A Trich-y Fungus: A Unique Presentation of Disseminated *Trichosporon mycotoxinivorans* Infection

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ABSTRACT

*Trichosporon mycotoxinivorans* is an emerging fungus which causes pulmonary infections in humans, with a predilection for patients with cystic fibrosis. In recent years, several case reports have described the role of *Trichosporon mycotoxinivorans* in disseminated infections, particularly in patients undergoing dialysis and those with various malignancies. However, this is the first case presentation of *Trichosporon mycotoxinivorans* dissemination to brain. We present our findings in a 42-year-old female undergoing treatment for acute liver failure and acute tubular necrosis, who had positive blood and stool cultures for *Trichosporon mycotoxinivorans* and a rapidly developing hypodense lesion in right basal ganglia during hospitalization.

Keywords: *Trichosporon mycotoxinivorans*; Fungus; Infection; Dissemination; Brain Lesion

CASE REPORT

A 42-year old female with history of autoimmune hepatitis and discoid lupus was hospitalized for acute liver failure secondary to alcoholic hepatitis. She was hypotensive at presentation and developed acute tubular necrosis resulting in acute kidney injury. The patient was started on hemodialysis via a tunneled dialysis central venous catheter. During her hospitalization, the patient reported dysphagia and underwent upper GI endoscopy with biopsy. Esophageal biopsies returned as squamous cell carcinoma of the esophagus. She also had persistent diarrhea during hospitalization for which extensive workup was negative, except for a stool culture that grew *T. mycotoxinivorans*. Flexible sigmoidoscopy was normal, and *T. mycotoxinivorans* infection was not treated at this point. Three weeks into her hospitalization, the patient began to experience periodic, diffuse, bilateral headaches that responded to acetaminophen. On day 32 of hospitalization, the patient suddenly became unresponsive. According to the nurse, two minutes prior to becoming unresponsive, the patient was speaking appropriately and took her medications by mouth without any difficulty. She was immediately intubated for respiratory failure. Given her sudden decline in mental status, she underwent an emergent CT of the head, which showed a new hypodense lesion in the right basal ganglia which was not present on a previous CT scan of the head done about a month earlier. Given the relatively rapid development of the lesion, an abscess or infarction was suspected. Of note, her blood cultures remained persistently positive for *T. mycotoxinivorans*. The patient was transferred to Intensive Care Unit (ICU), where she subsequently developed septic shock, requiring vasopressors at maximum dose. Despite efforts, her mental status did not improve, and three days after transfer to ICU, the patient died.

DISCUSSION

Although in 1970, Watson, et al. [1] described the first case report of invasive trichosporonosis due to *T. cutaneum* with development of a cerebral abscess, no similar cases involving *T. mycotoxinivorans* have been reported in the literature. Thus, this is the first case report of a
patient with possible brain abscess secondary to *T. mycotoxinivorans*. Fungi of genus *Trichosporon*, belonging to phylum *Basidiomycota*, are ubiquitously found in the environment [2,3]. In humans, *Trichosporon* species occasionally colonize skin and mucosa [2,4]. Rates of colonization vary from 1 to 3 percent in patients admitted to general hospital wards [5,6]. In patients with malignant hematological diseases, *Trichosporon* species have been reported as the second most common agent of systemic mycosis [7]. The main disease-causing species of genus *Trichosporon* in humans include *T. asahii*, *T. asteroides*, *T. cutaneum*, *T. inkin*, *T. mucoides*, *T. ovoides* and *T. mycotoxinivorans* [8,9]. Some of these species are responsible for causing superficial infections affecting skin and hair, whereas others are known to cause disseminated infections particularly in immunocompromised hosts [2-4,10].

*T. mycotoxinivorans* was first isolated from the hind gut of a termite in 2004 and was named for its ability to degrade mycotoxins [11]. In 2009, it was first described as a respiratory pathogen in a cystic fibrosis patient [9], and multiple similar cases have been reported since then [9,12]. In addition to its pulmonary manifestations, there is increasing data on the role of *T. mycotoxinivorans* in disseminated infections in transplant patients, in patients with indwelling dialysis catheters, and patients with various malignancies.

**Risk Factors for Trichosporonosis:** Invasive trichosporonosis occurs most commonly in immunocompromised patients. Reported risk factors include neutropenia [12-15], intravenous catheters [12,16-19], improperly sterilized endoscopes [20,21], cardiac valve surgery [22,23], mechanical ventilation, tracheostomy [24], extensive burns [25], immunocompromised status such as HIV infection [26], and immunosuppressive therapy such as glucocorticoids [27]. It has been suggested that chronic antibiotic therapy in diseases like cystic fibrosis could potentially be associated with emergence of *T. mycotoxinivorans* [28,29].

**Clinical Features of Trichosporonosis:** Trichosporonosis can present either as primary cutaneous [24] or as an invasive infection. Skin lesions in trichosporonosis are mostly localized on face, trunk, or limbs in the form of erythematous papules and nodules with an area of central necrosis or less commonly as multiple subcutaneous abscesses or hemorrhagic nodules [30]. Manifestations of disseminated disease include fever, positive blood cultures, pulmonary infiltrates, cutaneous lesions, renal failure, hepatic disease [3,25,31], summer-type hypersensitivity pneumonitis [32], neurological damage, chorioretinitis, and septic shock [14].

**Diagnostic Methods:** In addition to clinical symptoms associated with systemic trichosporonosis, diagnosis depends on identification of the organism in cultures from blood, urine, bronchial secretions, mucosal secretions, pericardial fluid, and stool [33,34]. In addition, (1,3)-β-D-glucan (BG), which is a unique cell-wall component of fungi [25] and galactomannan are non-culture-based biomarkers that can aid in diagnosis of trichosporonosis [34]. However, DNA analysis may be required to identify the species of *Trichosporon* [9,35] through extraction, amplification and sequencing of conserved genes such as D1/D2 domain of the large subunit (LSU) of ribosomal DNA (rDNA) or variable non-coding regions such as internal transcribed spacers 1 and 2 (ITS) or intergenic spacer 1 (IGS1) [2,24,33,36]. IGS1 is perhaps best able to delineate all presently known *Trichosporon* species [36]. Of note, diagnosis of invasive fungal infections is challenging due to atypical presentation, cost, time consumption, limited and difficult methods, difficulty in species identification and limited availability of DNA testing [28,37].

**Treatment and Prognosis of Trichosporonosis:** The goal of the treatment should be to reduce the high mortality rate associated with trichosporonosis and this can be achieved by early administration of antifungal agents [34,38,39]. The timing of administration of treatment following a positive blood sample may be a determinant of hospital mortality in infected patients [39]. Several studies have reported efficacies of different classes of antifungal drugs for trichosporonosis treatment [40]. Amphotericin, fluconazole, flucytosine and echinocandins lack fungicidal activity against *Trichosporon* [41,42]. On the other hand, azaoles such as voriconazole and posaconazole have higher bioavailability and greater effectiveness against *Trichosporon* [9,41,43,44]. Empiric therapy with voriconazole should be started for patients suspected of deep infection with *T. mycotoxinivorans* while waiting for antifungal susceptibility testing [9]. Although *Trichosporon* mucormycosis may be a possibility and should be considered when administering voriconazole to
patients [25]. With the increasing number of reported cases of infections due to emergent fungal species in immunocompromised patients, combined fungal therapy may be considered. However, combined fungal therapy is fraught with the risk of various drug-drug interaction and should be only used as the last resort [3]. Disseminated infection with emerging species such as T. mycotoxinivorans is usually associated with a poor outcome in patients with a reported mortality rate of up to 80% [3,12,44].

CONCLUSION

T. mycotoxinivorans is a relatively newly-identified fungus that can cause invasive infections in at-risk population. Invasive trichosporonosis has been shown to present with CNS infections and this may be the first reported case of a brain abscess caused by T. mycotoxinivorans. Further research is needed not only to identify the patient population at risk of developing invasive trichosporonosis, but also on the role of new diagnostic modalities, effective therapeutic options and prophylaxis for trichosporonosis. Additionally, more research is needed on species level identification methods that are cheaper and less time consuming.

REFERENCES
