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 developed fever with an episode of hypotension. Blood cultures were obtained, and patient was empirically started on antibiotics and micafungin. Blood cultures subsequently grew *T. mycotoxinivorans*, antibiotics were discontinued, micafungin was switched to voriconazole, and the tunneled dialysis catheter was removed. On day 36 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

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patient with possible brain abscess secondary to *T. mycotoxinivorans*.

Fungi of genus *Trichosporon*, belonging to phylum *Basidomycota*, 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, azoles 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

1. Basiri K, Meidani M, Rezaie F, Soheilnader S, Fatehi F. A rare case of trichosporon brain abscess, successfully treated with surgical excision and antifungal agents. *Neurol Neurochir Pol*. 2012;46(1):92-95.
2. Colombo AL, Padovan AC, Chaves GM. Current knowledge of trichosporon spp. and trichosporonosis. *Clin Microbiol Rev*. 2011;24(4):682-700.
3. Marine M, Brown NA, Riano-Pachon DM, Goldman GH. 2015. On and under the skin: Emerging basidiomycetous yeast infections caused by trichosporon species. *PLoS Pathog*. 2015;11(7):e1004982.
4. Arendrup MC, Boekhout T, Akova M, Meis JF, Cornely OA, Lortholary O, European Society of Clinical M, Infectious Diseases Fungal Infection Study G, European Confederation of Medical M. Escmid and ecmm joint clinical guidelines for the diagnosis and management of rare invasive yeast infections. *Clin Microbiol Infect.* 2014;20 Suppl 3:76-98.
5. Haupt HM, Merz WG, Beschorner WE, Vaughan WP, Saral R. Colonization and infection with trichosporon species in the immunosuppressed host. *J Infect Dis.* 1983;147(2):199-203.
6. Rose HD, Kurup VP. Colonization of hospitalized patients with yeast-like organisms. *Sabouraudia.* 1977;15(3):251-256.
7. Chagas-Neto TC, Chaves GM, Colombo AL. Update on the genus trichosporon. *Mycopathologia.* 2008;166(3):121-132.
8. Gueho E, Improvisi L, de Hoog GS, Dupont B. Trichosporon on humans: A practical account. *Mycoses.* 1994;37(1-2):3-10.
9. Hickey PW, Sutton DA, Fothergill AW, Rinaldi MG, Wickes BL, Schmidt HJ, Walsh TJ. Trichosporon mycotoxinivorans, a novel respiratory pathogen in patients with cystic fibrosis. *J Clin Microbiol.* 2009;47(10):3091-3097.
10. Hoy J, Hsu KC, Rolston K, Hopfer RL, Luna M, Bodey GP. Trichosporon beigelii infection: A review. Rev Infect Dis. 1986;8(6):959-967.
11. Molnar O, Schatzmayr G, Fuchs E, Prillinger H. Trichosporon mycotoxinivorans sp. Nov., a new yeast species useful in biological detoxification of various mycotoxins. *Syst Appl Microbiol.* 2004;27(6):661-671.
12. Kontoyiannis DP, Torres HA, Chagua M, Hachem R, Tarrand JJ, Bodey GP, Raad, II. Trichosporonosis in a tertiary care cancer center: Risk factors, changing spectrum and determinants of outcome. *Scand J Infect Dis.* 2004;36(8):564-569.
13. Ruan SY, Chien JY, Hsueh PR. Invasive trichosporonosis caused by trichosporon asahii and other unusual trichosporon species at a medical center in taiwan. *Clin Infect Dis.* 2009;49(1):e11-17.
14. Girmenia C, Pagano L, Martino B, D'Antonio D, Fanci R, Specchia G, Melillo L, Buelli M, Pizzarelli G, Venditti M *et al*. Invasive infections caused by trichosporon species and geotrichum capitatum in patients with hematological malignancies: A retrospective multicenter study from italy and review of the literature. *J Clin Microbiol.* 2005;43(4):1818-1828.
15. Tashiro T, Nagai H, Kamberi P, Goto Y, Kikuchi H, Nasu M, Akizuki S. Disseminated trichosporon beigelii infection in patients with malignant diseases: Immunohistochemical study and review. *Eur J Clin Microbiol Infect Dis*. 1994;13(3):218-224.
16. Vasta S, Menozzi M, Scime R, Indovina A, Speciale A, Liberti G, Spano C, Majolino I. Central catheter infection by trichosporon beigelii after autologous blood stem cell transplantation. A case report and review of the literature. *Haematologica*. 1993;78(1):64-67.
17. Spanik S, Kollar T, Gyarfas J, Kunova A, Krcmery V. Successful treatment of catheter-associated fungemia due to candida krusei and trichosporon beigelii in a leukemic patient receiving prophylactic itraconazole. *Eur J Clin Microbiol Infect Dis.* 1995;14(2):148-149.
18. Finkelstein R, Singer P, Lefler E. Catheter-related fungemia caused by trichosporon beigelii in non-neutropenic patients. *Am J Med*. 1989;86(1):133.
19. Almeida JN, Jr., Francisco EC, Barberino M, Silva LF, Brandao OM, Colombo AL, Padovan ACB. Emergence of trichosporon mycotoxinivorans (apiotrichum mycotoxinivorans) invasive infections in latin america. *Mem Inst Oswaldo Cruz*. 2017;112(10):719-722.
20. Schleupner CJ, Hamilton JR. 1980. A pseudoepidemic of pulmonary fungal infections related to fiberoptic bronchoscopy. *Infect Control*. 1(1):38-42.
21. Singh S, Singh N, Kochhar R, Mehta SK, Talwar P. Contamination of an endoscope due to trichosporon beigelli. *J Hosp Infect.* 1989;14(1):49-53.
22. Martinez-Lacasa J, Mana J, Niubo R, Rufi G, Saez A, Fernandez-Nogues F. Long-term survival of a patient with prosthetic valve endocarditis due to trichosporon beigelii. *Eur J Clin Microbiol Infect Dis.* 1991;10(9):756-758.
23. Keay S, Denning DW, Stevens DA. Endocarditis due to trichosporon beigelii: In vitro susceptibility of isolates and review. *Rev Infect Dis.* 1991;13(3):383-386.
24. Dabas Y, Xess I, Kale P. Molecular and antifungal susceptibility study on trichosporonemia and emergence of trichosporon mycotoxinivorans as a bloodstream pathogen. *Med Mycol*. 2017;55(5):518-527.

29. Miceli MH, Diaz JA, Lee SA. Emerging opportunistic yeast infections. *Lancet Infect Dis.* 2011;11(2):142-151.
30. Leaf HL, Simberkoff MS. Invasive trichosporonosis in a patient with the acquired immunodeficiency syndrome. *J Infect Dis*. 1989;160(2):356-357.
31. Walsh TJ, Melcher GP, Lee JW, Pizzo PA. Infections due to trichosporon species: New concepts in mycology, pathogenesis, diagnosis and treatment. *Curr Top Med Mycol.* 1993;5:79-113.
32. Shah AV, McColley SA, Weil D, Zheng X. Trichosporon mycotoxinivorans infection in patients with cystic fibrosis. *J Clin Microbiol.* 2014;52(6):2242-2244.
33. Goldenberger D, Hinic V, Prince SS, Tamm M, Balestra AM, Hohler D, Frei R. A case report of a cystic fibrosis patient with repeated isolation of trichosporon mycotoxinivorans identified by a novel short-extraction method. *BMC Infect Dis.* 2016;16(1):601.
34. Jannic A, Lafaurie M, Denis B, Hamane S, Metivier F, Rybojad M, Bouaziz JD, Bagot M, Jachiet M. Trichosporon inkin causing invasive infection with multiple skin abscesses in a renal transplant patient successfully treated with voriconazole. *JAAD Case Rep*. 2018;4(1):27-29.
35. Walsh TJ, Groll A, Hiemenz J, Fleming R, Roilides E, Anaissie E. Infections due to emerging and uncommon medically important fungal pathogens. *Clin Microbiol Infect.* 2004;10 Suppl 1:48-66.
36. Ando M, Suga M, Nishiura Y, Miyajima M. Summer-type hypersensitivity pneumonitis. *Intern Med*. 1995;34(8):707-712.
37. Arabatzis M, Abel P, Kanellopoulou M, Adamou D, Alexandrou-Athanasoulis H, Stathi A, Platsouka E, Milioni A, Pangalis A, Velegraki A. Sequence-based identification, genotyping and eucast antifungal susceptibilities of trichosporon clinical isolates from greece. *Clin Microbiol Infect.* 2014;20(8):777-783.
38. Bhatt VR, Viola GM, Ferrajoli A. Invasive fungal infections in acute leukemia. *Ther Adv Hematol*. 2011;2(4):231-247.
39. Sugita T, Nishikawa A, Ikeda R, Shinoda T. Identification of medically relevant trichosporon species based on sequences of internal transcribed spacer regions and construction of a database for trichosporon identification. *J Clin Microbiol.* 1999;37(6):1985-1993.
40. Sugita T, Nakajima M, Ikeda R, Matsushima T, Shinoda T. Sequence analysis of the ribosomal DNA intergenic spacer 1 regions of trichosporon species. *J Clin Microbiol.* 2002;40(5):1826-1830.
41. Hirschi S, Letscher-Bru V, Pottecher J, Lannes B, Jeung MY, Degot T, Santelmo N, Sabou AM, Herbrecht R, Kessler R. Disseminated trichosporon mycotoxinivorans, aspergillus fumigatus, and scedosporium apiospermum coinfection after lung and liver transplantation in a cystic fibrosis patient. *J Clin Microbiol.* 2012;50(12):4168-4170.
42. Erer B, Galimberti M, Lucarelli G, Giardini C, Polchi P, Baronciani D, Gaziev D, Angelucci E, Izzi G. Trichosporon beigelii: A life-threatening pathogen in immunocompromised hosts. *Bone Marrow Transplant.* 2000;25(7):745-749.
43. Peman J, Zaragoza R. Current diagnostic approaches to invasive candidiasis in critical care settings. *Mycoses.* 2010;53(5):424-433.
44. de Almeida Junior JN, Hennequin C. Invasive trichosporon infection: A systematic review on a re-emerging fungal pathogen. *Front Microbiol.* 2016;7:1629.
25. Pfaller MA, Diekema DJ. Rare and emerging opportunistic fungal pathogens: Concern for resistance beyond candida albicans and aspergillus fumigatus. *J Clin Microbiol.* 2004;42(10):4419-4431.
26. Denning DW. Echinocandin antifungal drugs. *Lancet.* 2003;362(9390):1142-1151.
27. Araujo Ribeiro M, Alastruey-Izquierdo A, Gomez-Lopez A, Rodriguez-Tudela JL, Cuenca-Estrella M. Molecular identification and susceptibility testing of trichosporon isolates from a brazilian hospital. *Rev Iberoam Micol*. 2008;25(4):221-225.
28. Suzuki K, Nakase K, Kyo T, Kohara T, Sugawara Y, Shibazaki T, Oka K, Tsukada T, Katayama N. 2010. Fatal trichosporon fungemia in patients with hematologic malignancies. *Eur J Haematol.* 2010;84(5):441-447