Medical Journal of Bakırköy

Med J Bakırköy 2021;17:130-134
DOI: 10.4274/BMJ.galenos.2021.54254

Research

Investigation of Antifungal Susceptibility of Trichosporon Asahii Isolated From Urine Samples

İdrar Örneklerinden İzole Edilen Trichosporon Asahii İzolatlarının Antifungal Duyarlılığının Araştırılması

Deniz Turan[1], Ayşe Barış[2], Fatma Özakkaş[3], Şölen Daldaban Dinçer[3], Sebahat Aksaray[4]

[1]University of Health Sciences Turkey, Haydarpaşa Numune Training and Research Hospital, Clinic of Medical Microbiology, İstanbul, Turkey
[2]University of Health Sciences Turkey, Şişli Hamidiye Etfal Training and Research Hospital, Clinic of Medical Microbiology, İstanbul, Turkey and İstanbul University Faculty of Medicine, Department of Medical Microbiology, İstanbul, Turkey
[3]University of Health Sciences Turkey, Ümraniye Training and Research Hospital, Clinic of Medical Microbiology, İstanbul, Turkey
[4]University of Health Sciences Faculty of Medicine, Department of Medical Microbiology, İstanbul, Turkey

ABSTRACT

Objective: As part of the normal human flora of the skin and gastrointestinal tract, Trichosporon species may lead to opportunistic infections through underlying facilitating factors. Urinary tract infections (UTIs) are the most common infections occurring in intensive care units (ICUs), where catheterization procedures are performed extensively. The aim of the study investigates the antifungal susceptibility of T. asahii strains isolated from urine samples.

Methods: Isolates were identified to the species level using the MALDI-TOF MS system (VITEK MS; bio-Mérieux). Antifungal susceptibility tests were conducted using the broth microdilution method, in accordance with the recommendations of the "Clinical and Laboratory Standards Institute (CLSI)".

Results: At a 48-hour assessment of the 100 T.asahii isolates included in the study, the minimal inhibitory concentration ($MIC)_{50}$ and MIC_{90} values were (2µg/mL, 8µg/mL) for fluconazole, (0.06µg/mL, 0.12µg/mL) for voriconazole, (0.25 µg/mL, 1 µg/mL) for posaconazole, (0.12 µg/mL, 0.25 µg/mL) for itraconazole and isavuconazole, (2 µg/mL) for amphotericin B and (>8) for micafungin.

Conclusion: The lowest and highest MIC values among the triazole antifungal agents were determined for voriconazole and fluconazole, respectively. Considering the high MIC values, care should be taken to prevent breakthrough infections of Trichosporon in at-risk patients undergoing empirical or prophylactic echinocandin or fluconazole therapies.

Keywords: Trichosporon asahii, urinary tract infection, antifungal susceptibility

ÖZ

Amaç: İnsanda deri ve gastrointestinal sistemin normal florasında bulunan Trichosporon türleri, altta yatan kolaylaştırıcı faktörlerin etkisi ile fırsatçı enfeksiyonlara neden olabilmektedir. Üriner sistem enfeksiyonları (ÜSE), yoğun kateterizasyon işlemlerinin uygulandığı yoğun bakım ünitesinde (YBÜ) en sık karşılaşılan enfeksiyonlardır.Trichosporon, ÜSE'de Candida' dan sonra en sık izole edilen maya cinsidir. Bu çalışmada idrar örneklerinden izole edilen T. asahii izolatlarının antifungal duyarlılıklarının araştırılması amaçlanmıştır.

Gereç ve Yöntem: İzolatların tür tanımı MALDI-TOF MS (VITEK MS; bio-Mérieux) sistemi ile yapıldı. Antifungal duyarlılık testleri "Clinical and Laboratory Standards Institute (CLSI)" önerileri doğrultusunda sıvı mikrodilüsyon yöntemi ile yapılmıştır.

Bulgular: Çalışmaya dahil edilen 100 T.asahii izolatının 48. saatte yapılan değerlendirmesinde izolatların minimum inhibitör konsant ($MİK)_{50}$, $MİK_{90}$ değerleri; flukonazol için (2µg/mL, 8µg/mL), vorikonazol için (0.06µg/mL, 0.12µg/mL), posakonazol için (0.25 µg/mL, 1 µg/mL), itrakonazol ve isavukonazol için (0.12 µg/mL, 0.25 µg/mL), amfoterisin B için (2 µg/mL) ve mikafungin için (>8) olarak belirlenmiştir.

Sonuç: Triazol grubu antifungal ilaçlar içinde en düşük MİK değerleri vorikonazol'de, en yüksek MİK değerleri flukonazolde saptanmıştır. Yüksek MİK değerleri göz önünde bulundurulduğunda; ekinokandin ve flukonazolün ampirik veya profilaktik olarak kullanıldığı, risk faktörleri bulunan hastalarda tedavi altında gelişebilecek Trichosporon enfeksiyonlarına karşı dikkatli olunmalıdır.

Anahtar Kelimeler: Tichosporon asahii, üriner sistem enfeksiyonu, antifungal duyarlılık

Address for Correspondence: Deniz Turan, University of Health Sciences Turkey, Haydarpaşa Numune Training and Research Hospital, Clinic of Medical Microbiology, İstanbul, Turkey
Phone: +90 216 542 32 32 E-mail: dennizturan@hotmail.com ORCID ID: orcid.org/0000-0001-7943-7536

Cite as: Turan D, Barış A, Özakka F, Daldaban Dinçer Ş, Aksaray S. Investigation of Antifungal Susceptibility of Trichosporon Asahii İsolated From Urine Samples. Med J Bakırköy 2021;17:130-134

Received: 08.09.2020
Accepted: 21.06.2021

INTRODUCTION

Trichosporon species are found widely in nature, comprising of yeast-like fungi belonging to the phylum Basidiomycota (1). A recent taxonomic revision identified 20 species within the genus, using IGS1 rDNA sequence analysis (2). Among these species, *T. asahii, T. asteroides, T. inkin, T. ovoides*, and *T. faecale* were reported as infectious in humans. The most common cause of invasive trichosporonosis and urinary tract infections (UTIs) is *T. asahii* (3,4).

Trichosporon species, which are members of saprophytic flora of the skin or found in the respiratory, gastrointestinal, and genitourinary tracts of humans, are causing superficial as well as invasive infections with increasing frequency (1,4). Nosocomial UTIs are the most common infections, particularly in intensive care units (ICUs). Most of these infections are reported to be related to the presence of a urinary catheter and tend to develop following urinary catheterization (5). *Candida* species are the most common types of yeasts isolated in UTIs, followed by *T. asahii* (6).

Virulence factors play an important role in the development of infection. *Trichosporon* species produce extracellular enzymes such as lipase, protease, and esterase and form biofilms (1,7). Most UTI-causing *T. asahii* isolates were shown to form biofilm on polystyrene plates (8,9). Moreover, studies have reported that a significant relationship exists between biofilm formation and antifungal resistance (8,10).

Amphotericin B and triazole antifungal agents are usually used for the treatment of trichosporonosis (1). Previous studies have reported that amphotericin B has inadequate fungicidal activity and limited *in vivo* activity with evidence of *in vitro* resistance (11). Triazole drugs, particularly voriconazole, are effective for treatment (12,13). Moreover, echinocandins, another drug group, are naturally ineffective against *Trichosporon* species (14-16). Thus, the present study aimed to determine the susceptibility of 100 *T. asahii* strains, isolated from urine samples, to various antifungal agents.

METHODS

Non-Invasive Research Ethics Committee approval was obtained from Haydarpasa Numune Education and Research Hospital (02.09.2019, HNHEAH-KAEK 2019/103-955). Among the 1,442 urine samples sent to the Central Laboratory of the Department of Public Hospital Services-2 in İstanbul between 2015 and 2016 that yielded yeast on culture, *Candida* species were detected in 1,332 (92.3%) samples, *T. asahii* in 106 samples (7.3%) and other yeasts in four samples (0.2%).

Identification was performed using the matrix-assisted laser desorption ionization-time of flight mass spectrometry-ITEK MS IVD V.2 (Bio-Mérieux, Marcy l'Etoile, France) automated system-as well as conventional methods (macroscopic and microscopic morphologies, appearance on corn meal agar with Tween 80, and urease positivity). Isolates were stored at -80 °C until the time of analysis and revived with two passages in Sabouraud dextrose agar.

Broth microdilution is standardized only for *Candida* and *Cryptococcus* species on CLSI M27-A3, which is intended for antifungal susceptibility testing; however, similar to previous studies, (3,4,9) our study investigated the *in vitro* susceptibility profiles of *T. asahii* for antifungal agents according to CLSI M27-A3 (17). Only the minimum inhibitory concentration (MIC) values obtained were specified because clinical thresholds of antifungals for the genus *Trichosporon* are still unestablished. Antifungal agents used in the study included amphotericin B (Sigma Chemical Co., St. Louis, MO, USA), fluconazole (Sigma Chemical Co.), voriconazole (Sigma Chemical Co.), itraconazole (Sigma Chemical Co.), posaconazole (Sigma Chemical Co.), and isavuconazole (Toronto Research). Microdilution plates were prepared with a final antifungal concentration of 32-0.06 µg/L for fluconazole; 16-0.03 µg/L for amphotericin B and itraconazole; 8-0.015 µg/L for voriconazole, posaconazole, and micafungin; and 4-0.008 µg/L for isavuconazole. The experiment was repeated twice for each strain. *C. krusei* ATCC 6258 and *C. parapsilosis* ATCC 22019 were used as quality control strains. The yeast suspensions resulted in concentrations of 2.5×10^3 cells/mL, and MIC was defined as the lowest antifungal concentration capable of promoting a 50% inhibition for azoles and 90% for amphotericin B at the end of 24 and 48 hours.

RESULTS

Among the 100 *T. asahii* strains isolated from the urine samples, 68 (68%) were isolated from male and 32 (32%) from female patients, and 66 (66%) of the total were from patients aged ≥70 years. The mean age of the patients was 69.94 (±20.30164) years. Among the 82 patients admitted in the ICU, 56 (68%) were male and 26 were female, and 68% were aged 70 and above. Table 1 presents the MIC ranges, MIC_{50}, MIC_{90}, and geometric mean values of isolates against amphotericin B, micafungin, and the five azole antifungal agents. The growth evaluation at 24 h revealed that most of the strains (89%) had a MIC value of ≥1 µg/mL for amphotericin B, while the rate was 96% at 48 h. Azole antifungal agents, including voriconazole, itraconazole, posaconazole, and isavuconazole, showed similar and low

Table 1. Results of *in vitro* susceptibility tests for *Trichosporon* asahii strains

	MIC (µg/mL) at 24 h				MIC (µg/mL) at 48 h			
Drug	MIC range	MIC_{50}	MIC_{90}	GM	MIC range	MIC_{50}	MIC_{90}	GM
Amphotericin B	0.25-2	1	2	0.99	0.5-4	2	2	1.81
Fluconazole	0.25-16	2	8	1.93	0.25-32	2	8	2.1
Voriconazole	≤0.015-1	0.06	0.12	0.05	≤0.015-1	0.06	0.12	0.06
Itraconazole	0.03-2	0.12	0.25	0.13	0.012-2	0.12	0.25	0.14
Posaconazole	≤0.015-0.5	0.25	0.5	0.18	0.012-1	0.25	1	0.18
Isavuconazole	≤0.008-0.5	0.12	0.25	0.09	≤0.008-2	0.12	0.25	0.12
Micafungin	>8	>8	>8	-	>8	>8	>8	-

GM: Geometric mean, MIC: Minimal inhibitory concentration

MIC values at both time points, while the MIC values for fluconazole were higher than those for other azole agents. The MIC values of all strains for micafungin were >8 mg/L Overall, *T. asahii* colonies became more prominent, and MIC values were more accurately determined at 48 h.

DISCUSSION

Infections caused by *Trichosporon* species often arise from endogenous flora, and the risk of such infections increases especially in patients with immunosuppression or in patients admitted in the ICU due to facilitating factors such as microbial translocation through the gastrointestinal mucosa and presence of vascular or urinary catheters (1). In a previous study, the prevalence of UTIs caused by *Trichosporon* in the ICU in a two-year period was 6% and the mortality rate was 20%. The prevalence was higher among men (65%) and individuals aged >70 years (55%) (6).

Among *Trichosporon* species, *T. asahii* is the most common cause of UTIs (4,9). *T. asahii* is an emergent pathogen in older patients with urinary catheter (12). Our study also identified *T. asahii* as the most commonly isolated species, with prevalence being higher among patients in the ICU (82%) and in male patients (68%). Furthermore, 66% of such patients were ≥70 years. Although UTIs are typically more common in women because of their anatomical structure (short urethra, vagina-anus proximity, etc.), (6) those caused by the genus *Trichosporon* were more common among men in our patient population, consistent with some other studies (6,12).

Triazole antifungal agents and amphotericin B are usually used for the treatment of *Trichosporon* infections (1). Previous studies have reported that amphotericin B has inadequate fungicidal activity against some *Trichosporon* strains and has limited *in vivo* activity along with evidence of *in vitro* resistance (11). Susceptibility test results vary from study to study. There are reports of low MIC (0.06-1) values, (8) as well as high MIC values (14). Although the fungus appears to be susceptible to amphotericin B *in vitro*, *in vivo* resistance may develop through a biofilm layer formed by the *Trichosporon* species; as a result, the desired effect is not observed (13). In our study, the MIC value for amphotericin B was ≥1 µg/mL in 89% and 96% of the strains at 24 h and 48 h, respectively.

Studies have reported that triazole antifungal agents, particularly voriconazole, are superior to amphotericin B in terms of efficacy in trichosporonosis treatment, and this group of agents are more commonly preferred for treatment (13,16). That said, there are reports of fatal pediatric cases (18) and treatment failures due to *T. asahii* infection, despite treatment with amphotericin B and voriconazole (19,20). In addition to the antifungal susceptibility of the agent, the patient's immunity system and neutrophil count play an important role in treatment success (21).

The 2014 clinical guidelines for the diagnosis and management of rare invasive yeast infections drawn up by the European Society for Clinical Microbiology and Infectious Diseases recommends the use of triazoles, particularly voriconazole, for the treatment of invasive infections caused by *T. asahii*. (15) Studies that compared the *in vitro* efficacy of triazole antifungal agents against *T. asahii* strains have reported fluconazole as the triazole antifungal agent with the lowest activity, whereas voriconazole demonstrated the highest activity. Other triazole antifungal agents, such as itraconazole, posaconazole, and isavuconazole, showed comparable activity (3,4,14,16,22,23) The findings of the present study were consistent with the results of such studies. To the best of our knowledge, only a few studies have investigated the susceptibility of the genus *Trichosporon* to isavuconazole, which is the newest member of triazole antifungals. The MIC_{50}-MIC_{90} values of

Table 2. ***In vitro*** **antifungal susceptibility test results of** ***Trichosporon asahii*** **isolates (µg/mL, 48 h), as reported by previous studies**

Authors	Number of isolates	Drugs	MIC range	MIC_{50}	MIC_{90}	GM
Montaya et al. (14)	39	AMB	0.25->16	2	4	1.84
		FLZ	0.12-16	0.5	1	0.78
		VOR	0.03-1	0.03	0.03	0.04
		POS	0.03-0.5	0.06	0.25	0.08
		MICA	>8	>8	>8	ND
Francisco et al. (4)	273	AMB	0.032-64	2	32	ND
		FLZ	0.25-64	2	8	ND
		VOR	0.03-2	0.06	0.125	ND
		POS	0.03-2	0.25	0.5	ND
Hazırolan et al. (22)	90	FLZ	0.5-16	4	8	3.24
		ITR	0.12-1	0.25	1	0.37
		VOR	≤0.015-0.25	0.06	0.12	0.06
		POS	0.06-1	0.25	0.5	0.25
		ISA	≤0.015-0.5	0.12	0.25	0.1
Kalkanci et al. (23)	87	FLZ	4-64	8	16	13.66
		ITR	0.25-2	1	2	0.985
Guo et al. (3)	108	AMB	0.125-4	1	2	1.36
		FLZ	0.5-512	4	8	3.56
		ITR	0.25-32	0.5	1	0.48
		VOR	0.03-16	0.064	0.25	0.09
		MICA	>8	>8	>8	>8
		CAS	>8	>8	>8	>8

FLZ: Fluconazole, ITR: Itraconazole, VOR: Voriconazole, POS: Posaconazole, ISA: Isavuconazole, CAS: Caspofungin, MICA: Micafungin, AMB: Amphotericin B, ND: Not determined, GM: Geometric mean, MIC: Minimal inhibitory concentration

clinical *T. asahii* isolates for isavuconazole, were found to be as follows: Hazirolan et al. (22) (n=90), 0.125-0.25 µg/mL; Thompson et al. (24) (n=40), 0.125 µg/mL; and the present study, 0.12-0.25 µg/mL, which is consistent with the previous data. Table 2 presents the *in vitro* susceptibility test results of *T. asahii* strains to several antifungal agents after 48 h of incubation, as reported in various studies.

Echinocandins, which are another group of antifungal agents, have demonstrated limited and inadequate *in vitro* activity against *Trichosporon* species (15,25). The MIC values for all strains against micafungin were >8 mg/L in the present study. Patients developing breakthrough invasive trichosporonosis while undergoing echinocandin therapy were also reported. Therefore, the risk of breakthrough infections of *Trichosporon* should not be ignored in patients with high risk status undergoing empirical or prophylactic therapy with echinocandins (16,25,26).

The generalization of the study's results is limited by the lack of differentiation between infection and colonization in patients; as a result, isolates deemed as potential causes are being considered as "related to the clinical picture." Standardization is required to differentiate between colonization and infection by *Trichosporon* species, particularly among patients in the ICU.

CONCLUSION

In conclusion, previous studies have identified various susceptibilities to antifungal agents and have shown that *in vitro* activity does not always correlate with efficacy *in vivo*. Our study established that voriconazole, an azole antifungal agent, was the most effective antifungal against *T. asahii* isolates *in vitro*. Considering the high MIC values, breakthrough infections of *Trichosporon* should be considered in patients with high risk status receiving

empirical or prophylactic therapy of echinocandin or fluconazole.

ETHICS

Ethics Committee Approval: The study were approved by the Haydarpasa Numune Education and Research Hospital of Local Ethics Committee (Protocol number: HNHEAH-KAEK 2019/103-955).

Informed Consent: Consent form was filled out by all participants.

Authorship Contributions

Surgical and Medical Practices: D.T., Concept: D.T., Design: D.T., S.A., Data Collection or Processing: D.T., Analysis or Interpretation: D.T., A.B., Literature Search: F.Ö., Ş.D.D., Writing: D.T., A.B.,

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

REFERENCES

1. Colombo AL, Padovan AC, Chaves GM. Current knowledge of Trichosporon spp. and Trichosporonosis. Clin Microbiol Rev 2011;24:682-700.
2. Liu XZ, Wang QM, Göker M, Groenewald M, Kachalkin AV, Lumbsch HT, et al. Towards an integrated phylogenetic classification of the Tremellomycetes. Stud Mycol 2015;81:85-147.
3. Guo LN, Yu SY, Hsueh PR, Al-Hatmi AMS, Meis JF, Hagen F, et al. Invasive Infections Due to Trichosporon: Species Distribution, Genotyping, and Antifungal Susceptibilities from a Multicenter Study in China. J Clin Microbiol 2019;57:e01505-18.
4. Francisco EC, de Almeida Junior JN, de Queiroz Telles F, Aquino VR, Mendes AVA, de Andrade Barberino MGM, et al. Species distribution and antifungal susceptibility of 358 Trichosporon clinical isolates collected in 24 medical centres. Clin Microbiol Infect 2019;25:909.e1-909.e5.
5. Urs TA, Kadiyala V, Deepak S, Karthik MK. Catheter associated urinary tract infections due to Trichosporon asahii. J Lab Physicians 2018;10:464-70.
6. Mattede Md, Piras C, Mattede KD, Ferrari AT, Baldotto LS, Assbu MS. Urinary tract infections due to Trichosporon spp. in severely ill patients in an intensive care unit. Rev Bras Ter Intensiva 2015;27:247-51.
7. Bentubo HD, Gompertz OF. Effects of temperature and incubation time on the in vitro expression of proteases, phospholipases, lipases and DNases by different species of Trichosporon. Springerplus 2014;3:377.
8. Sun W, Su J, Xu S, Yan D. Trichosporon asahii causing nosocomial urinary tract infections in intensive care unit patients: genotypes, virulence factors and antifungal susceptibility testing. J Med Microbiol 2012;61:1750-7.
9. Almeida AA, Crispim Bdo A, Grisolia AB, Svidzinski TI, Ortolani LG, Oliveira KM. Genotype, antifungal susceptibility, and biofilm formation of Trichosporon asahii isolated from the urine of hospitalized patients. Rev Argent Microbiol 2016;48:62-6.
10. Iturrieta-González IA, Padovan AC, Bizerra FC, Hahn RC, Colombo AL. Multiple species of Trichosporon produce biofilms highly resistant to triazoles and amphotericin B. PLoS One 2014;9:e109553.
11. Walsh TJ, Melcher GP, Rinaldi MG, Lecciones J, McGough DA, Kelly P, et al. Trichosporon beigelii, an emerging pathogen resistant to amphotericin B. J Clin Microbiol 1990;28:1616-22.
12. Treviño M, García-Riestra C, Areses P, García X, Navarro D, Suárez FJ, et al. Emerging Trichosporon asahii in elderly patients: epidemiological and molecular analysis by the DiversiLab system. Eur J Clin Microbiol Infect Dis 2014;33:1497-503.
13. Tanyildiz HG, Yesil S, Toprak S, Candir MO, Sahin G. Two Case Presentations Infected by Trichosporon asahii and Treated with Voriconazole Successfully. Case Rep Infect Dis 2015;2015:651315.
14. Montoya AM, Sánchez González A, Palma-Nicolás JP, Gómez-Treviño A, González JG, González GM. Genotyping, extracellular compounds, and antifungal susceptibility testing of Trichosporon asahii isolated from Mexican patients. Med Mycol 2015;53:505-11.
15. Arendrup MC, Boekhout T, Akova M, Meis JF, Cornely OA, Lortholary O, et al. 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.
16. de Almeida Júnior JN, Hennequin C. Invasive Trichosporon Infection: a Systematic Review on a Re-emerging Fungal Pathogen. Front Microbiol 2016;7:1629.
17. CLSI. Reference method for broth dilution antifungal susceptibility testing of yeasts Approved standard-third edition. Wayne, PA: Clinical and Laboratory Standards Institute; April 2008.
18. Thibeault R, Champagne M, de Repentigny L, Fournet JC, Tapiero B, Moghrabi A, et al. Fatal disseminated Trichosporon asahii infection in a child with acute lymphoblastic leukemia. Can J Infect Dis Med Microbiol 2008;19:203-5.
19. Kurnaz F, Kaynar L, Doğan S, Eser B, Metan G. Treatment Failure of Disseminated Trichosporon asahii Infection with Voriconazole in a Patient with Acute Myeloid Leukemia. Acta Oncol Turc 2010;43:32-5.
20. Chen J, Chen F, Wang Y, Yang LY, Miao M, Han Y, et al. Use of combination therapy to successfully treat breakthrough Trichosporon asahii infection in an acute leukemia patient receiving voriconazole. Med Mycol Case Rep 2014;6:55-7.
21. Hosokawa K, Yamazaki H, Mochizuki K, Ohata K, Ishiyama K, Hayashi T, et al. Successful treatment of Trichosporon fungemia in a patient with refractory acute myeloid leukemia using voriconazole combined with liposomal amphotericin B. Transpl Infect Dis 2012;14:184-7.
22. Hazirolan G, Canton E, Sahin S, Arikan-Akdagli S. Head-to-head comparison of inhibitory and fungicidal activities of fluconazole, itraconazole, voriconazole, posaconazole, and isavuconazole against clinical isolates of Trichosporon asahii. Antimicrob Agents Chemother 2013;57:4841-7.
23. Kalkanci A, Sugita T, Arikan S, Yucesoy M, Ener B, Otag F, et al. Molecular identification, genotyping, and drug susceptibility of the basidiomycetous yeast pathogen Trichosporon isolated from Turkish patients. Med Mycol 2010;48:141-6.
24. Thompson GR 3rd, Wiederhold NP, Sutton DA, Fothergill A, Patterson TF. In vitro activity of isavuconazole against Trichosporon, Rhodotorula, Geotrichum, Saccharomyces and Pichia species. J Antimicrob Chemother 2009 Jul;64:79-83.
25. Yang MF, Gao H, Li LL . A fatal case of Trichosporon asahii fungemia and pneumonia in a kidney transplant recipient during caspofungin treatment. Ther Clin Risk Manag 2014;10:759-62.
26. Liao Y, Hartmann T, Zheng T, Yang RY, Ao JH, Wang WL. Breakthrough trichosporonosis in patients receiving echinocandins: case report and literature review. Chin Med J (Engl) 2012;125:2632-5.