CASE REPORT

Clinical Significance of *Trichosporon* in Urine of Immunocompromised Host

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Abstract

Yeasts such as *Trichosporon* are being increasingly reported in catheterized urine of hospitalized patients. However, guidelines to interpret their clinical significance are lacking. The following case highlights the need for research and evidence-based recommendations for the management of funguria, especially for *Trichosporon* in urine for critically ill patients with nonresolving sepsis. This is a case of metastatic carcinoma lung on immunotherapy, which developed nonresolving sepsis along with repeated isolation of *Trichosporon* from urine. Patient had shown clinical response only after treatment with voriconazole.

Keywords: Echocardiography, Immunocompromised host, Sepsis.

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Case Description

A 60-year-old lady with diabetes mellitus and hypertension for last 15 years and reasonably controlled on oral medications was diagnosed with carcinoma right lung with brain and bone metastasis following admission to local hospital with new-onset seizure. Her lung biopsy showed epidermal growth factor receptor (EGFR) positivity in tumor cells; so, after receiving radiotherapy for her brain lesion, she was started on osimertinib, an EGFR tyrosine kinase inhibitor. She was transferred to a tertiary care cancer hospital with septic shock, poor sensorium, and hyponatremia. Urine analysis on admission showed 20–25 pus cells/high power field, leucocyte esterase positive, and nitrite positive. Her total leucocyte count was within normal limits. Culture subsequently showed carbapenem-resistant *Klebsiella pneumoniae*. She was treated with meropenem and colistin for 14 days as per hospital protocol. On day 30 of admission, she again became febrile and hypotensive, requiring low-dose of norepinephrine to maintain blood pressure. Appropriate cultures were sent, and central venous lines and urinary catheters were changed. Urine analysis again showed plenty of pus cells along with some yeast, leucocyte esterase positive, and nitrite negative. Considering probable candidemia, caspofungin was started along with broad-spectrum antibiotics as per hospital policy. On follow-up, *Candida* polymerase chain reaction and mannan antigen in blood were negative. Contrast-enhanced computed tomography scan chest and abdomen were normal; ophthalmological examination and transthoracic echocardiography were noncontributory. Subsequently, *Trichosporon asahii* (*T. asahii*) was grown in urine culture and identification was confirmed by deoxyribonucleic acid (DNA) sequencing of internal transcribed spacer locus of fungal DNA on day 37. Procalcitonin values were persistently very low. Her leucocyte count was always within the normal range during this clinical course. In the absence of any major immune-compromised state, *Trichosporon* is usually considered a urinary catheter colonizer, and urinary catheter was changed. Even then, antifungal was modified to liposomal amphotericin B due to poor clinical response. Repeat cultures, sent twice, grew only *T. asahii*. Meanwhile, patient had responded partially with amphotericin B, followed by clinical plateau. Because of its nonimproving clinical status, amphotericin B was replaced with voriconazole to cover *Trichosporon*. Within 48 hours of initiation of voriconazole therapy, patient showed clinical response as she became afebrile, hemodynamically stable, and with improvement of sensorium. Eventually she was weaned off from ventilator. Voriconazole was given for 2 weeks, and subsequent urine analysis and cultures were negative, along with clinical resolution of all symptoms.

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Highlights

Microbiological Perspective

Trichosporon is the most common non-*Candida* yeast found in intensive care units (ICU). Like *Candida*, they are reported to cause fungemia, especially in neutropenic and cancer patients.[1] Candiduria is common in ICU, especially in catheterized patients. Mostly it is colonizer, but it can cause ascending infection to kidney due to vesicoureteral reflux.[2] Caspofungin is the empirical choice of therapy for sick patients with "probable" *Candida* sepsis

and because of that, there has probably been an increasing frequency of trichosporonosis over last 2 decades. *T. asahii* is the most common species causing sepsis.[3] Microbiological findings of *T. asahii* are mentioned in Figure 1 and Table 1.

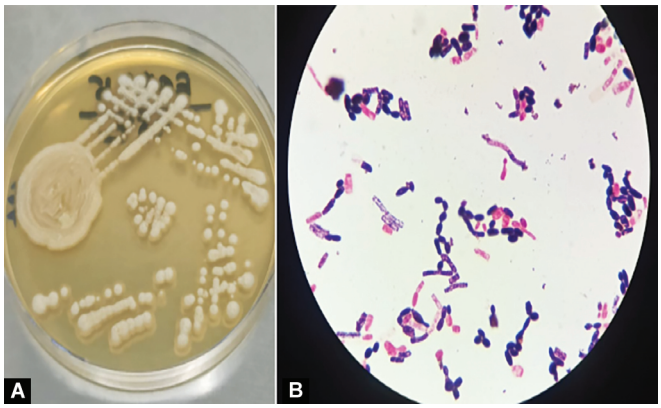
Clinical Perspective

Most common risk factors of trichosporonosis are neutropenia, central venous catheterization, prolonged antimicrobial therapy, and breakthrough over an antifungal, especially echinocandins. Mostly, it presents with disseminated trichosporonosis along with skin lesions, pulmonary lesions, hepatic and splenic lesions, and localized deep-seated infection.[4,5] There is limited literature on *T. asahii* causing urinary tract infection in ICU. Sun et al.,[6] had published a case series of 23 *T. asahii* isolates identified from urinary tract of ICU patients with urosepsis. All these patients were from ICU, elderly (>75 years), had multiple comorbidities (diabetes and hypertension) and had received antibiotic treatment. Notably, 60.8% of them had undergone urinary catheterization. The study found voriconazole to be the most effective antifungal, followed by amphotericin B; all the strains had high minimal inhibitory concentration because of biofilm formation.

In 2002, an International Consensus for defining "Opportunistic Invasive Fungal Infections in Immunocompromised Patients with Cancer and Hematopoietic Stem Cell Transplants" was published[7] and it has been revised in 2020 to define diagnosis of fungal sepsis.[8] However, trichosporonosis was not addressed. If we extrapolate those diagnostic criteria for *Trichosporon*, for example, presence of host criteria (persistent fever, diabetes mellitus, progressive metastatic disease, and steroid) and microbiological criteria (multiple positive culture from urine even after changing existing urinary catheter) and clinical criteria (hypotension); our case fits with the "probable" diagnosis of trichosporonosis.

Role of biomarkers for diagnosis of trichosporonosis needs further evaluation. Mannan antigen will be expected to be negative, as in our case. There are insufficient literature addressing sensitivity and specificity of β-D-glucan for diagnosis of trichosporonosis, and it varies from 50–81%. Glucuronoxylomannan (GXM) is a polysaccharide antigen present in the cell wall of *Trichosporon*. However, it has similarities with *Cryptococcus neoformans* antigen. The sensitivity of GXM serum assay is poor and was reported to be 26% in one study.[4]

Prognosis of disseminated trichosporonosis is poor. Advanced age, ICU admission, high dose of corticosteroid, disseminated infection, high median Acute Physiology and Chronic Health Evaluation II score, neutropenia at the time of diagnosis and breakthrough infection, and use of echinocandin as antifungal agent are poor predictors of outcome and 30-day mortality.[9] On the other hand, use of voriconazole in therapeutic management and recovery of normal neutrophil count have shown to has favorable outcomes. Voriconazole is the preferred therapy, followed by amphotericin B (which shows low success rate). *Trichosporon* is resistant to echinocandins and fluconazole.[10]



Figs 1A and B: (A) Colony morphology of *T. asahii* grown on Sabouraud's dextrose agar after 48 hours of aerobic incubation at 37°C, showing white to cream-colored, powdery colonies with radial furrows and irregular folds; (B) Microscopic morphology under 1000× magnification depicting gram-stained smear from culture isolate (colony) of *T. asahii* showing gram positive barrel shaped yeast cells measuring 2–5 µm × 2.5–9 µm

Table 1: Microbiological findings of *T. asahii*

Routine microscopy	*Appears like yeast (mimicking Candida)*
Sabauraud's dextrose agar	Dry wrinkled colonies
Cystine–lactose–electrolyte-deficient (CLED) agar	Dry creamy yellowish white colony
Lactophenol cotton blue mount	Septate hyaline hyphae, arthroconidia, and blastoconidia
Urease test	Positive
Antifungal susceptibility	VITEK 2 or broth dilution test

Conclusion

Trichosporon is the second most common yeast after *Candida* in clinical practice. Fungemia, disseminated or deep-seated infection, occurs especially in neutropenic hematological malignancies. Increasing trend of laboratory detection and infection with *Trichosporon* has been seen in ICU patients as breakthrough infection while on echinocandin therapy. The clinical significance of *Trichosporon* identified from nonsterile sites is difficult to ascertain diagnosis as biomarkers are also noncontributory. Heightened awareness about this fungus among clinicians and microbiologists will help in further elaboration of its epidemiology and prevent possible adverse clinical outcomes.

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