Comparison of the characteristics of patients with invasive infections and non-invasive infections caused by *Trichosporon asahii*

Jinyeong Kim, Min Jae Kim, Yong Pil Chong, Sung-Han Kim, Sang-Ho Choi, Sang-Oh Lee, Jun Hee Woo, Yang Soo Kim, Jiwon Jung*

Departments of Infectious Diseases, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea

*Contact Information: Jiwon Jung, MD
Department of Infectious Diseases
Asan Medical Center
University of Ulsan College of Medicine
E-mail: jiwonjung@amc.seoul.kr

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Abstract

- We performed retrospective study to identify the characteristics of *Trichosporon asahii* invasive infection. A total of 102 patients with *T. asahii* were identified including 18 (18%) with invasive infection. Invasive infection was associated with indwelling central venous catheter (94% vs. 54%, P=0.001), prior antifungal agent use (50% vs. 18%, P=0.01), hematologic malignancy (33% vs. 7%, P=0.006), and end-stage renal disease (28% vs. 7%, P=0.02). Patients with invasive infections had higher in-hospital mortality than patients with non-invasive infections (61% vs. 27%, P = 0.006). Those with the above risk factors should be monitored for the development of invasive *T. asahii* infection.

Background

- The ARTEMIS DISK global antifungal surveillance study reported that *Trichosporon* species represent the third most common non-*Candida* yeast infections causing invasive disease[1]. Many studies have shown that *Trichosporon asahii* is the most predominant species causing invasive infection among all various *Trichosporon* species, accounting for 35% to 84% of *Trichosporon* infections[2-5]. Despite the increasing attention focused on *T. asahii* infection, little is known about the current epidemiology of this emerging pathogen. Therefore, we conducted a retrospective study to investigate the epidemiology of *T. asahii* infections, and to identify risk factors and outcomes in South Korean patients.

Methods

- We retrospectively reviewed medical records of patients with at least one positive clinical isolate confirming *T. asahii* infection between January 2009 and July 2018 at a 2,700-bed tertiary care medical center in Seoul, South Korea. The study was approved by the Institutional Review Board of Asan Medical Center.
- All patients with positive cultures for *T. asahii* were divided into two groups: invasive and non-invasive disease. Invasive disease was defined according to the consensus statement of the Invasive Fungal Infections Cooperative Group of the European Organization for Research and Treatment of Cancer and the Mycoses Study Group (EORTC-MSG)[6]. Breakthrough invasive fungal infection was defined as occurring during exposure to an antifungal drug, including fungi outside the spectrum of activity of an antifungal agent[7].

Results

- During the study period, a total of 259 clinical *T. asahii* isolates (137 urine, 55 respiratory specimen, 26 blood, 16 surgical site drainage, 9 skin and soft tissue biopsy specimen, 9 open discharge, 3 toe/nail, 2 pleural fluid and 2 stool) were collected from 102 patients.

Results

- **Table 1. Characteristics of 102 patients with invasive and non-invasive *Trichosporon asahii* disease**

	Invasive (n=18)	Non-invasive (n=84)	P value
Age, median, years (IQR)	55 (45-72)	61 (51-74)	0.21
Male	13 (72)	54 (64)	0.52
Underlying disease and condition			
Indwelling of central venous catheter	17 (94)	45 (54)	**0.001**
Staying in intensive care unit	14 (78)	49 (58)	0.12
Hematologic malignancy	6 (33)	6 (7)	**0.006**
End stage renal disease requiring dialysis	5 (28)	6 (7)	**0.02**
Solid tumor	4 (22)	21 (25)	1.00
Diabetes mellitus	4 (22)	17 (20)	1.00
Solid organ transplant recipient	4 (22)	6 (7)	0.07
Liver cirrhosis	3 (17)	6 (7)	0.19
Neutropenia	3 (17)	3 (4)	0.07
Concurrent candidemia	1 (6)	5 (6)	1.00
Type of infection			
Fungemia	12 (67)	0 (0)	**<0.001**
Complicated skin and soft tissue infection[a]	3 (17)	0 (0)	**0.005**
Pneumonia with or without empyema[b]	2 (11)	0 (0)	**0.03**
Complicated intra-abdominal infection[c]	1 (5)	0 (0)	0.18
Prior antibiotics use within 30 days	18 (100)	74 (88)	0.20
Prior antifungal agent use within 30 days	9 (50)	15 (18)	**0.01**
Breakthrough infection	6 (33)	8 (10)	**0.02**
Fluconazole	0 (0)	0 (0)	N/A
Itraconazole	1 (6)	1 (1)	0.32
Voriconazole	0 (0)	4 (5)	1.00
Echinocandin	3 (17)	0 (0)	**0.005**
Polyene	2 (11)	3 (4)	0.21
In-hospital mortality	11 (61)	23 (27)	**0.006**

Data in parentheses are percentages (%) of patients unless otherwise indicated.
Abbreviation: IQR, interquartile range; N/A, not available.

- **Table 2. Univariable and multivariable analysis of risk factors for mortality in patients with *Trichosporon asahii* disease**

	Univariable analysis	Multivariable analysis	
	OR (95% CI)	Adjusted OR* (95% CI)	P value
Age	1.01 (0.98-1.04)	-	-
Sex	1.72 (0.70-4.25)	-	-
Indwelling of CVC	8.44 (2.68-26.56)	4.68 (1.37-16.02)	**0.01**
Staying in ICU	5.80 (2.00-16.77)	3.31 (1.02-10.78)	**0.047**
Breakthrough infection	10.36 (2.65-40.47)	6.15 (1.48-25.58)	**0.01**
Invasive *T. asahii* infection	4.17 (1.44-12.05)	-	-
Fungemia	4.92 (1.36-17.78)	-	-

*Adjusted by age, sex, indwelling CVC, staying in ICU, breakthrough infection, invasive *T. asahii* infection and fungemia.
Abbreviation: OR, odds ratio; CI, confidence interval; CVC, central venous catheter; ICU, intensive care unit.

- **Table 3. Antifungal susceptibilities of 15 *Trichosporon asahii* isolates**

Patient no.	Site of infection	Specimen	Minimum inhibitory concentration (μg/ml)													
			Fluconazole		Itraconazole		Voriconazole		Amphotericin B		5-Flucytosine		Micafungin		Caspofungin	
1	Fungemia	Blood	2	S	0.25	I	0.125	S	4	R	16	I	N/R		N/R	
2	Fungemia	Blood	2	S	N/R		≤0.12	S	1	S	4	S	N/R		≥4	R
3	Fungemia	Blood	4	S	N/R		≤0.12	S	N/R		≤1	S	N/R		N/R	
4	Fungemia	Blood	≤1	S	≤0.125	S	≤0.06	S	≤0.5	S	≤4	S	N/R		N/R	
5	Fungemia	Blood	2	S	0.25	I	0.125	S	>16	R	4	S	N/R		N/R	
6	Fungemia	Blood	1	S	0.125	S	0.06	S	1	S	≤4	S	N/R		N/R	
7	Fungemia	Blood	8	S	0.5	S	0.5	S	1	S	8	-	>8	R	>8	R
8	Fungemia	Blood	2	S	N/R		≤0.12	S	1	S	2	S	≥4	R	≥4	R
9	Fungemia	Blood	≤2	S	≤0.125	S	≤0.06	S	>16	R	≤4	S	N/R		N/R	
10	SSTI	Pus*	2	S	N/R		≤0.12	S	1	S	2	S	≥4	R	≥4	R
11	Colonization	Urine	32	I	4	R	2	I	≤0.5	S	>16	R	N/R		N/R	
12	Colonization	Urine	≤1	S	≤0.125	S	≤0.06	S	≤0.5	S	>16	R	N/R		N/R	
13	Colonization	Urine	N/R		N/R		N/R		≤0.5	S	≤4	S	N/R		N/R	
14	Colonization	Sputum	>127	R	>4	R	>8	R	≤0.5	S	>16	R	N/R		N/R	
15	Colonization	Sputum	2	S	0.25	S	≤0.12	S	2	R	N/R		N/R		≥4	R
Susceptible rates			12/14 (86%)		6/10 (60%)		12/14 (86%)		10/14 (71%)		9/14 (64%)		0/3 (0%)		0/5 (0%)	

Abbreviations: N/R. not reported; SSTI, complicated skin and soft tissue infection.
*Pus from infected wound of lower leg, left.

Conclusions

- *T. asahii* can cause life-threatening invasive infections, particularly in patients with indwelling central venous catheter, prior antifungal agent use, hematologic malignancy, and end-stage renal disease. As patients with invasive infections had fatal outcomes, those with the above risk factors should be monitored for the development of invasive *T. asahii* infection.

References

1. Pfaller MA, Diekema DJ, Gibbs DL et al. Results from the ARTEMIS DISK Global Antifungal Surveillance Study, 1997 to 2005. J Clin Microbiol. 2007; 45: 1735–1745.
2. Guo LN, Yu SY, Hsueh PR et al. Invasive infections due to Trichosporon: species distribution, genotyping, and antifungal susceptibilities from a multicenter study in China. J Clin Microbiol. 2019; 57.
3. Ruan S-Y, Chien J-Y, Hsueh P-R. Invasive trichosporonosis caused by Trichosporon asahii and other unusual Trichosporon species at a medical center in Taiwan. Clin Infect Dis. 2009; 49: e11–e17.
4. Chagas-Neto TC, Chaves GM, Melo AS, Colombo AL. Bloodstream infections due to Trichosporon spp.: species distribution, Trichosporon asahii genotypes determined on the basis of ribosomal DNA intergenic spacer 1 sequencing, and antifungal susceptibility testing. J Clin Microbiol. 2009; 47
5. Girmenia C, Pagano L, Martino B 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: 1818–1828.
6. Donnelly JP, Chen SC, Kauffman CA et al. Revision and update of the consensus definitions of invasive fungal disease from the European Organization for Research and Treatment of Cancer and the Mycoses Study Group Education and Research Consortium. Clin Infect Dis. 2019. E-pub ahead of print.
7. Cornely O,Hoenigl M, Lass-Flörl C et al. Defining breakthrough invasive fungal infection. Position Paper of the Mycoses Study Group Education and Research Consortium (MSG-ERC) and the European Confederation of Medical Mycology (ECMM). Mycoses. 2019; 62.