

Catheter-Associated *Rhodotorula mucilaginosa* Fungemia in an Immunocompetent Host

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Rhodotorula species live in the environment, but can also colonize human epithelium, as well as respiratory, and gastrointestinal tracts. Reports of infection, especially in the past 2 decades, have noted increasing numbers of *Rhodotorula* infections, particularly in immunocompromised hosts, leading it to be considered emerging opportunistic pathogen. The major risk factors for infection were prolonged use of central venous catheters in patients with hematological and solid malignancies who are taking corticosteroids or cytotoxic drugs. Herein, we report a case of catheter-associated fungemia due to *R. mucilaginosa* in an immunocompetent host. The patient was admitted to the intensive care unit with mechanical ventilation for treatment of community-acquired pneumonia. After 10 days, the patient developed new-onset fever confirmed to be a result of catheter-associated blood-stream infection by *R. mucilaginosa*. It was successfully treated by catheter removal and intravenous amphotericin B.

Key Words: Fungemia, *Rhodotorula*, Catheter-associated blood-stream infection

Introduction

Rhodotorula species have traditionally been considered as one of common non-virulent environmental inhabitant [1]. *Rhodotorula* species are airborne organisms that may be present on the skin and in sputum, urine, and feces. However, it has emerged as an opportunistic pathogen, particularly in immunocompromised hosts. It has been implicated as a cause of meningitis, endocarditis, ventriculitis, peritonitis, and keratitis [2]. Most infections caused by *Rhodotorula* species have been associated with intravenous catheter in patients with solid tumors, chronic renal failure, lymphoproliferative

disease, and acquired immunodeficiency syndrome [3-6]. Relatively few cases of *R. mucilaginosa* fungemia in immunocompetent hosts have been reported [7, 8]. Here, we report a case of catheter-associated fungemia due to *R. mucilaginosa* in an immunocompetent host.

Case Report

A 77-year-old man with a history of diabetes, hypertension, and Parkinson's disease developed new-onset fever 10 days after admission at the intensive care unit of our hospital. He

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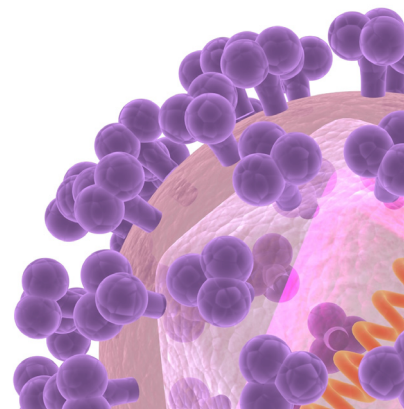
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was initially diagnosed with community-acquired pneumonia at right lower lung, and received ceftriaxone and azithromycin as empirical intravenous antibiotics. Because he was in a hypoxic state, he was transferred to the intensive care unit and started on mechanical ventilation. We inserted a central venous catheter for monitoring the central venous pressure and total parenteral nutrition. Six days after admission, a chest radiograph showed diffuse, peripherally located reticulonodular infiltrates in both lung fields. *Pseudomonas aeruginosa* was isolated in the sputum. We diagnosed the patient with ventilator-associated pneumonia and switched the antibiotic regimen to piperacillin-tazobactam. Following the modified treatment, the patient's fever decreased and other laboratory parameters stabilized. Ten days after admission, new-onset fever developed. The patient's vital signs were as follows: temperature was 38.4°C, pulse rate was 90 beats/min, respiratory rate was 24 breaths/min, and blood pressure was 130/80 mmHg. Further laboratory evaluation demonstrated the following results: white blood cell count 6,090/mm³ (neutrophils 86.4%), hemoglobin was 8.6 g/dL, platelet count was 119,000/mm³, blood urea nitrogen was 30 mg/dL, creatinine was 1.8 mg/dL, aspartate aminotransferase was 181 U/L and alanine aminotransferase was 81 IU/L. Two sets of blood culture were drawn, from peripheral venipuncture and the central venous catheter. After 72 hours, both blood culture sets had confirmed fungal growth with a yeast form. Blood cultures drawn from the central venous catheter demonstrated positive results 3 hours earlier than the peripheral cultures. We diagnosed the patient with central venous catheter-associated blood-stream infection and started intravenous fluconazole (400 mg/day) and removed the catheter. The yeast was subsequently subcultured on Sabouraud dextrose agar, producing multiple colonies. They were moist, glistening, smooth to mucoid and salmon pink to coral red color. Gram staining revealed budding yeast cells, which were short, ovoid, 2-6 µm in diameter and arranged in short chains and clusters. The organism was urease-positive and did not ferment conventional sugars. The isolate was identified as *R. mucilaginosa* on the basis of these characteristics and by an API 20C AUX system. (bioMerieux, Marcy l'Etoile, France). In addition, we identified the isolate using sequences of the D1/D2 domain of the large subunit (LSU) rRNA. Portions of the LSU rRNA gene were amplified using the primer sets LSU-F (5'-GCA TAT CAA TAA GCG GAG GAA AAG-3') and LSU-R (5'-GGT CCG TGT TTC AAG ACG-3') [9]. Unambiguously determined sequences (559 bp) were compared with the GenBank public database, using the BLASTn program (<http://blast.ncbi.nlm.nih.gov/>

Blast.cgi). The LSU rRNA gene sequence of the isolate showed 100% similarity with *R. mucilaginosa* ATCC32736T followed by 96.7% with *Rhodospiridium sphaerocarpum* SJ105 (AY953966). Thus, we could confirm that the isolate was *R. mucilaginosa*.

After 5 days, we changed fluconazole to amphotericin B deoxycholate. New sets of blood culture drawn 48 hours later were also positive for yeast, confirmed as *R. mucilaginosa*. After 3 days of amphotericin B treatment, we switched the patient to liposomal amphotericin B because he developed azotemia. The patients responded to this treatment; fever resolved and blood culture result converted to negative. Liposomal amphotericin was continued for 10 days and followed by fluconazole for an additional 14 days. After 34 days of additional hospitalization, he was discharged to a long-term care facility.

Discussion

Rhodotorula is a member of the basidiomycetous yeast genus, which produces mucoid colonies with a characteristic carotenoid pigment ranging from yellow to red. These organisms are frequently reported as contaminants in culture plates or medical equipment because of their ubiquitous existence in the natural environment, and have been known to cause nosocomial pseudoepidemics [10]. The first case of *Rhodotorula* species fungemia was reported in 1960 by Louria in a patient with endocarditis [11]. Subsequently, for the last two decades, the number of *Rhodotorula* infections has been increasing through a wider use of intensive treatments and central venous catheters. Studies of fungemia have demonstrated the incidence of *Rhodotorula* to be between 0.5 and 2.3% in the USA and Europe [12]. In Korea, a single center has reported a *Rhodotorula* fungemia incidence rate of 2.3% (5 cases) among all patients with fungemia, but the causative species were not identified [13]. In addition, central venous catheter-associated *R. rubra* fungemia in a leukemia patient, *R. mucilaginosa* peritonitis in a neonate undergoing continuous ambulatory peritoneal dialysis, and cases of *R. glutinis* peritonitis have been reported, likely related an increasing population of immunocompromised patients with chronic indwelling catheters that led to infections with this organism [3, 14, 15]. To the best of our knowledge, this is the first reported case of *R. mucilaginosa* fungemia occurring in an immunocompetent host in Korea.

R. mucilaginosa has been reported to cause fungemia, sepsis, endocarditis, meningitis, ventriculitis, endophthalmitis, keratitis, and peritonitis in immunocompromised hosts [16,

17]. However, most of the cases of infection due to *Rhodotorula* in humans were fungemia associated with central venous catheter use. *R. mucilaginosa* was responsible for most cases, followed by *R. glutinis*. The major risk factors were prolonged use of central venous catheters in patients with hematological and solid malignancies, who are taking corticosteroids or cytotoxic drugs [5]. Further, *R. mucilaginosa* fungemia in an immunocompetent, critically ill patient has been reported [7]. Some studies have been reported a correlation between *Rhodotorula* fungemia and the duration of catheter use [18, 19]. Association with catheter use could be attributed to *Rhodotorula* biofilm formation, similar to biofilms found in *Candida* species. Recently published data demonstrated *Rhodotorula* species' ability to form biofilms, in which the *R. mucilaginosa* and *R. minuta* were the best biofilm-producing species among *Rhodotorula*, and clinical isolate were better at forming biofilm than isolates derived from the environment [20]. Previous antibiotic use, parenteral nutrition, and abdominal surgery were also found to be risk factors of *Rhodotorula* fungemia. These factors might explain why most of the reported cases also entailed intensive care unit admission [8]. Our patient was immunocompetent patient but he was also in the intensive care unit and had used a central venous catheter as well as broad-spectrum antibiotics. These factors may have contributed to this unusual fungemia. We have demonstrated that immunocompetent host are also susceptible to these infections during long-term venous catheterization and broad-spectrum antibiotic therapy.

While there are no evidence-based guidelines for the management of this uncommon infection, previous cases have been managed successfully with removal of the indwelling catheter and appropriate antifungal agents. Susceptibility studies of *Rhodotorula* species have shown that all tested isolates were susceptible to amphotericin B (MIC range, 0.125 to 1.6 µg/mL), itraconazole (MIC range, 0.25 to 12.8 µg/mL) and resistant to fluconazole (MICs of ≥ 32 µg/mL) [10]. Further, it has poor activity of caspofungin and micafungin [19]. Because of high-level fluconazole resistance and high itraconazole MICs, these drugs are not recommended as treatment options for *Rhodotorula* infections. In our case, we also switched fluconazole to amphotericin B deoxycholate after we confirmed the fungal pathogen as *R. mucilaginosa*, however we could not confirm antifungal susceptibility before starting the course of treatment.

The results of this case demonstrate that before selecting empirical antifungal agents, we should consider the possibility of yeast pathogens such as *Rhodotorula*, and *Candida*, in

catheter-associated blood-stream infections in immunocompetent hosts.

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References

1. Fell JW, Boekhout T, Fonseca A, Scorzetti G, Stazzell-Tallman A. Biodiversity and systematics of basidiomycetous yeasts as determined by large-subunit rDNA D1/D2 domain sequence analysis. *Int J Syst Evol Microbiol* 2000;50:1351-71.
2. Pamidimukkala U, Challa S, Lakshmi V, Tandon A, Kulkarni S, Raju SY. Sepsis and meningoencephalitis due to *Rhodotorula glutinis* in a patient with systemic lupus erythematosus, diagnosed at autopsy. *Neurol India* 2007;55:304-7.
3. Chung JW, Kim BN, Kim YS. Central venous catheter-related *Rhodotorula rubra* fungemia. *J Infect Chemother* 2002;8:109-10.
4. Lo Re V, Fishman NO, Nachamkin I. Recurrent catheter-related *Rhodotorula rubra* infection. *Clin Microbiol Infect* 2003;9:897-900.
5. Lunardi LW, Aquino VR, Zimmerman RA, Goldani LZ. Epidemiology and outcome of *Rhodotorula fungemia* in a tertiary care hospital. *Clin Infect Dis* 2006;43:e60-3.
6. Tuon FF, de Almeida GM, Costa SF. Central venous catheter-associated fungemia due to *Rhodotorula* spp. --a systematic review. *Med Mycol* 2007;45:441-7.
7. Villar JM, Velasco CG, Delgado JD. Fungemia due to *Rhodotorula mucilaginosa* in an immunocompetent, critically ill patient. *J Infect Chemother* 2012;18:581-3.
8. Spiliopoulou A, Anastassiou ED, Christofidou M. *Rhodotorula fungemia* of an intensive care unit patient and review of published cases. *Mycopathologia* 2012;174:301-9.
9. Kurtzman CP, Robnett CJ. Phylogenetic relationships among yeasts of the 'Saccharomyces complex' determined from multigene sequence analyses. *FEMS Yeast Res* 2006;3:417-32.
10. Galán-Sánchez F, García-Martos P, Rodríguez-Ramos C, Marín-Casanova P, Mira-Gutiérrez J. Microbiological characteristics and susceptibility patterns of strains of *Rhodotorula* isolated from clinical samples. *Mycopathologia*

- 1999;145:109-12.
11. Louria DB, Greenberg SM, Molander DW. Fungemia caused by certain nonpathogenic strains of the family Cryptococcaceae. Report of two cases due to *Rhodotorula* and *Torulopsis glabrata*. N Engl J Med 1960;263:1281-4.
 12. Krcmery V, Laho L, Huttova M, Ondrusova A, Kralinsky K, Pevalova L, Dluholucky S, Pisarcikova M, Hanzen J, Filka J, Sejnova D, Lisková A, Purgelová A, Szovenyová Z, Koren P. Aetiology, antifungal susceptibility, risk factors and outcome in 201 fungaemic children: data from a 12-year prospective national study from Slovakia. J Med Microbiol 2002;51:110-6.
 13. Choi YH, Park YS, Jo JH, Hong SK, Chang KH, Song YG, Kim JM. Clinical evaluation of the incidence and outcome of patient with fungemia. Korean J Infect Dis 2000;32:373-9.
 14. Hong HK, Kim YM, Kim SD, Bae CW, Lee HJ. A case of *Rhodotorula mucilaginosa* peritonitis undergoing continuous ambulatory peritoneal dialysis in a neonate with acute renal failure. J Korean Soc Neonatol 2003;10:94-8.
 15. Park JH, Yang CW, Jin DC, Shin WS, Park IS, Chang YS, Bang BK. *Rhodotorula glutinis* peritonitis in patient undergoing continuous ambulatory peritoneal dialysis. Korean J Nephrol 1992;11:85-7.
 16. Tuon FF, Costa SF. *Rhodotorula* infection. A systematic review of 128 cases from literature. Rev Iberoam Micol 2008;25:135-40.
 17. Shinde RS, Mantur BG, Patil G, Parande MV, Parande AM. Meningitis due to *Rhodotorula glutinis* in an HIV infected patient. Indian J Med Microbiol 2008;26:375-7.
 18. Kiehn TE, Gorey E, Brown AE, Edwards FF, Armstrong D. Sepsis due to *Rhodotorula* related to use of indwelling central venous catheters. Clin Infect Dis 1992;14:841-6.
 19. Zaas AK, Boyce M, Schell W, Lodge BA, Miller JL, Perfect JR. Risk of fungemia due to *Rhodotorula* and antifungal susceptibility testing of *Rhodotorula* isolates. J Clin Microbiol 2003;41:5233-5.
 20. Nunes JM, Bizerra FC, Ferreira RC, Colombo AL. Molecular identification, antifungal susceptibility profile, and biofilm formation of clinical and environmental *Rhodotorula* species isolates. Antimicrob Agents Chemother 2013; 57:382-9.