Disseminated Trichosporonosis in a Burn Patient: Meningitis and Cerebral Abscess Due to *Trichosporon asahii*\(^\dagger\)

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A 44-year-old diabetic female presented to a hospital in Jamaica with thermal burns. *Trichosporon asahii* was isolated from facial wounds, sputum, and a meningeal swab. Dissemination of the fungus was demonstrated in stained histological sections of the meninges and a brain abscess at autopsy. Pure growth of the fungus from patient samples submitted and an environmental isolate obtained from a wash basin in the hospital supported the diagnosis.

**CASE REPORT**

A 44-year-old hypertensive, diabetic woman presented with partial and full-thickness thermal burns involving 50% of her total body surface area, including the face and neck, torso, upper limbs, and proximal portion of the lower limbs. She was admitted to the intensive care unit (ICU) for ventilatory support for suspected inhalational injury. Her initial hemoglobin level was 5.2 g/dl, her white blood cell count was 6.4 \( \times \) 10\(^9\)/liter, her platelet count was 239 \( \times \) 10\(^9\)/liter, and her blood urea nitrogen (BUN) and creatinine levels were 2 mmol/liter and 54 \( \mu \)mol/liter, respectively. Management included fluid resuscitation, topical and systemic antibiotic therapy, surgical intervention for control of wound sepsis, and limb perfusion. She also received ceftriaxone for empirical antibiotic coverage, tetracycline ointment for facial burn wounds, and twice daily application of dressings using flumazine to the wounds on the body. Nursing and dietary supportive measures were also instituted.

The patient was clinically stable on admission when a primary culture of sputum yielded a light growth of a fungus reported as “yeast not *Candida albicans*.” However, despite broad-spectrum antibiotic coverage, signs of sepsis appeared within 5 days of admission. She developed multiorgan infection of the burn wounds, which were culture positive for *Pseudomonas aeruginosa*, *Streptococcus* group D, *Bacteroides*, *Alcaligenes* sp., and *Stenotrophomonas maltophilia*. Blood culture and culture of a femoral central venous catheter tip were also positive for *Streptococcus* group D and *Acinetobacter* sp. Sputum and urine cultures were negative at that time. Appropriate antibiotic intervention following antibiotic susceptibility testing of isolates was commenced, and 0.25% acetic acid was included in the dressings applied to wounds that were positive for *Pseudomonas*. Despite the continued use of antibiotics, she persistently showed clinical, biochemical, and hematological signs of sepsis. The patient’s clinical status continued to deteriorate, and she developed multiorgan dysfunction.

Over the period of hospitalization, gradually increasing BUN levels (mean, 20.9 mmol/liter; range, 9.1 to 32.1 mmol/liter) and creatinine levels (mean, 287.2 \( \mu \)mol/liter; range, 54 to 353 \( \mu \)mol/liter) were recorded. Levels remained relatively high throughout the remainder of the patient’s hospital stay and were consistent with renal failure.

Subsequent sputum culture (23 days after admission) again demonstrated moderate growth of a fungus reported as “yeast not *Candida albicans*.” Repeat blood cultures were negative following specific antibiotic therapy after antibiotic susceptibility testing on the cultured isolates. However, a facial wound culture repeated 1 day before death was positive for multidrug-resistant *Acinetobacter* sp., *Streptococcus* group D, and coagulase-negative staphylococcus and *Acinetobacter* sp. It grew multidrug-resistant, coagulase-negative staphylococcus and *Acinetobacter* sp. In addition, a rapidly growing fungus was isolated from facial wounds and sputum. Characteristic microscopic features, growth at various temperatures, and assimilation of specific carbohydrates identified the fungus as *Trichosporon asahii*. The patient’s clinical status continued to deteriorate, and she died on day 32 after hospital admission.

An autopsy revealed infected thermal burns involving all of the anatomical locations noted clinically. On dissection, significant findings included hyperemia of the tracheobronchial tree and markedly overweight lungs with marked pulmonary congestion and consolidation consistent with adult respiratory distress syndrome. Other significant autopsy findings included perivascular opacity in the parasagittal region of the meninges suggestive of inflammation. Subsequent microbiological examination identified *T. asahii*. Dissection of the brain revealed an abscess in the right temporoparietal region. Histological examination of sections obtained from the meninges and brain abscess after hematoxylin-and-eosin and periodic acid-Schiff (PAS) staining showed numerous yeast cells and arthroconidia scattered within the acutely inflamed tissue (Fig. 1). No fungal elements were seen in stained histological sections of any other postmortem tissues.

Standard microbiological procedures, including Gram stain microscopy of sputum, a facial wound swab, and a meningeal

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swab, revealed Gram-positive budding yeast cells, pseudohyphae, and arthroconidia, while overnight cultures at 37°C on blood agar and MacConkey agar produced a rapidly growing fungus with chalky, white, pinpoint colonies. Colonies on both agar media became wrinkled and heaped up at the centers with characteristic radiating furrows following 7 days of incubation at 37°C (Fig. 2). All specimens except blood cultures and urine grew the fungus with detectable pure growth of the organism.

Mycological investigation, including culturing on Sabouraud dextrose agar, cornmeal agar (CMA), and mycobiotic agar incubated at 25°C, 28°C, and 37°C produced colonies morphologically similar to those seen on blood agar and MacConkey agar. Pellicles formed in broth cultures and growth after 48 h of incubation at 42°C were demonstrated by the fungus.

Lactophenol cotton blue staining of pure cultures demonstrated a microscopic morphology characteristic of Trichosporon species. Arthroconidia, hyphae, and pseudohyphae were more pronounced in older (7-day) cultures on CMA (Fig. 3 and 4). The barrel-shaped arthroconidia of T. asahii are diagnostic for this species (Fig. 4).

The API 20C system (bioMérieux) was employed for yeast identification, and the assimilation profiles readily identified all three isolates as T. asahii (API 20C, code 2744734). Positive assimilation was demonstrated for arabinose, cellobiose, galactose, lactose, maltose, and xylose, while negative reactions were documented for adonitol, inositol, and sorbitol. All isolates were urease positive, a diagnostic feature of Trichosporon
species aiding differentiation from urease-negative species of *Geotrichum*. Differential species characteristic of *T. asahii* include assimilation of arabinose, inability to assimilate melibiose, and growth at 37°C (5, 8).

Several attempts to identify the source of infection, including sampling of health care workers and the immediate environment, were mostly unsuccessful, but the fungus was later recovered from 1 of 13 wash basins designated for patient use. This isolate also produced carbohydrate assimilation reactions identical to those of the clinical isolates (API 20C, code 2744734). One representative isolate of *T. asahii* from the patient and one from the environmental source (basin) were deposited in the University of Alberta Microfungus Collection (Edmonton, Alberta, Canada).

*T. asahii* and other members of the genus *Trichosporon* are basidiomycetous yeasts characterized by the production of true hyphae and pseudohyphae, arthroconidia, and blastoconidia (5, 9). These fungi are rarely seen in human infections, and to date, just over 100 disseminated cases caused by *T. asahii* have been reported in the literature worldwide (21). The vast majority of these cases have been reported in leukemia or lymphoma patients who developed severe depletion of neutrophils (11, 21). Our report describes the first case fatality due to disseminated *T. asahii* infection seen at the University Hospital of the West Indies in Jamaica. The disseminated-infection case presented was not typical of those usually reported in the literature, where neutropenia is the major risk factor in invasive diseases (17).

For many years, invasive trichosporonosis not due to *T. cutaneum* was reported as *T. beigeli* infection. However, significant taxonomic revision in the early 1990s divided *T. beigeli* into several species, including *T. asahii*, and presumably, a significant number of the cases reported prior to the revision may have been due to *T. asahii* infection (8, 9, 13). Since the first case report of invasive disease in 1970, disseminated infections have been increasingly recognized in systemic illnesses of immunocompromised patients (4, 21, 23).

*Trichosporon* species have been isolated from the soil and other environmental sources and from surfaces in indoor environments (8, 19). They can also be a part of the normal flora of the human gastrointestinal tract, skin, and respiratory tract (22). Our isolation of *T. asahii* from a hospital wash basin in this study demonstrates the potential for environmentally acquired and nosocomial infections.

Dissemination of the fungus is rarely encountered, and only a few case reports of associated invasive trichosporonosis in patients with extensive burns have been documented (2). It is noteworthy that neutropenia is the primary predisposing risk factor in disseminated cases of trichosporonosis but notably absent in the present case. Despite the infrequency of invasive trichosporonosis, *T. asahii* is increasingly recognized as an important emerging opportunistic pathogen in the immunocompromised host and generally in patients with critical underlying conditions, including diabetes (3, 7). Several documented cases of trichosporonosis in aged and critically ill patients have been linked with ICU patients in different hospitals (6, 24). Invasive disease is not limited to elderly patients, affecting a wide age range, including neonates (1). Several prior reports of *Tricho-
T. asahii in invasive disease closely resembles systemic candidiasis in its clinical presentation and is difficult to differentiate histologically (14). Fungal infections of this nature are likely to be missed by clinicians who are encountering such cases for the first time. This may result in delays in diagnosis, antifungal intervention, and subsequently the choice of the appropriate antifungal drugs, where resistance is a major concern. In vitro resistance to amphotericin B and, to a lesser extent, the azoles has been demonstrated (24). However, the newer triazoles (e.g., voriconazole, posaconazole, ravuconazole) have shown excellent in vitro activity against Trichosporon species and are recommended for treatment (1, 6, 21). A review of the patient’s record revealed that no antifungal drugs were used in her management, a decision apparently made in the face of negative blood cultures and because dissemination of the fungus at the time was not indicated by early investigations. Importantly, when there is clear evidence of fungal dissemination, a considered approach to antifungal intervention is paramount. Early treatment has effectively reduced dissemination of the fungus, but resistance of Trichosporon species to many antifungals has been encountered and remains a major challenge to patient management (6, 18).

The challenge of determining the source of infection, together with several predisposing factors, may further compound the problem of eradication of Trichosporon species and the management of affected patients. Identifying these unusual fungal infections is even more difficult when signs and symptoms mimic those of other diseases with similar clinical manifestations. It is therefore incumbent on health care professionals, especially those involved in direct patient care, to be aware of (i) the risk factors that facilitate the spread of infection and the necessary steps toward prevention (this requires the ability to differentiate natural colonization of skin and mucosal surfaces by the fungus, as opposed to symptomatic and invasive cases of trichosporonosis; correspondingly, the progress of affected patients should be carefully monitored with regular laboratory investigations); (ii) the importance of sampling of health care workers, hospital commodes, and other potential environmental sources to stem the chain of transmission; and (iii) the real challenges of antifungal drug resistance and the appropriate choices to guide treatment policy. Nevertheless, early antifungal intervention in patient management is paramount to reducing dissemination of the fungus. New approaches to treatment may translate into improved prognoses and subsequently reduced hospital stay. The application of 1 to 5% sodium hypochlorite (bleach) in disinfecting the immediate environs, and in particular cubicles where affected patients are housed, is essential to infection control measures.

The recent fatal case of invasive trichosporonosis will undoubtedly serve to alert the medical fraternity that this and other rare and emerging infections are on the increase and are likely to pose similar problems.

REFERENCES