Candidiasis is the most common fungal infection in immunocompromised patients who are at greater risk for developing disseminated disease. Renal transplant recipients often are administered immunosuppressants and therefore are at an increased risk for developing disseminated candidal infections. Disseminated candidiasis generally does not present with cutaneous lesions, but when present, lesions usually are generalized or limited to the trunk and limbs. We describe the case of an immunosuppressed renal transplant recipient who developed a disseminated Candida kefyr infection and presented with oral mucosal lesions and cutaneous lesions limited to the left lower extremity. The lesions were localized due to a thrombus that was subsequently found in the patient’s left external iliac artery.


Case Report
A 22-year-old immunosuppressed woman with a recent history of a failed renal allograft due to bleeding in the graft anastomosis was being gradually tapered off prednisone and sirolimus and presented with annular, dusky, erythematous, indurated plaques with rare tense bullae on the left leg, thigh, and foot (Figures 1 and 2). The lesions ranged in size from 2 to 15 mm. Hydroxyzine and calamine lotion were administered, but the lesions progressively increased in size and number and the patient developed swelling and severe burning pain. She was febrile with a history of leukocytosis, and blood and catheter tip cultures were positive for Candida kefyr. Cultures from the respiratory tract and those taken during pulmonary thoracentesis grew Candida krusei; cultures taken during abdominal paracentesis grew Candida parapsilosis and Cryptococcus laurentii. The patient also developed oral candidiasis. Two punch biopsies were taken from lesions on the left leg and were submitted for tissue culture and histopathologic examination.

Histopathologic examination of the lesions showed a neutrophilic infiltrate within the deep dermis with extension into the subcutaneous fat and necrosis. Small round eosinophilic forms consistent with yeast were observed in the infiltrate (Figure 3). Gomori methenamine-silver staining revealed budding yeast forms and short hyphal forms with occasional bizarre shapes. Periodic acid–Schiff and Alcian blue staining highlighted these budding yeast and short hyphal forms (Figure 4). No capsule was identified. The findings were consistent with a disseminated yeast infection. The lack of capsular staining with periodic acid–Schiff and Alcian blue staining is evidence against a diagnosis of Cryptococcus. Tissue cultures did not grow any organisms. The patient’s prednisone was tapered off, and sirolimus was discontinued. Treatment with caspofungin was initiated, which initially led to an increase in the patient’s leukocytosis as well as the number of cutaneous lesions on the left leg. A thrombus in a previously placed stent in the left external iliac artery was subsequently discovered and replaced. Two days later, amphotericin B was added, followed by fluconazole, and the caspofungin was discontinued. Nystatin was prescribed for treatment of the oral lesions. Ophthalmology was consulted and no eye involvement was noted.

The patient later developed an infection at the abdominal incision site that grew C parapsilosis, and
most of the lesions on her leg progressed to become bullae and pustules. Although the lesions did not increase in number or size, they did not improve over the next 2 weeks. Incision and drainage of several of the lesions was performed; however, the drained lesions became fluctuant again. Pulses in her left leg were absent, and a new blood clot was discovered in her recently replaced left external iliac artery stent. The artery and stent were removed; cultures from her stent and the intima of the left common femoral and profunda femoris arteries grew *C. krusei* and *C. kefyr*, proving that the stent was the source of the infection. The compromised blood flow also prevented improvement of the lesions even after 2 weeks of treatment with intravenous and oral antifungals. Because *C. kefyr* was grown from cultures from the peripheral blood, catheter tip, stent, and arterial intima, we consider it to be the main pathogenic organism in this case.

An above-the-knee amputation was performed due to compromised blood flow, and it was decided that hemipelvectomy and hip disarticulation were future options if the infection worsened, as the intima of more proximal arteries still were infected. Over the next 2 months, a mixed gram-negative infection at the amputation site was treated with levofloxacin and cefepime hydrochloride, and a vancomycin-resistant *Enterococcus* and *Pseudomonas aeruginosa* infection involving the amputation site and thigh lesions as well as a sacral decubitus ulcer were treated with daptomycin, then linezolid and doripenem, respectively. Repeat blood cultures and further cultures of the lesions finally were negative, but the lesions on the left thigh failed to resolve. Incision and drainage
of all the lesions was performed, and more aggressive management of her nutrition was started. All antifungal treatment was discontinued due to increasing levels of alanine aminotransferase and aspartate aminotransferase. Because all cultures were negative and blood flow to the amputation site remained patent, it was decided that no further surgical intervention was required. After 125 days in the hospital, she was discharged with home health care for treatment of the amputation site, thigh lesions, abdominal incision site, and decubitus ulcer.

Comment
Solid organ transplant recipients are at an increased risk for infection, mainly due to necessary immunosuppressive therapy. Although less common than bacterial or viral infections, fungal infections in solid organ transplant recipients have an associated mortality rate of 27% to 77%; therefore, efforts must be made to diagnose and treat these infections in a timely manner. The incidence of systemic fungal disease in transplant recipients ranges from 2% to 45%, depending on the organ. In kidney transplant recipients, the rate is 2% to 14%; the incidence of infection is higher among other organ transplant recipients because these patients do not have the option of an alternative life support system (ie, dialysis) and there- are typically administered additional immunosuppressive therapy.

Candida albicans is the most common cause of disseminated candidiasis, but the incidence of candidiasis caused by other species, such as Candida tropicalis, C krusei, and Candida glabrata, is increasing. In one study, the total incidence of candidemia caused by non–C albicans species was higher than the incidence of candidemia caused by C albicans. Major risk factors for invasive Candida infections include colonization, treatment with broad-spectrum antibiotics, placement of a central venous catheter, parenteral nutrition, gastrointestinal or cardiac surgery, a prolonged hospital stay, an intensive care unit stay, burns, premature birth, neutropenia, corticosteroid treatment, human immunodeficiency virus infection, and diabetes mellitus. Our patient had several of these risk factors. Populations most commonly affected by invasive candidemia include those with neoplastic disease, those who have had complicated postoperative courses, burn patients, organ transplant recipients, and low-birth-weight infants.

The presence of fever, myalgia, and erythematous skin lesions in a septic patient who is not responding to antibiotic therapy is highly suggestive of disseminated candidiasis; however, all 3 components usually are not present. Cutaneous lesions with disseminated candidiasis are uncommon. Hematogenous spread to the skin occurs in 10% to 13% of patients with disseminated candidiasis.

Several different cutaneous lesions associated with fungemia in immunosuppressed patients have been reported. The most commonly reported lesions are erythematous or violaceous, asymptomatic maculopapular or nodular lesions, ranging from 5 to 10 mm in diameter and commonly are purpuric with or without associated thrombocytopenia. Lesions often have a pale center or a central pustule. They commonly are located on the extremities, particularly the proximal extremities, and the trunk; less commonly, they can appear on the head and neck. In 1 reported case, lesions were observed only on the face, palms, and soles. Although multiple lesions usually are present, a patient with a solitary nodule on the finger has been reported. Other unique reports of skin involvement associated with candidemia include generalized, micropustular, purpuric lesions on the scalp, trunk, and extremities; lesions that look clinically identical to erythema gangrenosum and purpura fulminans. Our patient presented with multiple lesions limited to one extremity due to the thrombus in her left external iliac artery. Culture of the thrombus demonstrated the source of septic emboli infected with Candida species infiltrating the distal aspect of the left lower extremity.

Conclusion
Disseminated candidiasis can have diverse presentations; therefore, a high index of suspicion should be maintained when a skin eruption occurs in a patient with associated risk factors. Rarely, cutaneous lesions are the only signs of the disease, but more commonly, cutaneous lesions occur in conjunction with systemic symptoms. Early diagnosis is critical, as disseminated candidiasis can be lethal in one-third of cases. Blood cultures often are negative 50% to 75% of the time, so skin lesions should be biopsied for histology and cultures.

REFERENCES