

Necrotic Ulcer on the Thigh



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A 29-year-old man with a history of acute lymphoblastic leukemia was admitted for acute encephalopathy and a necrotic ulcer on the right thigh of 2 weeks' duration. He had received chemotherapy with pegaspargase and vincristine 6 weeks prior to admission. He reported headache with nausea and vomiting of 2 weeks' duration and had sustained a fall in the bathtub a week prior that initially resulted in a right thigh abrasion. He denied recent travel, unusual food consumption, animal exposure, exposure to sick persons, and alcohol or other drug use. On examination the patient was alert but was not oriented to person, place, or time. A 10×10-cm necrotic ulcer with surrounding mild erythema and tenderness was noted on the right inner thigh.

WHAT'S THE DIAGNOSIS?

- brown recluse spider bite
- disseminated aspergillosis
- disseminated cryptococcosis
- disseminated fusariosis
- pseudomonal ecthyma gangrenosum

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The authors report no conflict of interest.

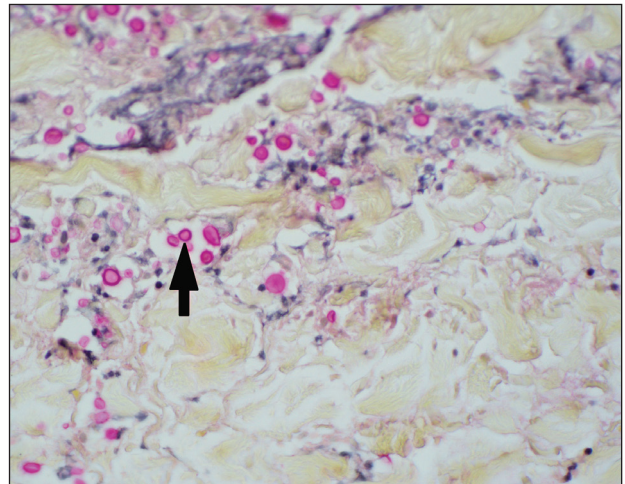
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THE DIAGNOSIS: Disseminated Cryptococcosis

Histopathologic examination of a 3-mm punch biopsy showed a diffuse dermal neutrophilic infiltrate with necrosis and subcutaneous tissue with round yeast surrounded by a prominent halo staining bright red with mucicarmine, representing a thick mucinous capsule (Figure). Grocott-Gomori methenamine-silver and periodic acid-Schiff stains also demonstrated fungal spores morphologically. Cerebrospinal fluid culture grew *Cryptococcus neoformans*, and cryptococcal antigen titers were positive in both serum and cerebrospinal fluid samples (>1:4096). The patient had autolytic debridement of the ulcer after completing a 4-week induction course of intravenous liposomal amphotericin B with oral flucytosine. He was transitioned to oral fluconazole for the consolidation phase of treatment.

Cryptococcus is an opportunistic basidiomycetous yeast with worldwide distribution and 2 primary pathogenic species in humans: *C neoformans* and *Cryptococcus gattii*. It is associated with bird feces, composted food, and decayed wood.^{1,2} A predilection toward an immunosuppressed host is recognized in 70% to 90% of the infections caused by *C neoformans*; however, *C gattii* commonly affects individuals with apparently intact immune systems.^{1,3} Risk factors for infection include advanced human immunodeficiency virus infection, solid organ transplantation, chronic liver disease, autoimmune disease, hematological malignancy, and underlying genetic susceptibility.^{1,2}

Initial exposure is through the respiratory tract with formation of latent reservoirs in the pulmonary lymph nodes with subsequent reactivation that can result in hematogenous dissemination.^{1,2} Cutaneous involvement was described in 108 patients (5%) in a large review of 1974 cases in France.⁴ Among those with cutaneous involvement, disseminated disease was diagnosed in 80 cases (74%), and 28 cases (26%) were considered primary cutaneous cryptococcosis. Primary cutaneous cryptococcosis typically presents as a single lesion, predominantly on the hand, with whitlow and more rarely with extensive cellulitis or necrotizing fasciitis.⁴ In disseminated cutaneous disease, there is no pathognomonic single lesion; however, it is commonly associated with multiple cutaneous lesions predominantly involving the head and neck. Plaques, abscesses, nodules, and pustular or umbilicated papules have been reported.^{1,5} There are few case reports that describe a single isolated necrotic ulcer with disseminated disease similar to our presented case, and more typically the necrotic ulcer is seen in transplanted patients.⁶ The differential diagnosis of a necrotic thigh ulcer includes pseudomonal ecthyma gangrenosum, cutaneous anthrax and aspergillosis, fusariosis, and a bite from the brown recluse spider.⁷ Our patient had an increased susceptibility to infection from



Diffuse dermal neutrophilic infiltrate with necrosis and subcutaneous tissue with round yeast surrounded by a prominent halo (arrow) staining bright red with mucicarmine, representing a thick mucinous capsule (original magnification $\times 400$).

his ongoing chemotherapy, a risk previously described in oncology patients with cell-mediated immunosuppression.⁸

Management for disseminated cryptococcosis is a 3-phase therapy including induction with intravenous amphotericin B and oral flucytosine for a minimum of 2 weeks, with consolidation and maintenance phases both with oral fluconazole for a length depending on underlying immunosuppression.⁹

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