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Letter to the Editor

# Breakthrough invasive *Trichosporon asahii* infection in an uremic patient with systemic calciphylaxis complicating necrotizing fasciitis during echinocandin therapy for *C. tropicalis*



Dear Editor,

Trichosporonosis, which emerged as an infectious disease in the past two decades, has become increasingly common in immunocompromised patients owing to the increasing number of antifungal agents used. Predisposing factors include malignancy, acquired immunodeficiency syndrome, organ transplantation, corticosteroid therapy, and hemodialysis.<sup>1–3,5</sup> Herein, we present the case of a female patient complicated with end stage renal disease with systemic calciphylaxis complicating necrotizing fasciitis (Fig. 1A and B) who developed a breakthrough *Trichosporon asahii* infection while receiving anidulafungin therapy for invasive candidiasis caused by *C. tropicalis*.

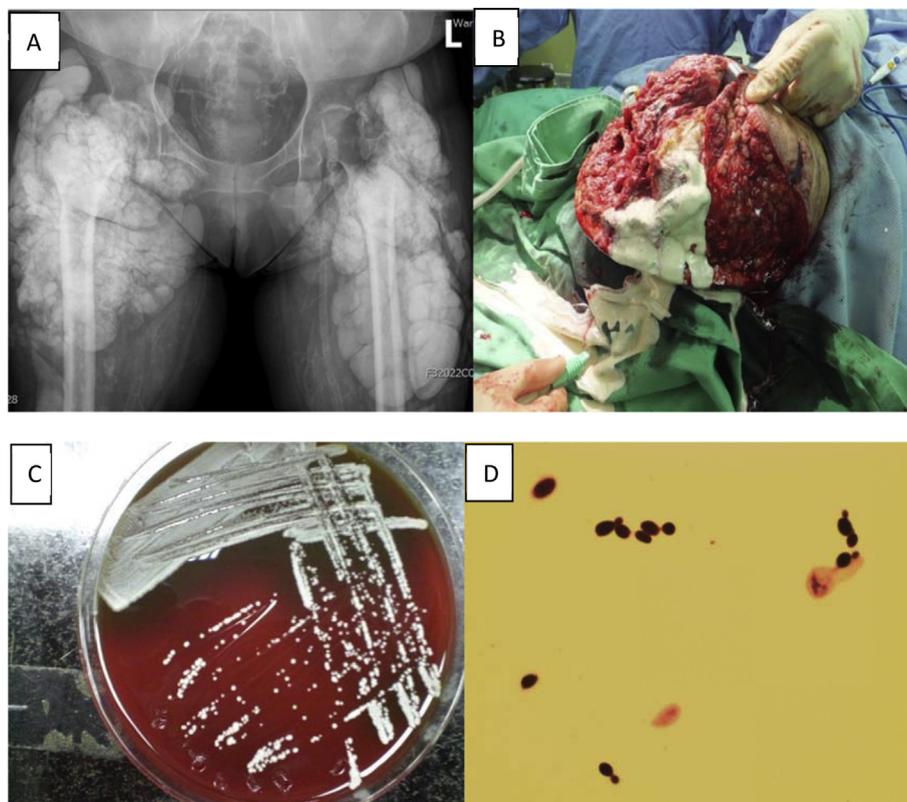
A 48-year-old woman was admitted to our hospital because of left diabetic foot infection with gangrene. She had uremia and underwent hemodialysis regularly for 8 years. She also had calciphylaxis (calcific uremic arteriolopathy) (Fig. 1A) due to tertiary hyperparathyroidism. Growth of vancomycin-resistance *Enterococcus faecium* (VRE), *Aeromonas caviae*, and *Stenotrophomonas maltophilia* was noted in the left foot wound culture sample obtained upon admission. An antibiotic regimen with tige-cycline 200 mg stat and 50 mg intravenously drip (ivd) every 12 h (q12h), plus ceftazidime 2 g ivd q24h, was administered. Computed tomography with angiography revealed diffuse calcification on the below knee arteries and total occlusion in the calcification site at the lateral circumflex femoral artery. After discussing with cardiovascular and orthopedic surgeons, left side above knee amputation for the progressive necrotizing fasciitis was performed on the 10th day of hospitalization. The pathologic report on the amputated part revealed a milky material discharge

(Fig. 1A and B), and fungal yeast in necrotic soft tissue. The wound tissue culture revealed *C. tropicalis* at the 8th admission day. She received the antifungal agent with anidulafungin 200 mg ivd stat and 100 mg ivd q24h for *C. tropicalis* infection. The wound/tissue culture was performed again at the 22th admission day due to the inflammation of the stump area became worsen. Growth of *T. asahii* colonies with a creamy, gray–white color morphology (Fig. 1C) was noted on the blood agar plate culture after 14 days of anidulafungin therapy. The Gram stain of *T. asahii* revealed pigmented yeast-like micro-organisms (Fig. 1D). The organism was identified by matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS Biotyper™, Bruker Daltonik GmbH, Bremen, Germany) with an identification score value of 2.166. Therefore, combination antibiotic therapy with intravenous linezolid, ceftazidime, sulbactam, voriconazole, and colistin were administered. In accordance with the patient's critical condition, she received surgical debridement over the left amputation stump wound 3 times due to poor wound healing. Moreover, the patient developed hypotension after the operation and received inotropes to maintain her blood pressure. A follow-up blood test revealed progressive leukocytosis with neutrophil predominance, and poor surgical wound healing was observed. Growth of carbapenem-resistant *Acinetobacter baumannii* in the surgical wound culture was noted on the 28th day of hospitalization. Unfortunately, the patient had a sudden cardiac arrest and died 24 h after the culture result was released.

Disseminated trichosporonosis has contributed to a high rate of morbidity and mortality, which may reach 100% in patients with persistent neutropenia.<sup>1–4</sup> *Trichosporon*

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**Figure 1.** (A). The plan film radiograph shows diffuse calcific lesions (calciophylaxis) in the bilateral hip and thigh of the patient. (B). The amputation site shows a milk-like material discharge from the infected tissue. (C). The blood agar plate shows *Trichosporon asahii* colonies with creamy, gray–white color. (D) The Gram stain morphology of *Trichosporon asahii* demonstrates pigmented yeast-like micro-organism.

species are resistant to flucytosine, while echinocandins and amphotericin B has been showed to have limited activity in vivo.<sup>5,6</sup> In general, *Trichosporon* species isolates are less susceptible to echinocandin agents (caspofungin, micafungin, and anidulafungin), similar to *Zygomycetes*, *Rhodotorula* species, and *Cryptococcus* species because of the lack of 1,3- $\beta$ -D glucan in the cell wall. As a result, patients with breakthrough fungal infections caused by these organisms during the use of echinocandins have been reported.<sup>2–4</sup> Another study in Japan<sup>6</sup> reported that the mechanisms for drug-resistance of *Trichosporon* species may be the same as the mechanisms found in *Candida* and *Aspergillus* species, namely modification of target molecules or decrease of access to the molecules. However, the optimal treatment for breakthrough trichosporonosis is yet to be established.

In conclusion, more cases have been reported recently on breakthrough *T. asahii* infections in patients receiving echinocandins therapy.<sup>2,4</sup> A large scale surveillance in Asia showed that *Cryptococcus* and *Trichosporon* species were the leading two non-*Candida* yeasts isolated from blood samples.<sup>7</sup> However, studies for identifying the optimal treatment are still lacking.<sup>2,4</sup> However, previous studies revealed that new azole drugs (voriconazole) showed significant activity against *Trichosporon* species.<sup>3</sup> However, prompt administration of antifungal drugs is a major concern in modern therapeutic modalities and invasive procedure for critically ill patients.

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