Candida albicans necrotizing fasciitis following elective surgery

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\section{1. Introduction}

Necrotizing fasciitis, a serious and rapidly spreading soft tissue infection, is associated with a high mortality rate. As such, prompt diagnosis and treatment are essential given the nonspecific presentation particularly in the early stages of disease \cite{1,2}.

Several major risk factors have been identified for necrotizing fasciitis including an immunocompromised state; however, any patient with a major or minor penetrating trauma, skin breach including surgical intervention are also at risk for infection \cite{1,2}.

Bacterial pathogens constitute the main etiology of necrotizing fasciitis. Clinically, necrotizing fasciitis is grouped into two types \cite{1,2}; type I is polymicrobial and includes anaerobes such as \textit{Bacteroides} and \textit{Peptostreptococcus}, as well as non-group A beta-hemolytic streptococci and members of the Enterobacteriaceae family \cite{1,2}. On the other hand, type II, which is more common, consists mainly of monomicrobial etiologies with group A beta-hemolytic streptococci and \textit{Staphylococcus aureus} being the most commonly isolated species \cite{1,2}. That said, rare cases of fungal pathogens, particularly \textit{Candida} species, have been described in the literature, although the majority are sequelae of trauma or contaminated wounds \cite{1,3–13}. To our knowledge, this is the first report of necrotizing fasciitis caused by \textit{C. albicans} following an elective surgical procedure.

\section{2. Case presentation}

A 60-year-old female patient had a past medical history of iron deficiency anemia, psoriasis, pituitary microadenoma, irritable bowel syndrome and resolved thrombocytopenia and splenomegaly presented with severe chronic back pain dating back to a back injury two years earlier. Medications included bromocriptine. Following evaluation, treatment plans were made for an elective lumbar anterior discectomy and fusion procedure. The surgical approach was through an open midline incision as well as a left sided retroperitoneal approach to perform a L3-L4 discectomy. The procedure was uncomplicated, and the patient was transferred to the floor.

On post-op day one, the patient experienced dyspnea requiring 40% oxygen by facemask to maintain normal oxygen saturation. She became tachycardic but remained normotensive. On physical exam, dusky coloration of the left flank was noted. Over the next several hours, the patient became progressively more dyspneic, tachycardic and developed hypotension with a clear spread of the bluish discoloration from the lower chest to the top of the pubis. Given the hemodynamic instability, acute renal failure and worsening hypoxia, the patient was transferred to the intensive care unit.

A computed tomography scan showed extensive subcutaneous emphysema, stranding and soft tissue swelling extending from the left lateral abdominal wall to the base of the thorax and groin (Fig. 1). In addition, low density fluid in the retroperitoneum of the abdomen and

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pelvis, and a small amount of intraperitoneal fluid and gas raised the possibility for necrotizing fasciitis. There was no pathology noted involving the visceral organs including the gastrointestinal tract.

Broad spectrum antibiotics were initiated with escalating combinations of ciprofloxacin, cefepime, clindamycin, vancomycin and imipenem, in addition to intravenous immunoglobulins. The patient was then taken to the operating room emergently for debridement, where extensive necrosis involving the entire anterior abdominal wall was encountered with extension to the lower thorax, bilateral extensive necrosis involving the entire anterior abdominal wall was then taken to the operating room emergently for debridement, where penem, in addition to intravenous immunoglobulins. The patient was nations of cipro

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Fig. 1. Computed Tomography of the abdomen. Coronal (Panel A), sagittal (Panel B), and axial (Panel C and D) sections of the abdomen demonstrating marked edema, extensive fat stranding and soft tissue emphysema of the left abdominal wall (arrows).

Fig. 2. Histopathology demonstrating Candida albicans necrotizing fasciitis. At low power (Panel A, 40X magnification), slides stained with hematoxylin and eosin revealed necrotic tissue with a blue-staining infiltrate traveling along tissue planes. At higher power (Panel B, 400X magnification) the infiltrate is revealed to consist not of inflammatory cells but rather budding yeast forms and pseudohyphae (circles), confirming fungal tissue invasion. Slides stained using Gomori’s methenamine silver (GMS) impregnation technique (Panel C, 40X magnification; Panel D, 400X magnification) highlighted the fungal elements, which are morphologically consistent with Candida albicans. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

species. The C. albicans isolates were susceptible to fluconazole using in vitro antimicrobial susceptibility testing using the disc-diffusion method. Despite surgical debridement and antimicrobial therapy, the patient passed on post-operative day two.

Of note, three years prior to this admission, the patient had presented with complaints of dysphagia. Upper esophagoscopy revealed esophageal candidiasis. There was no previous personal or family history of recurrent bacterial or fungal infections that would suggest a pre-existing immunodeficiency. Blood testing and immunologic workup, to include quantitative immunoglobulins, mannos binding lectin, human immunodeficiency virus, and lymphocyte phenotype profile including markers for CD3, CD4, and CD8 were found to be normal. Post-mortem examination revealed normal lymph node architecture and spleen size. One year before the current presentation, the patient presented with recurrent episodes of esophageal candidiasis, which were treated with short courses of fluconazole and oral nystatin. However, despite treatment she experienced six additional episodes of esophageal candidiasis, the last episode occurring 3 months prior to this event. During the last few months and leading up to the surgery, the patient was maintained on oral fluconazole 200mg daily with recurrence of disease.

3. Discussion

Given the high mortality rate related to necrotizing fasciitis, it is imperative to make an early diagnosis with prompt treatment. The clinical manifestations of necrotizing fasciitis, although often non-specific, include a progression of cutaneous erythema, swelling, blister and bulla formation, and then skin necrosis with a dusky discoloration [2]. Timing of treatment is critical and earlier antimicrobial therapy and surgical debridement are tied to improved outcomes [1,2].

Identified risk factors for necrotizing fasciitis include diabetes mellitus and trauma [1,2]. Other risk factors include alcohol use disorder, anemia, immunosuppressant therapy, as well as renal and liver disease [1,2]. The majority of infections are due to high virulence bacterial species including Staphylococci and beta-hemolytic streptococci. In the case described herein, the patient was found to have heavy infection by C. albicans, a very rare cause of soft tissue infection. Surprisingly, the patient was neither known to be immunocompromised nor to have any of the classic risk factors for necrotizing fasciitis. The laminectomy procedure was an elective procedure without any intraoperative complications. However, her history is significant for late adult-onset, recurrent episodes of esophageal candidiasis of unclear etiology, an uncommon opportunistic infection for an immunocompetent individual. The first episode of esophageal candidiasis

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was temporally associated with an epidural steroid injection for lower back pain and raises the spectre of a sub-clinical immunocompromised condition unmasked by the introduction of corticosteroids. In addition, the patient did have a history of bone marrow suppression of unknown etiology consisting of leukopenia and thrombocytopenia, as well as an episode of pancytopenia eight years earlier. However, upon presentation her cell counts were in the normal range, which fails to explain her severe infection with an opportunistic organism such as C. albicans. The patient’s history, including chronic abdominal symptoms and psoriasis suggests the possibility of an autoimmune syndrome. Despite this suspicion, the patient’s symptoms never required biologics or any immune modulator therapy.

The possibility exists that C. albicans, a normal colonizer of the gastrointestinal tract, translocated through a bowel perforation or disruption during the surgical procedure. The surgical approach was an anterior one, with a peri-umbilical incision to retract the great vessels as well as a lateral, retroperitoneal incision to access the lumbar spine. However, there were no complications noted. In addition, subsequent imaging of the abdomen did not reveal focal findings to suggest perforation or gastrointestinal injury.

Hypervirulent strains of C. albicans have been described [14–18]. Questions arose if the C. albicans strain in this case was indeed hypervirulent and the cause for this patient’s rapid deterioration. To determine virulence of the isolated Candida strain, we used the established invertebrate model of Galleria mellonella and compared survival to lab control C. albicans (SC5314, ATCC). Testing revealed that this patient’s C. albicans strain was not hypervirulent and, in fact, G. mellonella mortality was equal between both patient and lab control strains (data not shown).

In the literature, eleven cases of Candida species necrotizing fasciitis have been described [3–13]. The major risk factors include trauma, gunshot wounds and diabetes [1]. Moreover, an additional individual was immunocompromised being the recipient of a renal transplant [1]. Five cases identified C. albicans as the causative organism [3, 6, 7, 12, 13]. While not a contributor to this case, other species of Candida are known to cause necrotizing fasciitis including C. parapsilosis and C. glabrata [5, 8–10]. However, compared to published cases, this patient lacks obvious risk factors, which leads to further speculation about an underlying immunodeficiency. For instance, mutations or polymorphisms in receptors, specific cytokines and signaling components such as Dectin-1, interleukin (IL)-17, signal transducer and activator of transcription protein (STAT) and caspase recruitment domain-containing protein (CARD)-9, respectively, play a role in augmenting host immunity against pathogens, particularly yeast, and can manifest with mucosal candidiasis syndromes. Other syndromes, such as autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy (APECED), while include mucosal candidiasis, are unlikely to be the cause in this case given the lack of other components of the disease pattern [19]. Yet, current diagnostic assays have limited ability to characterize abnormalities pertaining to these pathways without use of specialized testing. This case highlights the need for development of improved immune profiling tools to better stratify those individuals at higher risk for invasive fungal infections, especially those with repeat infections such as mucosal candidiasis.

In conclusion, C. albicans, although very rare, should be considered as a potential causative organism of necrotizing fasciitis. Moreover, recurrent infections, particularly with opportunistic organisms such as fungi, should prompt a suspicion and evaluation of an immunocompromised state. Finally, this presentation raises concerns for deficits in our current diagnostics and highlights the need for novel assay development to help identify immune incompetency that warrant alternative clinical management of infectious complications.

Declaration of competing interestCOI

There are none.

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