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Case presentation

Disseminated *Candida tropicalis* presenting with Ecthyma-Gangrenosum-like Lesions

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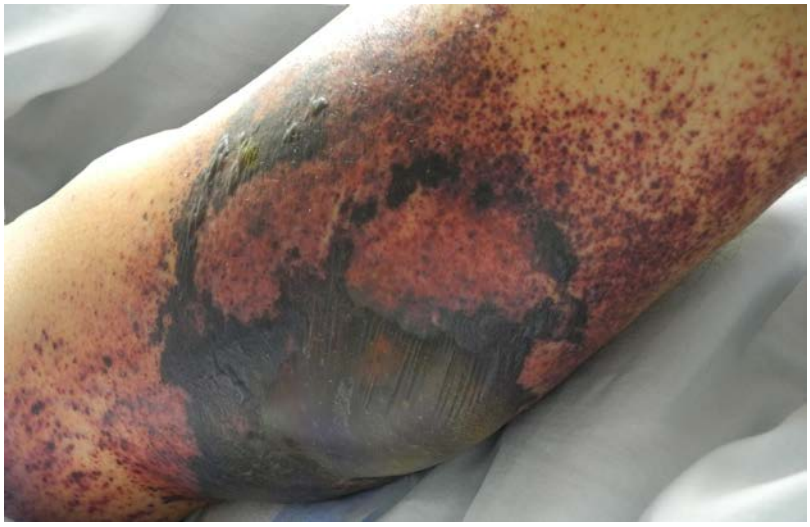
Abstract

Disseminated candidiasis in immunosuppressed patients has been classically associated with an erythematous papular eruption [1, 2, 3], however more severe presentations are possible. We present a patient who developed disseminated *Candida tropicalis* that presented with hemorrhagic bullae that progressed to large necrotic ulcers.

Keywords: Disseminated candidiasis, *Candida tropicalis*, Ecthyma Gangrenosum

Case Synopsis



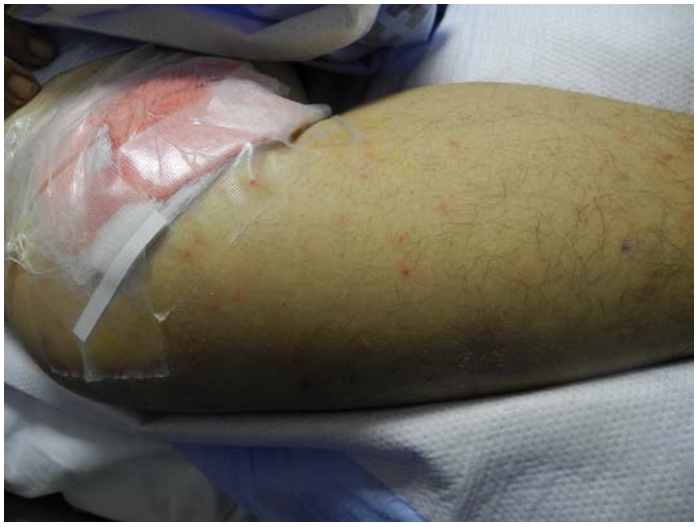


Figure 1. Diffusely scattered erythematous papules on his bilateral lower extremities. **Figure 2.** Left lower extremity with scattered erythematous and purpuric papules coalescing into a stellate purpuric plaque with overlying tense hemorrhagic bulla.

A 24-year-old male presented to our facility with lower extremity paralysis and urinary retention. His past medical history was significant for stage IV non-seminomatous germ cell tumor status post left orchiectomy and chemotherapy with progression of disease and high dose myeloablative therapy followed by autologous stem cell rescue twice two years prior. Unfortunately, he had lost his insurance and had been unable to follow up with his oncologist during that time. MRI of his lumbar spine

demonstrated a large heterogenous left paraspinal mass infiltrating into the spinal cord with mass effect on the cord at levels T10 to L3, as well as metastatic lesions. He underwent urgent decompressive laminectomy from T10 to L2 and partial resection of the epidural mass, which was consistent with a metastatic embryonal carcinoma on pathology. He was then started on paclitaxel, ifosfamide, cisplatin (TIP) chemotherapy that was complicated initially by tachycardia beginning six days after initiation, and was followed by neutropenia, fevers, and pancytopenia over the next several days. Blood and urine cultures were performed at the time, which initially grew *E. coli* from his blood, and he was started on empiric vancomycin and piperacillin/tazobactam.

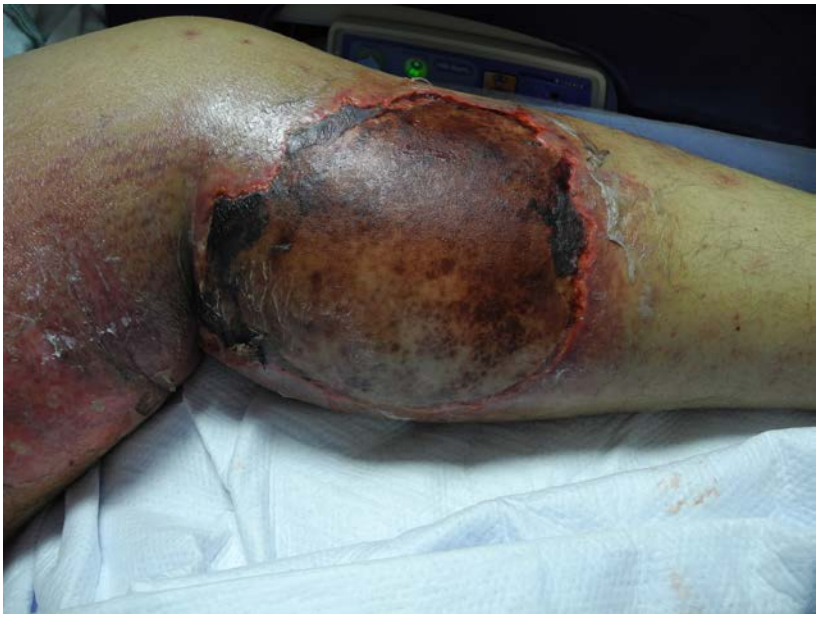
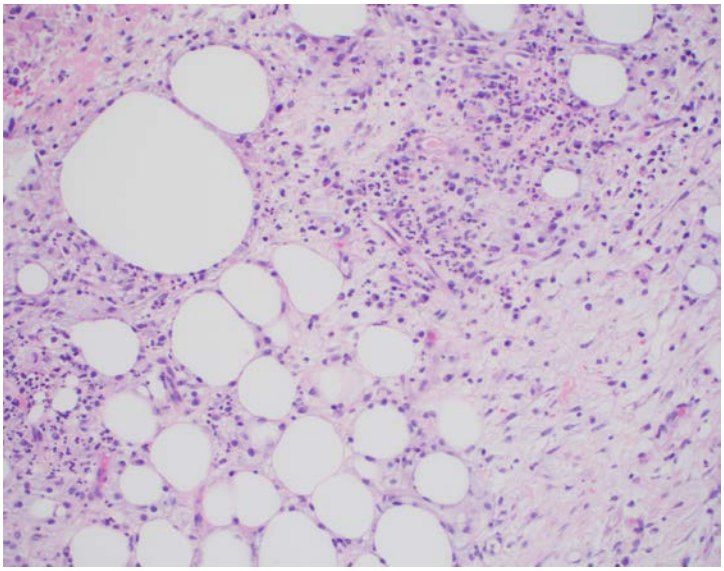


Figure 3. Necrotic ulcer with devitalized dermis (prior to debridement)

Dermatology was consulted for a new rash on his bilateral lower extremities, lower abdomen and flanks that had started about one week after onset of fevers. On examination, he initially had diffusely scattered erythematous papules on his bilateral lower extremities (Figure 1) as well as non-palpable purpura involving the lower abdomen and flanks. These lesions then progressed over the course of several days to large hemorrhagic bullae (Figure 2) that eventually became necrotic stellate ulcers. Punch biopsies showed suppurative granulomatous inflammation in the dermis and in the subcutis. PAS and GMS stains both highlight budding yeasts in the dermis. No vasculopathy or septic vasculitis was seen. Tissue and repeat blood cultures grew *Candida tropicalis*. (Figure 4a, 4b)



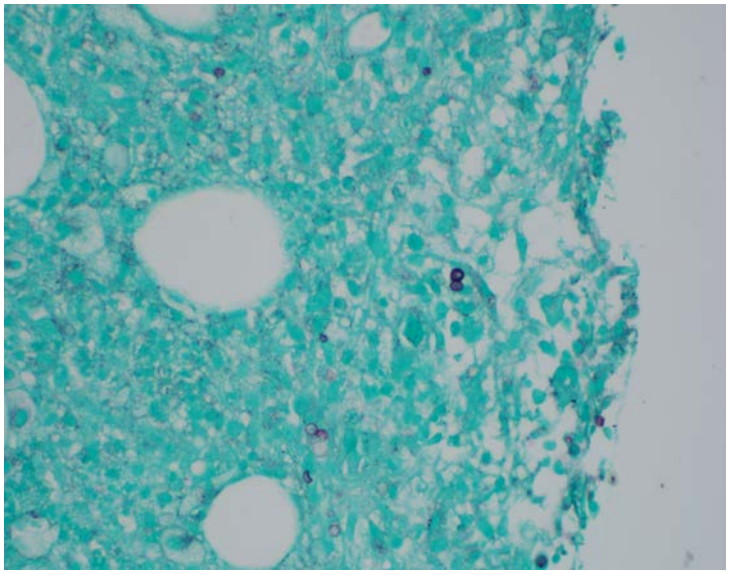


Figure 4A. Low power magnification demonstrating suppurative granulomatous dermatitis and panniculitis. **Figure 4B**. Grocott's methenamine silver (GMS) stain highlighting budding yeast.

The patient was treated initially with amphotericin and micafungin for empiric coverage, and was transitioned to fluconazole monotherapy once the speciation of *C. tropicalis* was determined. General surgery was also consulted and debrided 125 cm2 of necrotic tissue from his left lower extremity (Figure 3).

The patient's fevers initially improved, but then recurred and he was found to have a new pulmonary nodule concerning for fungal versus metastatic disease. At this point fluconazole was changed to voriconazole for aspergillus coverage. Amphotercin-B was also restarted, but stopped once voriconazole reached a therapeutic level. The lung nodule was biopsied and stained positive for fungal hyphae. Although the biopsy stained for fungal hyphae on GMS, there was no fungus isolated from the lung tissue cultures. There was also no acid-fast bacilli isolated or growth on the aerobic and anaerobic cultures.

The patient improved on voriconazole and was transferred to rehab. At the last follow-up 3 months after initial presentation, the patient was continued on voriconazole with a plan to repeat imaging the following month to determine length of therapy. Given

the biopsies, cultures, and clinical picture, our diagnosis was disseminated candidiasis presenting with ecthyma-gangrenosum-like lesions. Unfortunately, the patient has since been lost to follow-up.

Discussion

Disseminated candidiasis presenting as ecthyma gangrenosum-like lesions was first described by File et al. in 1978 [4]. The patient was immunosuppressed, and the causative organism was determined to be C. tropicalis. A more recent study showed that in patients with disseminated candidiasis and skin lesions, 63% were due to C. tropicalis [3]. In a study by Deorukhar et al., it was noted that 52% of C. tropicalis isolated were proteinase producers, allowing the organism to degrade host epithelial proteins like collagen and keratin [5].

Ecthyma gangrenosum is a vasculopathy that usually occurs in immunocompromised individuals and involves the occlusion of vessels by an organism, typically Pseudomonas aeruginosa. Lesions initially present as painless erythematous macules that can progress to hemorrhagic bullae and eventually form eschars as the organism proliferates. Histologically, organisms can be seen in the media and adventitia of vascular walls which can eventually cause occlusion of the vessel and the resultant clinical eschar. Fine et al. described a case of disseminated candidiasis mimicking ecthyma gangrenosum in 1981 where the biopsies showed numerous fungal pseudohyphae infiltrating into the dermis and epidermis [6].

In our patient, two biopsies were initially performed on “classic” looking erythematous papules, neither of which had fungal elements on biopsy or culture. Fortunately, biopsies taken from later-stage necrotic plaques were consistent with previous case reports and showed fungal elements on histology and C. tropicalis was isolated from cultures. The lack of vasculopathy or vasculitis on histopathology may be explained by the stage of the lesion as well as biopsy site selection. Blood cultures did eventually grow C. tropicalis, however this was several days after the diagnosis had been made from skin biopsies, emphasizing the importance of tissue as a diagnostic aid.

A distinctive triad of high fever, papular erythematous skin lesions, and diffuse muscle tenderness has been proposed as a diagnostic clue in disseminated candidiasis [2]. While our patient did have fevers and skin lesions, he did not have any feeling in his legs due to tumor compression of his spine.

Treatment of a disseminated C. tropicalis infection typically involves either amphotericin B or an azole. In a study of 125 C. tropicalis isolates, amphotericin B has the lowest resistance rate at 17.6%, followed by itraconazole (67.2%), ketoconazole (68%), and fluconazole (71.2%)[5]. Increased resistance to fluconazole was noted in C. tropicalis that has been isolated from blood cultures, and when the organism was able to form a biofilm [5]. In addition to medical therapy, debridement is also an important form of source control, as our patient had persistent positive wound cultures despite days of antifungal treatment.

In summary, although ecthyma gangrenosum-like lesions have been described classically as occurring in Pseudomonas infection, many organisms have been also been implicated. In neutropenic patients angioinvasive fungi such as Aspergillius, Fusarium and Zygomyces more commonly cause ecthyma-like lesions, however, disseminated candidiasis, specifically C. tropicalis, should be included in the differential in an immunosuppressed patient presenting with necrotic ulcers.

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