Systemic Trichosporonosis: A Mini-Review

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Abstract

The occurrence of systemic fungal infections has increased during the past 2 decades, probably due to the immunosuppressed status caused by aggressive chemotherapy, transplantation, HIV infection, and malignancy both solid and hematologic malignancies. *Trichosporon* species are among emerging causative agents of systemic mycosis in these patients. *Trichosporon* spp. are medically important basidiomycetous yeasts which can be found in environment as well as the skin and respiratory tract of immunocompromised patients. *Trichosporon* can cause three categories of infection including hypersensitivity pneumonitis, superficial (scalp and skin white piedra) and systemic infections. Clinical manifestations of systemic trichosporonosis include fever with or without dissemination to multiple deep seeded organs; it is very difficult to distinguish between systemic trichosporonosis and candidiasis. Treatment of systemic trichosporonosis is difficult. Voriconazole is one of the best antifungal agents with good activity against *Trichosporon*. Surgical drainage and central venous catheter removal should be considered if indicated. The mortality of systemic trichosporonosis is high. (J Infect Dis Antimicrob Agents 2013;30:57-61.)

*Trichosporon* species are medically important basidiomycetous yeasts which can be found in environment including soil, water, wood, and vegetables. In addition, they can be presented in normal skin and occasionally in the respiratory and gastrointestinal tracts of humans.

The occurrence of systemic mycosis has increased over the past few decades worldwide, likely due to the suppressed immune status of patients from aggressive chemotherapy, trans-plantation, HIV infection, and malignancy both solid and hematologic malignancies. *Trichosporon* spp. are among emerging causative agents of systemic mycosis in these patients.

Microbiology

*Trichosporon* spp. can produce blastoconidia, arthroconidia, pseudohyphae, and true septate hyphae. Their yeast-like colonies on Sabouraud’s dextrose agar appear as white to cream color, with typical cerebriform and radial surfaces. The aged colonies become dry and membranous. Apart from molecular microbiology techniques, the species of *Trichosporon* can be determined by the presence or absence of other morphological structures including appresoria, macroconidia and meristematic conidiation as well as biochemistry tests including the capability to assimilate different kinds of carbohydrates and carbon sources. More than 50 species of *Trichosporon* have been reported worldwide. The most common species causing human systemic trichosporonosis include *T. asahii*, *T. mucoides*, *T. cutaneum*, *T. inkin*, and *T. ovoides.*
Epidemiology

The first patient with systemic trichosporonosis was reported in 1977 in a patient with hematopoietic stem cell transplant. In Thailand, the first case was described in a 27-month-old patient with chronic granulomatous disease in 2001. The diagnosis was made from the postmortem tissue culture. A recent study in Khon Kaen University from 1999 to 2003 showed that Trichosporon was the second most common causative agent of fungal bloodstream infection in non-HIV-infected patients. Another study in Thai patients with yeast infections from 2003 and 2007 showed that Trichosporon spp. were the third most common pathogen followed by Candida spp. and Cryptococcus neoformans. A retrospective study at the University of Texas MD Anderson Cancer Center among patients with fungemia by opportunistic yeasts from 1998 to 2010 showed that Candida spp. and non-Candida yeasts accounted for 96.9% and 3.1% of 2,984 patients, respectively. Trichosporon spp. were noted in 8 patients. Catheter-associated fungemia was observed in 21 (51%) patients. A multicenter retrospective study among Italian patients with hematological diseases reported that 17 and 35 of 52 episodes of proven or probable systemic trichosporonosis from 1983 to 2002 over the past 20 years were Trichosporon spp. and Geotrichum capitatum, respectively. The prevalence of infections caused by Trichosporon and G capitatum in acute leukemic patients were 0.4% and 0.5%, respectively.

Mode of transmission

The mode of transmission of superficial trichosporonosis such as scalp or white piedra remains unknown, but poor hygiene and bathing in contaminated water may play a significant role. Regarding systemic trichosporonosis, prior gastrointestinal colonization and further translocation through the gut wall into the systemic circulation will probably be the primary site of systemic trichosporonosis. Apart from endogenous acquisition from the gastrointestinal tract, some evidence suggests that some patients with systemic trichosporonosis may acquire the fungus exogenously. Colonized Trichosporon on the skin of patients may enter the bloodstream after a contamination of central venous catheter or percutaneously inserted intravascular catheter insertion. Kontoyiannis and colleagues claimed that central venous catheter-related bloodstream infection was the major cause (70% of all episodes) of systemic trichosporonosis in 17 cancer patients. In King Chulalongkorn Memorial Hospital, 5 patients were diagnosed as systemic trichosporonosis during a 5-year period from 2008 to 2012. (unpublished data). All patients had central venous catheter-related bloodstream infection.

Clinical manifestations

Trichosporon spp. can cause three categories of infection including hypersensitivity pneumonitis, superficial and systemic infections. Trichosporonosis in patients with hematologic malignancy is frequently categorized as systemic infection. Clinical manifestations of systemic trichosporonosis include acute or subacute fever with or without dissemination to multiple deep seated organs. Pneumonia is usually an early manifestation, and renal involvement is commonly observed in disseminated infection. Cutaneous lesions occur in approximately one-third of patients with systemic trichosporonosis. The most common skin lesions are purpuric papules and/or nodules with central necrosis or ulceration, frequently involving the trunk, face, and extremities. Some patients may present as acute cellulitis mimicking that caused by
bacterial infection. In conclusion, the clinical manifestations of systemic trichosporonosis are similar to systemic candidiasis.

Diagnosis and laboratory investigations

Blood culture is considered the standard diagnostic test for early diagnosis of systemic trichosporonosis. Regarding tissue pathology, *Trichosporon* is usually presented as a mixture of blastoconidia, arthroconidia, pseudohyphae, and true hyaline hyphae; it can be easily mistaken as *Candida* with non-expert microbiologists. In addition, serum beta-D-glucan is generally not positive in patients with systemic trichosporonosis. A false-positive result of cryptococcal antigen may occur in patients with systemic trichosporonosis due to the presence of a cell wall antigen in *Trichosporon* cross-reacting with *C. neoformans* capsular antigen. Molecular microbiology techniques have not yet been adopted as routine clinical procedures.

Treatment

Treatment of systemic trichosporonosis is very difficult due to antifungal resistance, a need for surgical debridement, and immunocompromised status of patients. Clinical Laboratory Standards Institute (CLSI) documents do not include the genus *Trichosporon* for antifungal susceptibility testing. To date, most studies evaluated *Trichosporon* in vitro antifungal susceptibility based on the recommendations of CLSI 2002 methods. In the past, amphotericin B was considered as the agent of first choice for the treatment of systemic trichosporonosis. However, there were several case reports with poor response to amphotericin B treatment. In addition, there is a high rate of amphotericin B-resistant among *Trichosporon asahii*. The new triazoles have recently been shown to have a good antifungal activity against *Trichosporon* spp. both in vitro, in animal studies, and case series. Voriconazole is considered as one of the most effective agents against *Trichosporon* spp. Echinocandins have poor in vitro activity, and there were several case reports of breakthrough infections during its use.

In addition to appropriate antifungal treatment, adequate surgical drainage should be carried out in all patients with relatively large size of abscess or necrotic tissues. Central venous catheter must be removed in all patients with suspected central venous catheter-related bloodstream infection caused by *Trichosporon*.

Outcome

The clinical outcome of systemic trichosporonosis is generally poor. The mortality rate in different case series ranged from 42 to 76%; this number was relatively high in patients with hematologic malignancy.

Conclusion

*Trichosporon* spp. are among emerging causative agents of systemic mycosis in immunocompromised patients over the past 2 decades. Clinical manifestations are similar to systemic candidiasis. Voriconazole is one of the antifungal agents with good in vitro activity against *Trichosporon* spp. Surgical drainage and central venous catheter removal must be considered if indicated. The mortality of systemic trichosporonosis is very high.

References

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