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Case Report Open Access

A *Trichosporon asahii* Bloodstream Infection in a Preterm Newborn with a Successful Outcome: A Case Report

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Abstract

Trichosporon asahii is a rare opportunistic fungal pathogen that causes fatal systemic infections in immunocompromised patients. We have reported a case of *T. asahii* fungemia in a low birth weight preterm newborn baby in the neonatal intensive care unit (NICU). This case of *T. asahii* fungemia was unresponsive to treatment with a combination of Amphotericin B and Fluconazole. However, Treatment with a combination of Voriconazole and Caspofungin was successfully eliminated the fungus from the blood of the infected patient.

Keywords: *Trichosporon asahii*; Bloodstream infection; Preterm newborn

Background

The mortality rate among patients with fungal bloodstream infection is high, ranging from 50% to 80% [1]. Candida species are usually susceptible to standard antifungal agents. Whereas, the treatment of non-candida yeasts is more difficult because they have innate resistance to standard antifungal agents which limits treatment options [2]. *Trichosporon asahii* (previously known as *T. beigelii*) is an emerging, opportunistic non-candida yeast pathogen that causes superficial dermatologic infections (white piedra and onychomycosis) in immunocompetent individuals, however, among immunocompromised patients, it causes severe complications, disseminated disease with poor prognosis and fatal infections for neonatal [3]. Prematurity is an important predisposing factors for invasive *Trichosporon* infections [4].

Case presentation

A 30 weeks, low birth weight (about 1500 g), preterm girl baby was delivered by Cesarean Section (due to maternal antepartum hemorrhage) in the Maternity and Children Hospital, Makkah, Saudi Arabia. Immediately after delivery, the baby suffered from respiratory distress and cardiac arrest and lifesaving resuscitation was done successfully and the baby was admitted to the Nursery Intensive Care Unit (NICU) where the baby developed manifestations of pneumothorax, for which, emergency intercostal drainage tube, high frequency ventilation, central venous catheter, as well as a prophylactic course of broad-spectrum antibiotics were necessary with subsequent recovery. In the NICU, *T. asahii* was isolated from the baby nasal swab culture on the 19th day of life. On 21st day it was isolated from both nasal and groin swabs. On 27th day, *T. asahii* was isolated from blood culture for the first time and treatment started using Amphotericin B and Fluconazole. No specific clinical manifestations were recognized on the preterm baby.

Despite of the treatment, The fungus continued to be isolated again from blood cultures on 29th, 34th, 37th, 43rd, 50th, 54th, 59th days. On the 60th day, Amphotericin B and Fluconazole were replaced by a combination of Voriconazole and Caspofungin. From the 74th day of life and onward, *T. asahii* could not be isolated from blood cultures. Routine laboratory investigations were within normal values for anemia (Hemoglobin: 8.7 g/dL), thrombocytopenia (Platelets: 70,000/µL), prolonged prothrombin time (PT: 17 seconds), metabolic and respiratory acidosis. For the isolation of *T. asahii*, blood culture bottles were incubated inside the automated Bact/Alert blood culture System (BacT/ALERT® 3D; BioMérieux, Marcy-l'Etoile, France). On positive signal, blood samples from positive bottles were examined directly under light microscope (oil lens X 1000) and showed yeast like fungi and elongated blastoconidia. In the same time, blood samples from positive bottles were cultured on Sabouraud's dextrose agar (SDA), blood agar and chocolate agar (nasal and groin swabs were cultured on the same media). After 48 h of incubation at 37°C, colonies of yeast-like fungi were isolated. Even though, colonies needed 7 days at 37°C to reach the characteristic white, rosette- shaped, wrinkled colonies with radiating furrows and umbonate centers.

Microscopic examination of gram-stained smears of these colonies, demonstrated round to oval, budding yeast-like cells, elongated blastoconidia, septate pseudohyphae and cylindrical arthroconidia. Identification of the isolate as *T. asahii* as well as antifungal susceptibility testing were done by the Vitek 2 automated system (BioMerieux, Marcy l'Etoile, France) using the card kits for yeast identification (YST) and sensitivity (AST-YS07). Minimum Inhibitory Concentrations (MICs) were as follows: Amphotericin B 2 µg/mL; Fluconazole 1 µg/mL; Voriconazole ≤ 0.12 µg/mL; Micafungin ≤ 0.06 µg/mL ; Caspofungin ≤ 0.25 µg/mL and Flucytosine ≤ 1 µg/mL (Figures 1 and 2).

Discussion

Over the last two decades, Trichosporon species have been increasingly reported as opportunistic pathogens that can cause invasive infections. Trichosporon species were isolated from different types of clinical specimens, including blood, urine and skin specimens. Moreover, they were recognized in colonization of the gastrointestinal

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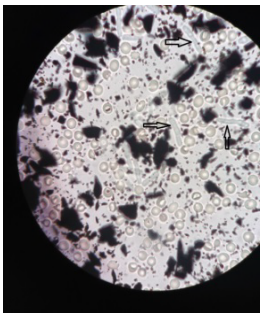

Figure 1: Direct microscopic examination of blood sample from positive blood culture bottles show oval elongated yeast-like cells, elongated blastoconidia of *T. asahii* (light microscope oil lens X 1000).

Figure 2: *T. asahii* colonies on SDA after incubation at 37°C for 7 days.

tract, skin, mucosal surfaces, sputum, central venous catheter, stool, and hair. Six Trichosporon species (*T. asahii*, *T. asteroides*, T. *cutaneum, T. inkin, T. mucoides,* and *T. ovoides*) cause superficial and/or invasive infections. *T. asahii* is the most frequent Trichosporon species involved in disseminated human infections [5-10]. To date, only few cases of *Trichosporon asahii* fungemia were reported in Saudi Arabia [11]. In the present case, *T. asahii* was isolated from nasal and groin swabs before the isolation from blood cultures. This is consistent with a study by Yamamoto et al. [12] who found that colonization by the causative organisms prior to fungemia onset was noted in 72.7% of non-Candida fungemia patients. These findings could be important for predicting the occurrence of non-candida fungemia. In addition, it might be important for prescribing prophylactic treatment with systemic suitable antifungal agents once the fungus is isolated from peripheral swabs.

The most common reported predisposing risk factors of invasive *T. asahii* infection included malignancies (mainly hematological malignancies with marked neutropenia), central venous catheters, prematurity with low birth weight, admission to intensive care units, administration of immunosuppressive agents, prior use of broad-spectrum antibiotics, Corticosteroid therapy, organ failure, organ transplantation, prosthetic valve surgery, HIV infection, extensive burns and peritoneal dialysis [13]. In the current case, several predisposing factors (in addition to prior colonization by the causative organism) may have acted singly or collectively for predisposition to bloodstream infection with *T. asahii*, namely, prematurity and low birth weight, central venous catheter, parenteral nutrition, insertion of intercostal drainage tube and the prior prophylactic course of broad spectrum antibiotics. However, in our case, Prematurity and low birth weight are thought to be the main factors that facilitated colonization and subsequent sepsis of the preterm baby because of the deficiency of normal flora that competes with the opportunistic pathogens and by the fact that components of body defense systems are still immature enough in the preterm babies especially those with low birth weight.

In the present case of *T. asahii* fungemia, no specific clinical manifestations were registered on the preterm baby, however, regarding the laboratory investigations, there were anemia, thrombocytopenia, prolonged prothrombin time, metabolic and respiratory acidosis. Our results are nearly consistent with a previous case study by Pereira et al., [14,15] who reported anemia, thrombocytopenia and metabolic acidosis in a low birth weight preterm baby with *T. asahii* fungemia [16] recently reported severe throbmocytopenia, lethargy, feeding intolerance, bleeding manifestations in cases of *T. asahii* fungemia in preterm babies with low birth weight. Unexplained thrombocytopenia was again reported by John et al., [17] in an immunocompetent adult patient with *T. asahii* fungemia.

Treatment for invasive Trichosporon infections is still difficult and controversial. Few and variable data are available on the *in vitro* and *in vivo* activities of antifungal drugs against clinically relevant species of Trichosporon. In addition, the *in vitro* activity of antifungal drugs does not always correlate with good clinical response. Accordingly, No optimal therapy regimen for trichosporonosis has been identified. Amphotericin B has limited activity against Trichosporon species *in vitro* and *in vivo* while echinocandins are nearly not effective as a mono-therapy for invasive Trichosporon infections [18]

Triazoles are the drug of choice for antifungal treatment and Trichosporon infections in particular. Studies have shown that Voriconazole is highly active against *T. asahii* isolates *in vitro* and *in vivo*; including isolates with reduced susceptibility to Amphotericin B, Itraconazole, and Fluconazole. However, a case of breakthrough of *T. asahii* infection has been reported recently against Voriconazole [19].

Several studies and clinical trials have strongly recommended the use of combined antifungal synergistic therapy for Trichosporon infections as these combinations increase clinical efficacy e.g. the combination of Amphotericin B with Azoles and the combination of Echinocandins with Azoles or Amphotericin B [20]. In the present case, the treatment was initiated with failure by using a combination of Amphotericin B and Ketoconazole for 4 weeks. After that the treatment was replaced by a combination of Voriconazole and Caspofungin which eradicated *T. asahii* from the blood of the patient by the end of 2nd week of treatment.

Conclusion

We have described a rare case of *T. asahii* invasive infection in a low birth weight preterm newborn baby in the neonatal intensive care unit (NICU), Maternity and Children Hospital, Makkah, Saudi Arabia. *T. asahii* was isolated from the patient nasal swabs, groin swabs and then from blood cultures. No specific clinical manifestations could be detected on the preterm baby. Thrombocytopenia was the most prominent laboratory finding. This case of *T. asahii* fungemia was resistant to treatment with a combination of Amphotericin B and Fluconazole, However, the case was successfully treated using a combination of Voriconazole and Caspofungin.

Conflicts of Interest

All authors declare no conflict of interests in this work.

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