

CASE REPORT

***Trichosporon asahii* fungaemia in an immunocompetent polytrauma patient who received multiple antibiotics**

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Abstract

Trichosporon asahii is a yeast-like fungus that is emerging as an important cause of invasive infections in tertiary medical centres. A 58-year-old Chinese man with no known medical illnesses presented with liver lacerations and multiple fractures following an alleged 12-foot fall at a construction site. The gravity of his injuries and poor haemodynamic status necessitated an intensive care unit (ICU) admission, during which several febrile episodes were detected and multiple antibiotics were administered. After being in the ICU for at least two weeks, a urease-positive yeast was isolated from the patient's blood. The yeast formed dry, fuzzy and wrinkled white colonies on Sabouraud dextrose agar following prolonged incubation, and produced blastoconidia, true hyphae, pseudohyphae and arthroconidia on slide culture. It was identified biochemically by the ID 32 C kit as *T. asahii*. The yeast had elevated minimal inhibitory concentration (MIC) values to fluconazole, amphotericin B, flucytosine and all echinocandins tested. In view of this, the patient was treated with voriconazole and was successfully transferred to the general medical ward.

Keywords: *Trichosporon asahii*, polytrauma, ID 32 C, voriconazole

INTRODUCTION

Trichosporon spp. are widely distributed in the environment but can also be found regularly on the skin and in the gastrointestinal and upper respiratory tracts of normal humans.¹ *Trichosporon* is a very old genus, with its discovery dating back to 1865 when it was identified as the causative agent of a benign hair infection known as white piedra.² The genus is rather large, containing at least 50 described species, of which 16 are considered to be of clinical relevance.³ Thus, depending on the species, trichosporonosis can either be a superficial or invasive infection, with the former infection category being associated with *T. inkin*, *T. cutaneum* and *T. ovoides*, and the latter with *T. asahii*, *T. mucoides* and *T. asteroides*.² *Trichosporon asahii* (formerly known as *T. beigeli*) has been increasingly implicated as an opportunistic fungal pathogen

in disseminated infections in patients with severe granulocytopenia.⁴ We report a rare case of *T. asahii* fungaemia which developed in a seemingly immunocompetent patient who was admitted to our medical centre for polytrauma management.

CASE REPORT

A 58-year-old Chinese man with no known underlying medical illnesses presented to UKM Medical Centre with polytrauma following an alleged 12-foot fall at a construction site. He sustained a left parietal scalp haematoma measuring 4 cm x 4 cm, a closed right humeral fracture, 6th - 10th rib fractures complicated by a flail chest and right haemothorax, as well as T4 - L5 vertebral spinous process fractures. Following a chest tube insertion for the right haemothorax, he underwent an emergency exploratory laparotomy. Grade 3

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liver lacerations involving segments VII and VIII were detected and packing was performed to arrest the bleeding. Following the abdominal surgery, he was admitted to the ICU because his haemodynamic status deteriorated, necessitating endotracheal intubation, multiple blood product transfusions and inotropic support. Two days post-admission, the patient was febrile and a septic workout was ordered. Despite negative blood, tracheal aspirate and urine cultures, and an only marginally elevated total white blood cell (TWBC) count of $12.6 \times 10^9/L$, the serum procalcitonin level was elevated at $>100 \text{ ng/mL}$. This prompted empirical antibiotic coverage for sepsis to be administered, with ceftriaxone being given initially and later piperacillin-tazobactam.

By day-12, the patient was still febrile despite being on piperacillin-tazobactam. The TWBC was now $25.5 \times 10^9/L$. New specimens (including a blood specimen from a femoral catheter used for hemodialysis) were taken for culture and imipenem-cilastatin was commenced. Both the central and peripheral blood specimens grew cloxacillin-resistant coagulase-negative *Staphylococcus*, although this was not a catheter-related bloodstream infection. With the assumption that the patient had gram-positive bacteraemia, a course of vancomycin was started. Blood cultures were repeated again after five days. The peripheral blood was now positive for a urease-positive yeast which formed dry, fuzzy and wrinkled (or folded) white colonies on

Sabouraud dextrose agar after at least 48 hours of incubation (Fig. 1). When a slide culture on cornmeal agar was performed, the yeast produced blastoconidia, true hyphae, pseudohyphae and barrel-shaped arthroconidia, as depicted in (Fig. 2). The biochemical yeast identification kit ID 32 C (bioMérieux, France) identified the yeast as *Trichosporon asahii* with a %ID of 99.9 (numerical profile: 7756645321). Antifungal susceptibility testing was also performed using the colourimetric broth microdilution kit Sensititre YeastOne YO10 (TREK Diagnostic Systems, USA) and the antifungal minimal inhibitory concentration (MIC) results are as presented in Table 1. Due to the low voriconazole MIC, a course of voriconazole (loading dose: 400 mg bd; maintenance dose: 200 mg bd) was started, which resulted in clinical improvement and a successful transfer out of the ICU to the general medical ward.

DISCUSSION

In general, where fungaemia is concerned, yeast causative agents that do not belong to either the *Candida* or *Cryptococcus* genus are classified as “rare yeasts”.⁵ Despite its relative rarity, the mortality rates of invasive fungal infections caused by rare yeasts can be high and some of these yeasts have intrinsic resistance to key antifungal agents.¹ Fungaemia attributable to rare yeasts are largely opportunistic, and are seen



FIG. 1: Dry, fuzzy and folded/wrinkled *Trichosporon asahii* colonies on Sabouraud dextrose agar after ≥ 48 hours of incubation.

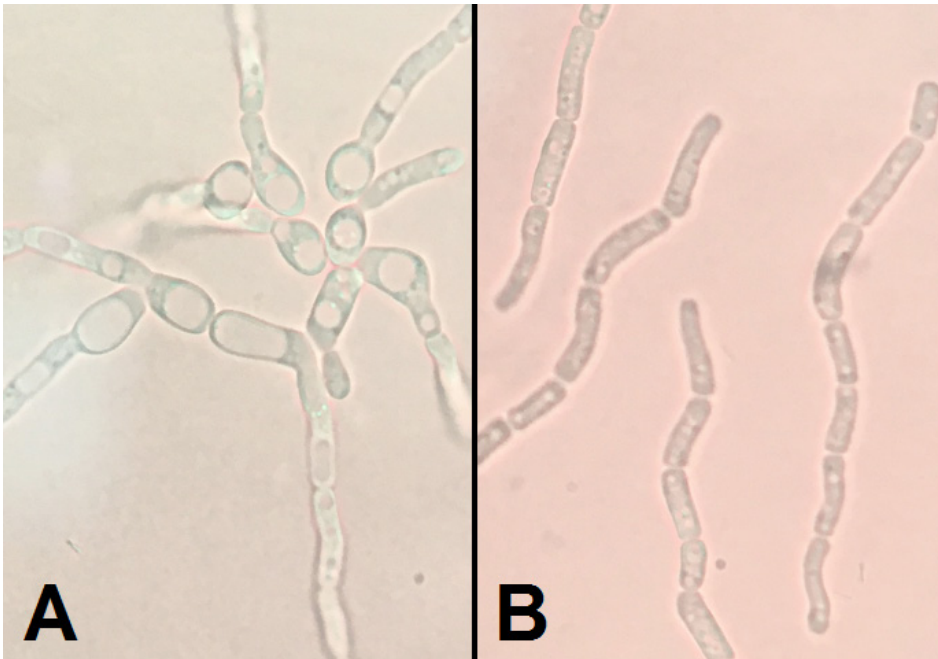


FIG. 2: Microscopic morphology of *Trichosporon asahii* on cornmeal agar (1000x) showing the formation of blastoconidia and pseudohyphae (A), as well as barrel-shaped arthroconidia (B).

mostly in patients with malignancies (especially haematological), chronic airway diseases and/or immunosuppression (e.g. neutropenia).⁵ Amongst the rare yeasts, *Rhodotorula* spp. accounted for slightly more than half of all the rare yeasts isolated in an American study, while *Trichosporon* spp. only contributed 20%.⁶ Thus, the isolation of *Trichosporon asahii* from the blood of our patient who had no previous medical history was a rather surprising finding.

Invasive trichosporonosis has been reported to have a mortality rate of up to 80% among immunocompromised patients.¹ Thus, it is imperative not to overlook this condition in patients who lack the typical risk factors mentioned above. A history of ICU admission,

mechanical ventilation, trauma, the administration of broad-spectrum antibiotics and the use of indwelling catheters have been reported to be risk factors for trichosporonosis in non-granulocytopenic patients.⁴ Our patient had all of these risk factors and was in fact on two truly broad-spectrum antibiotics (i.e. piperacillin-tazobactam and imipenem-cilastatin) prior to the onset of fungaemia. Even his traumatic injuries were multiple, with liver lacerations as well as vertebral, rib and humeral fractures. Rubic *et al.* also reported a case of trichosporonosis in a non-immunodeficient comatose patient with polytrauma who was given broad-spectrum antibiotics for a long duration.⁷

The microscopic visualisation of arthroconidia

TABLE 1: Antifungal minimal inhibitory concentration results for *Trichosporon asahii*

Antifungal agent	Minimal inhibitory concentration (in $\mu\text{g/mL}$)
Fluconazole	4
Itraconazole	0.25
Voriconazole	0.06
Posaconazole	0.12
Amphotericin B	2
Micafungin	≥ 8
Anidulafungin	≥ 8
Caspofungin	≥ 8
5-Flucytosine	≥ 64

in slide cultures is an integral clue to the presence of *Trichosporon* whenever yeasts are isolated from a clinical specimen. Although *Geotrichum* (another example of a rare yeast genus) also produces arthroconidia, differentiating it from *Trichosporon* can be accomplished through a urea hydrolysis test, with only the latter typically testing as urease-positive.² Even the arthroconidia appearance by itself differs between the two genera, with *Trichosporon* producing barrel-shaped arthroconidia with rounded ends, and *Geotrichum* typically forming rectangular arthroconidia with flattened ends.³ The colony morphology of *Trichosporon* is unique – its dry and fuzzy colonies resemble mould rather than yeast colonies. However, both *Trichosporon* from *Geotrichum* produce similar colonies and cannot be reliably differentiated through colony morphology alone.³ Thus, commercial biochemical yeast identification kits based on carbohydrate assimilation (e.g. ID 32 C and API 20 C AUX) are commonly employed by clinical laboratories for formal identification of *Trichosporon* spp.^{2,4}

Breakpoints for antifungal susceptibility testing of *Trichosporon* have not been published by either the Clinical and Laboratory Standards Institute (CLSI) or the European Committee on Antimicrobial Susceptibility Testing (EUCAST). However, consistent with our own finding, it has been reported that the amphotericin B MICs of *T. asahii* are typically $\geq 2 \mu\text{g/mL}$, and as such the yeast should be regarded as polyene-resistant.² This is particularly important to note because amphotericin B is one of the first-line treatments for invasive yeast infections.¹ MICs to flucytosine and echinocandins have also been reported to be elevated, with values exceeding $4 \mu\text{g/mL}$ and $16 \mu\text{g/mL}$, respectively.¹ These MIC values are also consistent with our finding, although we were unable to confirm if the echinocandin MICs have actually reached (or exceeded) $16 \mu\text{g/mL}$, because the echinocandin MIC range of the Sensititre kit is only up to $8 \mu\text{g/mL}$. Fortunately, not all hope is lost because with the exception of fluconazole, *T. asahii* strains are typically triazole-susceptible and its infections respond especially favourably to voriconazole.²⁻³ Looking at our own isolate's antifungal susceptibility results, the lowest recorded MIC was to voriconazole, followed by posaconazole.

In conclusion, a high index of suspicion is the cornerstone to diagnosing invasive trichosporonosis. Polytrauma patients who receive

broad-spectrum antibiotics are predisposed to this infection, particularly if they are also nursed in an ICU. A history of immunosuppression need not be present in these patients, despite the widely held hypothesis that invasive fungal infections are largely opportunistic in nature. *T. asahii* is relatively easy to isolate on standard mycological media and identify through conventional techniques such as slide culture and carbohydrate assimilation. Once invasive trichosporonosis is confirmed, voriconazole is the antifungal agent of choice.

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Conflict of interest: The authors declare they have no conflict of interests.

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