-like appearance of the tissues. Tissue necrosis is an expected component in these infectious entities, but the tissue in this case was not only necrosed, but liquified and congealed in manner not previously described. Thick, viscous and tenaciously adherent to itself and other surrounding tissues, the involved planes were difficult to separate from uninvolved areas. There were no signs of vascular thrombosis, as is commonly identified in necrotizing infections. Additionally, the infection skipped over tissue planes, and involved deeper areas. For example, the skin and fascia was not involved, except near the sentinel laparoscopic port site, while the subcutaneous tissue and underlying muscle had extensive necrosis. This presented a surgical dilemma in determining the extent and depth of tissue involvement. With these unanticipated findings, we began empiric systemic treatment with amphotericin B for a suspected fungal infection during the initial operation.

Treatment of candidal infections typically involves the use of systemic fluconazole. *Candida glabrata* and other non-albicans species of *Candida* are frequently resistant to standardazole antifungals, and require an echinocandin class of antimicrobials. Similarly, *C. dubliniensis* readily develops resistance to fluconazole, and requires either echinocandins or amphotericin B [6]. For these reasons, in the face of a potentially-fatal necrotizing soft tissue fungal infection, we recommend empiric amphotericin B in addition to wide surgical debridement. Antimicrobials may be tailored to local resistance patterns once
cultures have been finalized. As is the case with all necrotizing soft tissue infections, wide and aggressive surgical debridement must be employed immediately with simultaneous initiation of systemic chemotherapeutic regimens.

**Conclusion**

This is the first reported case of a fungal necrotizing soft tissue infection caused by *Candida dubliniensis* in an immunocompetent patient. Wide, immediate surgical debridement remains the mainstay of treatment, and when fungal sources are expected, empiric systemic amphotericin B is recommended.

**Figure**

![Figure 1: Left flank, abdominal wall and thigh. Skip lesions with tar-like, black areas of necrosis and sparing of fascial planes is identified. On the thigh, normal skin, subcutaneous fat and fascia can be seen overlying the necrotic muscle beneath.](image)

**References**


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