Short Communication

Trichosporon asahii Fungemia in a Patient with Non-Hematological Malignancy

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SUMMARY: Trichosporon fungemia is usually seen in neutropenic patients with underlying hematological malignancies. In this report we describe a fatal case of Trichosporon asahii fungemia in a non-neutropenic patient with a non-hematological malignancy. For 1 week the patient exhibited hematuria, weakness, easy fatigability and headaches. At admission she had anemia, renal failure and evidence of right hydronephrosis and bladder wall masses as detected by CT scan. She did not have a history of tobacco abuse, contact with urinary carcinogens or Schistosoma infestation; her clinical picture was suggestive of bladder cancer. After some investigations the patient underwent radical cystectomy and ileal conduit surgery because of transitional cell carcinoma in the urinary bladder. After an initial uneventful improvement postoperatively the patient deteriorated and died of septic shock despite all reanimation efforts and antibiotic therapy including fluconazole. The blood culture obtained 4 days before the patient died revealed T. asahii, which was isolated on the day she died and found to be resistant to fluconazole and caspofungin. This report suggests that clinicians remain aware that fungemia in a patient with non-hematological malignancy. The remarkable findings in our case include a lack of neutropenia, borderline MIC of the isolate for fluconazole, and the fatal course of the disease despite the use of fluconazole and caspofungin.

A 75-year-old female without a previous medical history was admitted to our hospital, having exhibited hematuria, weakness, easy fatigability and headaches for 1 week. At admission she had anemia (hemoglobin, 7.5 g/dl), renal failure (creatinine, 4.5 mg/dl), and evidence of right hydronephrosis, left atrophic kidney and bladder wall masses as detected by CT scan. Although the patient did not have a history of tobacco abuse, contact with urinary carcinogens or Schistosoma infestation, her clinical picture was suggestive of bladder cancer. She required the insertion of a right percutaneous nephrostomy tube followed by a cystoscopy with multiple biopsies. No chemotherapeutic agents or Bacille Calmette-Guerin (BCG) were instilled following the procedure. The pathology results were consistent with high-grade T2 transitional cell carcinoma, and the patient underwent radical cystectomy and ileal conduit surgery.

Trichosporon asahii fungemia has been described in organ transplant recipients, patients with HIV infection, burn patients, individuals with end-stage renal disease on hemodialysis, and recipients of prosthetic heart valves (1). However, the overwhelming majority of cases occur in patients with leukemia or lymphomas who have developed profound granulocytopenia (2). Fewer cases have been reported in patients with solid malignancies, and the majority of these individuals also have severe depletion of neutrophils as the most prominent risk factor (3). We report a case of T. asahii fungemia in a patient with non-hematological malignancy. The remarkable findings in our case include a lack of neutropenia, borderline MIC of the isolate for fluconazole, and the fatal course of the disease despite the use of fluconazole and caspofungin.

After an initial uneventful recovery the patient developed pneumonia (treated with ceftriaxone and clarithromycin) and, later, an abdominal evisceration which required transfer to the intensive care unit. At that time the patient was hemodynamically unstable with a temperature of 39.1°C, a respiratory rate of 28 breaths/min, a heart rate of 112 beats/min, and blood pressure of 80/40 mmHg. She looked acutely ill, diaphoretic and pale. Her oral mucosa was dry. Her lungs were clear to auscultation. Her cardiovascular sounds were regular and rhythmic but tachycardiac, and a functional systolic murmur II/VI was heard in the precordium. Intra-abdominal viscera were visible in her abdominal wound. There was no obvious drainage or erythema surrounding the open wound. The patient was stuporous.

Six blood cultures were negative, but a urine culture yielded Enterococcus spp. resistant to ampicillin, and deep-wound cultures grew Candida albicans and Pseudomonas aeruginosa. The patient had an initial clinical improvement while receiving intravenous imipenem, gentamicin, teicoplanin, and fluconazole. After the initial clinical improvement, her condition deteriorated. The patient developed leukocytosis, elevated liver enzymes (aspartate aminotransferase, 125 U/L; alanine aminotransferase, 164 U/L) and renal dysfunction (blood urea nitrogen, 67; creatinine, 2.1 mg/dl). Consequently, the dose of teicoplanin was decreased, and after 5 days of fluconazole therapy it was exchanged for IV caspofungin (70 mg once then 50 mg/day). On the 4th day of therapy with caspofungin, a new blood culture grew T. asahii. On the same day the patient went into cardiorespiratory arrest and expired, despite reanimation efforts. Her relatives refused an autopsy.

The identification of T. asahii was performed in our microbiology laboratory. Yeasts were recovered from blood cultures after 48 h of incubation at 30°C on Sabouraud glucose agar (SGA) supplemented with 50 μg of chloramphenicol.
Selected colonies of each isolate were transferred to fresh SGA and maintained at 30°C. Germ tube negative yeasts were then tested for carbohydrate assimilation using the API 20C AUX yeast assimilation system (bioMérieux, Marcy l’Etoile, France). Susceptibility testing of the T. asahii isolate for caspofungin and fluconazole was performed using the National Committee for Clinical Laboratory Standards guidelines for broth microdilution antifungal susceptibility testing of yeasts on RPMI 1640 media. The MIC-2 for both drugs, caspofungin and fluconazole, was 16 µg/ml. The MICs were defined as prominent (80%) or complete (100%) growth inhibition after 48 h of incubation.

The availability of chemotherapy for the treatment of malignancies and the broad use of antifungal agents has been associated with a dramatic increment in opportunistic fungal infections (4). Trichosporonosis has emerged as a potentially life-threatening human condition, especially in neutropenic patients with hematological malignancies. In fact, Trichosporon spp. was ranked first among non-Candida causes of fungemia in a European cancer institute report (5).

Trichosporon spp. is a basidiomycete that inhabits the soil and fresh water and may also colonize skin, nails and oral mucosa in humans (6). The organism is usually not isolated in hospital environments, although there have been outbreaks associated with bronchoscopes and endoscopes. According to a proposed classification there are 17 species of Trichosporon, 6 of which are pathogenic to humans. T. inkin, T. ovoides, T. cutaneum and T. asteroides cause superficial infections, whereas T. asahii and T. mucoides cause deep-seated infections. Due to the change in nomenclature many isolates reported previously as T. beigelli or T. cutaneum will be classified now as T. asahii (7).

Our patient did not develop neutropenia, but she had other risk factors for the acquisition of fungemia, including extensive abdominal surgery and the presence of an intravascular catheter (both conditions breach the cutaneous barrier, and the first may also alter the normal bowel flora). In addition, our patient received a broad-spectrum antibiotic as well as antifungals, which may have selected a less susceptible yeast. We think that the port of entrance for T. asahii fungemia may develop in clinically deteriorated patients even if they do not have a hematological malignancy.

The treatment of Trichosporon fungemia is difficult, and the mortality rate is high, ranging from 35% to up to 80% (9). In addition, the methods for determining in vitro susceptibilities to various antifungals are not standardized, and MIC breakpoints for Trichosporon have not been determined. Amphotericin B and fluocytosine have poor activity against Trichosporon and are not recommended as treatment (9). Caspofungin also has poor activity in vitro; however, one case of fungemia and one of peritonitis associated with a peritoneal dialysis catheter have been successfully treated with this drug (10,11). Trichosporon spp. tends to be susceptible to azoles in vitro, but cases of resistance, and high “borderline MICs” (as in our case) have been reported (4). Also, clinical cases of breakthrough fungemia despite treatment with azoles have appeared in the literature (9). In these circumstances, voriconazole has been described as still being effective, at least in vitro (12). However, unfortunately, we did not have the chance to test the resistance to voriconazole, which may be considered as an important shortcoming of this report.

As a result, we suggest that clinicians remain aware that T. asahii fungemia may develop in clinically deteriorated patients even if they do not have a hematological malignancy. 

REFERENCES


