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. 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-resistant *Enterococcus faecium* (VRE), *Aeromonas caviae*, and *Stenotrophomonas maltophilia* was noted in the left foot wound culture sample obtained upon admission. An antibiotic regimen with tigecycline 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 microorganisms (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. 

*Trichosporon*
species are resistant to flucytosine, while echinocandins and amphotericin B has been showed to have limited activity in vivo.\textsuperscript{5,6} 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-\(b\)-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.\textsuperscript{2-4} Another study in Japan\textsuperscript{6} 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 \textit{T. asahii} infections in patients receiving echinocandins therapy.\textsuperscript{2-4} A large scale surveillance in Asia showed that \textit{Cryptococcus} and \textit{Trichosporon} species were the leading two non-Candida yeasts isolated from blood samples.\textsuperscript{7} However, studies for identifying the optimal treatment are still lacking.\textsuperscript{2-4} However, previous studies revealed that new azole drugs (voriconazole) showed significant activity against \textit{Trichosporon} species.\textsuperscript{3} However, prompt administration of antifungal drugs is a major concern in modern therapeutic modalities and invasive procedure for critically ill patients.

**Figure 1.** (A). The plan film radiograph shows diffuse calcific lesions (calciphylaxis) 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 \textit{Trichosporon asahii} colonies with creamy, gray–white color. (D) The Gram stain morphology of \textit{Trichosporon asahii} demonstrates pigmented yeast-like micro-organism.

**References**


Yi-Hsuan Tsai

\textit{Department of Family Medicine, Wan Fang Medical Center, Taipei Medical University, Taipei, Taiwan}
Cheng-Hui Wang  
Department of Laboratory Medicine, Wan Fang Medical Center, Taipei Medical University, Taipei, Taiwan  
School of Medical Laboratory Science and Biotechnology, College of Medical Science and Technology, Taipei Medical University, Taipei, Taiwan

Po-Ren Hsueh  
Departments of Laboratory Medicine and Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan  
National Taiwan University College of Medicine, Taipei, Taiwan

Shio-Shin Jean  
Departments of Emergency, Wan Fang Medical Center and School of Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan

Fu-Lun Chen  
Division of Infectious Diseases, Departments of Internal Medicine, Wan Fang Medical Center, Taipei Medical University, Taipei, Taiwan

Department of Internal Medicine, School of Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan  
Wen-Sen Lee*  
Division of Infectious Diseases, Departments of Internal Medicine, Wan Fang Medical Center, Taipei Medical University, Taipei, Taiwan  
Department of Internal Medicine, School of Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan

*Corresponding author. Division of Infectious Diseases, Department of Internal Medicine, Wan Fang Medical Center, Taipei Medical University, Taipei  
E-mail address: 89425@wanfang.gov.tw (W.-S. Lee)

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