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Case report

Rapidly progressive necrotizing cellulitis secondary to *Candida tropicalis* infection in an immunocompromised host

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ABSTRACT

The incidence of invasive fungal infection is increasing as the population of immunosuppressed patients grows. Many species that were previously thought to be benign are now known pathogens. The most commonly isolated organisms (>80 %) include *Candida albicans, Cryptococcus neoformans* and *Aspergillus fumigatus*. However, there are several new and emerging organisms. The Non-albicans species of Candida are one of the emerging invasive fungal organisms that are beginning to affect high-risk patients such as those with bone marrow transplant, neutropenia, HIV/AIDS or on immunosuppressive therapy. We present a case of a patient who suffered with angioinvasive non-Albicans Candidal infection, leading to a life-threatening necrotizing cellulitis.

Introduction

Immunocompromised patients are at high risk of developing serious disseminated infections by opportunistic fungi such as Aspergillus, Candida, and Fusarium spp [1]. These may have several manifestations, including cutaneous lesions. Severe and prolonged neutropenia, immunosuppressive treatments and severe T-cell immunodeficiency are well known important risk factors. We report the case of a 60-year-old man with large T-cell lymphoma status post chemotherapy, who presented with a fever and a tender skin lesion on the right side of his medial thigh. The rash continued to progress, becoming more necrotic and appearing to extend to the fascia. A skin biopsy was performed and demonstrated angioinvasive deep fungal organisms, both yeast and hyphal forms. Tissue culture revealed the presence of fluconazole-resistant Candida tropicalis. The atypical presentation of a tender, erythematous, macular rash progressing to a rapidly expanding bullous necrotic lesion led to a delayed diagnosis of angioinvasive cellulitis in our patient. Early diagnosis and treatment is very important to improve the prognosis, due to the high mortality rate of invasive candidal infections in immunocompromised hosts.

Case presentation

We report here the case of a 60-year-old man with history of large T-cell lymphoma, status post chemotherapy with rituximab, cyclophosphamide, hydroxydaunomycin, oncovin, prednisolone (RCHOP), who presented with fever and a tender skin lesion on the medial side of his right thigh. The lesion started as a localized, superficial rash following his first round of inpatient ifosphamide carboplatin-etoposide (ICE) chemotherapy for relapsed lymphoma, along with corticosteroids, intravenous immunoglobulin and romiplastin for the treatment of Evan's Syndrome, refractory and recurrent cytopenic episodes. At the time of presentation, the patient was found to be septic. He had a peripherally inserted central catheter (PICC) in place from a prior hospital stay for administration of chemotherapy. The line was suspected to be the source of sepsis and therefore was immediately removed. Meropenem and vancomycin were initiated, for empiric coverage, in the setting of severe neutropenia and sepsis. Clinical examination revealed a faint, well-demarcated and extremely painful 3×4 cm light red macule with no evidence of induration (Fig. 1) on his right medial thigh. The patient denied any inciting trauma to the area. Empiric acyclovir was added to his regimen for treatment of suspected herpes zoster, however, he had no clinical improvement. On day 3 following onset, the lesion became confluent and violaceous, extending to involve the majority of the medial aspect of the right thigh. It was no longer tender and now appeared indurated and plaque-like with newly developed bullae. An ultrasound of the affected area was unremarkable for any fluid collection or abscess. His admission blood cultures started growing

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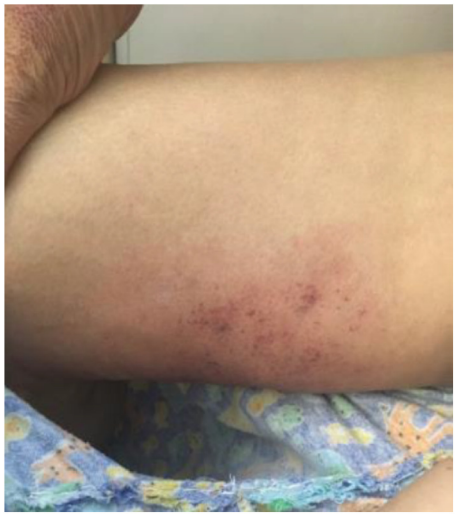

Fig. 1. 3 × 4 cm light red macule with no evidence of induration.

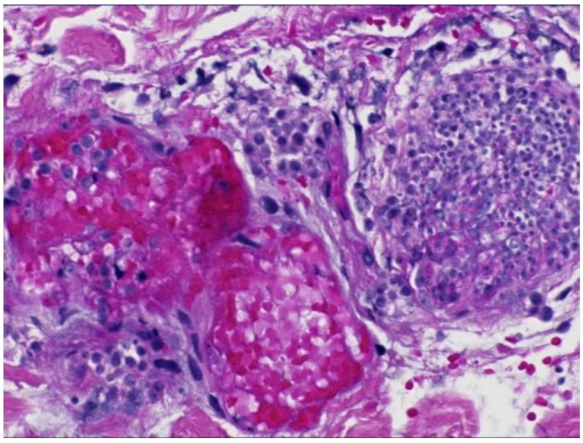

Fig. 2. Angioinvasive deep fungal organisms, both yeast and hyphal forms.

Candida tropicalis (C. tropicalis). PICC tip culture was also positive for the same organism. He was started on caspofungin. A skin biopsy was performed and demonstrated angioinvasive deep fungal organisms, both yeast and hyphal forms (Fig. 2). Tissue culture revealed the presence of fluconazole-resistant C. tropicalis. The rash continued to progress, became more necrotic and appeared to extend to the fascia (Fig. 3). At that point, General Surgery was consulted, but surgical intervention was deferred due to lack of any drainable fluid collection. With continued antifungal treatment, the patient's clinical condition stabilized and the skin manifestations slowly started to improve. Caspofungin was continued for a total of 6 weeks. All other antimicrobials were discontinued. At a 4-month follow up appointment, the lesions showed significant improvement, however the area remained deeply pigmented with a slowly healing ulcer with central clearing.

Discussion

Most cutaneous Candida spp infection manifestations are a result of hematogenous spread [2]. While in this case it was not the primary manifestation, primary cutaneous candidiasis can occur and should be included in the differential diagnosis for immunosuppressed patients presenting with cellulitis that fails to respond to antimicrobial therapy. Primary Candida spp infections of the deep skin and soft tissue are extremely rare. The majority of cutaneous Candida spp infections are secondary to Candida albicans and can have a wide variety of presentations including superficial dermatitis, intertrigo and balanitis [2]. A wider variety of fungal infections can occur in immunosuppressed patient populations such as those receiving intravenous cytotoxic chemotherapy. The presence of an indwelling catheter or port-a-cath for cytotoxic chemotherapy in a patient who presents with sepsis should always prompt investigation and consideration of potential fungal etiologies of the disease process. The most prevalent pathogenic Candida spp of the non-albicans group is C. tropicalis. There has been a marked global increase in infection due to this pathogenic yeast, and it is currently emerging as a significant threat to immunocompromised patients [3]. In addition to the ascendance of C. tropicalis as an etiologic agent of nosocomial infections, this organism has also shown high-levels of acquired resistance to fluconazole, fact which remains under investigation by researchers [3]. As in our patient, invasive candidiasis can be present through blood stream infection, deep tissue infection or meningoencephalitis. Immunocompromised patients are at increased risk of disseminated candidiasis. The mortality rate is high, especially in critically ill patients, post-surgical patients, patients with malignancy, neutropenia or who are on broad-spectrum antibiotics [4]. Invasive candidiasis is common in patients who have severe congenital neutropenia or leukocyte adhesion disorder, demonstrating the role played by granulocytes in protecting against disseminated fungal disease [4]. Guidelines for the treatment of invasive candidiasis were last published in 2009, but resistance to the recommended treatment has recently been described in the literature. Awareness of the increasing resistance patterns of Candida spp. When caring for immunocompromised patients may improve treatment and create better patient outcomes, given the high mortality rates in these patients.

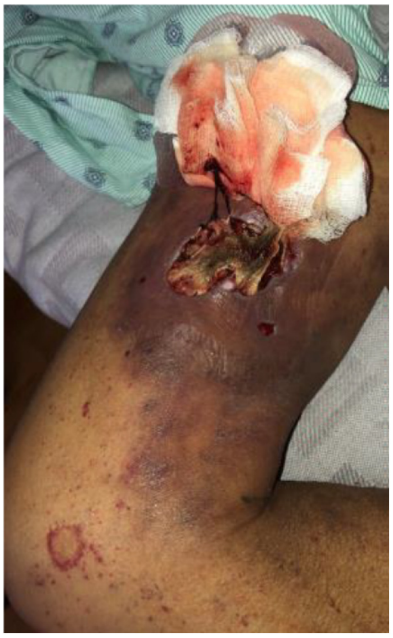

Fig. 3. Necrotic rash extending to fascia.

Conclusion

Skin lesions seen in immunocompromised patients may not manifest in a typical manner as in the case of immunocompetent patients. The atypical presentation of a tender, erythematous, macular rash progressing to a rapidly expanding bullous necrotic

lesion led to a delayed diagnosis of angioinvasive fungal cellulitis in our patient. Early diagnosis and treatment is very important to improve the prognosis, due to the high mortality rate of invasive candidal infections in immunocompromised hosts.

CRediT authorship contribution statement

Nithya Krishnan: Conceptualization, Writing - original draft. **Bijal Patel:** Conceptualization, Writing - review & editing. **William Palfrey:** Writing - review & editing. **Carmen Isache:** Supervision.

Declaration of Competing Interest

The authors whose names are listed immediately below certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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