A Rare Case Report of Central Line-associated Bloodstream Infection Caused by Cryptococcus arboriformis

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Abstract

Cryptococcus arboriformis (C. arboriformis) is a novel Cryptococcus species belonging to the genus Trichosporonales. This novel species was identified definitively in 2007 using D1/D2 26S ribosomal DNA gene sequencing. In this article, we present a rare case of central line-associated bloodstream infection caused by C. arboriformis with successful treatment of this infection.

Key words: Cryptococcus arboriformis, rare species, central venous catheter-related bloodstream infection


Introduction

Cryptococcus arboriformis (C. arboriformis) is a novel Cryptococcus species belonging to the genus Trichosporonales. In 2007, this species was accurately identified using D1/D2 26S ribosomal DNA gene sequencing of a urine sample obtained from a patient with chronic renal failure. However, the pathogenicity remains unclear, and only one infection caused by this species has been reported to date (1, 2). In this article, we present a rare case report of central line-associated bloodstream infection caused by C. arboriformis with successful treatment of the infection.

Case Report

A 69-year-old Japanese woman with a stable status of rheumatoid arthritis and diabetes mellitus was admitted to our hospital due to septic shock complicating septic bursitis of the left elbow. Her medications included prednisolone at a dose of 7 mg/day, bucillamine at a dose of 200 mg/day and miglitol at a dose of 150 mg/day. On day 1, a central venous catheter (CVC) was inserted, and treatment was started with meropenem at a dose of 1 g every eight hours and vancomycin at a dose of 1 g every 12 hours for a final diagnosis of infectious endocarditis and septic bursitis of the left elbow caused by Methicillin-resistant Staphylococcus aureus (MRSA). The minimum inhibitory concentration (MIC) of vancomycin for MRSA isolated via blood culture was 2 μg/mL, as tested according to the broth dilution method. Starting on day 4, due to persistent bacteremia, meropenem was discontinued, and the antibiotic therapy was switched to daptomycin at a dose of 8 mg/kg/day. After switching to daptomycin, the patient’s condition gradually improved without the need for surgery, and her clinical course remained stable; however, on day 14, she developed a fever and chills.

On a physical examination, the patient’s blood pressure was 125/74 mm Hg, her pulse rate was 110 beats per minute, her temperature was 38.5°C, her respiratory rate was 24 breaths per minute and her peripheral arterial oxygen saturation was 97% while she breathed ambient room air. The results of the physical examination were unremarkable, except for mild abdominal distension. The laboratory data obtained on day 14 revealed a white blood cell (WBC) count of 9.900/μL with 88% neutrophils, 8% lymphocytes and 2% monocytes, a hemoglobin level of 10.2 mg/dL and a platelet count of 142,000/μL. Serum chemistry disclosed the following results: sodium= 143 mEq/L, potassium= 4.3 mEq/L, chloride= 105 mEq/L, blood urea nitrogen= 34.9 mg/dL, creatinine= 0.8 mg/dL, albumin= 2.4 g/dL, total protein= 6.4 g/dL, aspartate aminotransferase (AST)= 39 IU/L, alanine

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aminotransferase (ALT)= 51 IU/L, total bilirubin= 0.6 mg/dL, lactate dehydrogenase (LDH)= 279 IU/L, alkaline phosphatase= 404 U/L, C-reactive protein (CRP)= 7.5 mg/dL and HbA1c= 6.0%. The results of a urinalysis demonstrated no abnormalities.

On day 14, a blood culture was obtained, the CVC was removed and micafungin at a dose of 100 mg every 24 hours was added to the treatment regimen, as Gram staining of the catheter tip showed yeast-like organisms. In addition, the dose of daptomycin was continued, and a CVC was inserted in another site due to the difficulty of intravenous catheterization. On day 15, a blood culture of a sample obtained from the CVC showed positive growth of a yeast-like fungus, while the peripheral blood culture was negative. On day 18, yeast species was isolated from the CVC blood culture, Gram staining of the isolated colonies revealed yeast-like fungi (Fig. 1) and the colonies in the blood culture grown on Sabouraud agar were shiny and cream-colored (Fig. 2). In contrast, the patient showed negative test results for beta-D glucan and cryptococcal antigens as well as a urine culture, and obtaining a precise identification of the isolated organisms was difficult using the BacT/Alert 3D and API ID 32C systems (Sysmex bioMórieux, Tokyo, Japan). The patient’s fever persisted, and a sample for blood culture was obtained on day 18, which again showed CVC. On day 20, blood cultures of two sets of peripheral and central venous blood samples were found to be positive, and Gram staining revealed a yeast-like fungus once again. The colonies obtained from the blood cultures and the catheter tip removed on day 18 grown on Sabouraud agar were also shiny and cream-colored.

The patient was switched to treatment with liposomal amphotericin B at a dose of 3 mg/kg every 24 hours. The follow-up blood culture performed on day 22 was negative. She was successfully treated with a 17-day course of intravenous liposomal amphotericin B, and no evidence of relapse of infection was noted at the six-month follow-up.

After treatment, we performed molecular identification by sequencing the D1/D2 26S ribosomal DNA gene (1). The sequences were compared using the BLAST database (www.ncbi.nlm.nih.gov/BLAST), and all isolates derived from the blood and catheter tip were identified to be Cryptococcus arboriformis (100% homology with GenBank accession no. AB260936). Micafungin exhibited a MIC for the isolate of >16 μg/mL, while the MICs of amphotericin B, flucytosine, itraconazole and voriconazole were 2 μg/mL, 4 μg/mL, 0.06 μg/mL and 0.12 μg/mL, respectively, as measured using CLSI M27-A3.

**Discussion**

Cryptococcus infection, most commonly caused by *C. neoformans*, is considered to be one of the most serious fungal infections, especially in immunocompromised patients. Recently, the incidence of infections caused by *non-neoformans* cryptococci has increased; these microbes are generally considered to be non-pathogenic. For example, *C. laurentii* and *C. albidus* are responsible for 80% of reported cases of infection with *non-neoformans* cryptococci and *non-gattii* cryptococci (3). *C. arboriformis*, a novel *Cryptococcus* species belonging to the genus Trichosporonales and definitively identified in 2007, is a very rare causative organism of infections in humans (1). To the best of our knowledge, there is only one case of human infection reported in the literature. Im et al. reported a case of *C. arboriformis* peritonitis in a patient undergoing continuous ambulatory peritoneal dialysis (2). An accurate identification of this organism was achieved with D1/D2 26S ribosomal DNA gene sequencing of a urine sample obtained from a patient with chronic renal failure, although the pathogenicity remains unclear. The characteristics of this strain are similar to those of its closest relative, *C. haglerorum* (4). In the present case, we were able to definitively identify the isolated organism as *C. arboriformis* using D1/D2 26s ribosomal DNA gene sequencing, which has been demonstrated to be a useful method for making precise identifications (1); this method improves the accuracy of clinical microbiological identification by allowing for better identification of poorly described organisms, such as *C. arboriformis*. With respect to treatment, we consider that voriconazole and itraconazole are effective against *C. arboriformis* based on the results of
the MIC evaluation and the similar traits of the organism to those belonging to the genus Trichosporonales. Recent data regarding the susceptibility profile of non-\textit{neoformans} non-\textit{gattii} \textit{Cryptococcus} species show that amphotericin B is the most active agent \textit{in vitro}, while flucytosine and the candins are inactive and voriconazole,itraconazole and posaconazole are active against most isolates (5). In the present case, the patient was successfully treated with a 17-day course of liposomal amphotericin B. Based on the results of the susceptibility testing, micafungin was not active against \textit{C. arboriformis} in our patient. In general, the Infectious Diseases Society of America (IDSA) guidelines recommend catheter removal in patients with catheter-related bloodstream infection caused by yeast-like organisms (6). In the current case, we consider that removing the CVC may have played an important role in our ability to successfully control the infection. The pathogenicity of this organism remains unknown; therefore, further studies are needed to clarify the clinical characteristics of infections caused by \textit{C. arboriformis}.

In conclusion, we herein reported a case of central line-associated bloodstream infection caused by \textit{C. arboriformis} that was successfully controlled with antifungal therapy. To the best of our knowledge, this is the first case of isolation from the blood in a patient with bacteremia caused by \textit{C. arboriformis}. The causative organism was identified to be \textit{C. arboriformis} by sequencing the D1/D2 26S ribosomal DNA gene, and we conclude that \textit{C. arboriformis} may be a causative pathogen of septicemia and catheter-related bloodstream infection.

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

References