Fatal Lower Limb Infection by *Trichosporon asahii* in an Immunocompetent Patient

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SUMMARY *Trichosporon (T.) asahii* can cause superficial skin infections and can be an opportunistic pathogen that produces potentially fatal systemic infections in immunocompromised hosts. We report a case of lower limb infection due to *T. asahii* in an immunocompetent patient who displayed no evidence of underlying disease. There is a strong possibility that our patient had been colonized at the infection site as part of the normal skin flora. After one-month bed rest due to an accidental fall and fracture of the right shoulder blade, a 61-year-old woman experienced severe edema and redness in the right lower limb and received topical treatment with iodine solution and antibiotics without improvement. She presented at our Outpatient Clinic with cellulitis and lymphedema. Samples collected from the affected areas revealed *T. asahii* and the patient was referred to a hospital for infectious diseases for appropriate therapy. The patient was treated with wound dressings until she was admitted to our intensive care unit when her general condition abruptly deteriorated. Despite *in vitro* susceptibility results, therapy with liposomal amphotericin and voriconazole could not change the fatal outcome. Nowadays, physicians must suspect this emerging difficult-to-treat fungal pathogen and treatment must start promptly in these infections.

KEY WORDS: *Trichosporon asahii*, lower limb infection, immunocompetent patient

INTRODUCTION

Trichosporon asahii is a basidiomycetous, nondermatophytic fungus widely distributed in soil, vegetation, and water and may be part of the normal human skin and respiratory tract flora (1). *Trichosporon (T.) asahii* has been recognized as the cause of superficial skin infections, such as white piedra. It can also be an opportunistic pathogen that produces potentially fatal systemic infections in immunocompromised hosts, particularly those with underlying hematologic malignancy (2). Rarely, *T. asahii* has been isolated from patients who displayed no evidence of underlying disease (3-5).

CASE REPORT

We report a case of lower limb infection due to *T. asahii* in an immunocompetent patient who displayed no evidence of underlying disease but developed an ultimately lethal *T. asahii* systemic infection. There is a strong possibility that our patient had been colonized at the infection site as part of the normal skin flora. After one-month bed rest due to an accidental fall and fracture of the right shoulder blade, a 61-year-old woman experienced severe edema with an overlying erythematous patch in the right lower limb. The patient used iodine solution to the affected area for about two weeks. Furthermore, the skin le-

sions were mistaken by the family doctor as erysipelas and antibiotics were prescribed without improvement. She presented at our Outpatient Clinic with fever, cellulitis and lymphedema. She was in otherwise good health. No one in her family or friends had similar lesions and she had no pets in her house. Physical examination revealed no pathology of the venous or arterial system and there was no regional or generalized lymphadenopathy or hepatosplenomegaly. Routine blood cell count and serum electrolytes were within the normal limits.

Direct microscopic examination with 15% potassium hydroxide (KOH) solution of the material collected from the affected area showed pseudohyphae. Culture on Sabouraud dextrose agar medium (Oxoid Ltd., Basingstoke, UK) supplemented with chloramphenicol (Sigma, St. Louis, MO, USA) and cycloheximide (Sigma, St. Louis, MO, USA) incubated for 2 weeks at 25 °C yielded white to deep-cream colored, wrinkled colonies (Fig. 1). Microscopic examination after staining with lactophenol cotton blue showed true hyphae, pseudohyphae, a few blastoconidia, and rectangular arthroconidia typical of *Trichosporon* species. The identification of *T. asahii* was confirmed by using the Vitek 2 automated biochemical testing system (BioMerieux, Marcy l'Etoile, France). These colonies were identified as *T. asahii* using the API 20C AUX assimilation assay (BioMerieux, Inc., Lyon, France). MICs were as follows: for amphotericin B, 16 µg/mL; fluconazole, 1 µg/mL; itraconazole, 0.25 µg/mL; and voriconazole, 0.06 µg/mL. To confirm our findings, second samples from the affected limb were collected with the same results. She was referred to another hospital for appropriate antifungal therapy. For a period of one month, the patient received local treatment with wound dressings and topical corticosteroids but the skin lesions did not respond to this therapy, and instead spread to the whole limb (Fig. 2). Subsequently she developed high fever with hemodynamic deterioration and was admitted to our Intensive Care Unit. Despite *in vitro* susceptibility results, intravenous therapy with liposomal amphotericin B (5 mg/kg daily) and voriconazole (6 mg/kg twice daily) could not change the outcome and the patient expired after the first 24 hours of therapy due to multiorgan failure and septic shock. Since *T. asahii* can be a life-threatening pathogen, it is imperative nowadays that physicians suspect this emerging difficult-to-treat fungal pathogen and start the treatment promptly in these infections.

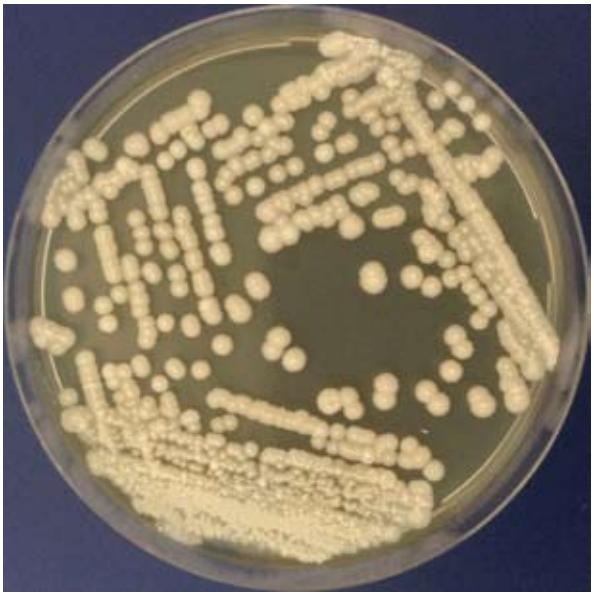

Figure 1. *Trichosporon asahii* culture on Sabouraud dextrose agar.

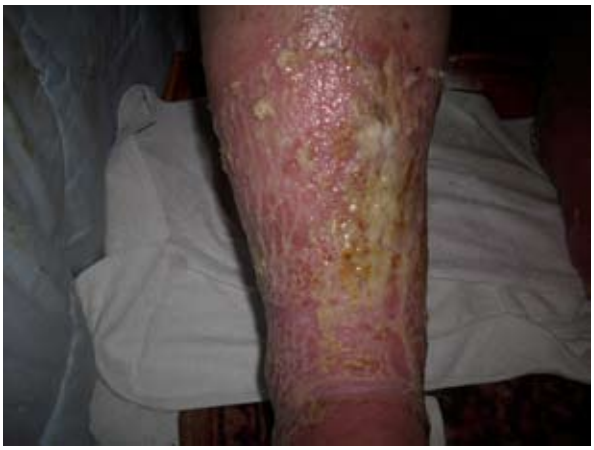

Figure 2. Lower limb infection by *Trichosporon asahii*.

DISCUSSION

Trichosporon asahii has been recognized as the main *Trichosporon* species that causes systemic infection in humans (6). Recently, after examining skin samples from 380 healthy individuals using a nested PCR assay, it was found that this opportunistic yeast pathogen is part of the cutaneous fungal microbiota in humans and this may be one of the routes through which trichosporonosis is acquired (7).

Most cases of superficial *Trichosporon* infections have involved immunocompromised, neutropenic patients with hematologic malignancies, usually mimicking an eczema (8). Nevertheless, there are few reports involving immunocompetent hosts presenting with superficial cutaneous infections (9-11).

Predisposing risk factors associated with infections caused by *T. asahii* include treatment with immunosuppressive drugs, presence of implanted

prosthetic devices, transplantation, acquired immunodeficiency syndrome, extensive burns (12) and prolonged use of antibiotics (13). However, a case of fatal septic shock by *T. asahii* has been reported in a patient who did not have cancer or neutropenia (3), while a case of disseminated trichosporonosis by *T. asahii* in a healthy adult woman with no underlying disease has been reported in China (9).

Disseminated infections due to *T. asahii* are difficult to resolve, while the antifungal agents approved for the treatment of *Trichosporon* infections are limited. It has been demonstrated that monotherapy of disseminated trichosporonosis is usually unsuccessful (3,6). A previous study of the *in vitro* antifungal susceptibility of *Trichosporon* species showed that voriconazole, posaconazole, and ravuconazole were more active than amphotericin B or fluconazole (14). On the other hand, combination regimens with synergistic antifungals could provide additional options for treating these infections. Interestingly, in a recent study, the combined antifungal activities of the echinocandin caspofungin and the polyene amphotericin B against clinical isolates of *T. asahii* were more effective than monotherapy, suggesting that combined antifungal therapy may be a potential strategy for treating disseminated trichosporonosis (15). The automated commercial system VITEK 2 used for the identification and susceptibility testing of our *T. asahii* isolate was found comparable to the Clinical and Laboratory Standards Institute (CLSI M27-A3) reference broth microdilution method (16).

Cutaneous infection by *T. asahii* in immunocompetent hosts, as observed in our patient, is not usual. Our patient had suffered from gradually expanding skin lesions to which various treatments, including antibiotics, were ineffective. It can be easily speculated that, at the initial stage, the patient may have been affected by a superficial form of trichosporonosis that, due to the delay in diagnosis and treatment, may have disseminated. In the immunocompromised body, dissemination may occur, but this is usually unexpected in the immunocompetent host. In our patient, it is possible that the prolonged use of topical corticosteroids, due to misdiagnosis of the cutaneous lesions, induced a localized immune deficit that facilitated the subsequent dissemination of the infection. Infection with this unusual pathogen should be considered in those immunocompetent patients presenting with skin lesions that continue to persist after prolonged treatment with topical steroids.

CONCLUSION

We have described a fatal case of lower limb cutaneous infection by *T. asahii* in an immunocompetent woman. In conclusion, it is important to acknowledge the poor prognosis that can be associated with infections due to *T. asahii*, which has the potential for invasive infection in the immunocompromised patient as well as in the immunocompetent host.

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REFERENCES

1. Itoh T, Hosokawa H, Kohdera U, Toyazaki N, Asada Y. Disseminated infection with *Trichosporon asahii*. Mycoses 1996;39:195-9.
2. Groll AH, Walsh TJ. Uncommon opportunistic fungi: new nosocomial threats. Clin Microbiol Infect 2001;7:8-24.
3. Ebright JR, Fairfax MR, Vazquez JA. *Trichosporon asahii,* a non-*Candida* yeast that caused fatal septic shock in a patient without cancer or neutropenia. Clin Infect Dis 2001;33:e28-30.
4. Yun SJ, Lee JB, Shin MG, Kim SJ, Won YH, Lee SC. Cutaneous abscess by *Trichosporon asahii* developing on a steroid injection site in a healthy adult. Clin Exp Dermatol 2006;31:545-7.
5. Rastogi VL, Nirwan PS. Invasive trichosporonosis due to *Trichosporon asahii* in a non-immunocompromised host: a rare case report. Indian J Med Microbiol 2007;25:59-61.
6. 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;10:48-66.
7. Zhang E, Sugita T, Tsuboi R, Yamazaki T, Makimura K. The opportunistic yeast pathogen *Trichosporon asahii* colonizes the skin of healthy individuals: analysis of 380 healthy individuals by age and gender using a nested polymerase chain reaction assay. Microbiol Immunol 2011;55:483-8.
8. Nakagawa T, Nakashima K, Takaiwa T, Negayama K. *Trichosporon cutaneum (Trichosporon asahii)* infection mimicking hand eczema in a patient with leukemia. J Am Acad Dermatol 2000;42:929-31.
9. Abliz P, Fukushima K, Takizawa K, Yang R, Li R, Nishimura K. Identification of the first isolates of *Trichosporon asahii* var. *asahii* from disseminated trichosporonosis in China. Diagn Microbiol Infect Dis 2002;44:17-22.
10. Pulvirenti N, Dall'Oglio F, Greco AM, Oliveri S, Schwartz RA, Micali G. Superficial cutaneous *Tri-*

chosporon asahii infection in an immunocompetent host. Int J Dermatol 2006;45:1428-31.

11. Kim SH, Kim DH, Joo SI, Yoo JI, Kim HB, Kim NJ, *et al*. Chronic cutaneous disseminated *Trichosporon asahii* infection in a nonimmunocompromised patient. J Am Acad Dermatol 2008;59:S37-9.
12. Wolf DG, Falk R, Hacham M, Theelen B, Boekhout T, Scorzetti G, *et al*. Multidrug-resistant *Trichosporon asahii* infection of nongranulocytopenic patients in three intensive care units. J Clin Microbiol 2001;39:4420-5.
13. Mori Y, Hiraoka M, Katsu M, Tsukahara H, Mikami Y, Mayumi M. Marked renal damage in a child with hydronephrosis infected by *Trichosporon asahii*. Pediatr Nephrol 2005;20:234-6.
14. Paphitou NI, Ostrosky-Zeichner L, Paetznick VL, Rodriguez JR, Chen E, Rex JH. *In vitro* antifungal susceptibilities of *Trichosporon* species. Antimicrob Agents Chemother 2002;46:1144-6.
15. Li H, Lu Q, Wan Z, Zhang J. *In vitro* combined activity of amphotericin B, caspofungin and voriconazole against clinical isolates of *Trichosporon asahii*. Int J Antimicrob Agents 2010;35:550-2.
16. Cejudo MA, Gallego AG, Lacasa EC, Aller AI, Romero A, García JP, *et al*. Evaluation of the VITEK 2 system to test the susceptibility of *Candida* spp., *Trichosporon asahii* and *Cryptococcus neoformans* to amphotericin B, flucytosine, fluconazole and voriconazole: a comparison with the M27-A3 reference method. Med Mycol 2010;48:710-9.