Case of Fatal Blastoschizomyces capitatus Infection Occurring in a Patient Receiving Empiric Micafungin Therapy

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The febrile neutropenic patient has been and continues to be a major therapeutic challenge (5). As our armamentarium of effective prophylactic and empirical treatment options has expanded, the pathogens causing infections have evolved in response to those changes. Using antimicrobial agents with good activity against particular organisms has led to an increasing prevalence of infections with organisms not typically covered by these agents. As an example of this phenomenon, we report the first known case of Blastoschizomyces capitatus infection occurring in a patient receiving empirical therapy with an echinocandin.

A 65-year-old Caucasian male was admitted to our institution with complaints of fatigue and shortness of breath. A complete blood count at admission revealed pancytopenia, with circulating blasts. The results of a bone marrow biopsy confirmed a diagnosis of acute myelogenous leukemia. A peripherally inserted central venous catheter (PICC) was placed in the patient, and he was treated with cytarabine and daunorubicin. After initial prophylaxis with moxifloxacin, fluconazole, and acyclovir, he became neutropenic and febrile on hospital day 8, at which time he was started on vancomycin and cefepime treatment. A coagulase-negative staphylococcus PICC-associated bloodstream infection was diagnosed, and he responded well to treatment with retention of the PICC. On hospital day 20, he again developed fevers, and fluconazole was changed to micafungin (100 mg daily). The blood cultures were negative, and the patient defervesced while on the same antimicrobial regimen. On hospital day 34, he was begun on total parenteral nutrition due to inadequate oral intake and again developed fevers. His cefepime was changed to meropenem, but his fevers persisted. Over the next 3 days, he manifested worsening renal, hepatic, and pulmonary dysfunction. Multiple blood cultures obtained on hospital days 34, 35, 36, and 37 ultimately all grew Blastoschizomyces capitatus. His PICC was removed on hospital day 35; a culture of the catheter tip was negative. On hospital day 37, the patient’s micafungin was changed to amphotericin B lipid complex and intravenous voriconazole on the basis of the first set of cultures yielding positive results, but he died later that day after a cardiopulmonary arrest.

Susceptibility testing was performed by colorimetric microdilution using Sensititre YeastOne panel (Trek Diagnostic System, Cleveland, OH) containing serial twofold dilutions of the agents listed in Table 1. The concentration range tested for micafungin was 0.008 to 8 μg/ml. A fresh culture of the organism was used to prepare the inoculum, which was standardized to a 0.5 McFarland turbidity standard. The inoculum was further diluted by transferring 20 μl of the yeast suspension into 11 ml of YeastOne inoculum broth to obtain a final inoculum concentration of 1.5 × 10^3 to 8 × 10^3 CFU/ml as recommended by the manufacturer. The dried YeastOne panel was rehydrated with the working yeast suspension by dispensing 100 μl into each well. The YeastOne panel was covered with adhesive seal and incubated at 35°C for 24 h in a non-CO_2 incubator. The panel was read using a reading mirror, which displays the underside of the wells. Yeast growth in the antifungal solution was evident as a color change from blue (no growth) to red (growth). Colorimetric MIC results for all agents tested were defined as the lowest concentration of antifungal agent that prevented the development of a red color (first blue well). Quality control was performed by testing strains with known endpoints (Candida parapsilosis ATCC 22019 and Candida krusei ATCC 6528) to check the potency of the antifungal agent dilutions.

Blastoschizomyces is a yeast similar to Trichosporon species but is distinguished by the ability to produce annelloconidia. Invasive disease is quite rare and almost exclusively limited to hosts with hematologic malignancies (1). In the largest case series published thus far, the vast majority of patients with B. capitatus infection had hematologic malignancies, recent chemotherapy, neutropenia, central venous catheters, and broad-spectrum antibiotic use (9). Mortality rates with this infection are quite high regardless of treatment.

The optimal antifungal therapy for B. capitatus remains somewhat unclear. In vitro susceptibility data are limited and vary widely for different classes of antifungals (1), though data
from the early 1990s suggested that fluconazole and flucytosine were four- to eightfold more active than amphotericin B was (13). Similarly, high-dose fluconazole was more effective than amphotericin B or voriconazole in a murine model (12), though there are also reports of fluconazole resistance occasionally occurring while on therapy (3, 9). In contrast, clinical experience suggests that amphotericin B is the most effective treatment, and most experts currently recommend this agent, alone or in combination with another drug. A review of the literature in the late 1990s found a better survival rate in those treated with amphotericin-based regimens versus fluconazole-based regimens (7). In the case series of Martino et al., while the numbers were too small to draw any formal conclusions, it is notable that only 1 of 13 patients with successful outcomes was not treated with amphotericin in some form (9). Central venous catheter removal (if present) also seems to be an important aspect of treatment (9). Adjuvant therapies advocated by some include hematopoietic growth factors (10), gamma interferon (4), and granulocyte transfusions (8, 11).

It is uncertain what activity, if any, echinocandins have against B. capitatus. There is some thought that they are inactive against this yeast, primarily on the basis of extrapolation of data for Trichosporon species. In vitro data, though limited, have at times suggested that at least some isolates are susceptible to echinocandins (2). We found only one case treated with an echinocandin (caspofungin [50 mg daily]), which ultimately was fatal 7 days after the onset of infection (9). Our isolate was interpreted as susceptible (using Candida species breakpoints) with an MIC of 0.5 µg/ml to micafungin despite the fact that it grew repeatedly for four consecutive days despite micafungin therapy. Notably, the correlation between MIC and treatment outcome for echinocandins in invasive candidiasis has not been fully established (6), calling into question the utility of in vitro susceptibility data for echinocandins against B. capitatus.

Clinicians should consider B. capitatus infection in those neutropenic patients who remain febrile despite echinocandin therapy or who develop yeast bloodstream infections while receiving an echinocandin. While there are limited treatment options available for this pathogen, it would appear that echinocandins have no role in management at this time.

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