Cutaneous presentation of Candida krusei fungemia refractory to amphotericin B

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To the Editor:

Disseminated candidiasis typically manifests with severe symptoms in immunocompromised patients and may infrequently present with cutaneous findings. The mortality rate of candidemia in patients who develop skin involvement approaches 80%.¹ While Candida albicans is the predominant causative pathogen, Candida krusei is on the rise and accounts for approximately 1.5-8% of cases.² We illustrate an atypical case of C.
Candida krusei fungemia that presented with subtle skin findings in an afebrile oncology patient, despite amphotericin B prophylaxis.

A 23-year-old female with a one-year history of BCR/ABL-negative B-cell acute lymphoblastic leukemia with leptomeningeal disease treated with craniospinal irradiation, refractory to multiple lines of chemotherapy and CART-cell infusion, was consulted by the dermatology service for an asymptomatic rash present for two days. The rash started on the face and spread caudally. On physical examination, she had a diffuse eruption consisting of multiple pink-to-red macules and papules with surrounding erythema most prominent on the face and trunk (Fig 1). There were no vesicles, pustules, erosions, or ulcers with sparing of the oral mucosa and conjunctiva. Her current medications included venetoclax and ibrutinib, as well as levofloxacin, valacyclovir, atovaquone, and micafungin for infection prophylaxis. Blood cultures revealed candidemia and bacteremia prior to consult, and she was started on amphotericin B, voriconazole, daptomycin, and meropenem. Given the morphology and frequent medication changes, a drug reaction was suspected. We also considered viral exanthem, thrombocytopenic purpura, and fungemia. While she had previously experienced neutropenic fevers, vital signs at the time of consult were within normal limits. Significant laboratory results included pancytopenia with a neutrophil count of 0.0 k/uL. Skin punch biopsy of the right leg demonstrated aggregated yeast in and around a blood vessel in the papillary dermis, highlighted with PAS-D stain (Fig 2). The biopsy findings were compatible with hematogenous yeast dissemination. Blood culture eventually confirmed the fungal species as Candida krusei and bacterial species as Enterococcus faecium. Despite aggressive therapy, she expired three days later.

Candida krusei is a rare, often fatal cause of fungemia, most commonly observed in severely neutropenic patients with hematologic malignancies. Its intrinsic resistance to azole antifungal agents, specifically fluconazole, and reduced susceptibility to other azoles and polyenes, including amphotericin B, makes prophylaxis and treatment challenging. Furthermore, azole prophylaxis is reported to increase the risk of C. krusei candidemia. Although reports are limited, cutaneous lesions may be an initial sign of disseminated C. krusei and vary from erythematous papules, with or without necrosis and crusting, to pustulonodular lesions. Neutropenic patients are at risk of severe cutaneous manifestations, including diffuse necrotic varicelliform papules associated with pain and pruritis. Though our patient was severely neutropenic, her eruption only consisted of asymptomatic red-to-violaceous macules and papules predominantly localized to the face and upper trunk.

While less prevalent, C. krusei infection carries higher mortality than C. albicans. Unlike C. albicans, which is typically associated with catheter-related bloodstream infection, the source of C. krusei is frequently unidentified. However, C. krusei is commonly linked to gastrointestinal colonization, which is more likely in the setting of poly-antimicrobial use. We theorize that our patient’s immunosuppression and antimicrobial prophylaxis for opportunistic infections placed her at risk of gastrointestinal colonization and dissemination.

This case highlights the diagnostic and treatment challenges surrounding C. krusei. Since the most susceptible individuals have pancytopenia on numerous medications, a purpuric eruption may be attributed to drug reactions or thrombocytopenia. Therefore, new disseminated cutaneous lesions in an oncology patient, even without fever, should raise concern for fungemia. There should be a low threshold for obtaining skin biopsy in these high-risk patients. Increasing the awareness of the heterogeneous manifestations of C. krusei is essential given the high mortality rate.

Ethics Statement: Informed patient consent was obtained for publication of the case details and photographs.

Abbreviations

CART-cell – chimeric antigen receptor T-cell

PAS-D – Periodic acid–Schiff–diastase

References


**Figure Legend**

Figure 1. Pink to red macules and papules with surrounding erythema on the face and chest.

Figure 2. A) Skin punch biopsy showing superficial perivascular inflammatory infiltrate (Hematoxylin and Eosin stain, 20x). B) Aggregates of yeast are seen in and around a blood vessel in the papillary dermis (Hematoxylin and Eosin stain, 200x). C) Fungal organisms are highlighted with a PAS-D stain and are compatible with hematogenous dissemination (PAS-D stain, 400x).