A 70-Year-Old Kidney Transplant Recipient Presenting With Persistent Leg Cellulitis

(See page 688 for the Photo Quiz.)

Diagnosis: Disseminated cryptococcosis with cutaneous manifestations.

The patient presented with well-demarcated cellulitis (Figure 1). Histologic sections of skin demonstrated an unremarkable epidermis. In the dermis, there was a mixed inflammatory cell infiltrate surrounding numerous yeast-like fungal organisms that, when highlighted with mucicarmine and Fontana-Masson stains, were consistent with *Cryptococcus* (Figure 2). Fungal culture of skin biopsy grew *Cryptococcus neoformans*. Serum cryptococcal antigen from day 3 was positive. Cerebrospinal fluid (CSF) obtained on day 3 revealed 7 white blood cells/mm³, 378 red blood cells/mm³, glucose of 51 mg/dL, and protein of 41 mg/dL and was positive by cryptococcal lateral flow assay. The CSF Gram stain demonstrated fungal organisms, and culture grew *C. neoformans* 4 days later. Blood cultures obtained on hospital day 2 also grew *C. neoformans* on hospital day 7. A diagnosis of disseminated cryptococcosis with cutaneous involvement was made.

Cryptococcosis is a serious infectious complication in recipients of solid organ transplant (SOT). *Cryptococcus neoformans*, a basidiomycetous, encapsulated yeast, has been identified in soil samples worldwide, particularly in areas contaminated by bird or pigeon droppings. The estimated incidence of cryptococcosis in SOT recipients is 1.56% (range, 0.45%–4.1%) [1, 2].

Cutaneous cryptococcosis in SOT typically arises from hematogenous spread following primary pulmonary infection, although direct skin inoculation has been reported [3]. Early data on cutaneous cryptococcal disease was limited to case reports and case series [2], but in a recent prospective SOT cohort study, cutaneous cryptococcosis was the third most common manifestation [4]. It was the most common manifestation in a case series of liver transplant recipients receiving tacrolimus [5], and patients receiving tacrolimus have been shown to have more cutaneous involvement than patients receiving non-tacrolimus-based immunosuppression [2]. Cutaneous manifestations of cryptococcosis are incredibly varied and include acneform lesions, purpura, papules, vesicles, nodules, tumors, abscesses, ulcers, sinus tracts, plaques resembling ecchymoses, and superficial granulomas [6]. SOT patients with cryptococcal cutaneous disease often present with cellulitis [2, 4], and lower extremity involvement is most common [4], with multiple sites involved.

Figure 1. Photograph of the lower extremities showing well-demarcated cellulitis diagnosed as cutaneous cryptococcosis.

Figure 2. Skin biopsy (original magnification ×600). Fontana-Masson stain revealing melanin precursors in the yeast cell wall and accentuating the variable yeast size and morphology (red arrows) and narrow-based budding (yellow arrows).
frequently (48%) [3]. Therefore, cutaneous cryptococcosis should be considered in immunocompromised patients presenting with presumed nonresolving bacterial cellulitis in the appropriate context, as in our patient [3].

Because of the protean manifestations of cutaneous disease, the diagnosis can be challenging. Demonstration of cryptococcal organisms in tissue confirms the diagnosis. Variably sized (2–15 µm) Cryptococcus yeast forms can be identified in histopathologic specimens using methenamine silver stain. Mucicarmine stain highlights the secreted capsule and is highly specific for Cryptococcus; however, this staining may not be apparent in capsule-deficient variants, in which case Fontana-Masson stain uniformly highlights melanin precursors contained in the yeast cell wall.

Because our patient also had evidence of central nervous system disease, he received liposomal amphotericin and 5-fluorocytosine. Cyclosporine and mycophenolate mofetil were discontinued. He developed progressive renal failure and required initiation of hemodialysis. He was discharged 29 days after admission to complete a 4-week course of liposomal amphotericin, but was readmitted after 2 days for peritonitis secondary to a ruptured liver cyst. Unfortunately, he developed sepsis and respiratory failure, received comfort measures, and died.

Notes

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George E. Nelson,1 Dionysis Neofytos,1,3 Max Fischer,2 and Christine M. Durand1

1Division of Infectious Diseases, and 3Division of Dermatopathology, School of Medicine, Johns Hopkins University, Baltimore, Maryland, and 2Department of Medicine, Division of Infectious Pathology, Memorial Sloan Kettering Cancer Center, New York, New York

References


Correspondence: George Nelson, MD, Johns Hopkins University School of Medicine, 1830 E Monument St, Ste 450B, Baltimore, MD 21287 (george.nelson@jhmi.edu).