

[CASE REPORT]

Asymptomatic Fungemia Due to *Rhodotorula* spp. Caused by a Subcutaneously Implanted Central Venous Port Catheter

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Abstract:

A 66-year-old man was admitted to our hospital for gastrointestinal perforation. He had a history of surgery and chemotherapy for colorectal cancer and had a subcutaneously implanted central venous port catheter. After surgery for gastrointestinal tract perforation, he developed an intra-abdominal abscess, which was treated with broad-spectrum antimicrobial agents and improved. Following this improvement, *Rhodotorula* spp. was detected in a blood culture and at the catheter tip. He was asymptomatic despite having fungemia. His condition improved after the removal of the catheter and the administration of antifungal drugs. Fungemia due to *Rhodotorula* spp. is rare, and asymptomatic fungemia is even rarer.

Key words: fungemia, asymptomatic, *Rhodotorula*, central venous port catheter

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Introduction

In recent years, with the development of new immunosuppressive drugs and biologic therapy, advances in cancer treatment, and the increasing use of intravascular catheters and implantable devices, various uncommon fungal infections are being encountered. *Rhodotorula* spp. is a yeast-like fungus that can cause bacteremia in immunocompromised patients with indwelling catheters and is generally recognized as a rare fungal infection (1, 2).

We herein report a case of asymptomatic fungemia due to *Rhodotorula* spp. caused by a subcutaneously implanted central venous port catheter.

Case Report

The patient was a 66-year-old man (height, 170 cm; weight, 49 kg; body mass index, 16.9). Two years previously, he had undergone high anterior resection for rectal

cancer and right hemicolectomy for transverse colon cancer. After the surgery, a central venous port catheter had been inserted into the right internal jugular vein, and 12 courses of mFOLFOX-6 therapy had been administered.

He visited the hospital with complaints of abdominal pain and vomiting after eating. He was diagnosed with a gastrointestinal tract perforation after computed tomography (CT) showed intra-abdominal free air, and he subsequently underwent emergency surgery. The surgical findings included intestinal fluid in the abdomen, which was thought to be due to perforation; however, the site of perforation was unknown, so the surgery was completed after abdominal lavage. Eventually, he was diagnosed with small bowel perforation due to dietary ileus.

At two weeks after surgery, a fever and an increased inflammatory response were observed, and CT showed intra-abdominal abscess and peritonitis. Meropenem was started, and after 13 days of treatment, the patient's fever and inflammatory response showed improvement, and CT showed improvement of the intra-abdominal abscess and peritonitis;

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Table 1. Laboratory Data.

Hematology		Biochemistry	
Red blood cell count	398×10 ⁴ /μL	Total protein	6.6 g/dL
Hemoglobin	11.5 g/dL	Albumin	2.8 g/dL
Hematocrit	33.6 %	Total bilirubin	1.26 mg/dL
White blood cell count	5,280 /μL	AST	39 IU/L
Neutrophil	74 %	ALT	74 IU/L
Eosinophil	4 %	LDH	140 IU/L
Basocyte	0 %	ALP	862 IU/L
Lymphocyte	16 %	γGTP	124 IU/L
Monocyte	1 %	Urea nitrogen	22 mg/dL
Platelet count	19.0×10 ⁴ /μL	Creatinine	0.68 mg/dL
		Glucose	96 mg/dL
		Sodium	136.9 mEq/L
Serology		Potassium	3.86 mEq/L
CRP	0.26 mg/dL	Chloride	101.6 mEq/L
β-D glucan	<2.8 pg/mL		

CRP: C-reactive protein, AST: aspartate aminotransferase, ALT: alanine aminotransferase, LDH: lactate dehydrogenase, ALP: alkaline phosphatase, γGTP: gamma glutamyl transpeptidase, β-D glucan measured by Fujifilm/Wako assay

Table 2. Susceptibility Testing of *Rhodotorula* spp.

Amphotericin B	0.5	(μg/mL)
Flucytosine	0.5	
Fluconazole	>64	
Itraconazole	2	
Miconazole	8	
Micafungin	>16	
Voriconazole	4	
Casposfungin	16	

thus, the treatment was terminated.

Blood cultures taken for screening at the end of treatment showed yeast-like fungi. Blood cultures were performed in an aerobic bottle (BD BACTEC 23F Aerobic resin bottle P; Becton, Dickinson and Company, Franklin Lakes, USA) and an anaerobic bottle (BD BACTEC 21F Hemolytic type Anaerobic bottle P; Becton, Dickinson and Company) using the FX System (BD BACTEC; Becton, Dickinson and Company). Although there was no fever or elevated inflammatory response in the blood test (Table 1), micafungin administration was started due to the possibility of candidemia. However, yeast-like fungus was repeatedly detected in subsequent blood cultures (aerobic bottles). We considered the possibility of candidemia due to peritonitis, but since it was persistent candidemia, we thought that a catheter-associated infection had occurred. The yeast-like fungus was identified as *Rhodotorula mucilaginosa* using the API 20C AUX system (bioMérieux, Marcy-l'Étoile, France). To confirm the identification, mass spectrometry was performed using a MALDI Biotyper (Bruker, Billerica, USA). The isolate was identified as *R. mucilaginosa*. The score was 1.950, which is the genus level (a score of ≥2.00 represents high confidence; a score of 1.70-1.99 represents low confidence; and a score of <1.69 is considered unreliable). Antifungal susceptibility

testing was performed using Yeast-like fungi FP “Eiken” (Eiken Chemical, Tokyo, Japan) according to the Clinical and Laboratory Standards Institute (CLSI) document M27-A 3 (3) (Table 2).

Considering the possibility of catheter-associated infection due to *Rhodotorula* spp., the catheter was removed, and liposomal amphotericin B (L-AMB) was started. *Rhodotorula* spp. was also cultured from the tip of the removed catheter. We performed tests that ruled out endophthalmitis and endocarditis. A blood culture from three days after the start of L-AMB was negative. However, renal dysfunction appeared, and the administration of L-AMB had to be terminated after seven days. Thereafter, he was carefully monitored with blood cultures, but no relapse was observed.

Discussion

We experienced a case of asymptomatic fungemia due to *Rhodotorula* spp. that was caused by a subcutaneously implanted central venous port catheter. Our present report differs from previously reported cases in that the patient was asymptomatic despite the presence of fungemia. This suggests the importance of obtaining blood cultures regularly in patients with an implanted intravascular device, even when they are asymptomatic.

Rhodotorula spp. are yeast-like fungi that belong to the phylum Basidiomycota and are widely found in the environment in soil, waterways, and air. *Rhodotorula* spp. are characterized by the formation of pink colonies due to the production of carotenoids and may be involved in pink mold around water. In humans, it is a constituent of the normal human skin, mucosal surface (4). *R. mucilaginosa* is the most common species that can cause infection in humans, but other species, such as *R. glutinis* and *R. minuta*, are also known (5). Human infections mainly occur as bacteremia, meningitis, endocarditis, and peritonitis in immunocom-

promised patients, and catheter-related bloodstream infections are also frequently reported (6).

We considered the possibility that the blood culture results were contaminated; however, since it is unusual for fungi to be identified from blood cultures as a result of contamination (7), and since fungi were repeatedly identified from blood cultures and detected at the tip of the removed catheter, we considered the possibility of catheter-induced fungemia. Our search of the relevant literature yielded a limited number of reports on asymptomatic fungemia, due to species other than *Rhodotorula* spp. (8-11). There have been no reports on asymptomatic fungemia due to *Rhodotorula* spp.; thus, this is considered a valuable case. Vasquez et al. noted that asymptomatic fungemia may occur because the optimal growth temperature of the pathogen differs from the body temperature (11). Indeed, the optimal growth temperature for *Rhodotorula* spp. is 18-22°C, and the growth is reduced at temperatures above 33°C (12). In addition to the fact that the virulence of *Rhodotorula* spp. is considered low (13), its optimal growth temperature is lower than that of the human body, which may be why this case was asymptomatic.

According to the Centers for Disease Control and Prevention (CDC)/National Healthcare Safety Network (NHSN) definition (14), central line-associated bloodstream infections (CLABSI) are those with clinical symptoms, such as a fever, in addition to bacteriological detection. According to this definition, our patient did not have a CLABSI and was asymptomatic; therefore, the removal of the catheter alone was considered. However, the patient was in a state of persistent bacteremia, and since dissemination to multiple organs and the appearance of symptoms might have occurred in the future, treatment according to CLABSI was deemed necessary. There is a pediatric report suggesting an association between asymptomatic catheter-related bacteremia and right-sided infective endocarditis (15). Therefore, even in asymptomatic cases, it is considered necessary to use the same treatment as for CLABSI.

Treatment of CLABSI caused by *Rhodotorula* spp. is similar to that of CLABSI caused by *Candida* spp., and removal of the catheter is particularly important (16). It has been reported that the prognosis is poor when CLABSI caused by *Rhodotorula* spp. is treated by catheter removal alone (17). In the treatment of *Rhodotorula* spp., amphotericin B (AMPH) is considered the first choice of antifungal drug (18). Flucytosine has also been shown to be effective. It is generally resistant to echinocandins, unlike *Candida* spp. (19). When a yeast-like fungus is detected by Gram staining of blood cultures, as in this case, echinocandin is generally administered in consideration of *Candida* spp. fungemia, and caution should be exercised. *Rhodotorula* spp. also has a high minimum inhibitory concentration (MIC) to azoles (20), which is important, as susceptibility is often not expected. When AMPH is used, the associated side effects may make it impossible to continue administration, as in the present case. In addition, flucytosine is

difficult to use as a single agent because it tends to create resistance. Since there are only a limited number of antifungal drugs that can be used for *Rhodotorula* spp., there are no clinical breakpoints for drug susceptibility testing; thus, MICs is only a reference value. However, we consider it important to measure the MICs and confirm the drugs that may be used. Drug susceptibility testing in this case showed that AMPH and flucytosine had low MICs, while other antifungal drugs tended to have high MICs, suggesting that efficacy of azoles and micafungin may not be expected. Although the duration of antifungal treatment was short, we were fortunate to obtain a therapeutic effect with catheter removal and the short-term administration of antifungal drugs. After the interruption of treatment, the patient was carefully followed up with blood cultures, but no relapse was observed.

The number of patients in an immunosuppressed state and with subcutaneous central venous port catheter insertion will increase due to the aging of the population, the development of cancer treatments, and the development of immunotherapy. As a result, the chance of encountering rare fungal infections is likely to increase. It is important to note that *Candida* spp. are not the only yeast-like fungi to cause CLABSI. It may be important to perform blood culturing periodically for patients with intravascular devices, such as central venous catheters, as asymptomatic fungemia may occur.

The authors state that they have no Conflict of Interest (COI).

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