

Disseminated Candidiasis in a Patient With Acute Myelogenous Leukemia

Richard Grabowski, MD; Elizabeth Dugan, MD

Disseminated candidiasis is a frequently fatal condition that is rising steadily in immunocompromised patients. We present the case of a 62-year-old African American woman with acute myelogenous leukemia who developed characteristic cutaneous signs of systemic candidiasis. Early cultures and biopsies resulted in early diagnosis, which prompted proper antifungal therapy and a positive outcome.

Cutis. 2003;71:466-468.

Systemic candidiasis is a frequently fatal condition that has become increasingly common with the advent of systemic immunosuppressive medications and broad-spectrum antibiotics. The ability to detect these infections early is exceedingly important, because early intervention with antibiotics is the best defense. In the hospital setting, dermatologists are frequently called on to assist oncologists in the management of both iatrogenic and inherently immunosuppressed patients with cutaneous abnormalities. Often, these benign conditions are the ones we see on a daily basis in immunocompetent patients. However, in a febrile neutropenic patient with concomitant exanthema, the clinician has to be particularly vigilant. This article presents a case report of such a scenario.

Case Report

A 62-year-old African American woman with a history of hypertension and asthma was admitted to our hospital for fatigue, weight loss, and easy bleeding. A biopsy of the bone marrow was performed, and results confirmed the diagnosis of acute myelogenous leukemia. She was given a 6-day course of chemotherapy including idarubicin and cytarabine.



Figure 1. View of erythematous to purpuric palpable papules on the ankles.

Five days after finishing the treatment, the patient became febrile (temperature, 103°F) and developed numerous erythematous to purpuric papules in a generalized distribution (Figure 1). Results of blood cultures were positive for yeast.

When dermatology was consulted, two 4-mm punch biopsies were performed, one for histopathologic examination and one for culture. Figures 2 and 3 show a superficial, primarily perivascular inflammatory infiltrate consisting mostly of lymphocytes, neutrophils, nuclear dust, and extravasated red blood cells. Periodic acid–Schiff stain with diastase and Gomori methenamine-silver stain facilitated the visualization of sporelike and hyphal forms within some of the vessels. Skin culture as well as blood cultures eventually became positive for *Candida tropicalis*. Her Groshen catheter was removed, and the findings from an echocardiogram were normal, with no evidence of cardiac vegetations. The patient was started on amphotericin B

Accepted for publication October 25, 2002.

From the Department of Dermatology, Washington Hospital Center, Washington, DC.

The authors report no conflict of interest.

Reprints: Richard Grabowski, MD, 1712 Eye St, NW, Suite 712, Washington, DC 20006 (e-mail: richgrabowski@cox.net).

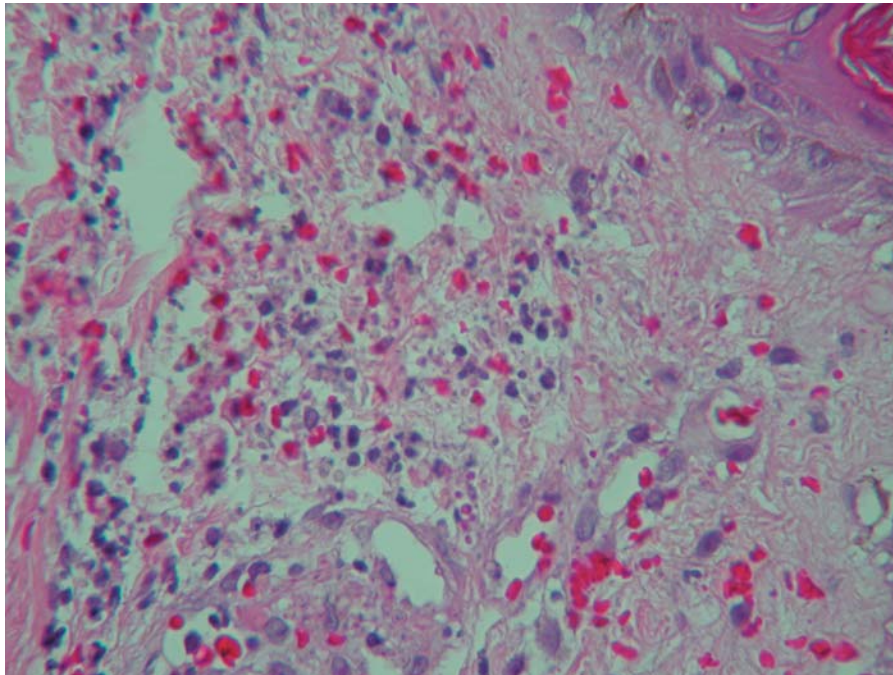


Figure 2. Perivascular neutrophils, karyorrhexis, and extravasated red blood cells (H&E, original magnification $\times 40$).

but was subsequently switched to Abelcet® as a result of elevated serum creatinine levels. Her skin gradually cleared. Then, she was transferred to a subacute care facility for continued intravenous (IV) amphotericin B, with the intent to convert her final treatment to a 14-day course of oral fluconazole. The total candidal treatment course was 6 weeks. After the patient's transfer to the subacute care facility, she was lost to follow-up. However, her infectious disease physician reports that the patient did very well in subacute care and was later released.

Comment

The incidence of systemic candidiasis is rising steadily and is a frequent cause of death in immunocompromised patients.¹ This is especially relevant in febrile neutropenic patients with indwelling IV catheters and recent treatment with broad-spectrum antibiotics.² Although cutaneous involvement is rare, biopsy of skin lesions for histopathologic analysis and culture can facilitate early diagnosis. In classic disseminated candidiasis, erythematous macules and papules measure from 0.5 to 1.0 cm in diameter, some with pale centers, purpuric papulonodules, or necrotic plaques resembling ecthyma gangrenosum, all of which are found on the trunk and extremities.^{3,4} Some authors have even described a triad of fever, rash, and muscle tenderness, symptoms our patient did not volunteer.⁵ Cutaneous involvement is cause for initiating anti-

fungal therapy. Although blood cultures are essential in a febrile hospitalized patient, they are frequently negative for candidemia. Thus, negative cultures should not override clinical judgment in this setting. Fortunately, skin cultures from involved skin often test positive for *Candida*.

C. tropicalis has become a well-known pathogen in patients with hematologic and lymphoreticular malignancies, especially acute myelogenous leukemia, as in our patient.⁶ A review of the literature reveals that in classic disseminated candidiasis, 60% of cases are secondary to *C. tropicalis*, with an additional 20% due to *Candida albicans*. A study conducted by Bielsa et al⁷ reported that in heroin-addicted patients, 100% had systemic candidiasis as a result of *C. albicans*. The exact reason for this discrepancy has not been elucidated entirely. Heroin abusers develop dermal candidal abscesses, likely caused by heroin diluted with *C. albicans*-contaminated lemon juice.⁷ In neutropenic patients, the gastrointestinal tract and, to a lesser extent, IV catheters play a role in dissemination.²

Histopathologic evaluation is a valuable tool in these cases. However, it may be difficult to identify organisms on standard hematoxylin-eosin (H&E) staining unless there are large numbers of organisms. Hence, clinical history is essential to heighten the dermatopathologist's index of suspicion. Visualization of *Candida* is facilitated by periodic acid-Schiff stain with diastase, Gomori methenamine-silver stain, or both. The pathology

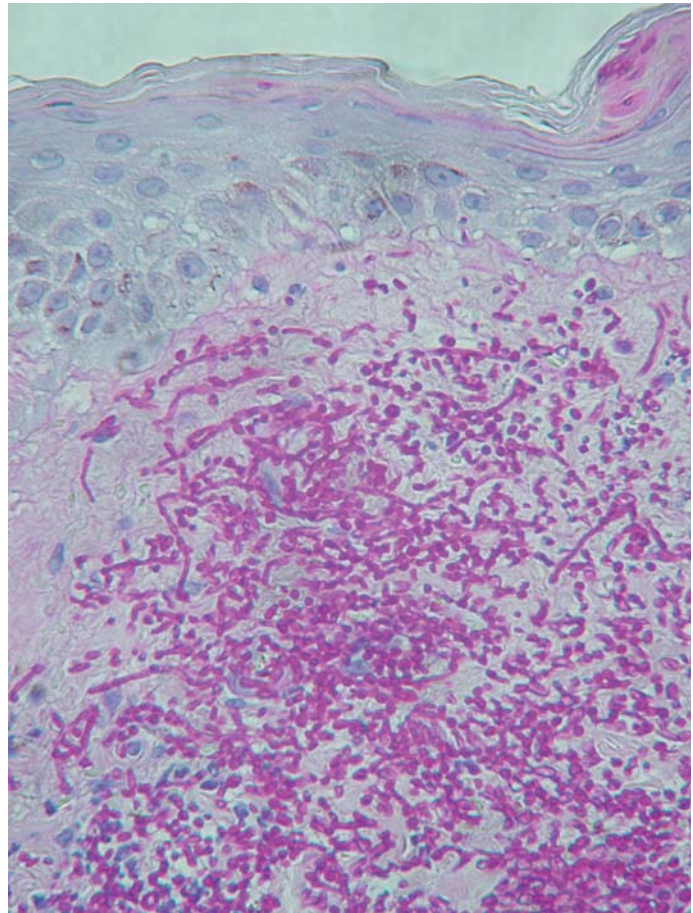


Figure 3. Numerous branching hyphae (periodic acid–Schiff stain with diastase, original magnification $\times 40$).

ranges from a leukocytoclastic vasculitis to a perivascular mononuclear infiltrate.⁸ In either case, adequate tissue is needed because early changes may be subtle, and it is a focal process within the dermis at sites of vascular damage from previously presumed fungal microthrombi.

In our institution, neutropenic patients receive an especially vigilant physical examination, and we maintain a high index of suspicion for performing biopsies for not only H&E staining but also bacterial and fungal cultures. By intervening in cutaneous disease processes early, we can have a positive effect on patients' lives.

REFERENCES

1. Martin AG, Kobayahi GS. Yeast infections: candidiasis, pityriasis versicolor. In: Freedberg IM, Eisen AZ, Wolff K, et al, eds. *Dermatology in General Medicine*. Vol 2. New York, NY: McGraw-Hill; 1999:2358-2368.
2. Anaissie E, Pinczowski H. Invasive candidiasis during granulocytopenia. *Cancer Res*. 1993;132:137-145.
3. File TM, Marina OA, Flowers FP. Necrotic skin lesions associated with disseminated candidiasis. *Arch Dermatol*. 1979;115:214-215.
4. Fine JD, Miller JA, Harist TJ, et al. Cutaneous lesions in disseminated candidiasis mimicking ecthyma gangrenosum. *Am J Med*. 1981;70:1133-1135.
5. Jarowski CI, Fialk MA, Murray HW, et al. Fever, rash, and muscle tenderness: a distinctive clinical presentation of disseminated candidiasis. *Arch Intern Med*. 1978;138:544-546.
6. Benson PM, Roth RR, Hicks CB. Nodular subcutaneous abscesses caused by candida tropicalis. *J Am Acad Dermatol*. 1987;16:623-624.
7. Bielsa I, Miro JM, Herrero C, et al. Systemic candidiasis in heroin abusers: cutaneous findings. *Int J Dermatol*. 1987;26:314-319.
8. Grossman ME, Silvers DN, Walther RR. Cutaneous manifestations of disseminated candidiasis. *J Am Acad Dermatol*. 1980;2:111-116.