



Case Report

Nosocomial *Trichosporon asahii* Fungemia in a Patient with Secondary Hemochromatosis: A Rare Case Report

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Trichosporon asahii (formerly known as *T. beigeli*) is an emerging, life-threatening opportunistic pathogen, especially in severely granulocytopenic patients with underlying hematological malignancies. Other reported predisposing factors for infection with this pathogen include organ transplantation, extensive burns, human immunodeficiency virus infection, corticosteroid therapy, prosthetic valve surgery, and peritoneal dialysis. We report a 53-year-old nongranulocytopenic female with secondary hemochromatosis, who developed nosocomial fungemia caused by *T. asahii*. This case suggests that clinicians should be aware that *T. asahii* fungemia can develop in nongranulocytopenic patients with secondary hemochromatosis.

KEYWORDS: fungemia, hemochromatosis, *Trichosporon asahii*, trichosporonosis

Introduction

Over the past decade, *Trichosporon* spp. have been recognized as opportunistic pathogens capable of causing invasive infections, especially in immunosuppressed patients.¹ Infection with *Trichosporon* spp. has been associated with a high mortality rate in a retrospective study.² These pathogens have rarely been reported to cause nosocomial

infections in the literature.³ Here, we report the case of a nongranulocytopenic patient with nosocomial fungemia caused by *Trichosporon asahii* (formerly known as *T. beigeli*).

Case Report

A 53-year-old female was admitted to our hospital with a 2-day history of lower back soreness and shortness of breath. She had also had 17-year history of paroxysmal nocturnal hemoglobinuria and anemia. Frequent blood transfusions resulted in secondary hemochromatosis and chronic renal insufficiency. A prior renal biopsy showed tubular deposition of hemosiderin. On admission, she appeared pale and dyspneic with a blood pressure of 95/41 mmHg, a heart rate of 118 beats/min and a respiratory rate of 28 breaths/min. Physical examination showed ecchymoses and pitting edema in the lower extremities. The white cell count was 7,500/mm³ (96% neutrophils); hemoglobin was 9.7 g/dL; and hematocrit was 27.7%.

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Blood biochemistry revealed ferritin, blood urea nitrogen, and creatinine values of 14,135 ng/mL, 263 mg/dL, and 13.3 mg/dL, respectively. Arterial-blood gas analysis showed severe metabolic acidosis with a pH of 7.05 and a HCO₃ content of 3.1 mmol/L. Because both the blood and urine cultures revealed *Klebsiella pneumoniae* infection, the patient initially received intravenous imipenem/cilastatin therapy. She also received continuous venovenous hemodialysis for severe azotemia and metabolic acidosis. Two sets of blood cultures collected on hospital day 9 showed growth of *T. asabii*, which was identified by use of the Vitek 2 YST yeast identification kit (Vitek 2 YST, Biomèrieux, Durham, NC, USA). Antifungal susceptibility testing, which was performed using the microbroth dilution technique in accordance with the guidelines of the Clinical and Laboratory Standards Institute,⁴ showed the following minimum inhibitory concentrations (susceptibility break-points): amphotericin B, 0.5 mg/L (≤ 1); fluconazole, 4 mg/L (≤ 8); and voriconazole, 0.125 mg/L (≤ 1). The patient then received combination antifungal therapy with amphotericin B deoxycholate (0.4 mg/kg/day, intravenously) and voriconazole (200 mg twice daily, orally) for 14 days. However, the patient eventually died from ventilator-associated pneumonia with tension pneumothorax 30 days after admission (or day 14 after the start of antifungal therapy). Blood cultures showed no fungemia at time of death.

Discussion

In the past 3 decades, the non-*Candida* yeast *Trichosporon* spp. have been increasingly recognized as opportunistic pathogens capable of causing invasive infections, especially in immunosuppressed patients.¹ Guého et al described human colonization with *Trichosporon* spp.⁵ The gastrointestinal tract, skin, and mucosal surfaces have been reported as the sites of colonization, and *Trichosporon* spp. have also been detected in stool, central venous catheter, sputum, and hair.³

Thirty-eight *Trichosporon* spp. have been described in the current literature, and among these, eight are considered as potential human pathogens: *T. asabii*, *T. asteroides*, *T. cutaneum*, *T. inkin*, *T. mucoides*, *T. ovoides*, *T. domesticum*, and *T. montevidense*.⁶ Invasive *Trichosporon* infections are usually preceded by respiratory or gastrointestinal tract colonization, and are commonly associated with the use

of central venous catheters.⁶ More recently, *T. asabii* and *T. mucoides* have emerged as major opportunistic pathogens responsible for invasive infections in immunosuppressed patients, and *T. asabii* has been described as the most frequently isolated species.^{5,6}

Trichosporon spp. are characterized by their ability to form hyphae, pseudohyphae, arthroconidia and blastoconidia.^{6,7} *Trichosporon* spp. grow on ordinary Sabouraud-dextrose agar as yeast with cream-colored cerebriform colonies.⁶ Culture identification can be confused with *Candida* spp. morphologically. Furthermore, invasive trichosporonosis is difficult to differentiate histologically from invasive candidiasis, making definitive diagnosis more problematic.^{7,8} The presence of arthroconidia is the major microscopic feature that differentiates *Trichosporon* from *Candida*.^{2,7} In addition, the *Trichosporon* spp. are morphologically similar to *Cryptococcus*, and the cell wall antigen of *Trichosporon* spp. cross-reacts with the capsular polysaccharide of *Cryptococcus neoformans*; therefore the assay for the cryptococcal polysaccharide antigen may be positive in patients with trichosporonosis.⁹

There has been a considerable increase in the incidence of the invasive *Trichosporon* infection over the past 2 decades. Invasive infections are more common in patients with hematological malignancies.² A shift to a predominance of catheter-related fungemia, without evidence of organ involvement, has been reported.¹⁰ The proposed explanation for this change is the increased use of central venous catheters and the widespread use of fluconazole prophylaxis. Wolf et al reported six nongranulocytopenic patients with invasive *Trichosporon* infection, in whom the isolates of *T. asabii* shared a similar phenotype and genotype, thereby suggesting a common nosocomial origin.³ In a recent review of the literature, *Trichosporon* fungemia was found to occur in 74% of all reported *Trichosporon* spp. infections; 50% of the cases were classified as disseminated, 16% of the cases had disease restricted to the lung, and 3.2% had focal hepatosplenic involvement.² Although *Trichosporon* spp. have most often been implicated in invasive infections in immunosuppressed hosts, trichosporonosis in immunocompetent patients has rarely been reported.¹¹

Profound granulocytopenia in patients with hematological malignancies has been reported as the most common risk factor for *T. asabii* fungemia. Other reported

predisposing factors include organ transplantation, extensive burns, human immunodeficiency virus infection, corticosteroid therapy, prosthetic valve surgery, and peritoneal dialysis.^{3,12} Hemochromatosis is a separate risk factor for trichosporonosis.¹² Two potential mechanisms have been described that increase the risk of fungal infection. First, iron serves as a nutrient for fungal growth, and is an important cofactor for enzymes involved in many basic cellular functions.¹³ *Trichosporon* grows rapidly *in vitro* in iron-supplemented media, and iron overload has been implicated as a factor in invasive *Trichosporon* infections.¹² Second, an environment free of excess iron is required for the effective innate and acquired immune responses.¹⁴ Iron overload decreases T-cell antifungal immunity, natural killer cell activity, and the phagocytic capacity of neutrophils and monocytes, thereby greatly increasing the possibility of invasive fungal infections.^{15,16}

Although there have been many advances in antifungal treatment of invasive fungal infections,¹⁷ the optimal therapy for trichosporonosis has yet to be identified. The new triazole voriconazole, alone or in combination, is probably the drug of choice for this infection, especially in a granulocytopenic patient.^{18,19} In patients who cannot be treated with voriconazole because of its side effects, amphotericin B, flucytosine, fluconazole, and itraconazole might be alternative antifungals,² although multidrug resistance to these agents leading to treatment failure has been reported.³ Other new triazoles, namely, posaconazole and ravuconazole, have also shown potent *in vitro* activity against isolates of *T. asahii* and other *Trichosporon* species.²⁰ Reportedly, echinocandins have low activity against *Trichosporon* spp. and are not recommended for the treatment of trichosporonosis.^{17,21} The prognosis of invasive trichosporonosis has been dismal because the crude mortality rate is as high as 77% in published cases.³ The poor results of treatment are mostly due to the advanced nature of the underlying illness.

In conclusion, *T. asahii* causes life-threatening infections, particularly in granulocytopenic patients. It is important to consider that emerging *Trichosporon* spp. infections are usually difficult to diagnose, are refractory to conventional antifungal agents, and are associated with a high mortality rate.^{2,6} Early diagnosis is crucial for successful therapy. Clinicians should be aware that *Trichosporon* fungemia might develop in patients with

secondary hemochromatosis. Early detection and accurate identification of this unusual pathogen are necessary to provide specific and timely antifungal therapy, and offer the patient a better chance of survival.

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