Invasive Trichosporon Mucoides Infection in a Uremic Patient with Type 2 Diabetes Mellitus on Maintenance Hemodialysis

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Abstract

Invasive Trichosporon mucoides infections are very rare in uremic patients. They are almost exclusively seen in immunocompromised patients, especially in the setting of neutropenic patients with hematologic malignancies. We report the case of a 62-year-old uremic woman, without neutropenia and on maintenance hemodialysis for four years, who developed nosocomial disseminated Trichosporonosis mucoides during a hospital admission for shortness of breath. The blood culture yielded Trichosporon mucoides, and amphotericin-B (0.5 mg/kg/day) was given with a successfully completed therapy in addition to the immediate removal of the Hickman catheter. However, sepsis recurred and pus culture from the stump of the left knee yielded T. mucoides. In addition to increasing the dosage of amphotericin B to 1 mg/kg/day, oral voriconazole 300 mg every 12 h were added, too. Stump revision was also performed and her condition improved thereafter. Disseminated trichosporonosis should be considered in the differential diagnosis of elderly uremic patients with diabetes, severe peripheral arterial occlusive disease and intravenous catheter, when sepsis does not improve after prolonged treatment with broad-spectrum parenteral antibiotics. Removal of intravenous catheter, management for the infectious wound and aggressive anti-fungal agents are necessary for a successful Trichosporon mucoides treatment.

(KEY WORDS: diabetes mellitus type 2, hemodialysis, Trichosporon mucoides, uremia)

Introduction

Invasive Trichosporon mucoides infections are almost exclusively seen in immunocompromised patients. The majority of trichosporonosis cases are seen in neutropenic individuals, usually in the setting of a hematologic malignancy (1). They are very rare in uremic patients but may be observed in renal transplant patient. Other reported risk factors include AIDS, extensive burns, intravenous catheters (2), corticosteroid treatment, and heart valve surgery. And several cases of fungal peritonitis in patients on continuous ambulatory peritoneal dialysis had been reported. To the best of my knowledge, this is the only reported case, that got an invasive nosocomial Trichosporon mucoides infection with an underlying disease of type 2 diabetes mellitus and uremia on maintenance hemodialysis.

Case Report

A 62-year-old woman with type 2 diabetes...
mellitus and diabetic nephropathy, had been on chronic maintenance hemodialysis since 10 October 2002. The most recent four admissions were for osteomyelitis in the right talus and necrotizing fasciitis of the right leg, and peripheral arterial occlusive disease, resulting in amputation above the knee of the left leg.

Reportedly, she had general weakness and consciousness fluctuated for 2 days prior being brought to the emergency department on 5 April 2006. Physical examination upon arrival revealed a 62-year-old woman with drowsy consciousness. Her blood pressure was 127/53 mmHg with body temperature 36°C, pulse rate 64 beats/min, and respiration rate 25 breaths/min. Chest auscultation revealed crackles over both lung fields. A 5 × 4 × 3-cm deep, dirty, and poorly healing wound in the inner aspect of her right thigh and a 5 × 4 × 0.5-cm ulcerated wound in the posterior aspect of her right lower leg were noted; her left leg had been amputated above the knee. The laboratory data showed white blood cells of 14,000/µL, with 68% neutrophils. The initial chest X-ray showed cardiomegaly, with mild bilateral infiltrations. She was admitted to the intensive care unit under the assumption of sepsis, with the suspected focus at the right Hickman catheter and the wound in the right thigh or pneumonia.

Empirical antibiotics were given with piperacillin 4.0 g, tazobactam 0.5 g every 12 h, and gentamicin 40 mg following hemodialysis three times weekly. The patient’s fever rose to 38°C 2 days after admission; teicoplanin 200 mg every 3 days was added to cover the probability of methicillin-resistant Staphylococcus aureus infection in the wound. The blood and sputum cultures on admission yielded nothing peculiar, but the pus cultures on 25 April 2006 from the exit site of the right Hickman catheter and the wound in the right lower extremity yielded yeast-like organism. So that the Hickman catheter was removed promptly and intravenous fluconazole 100 mg daily was given. However, her fever did not subside, and repeated blood cultures on 28 April 2006 yielded T. mucoides. Amphotericin B (0.5 mg/kg/day) was given instead of fluconazole, according to the sensitivity test of T. mucoides. For T. mucoides, the minimal inhibitory concentration (MIC) obtained by broth microdilution method for Amphotericin B was < 0.5 mg/L; that for 5-Flucytosine was < 0.5 mg/L; that for Fluconazole was > 128 mg/L, and that for Itraconazole was > 4 mg/L. Her conditions improved dramatically following amphotericin B treatment. She was discharged on 10 June 2006, and amphotericin B 50 mg was administered thrice weekly during maintenance hemodialysis.

Unfortunately, she was admitted again on 14 June 2006, with the chief complaint of shortness of breath. In addition to increasing the amphotericin B dosage to 1 mg/kg/day, piperacillin 4.0 g and tazobactam 0.5 g every 12 h were added due to a fetid odor and discharge from the stump of the left knee noted on 16 June 2006 with the stump culture on 16 June 2006 yielded T. mucoides mixed with bacterial floras. In the meanwhile, oral voriconazole 300 mg every 12 h were given. Blood culture and fungus culture on 14 June 2006 showed no findings. Stump revision was performed on 21 June 2006. And her condition improved dramatically thereafter.

Discussion

The genus Trichosporon includes approximately 30 species, at least six of which (T. asahii, T. mucoides, T. inkin, T. ovoides, T. cutaneum, and T. asteroides) are known as Trichosporon beigelii (3) and are associated with human infections (trichosporonosis) (3). These fungi are found in nature, predominately in soil. Mucosal surfaces, skin, throat, stools, the lower urinary tract, sputum, nails and hair are reported as sites of colonization with Trichosporon beigelii. In clinical specimens, a yeast-like organism that is urease positive and forms arthroconidia can be presumptively identified as Trichosporon beigelii. The specimen from our patient was identified as T. mucoides according to the API 20C AUX system (bioMerieux, Basingstoke, UK).

Most invasive T. mucoides infections probably start with colonization of the mucosal surfaces, with a break in the integrity of the surface subsequently seeding the bloodstream. Antibiotics probably increase the incidence and extent of colonization and play a role in increasing the risk of human infections. For our patient without neutropenia, the predisposing risk factors included the indwelling right side intravenous Hickman catheter, prolonged antibiotic treatments during several repeated admissions, and type 2 diabetes. The specific clinical picture of this patient was one of severe peripheral arterial occlusive disease, with multiple gangrenous areas in the lower extremities. Even though the pus cultures from these wounds grew what was identified initially as C. albicans, it was probably T. mucoides. T. mucoides was likely to be confused with C. albicans because of their close resemblance on histological examination (4). However, mixed infection could not be excluded absolutely without doubt. The common presentations described in the literature comprise pneumonia, hypersensitivity pneumonitis, peritonitis, skin lesions, chronic urinary tract infection, brain abscess, endophthalmitis, endocarditis, or septic shock. The patient’s presenting symptoms were sepsis, and disturbed consciousness.

Voriconazole, a new extended-spectrum triazole, posaconazole, and ravuconazole reportedly have good activity against Trichosporon species in vitro (5). Thus, we added oral variconazole species 300 mg every 12 h and increased the amphotericin B dosage to 1 mg/kg/day due to progression of disseminated T. mucoides. The
prognosis is poor and most often fatal in patients in poor physical and immune condition, despite treatment. So, the right Hickman catheter was removed promptly during the first admission because a biofilm in the catheter may be a major factor in determining persistence of the infection in spite of in vitro susceptibility of clinical isolates (6) and a stump revision was also performed during the second admission. As a consequence, her condition dramatically improved thereafter.

Invasive T. mucoides infections should be considered in the differential diagnosis of elderly uremic nonneutropenic patients with diabetes, severe peripheral arterial occlusive disease, and indwelling intravenous catheters when sepsis does not improve after prolonged treatment with broad-spectrum parenteral antibiotics. Removal of the intravenous catheter, and managements for the infectious wound, in addition to aggressive antifungal agents, are necessary for a successful T. mucoides treatment.

References