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CASE REPORT

Catheter-related fungemia caused by *Candida dubliniensis*

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Infections caused by *Candida dubliniensis* in humans are rare and have never been reported in Taiwan. We report two cancer patients with catheter-related fungemia due to *C. dubliniensis* infection in Taiwan. The two isolates were confirmed to the species level using an oligonucleotide array system and sequence analysis, and both showed high *in vitro* susceptibilities to nine antifungal agents. The catheters were removed, and both patients responded well to antifungal treatment. Although this type of infection is rare, physicians should consider *C. dubliniensis* as one of the possible pathogens causing catheter-related infections in Taiwan.

Introduction

Candida species are important causative agents of healthcare-associated infections, especially in critically ill patients with intravascular catheters, those on broad-spectrum antibiotics, those on mechanical ventilation, and those on immunosuppressive agents and parenteral nutrition.[1] *Candida albicans* remains the predominant cause of invasive candidiasis and accounts for more than 50% of all cases; however, the incidence of invasive candidiasis due to non-*albicans Candida* species such as *C. tropicalis*, *C. glabrata*, and *C. parapsilosis* is increasing.[2,3]

Candida dubliniensis was first characterized by Sullivan et al in 1995.[4] Since then, however, very few cases of

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candidiasis due to this rare pathogen have been reported. *C. dubliniensis* shares many features with *C albicans* and, therefore, can be misidentified in routine laboratory methods in clinical microbiology laboratory. Thus, the incidence of infection due to this causative pathogen may be underreported. In Taiwan, *C. dubliniensis* has only been reported in association with oropharyngeal carriage in HIV-infected patients.[5] In this report, we describe two cancer patients with catheter-related fungemia due to *C. dubliniensis* in Taiwan.

Case reports

Case 1

A 62-year-old woman with rheumatic heart disease status after mitral valve replacement and thyroid papillary carcinoma was admitted to the National Taiwan University Hospital because of congestive heart failure and progressive dyspnea. She was intubated for acute respiratory failure and was placed on dialysis. Several episodes of healthcare-associated infections developed during hospitalization for which she received piperacillin—tazobactam, ertapenem, and cefepime. One month later, a new onset of fever occurred, and ceftazidime was prescribed after collecting blood for culture. Five days later, blood cultures (Becton Dickinson Microbiology Systems, Sparks, MD, USA) from the central venous catheter (CVC) yielded *C. dubliniensis*. The CVC was removed, and intravenous amphotericin B (50 mg/day) for 14 days was added to the regimen to cover candidemia. Thereafter, there was no fever and repeated blood culture did not yield *Candida* spp.

Case 2

A 71-year-old man had received three courses of gemicitabin and cisplatin as treatment for bladder cancer. Two months after the final treatment, the patient presented with symptoms and signs of progressive bladder cancer. A radical cystectomy was performed. Approximately 8 days after the operation, the patient developed fever. Empirical therapy with ceftazidime was initiated but the patient responded to the therapy unsatisfactorily. Culture of peripheral blood and blood from the CVC yielded *C. dubliniensis*. The CVC was removed, and intravenous fluconazole (400 mg/day) was administered for 14 days. His clinical condition gradually improved, and the patient was discharged uneventfully after completing the full course of antibiotics.

The two isolates of *C. dubliniensis* were identified to the species level by conventional laboratory procedures and the Vitek Yeast Biochemical Card identification system (bioMérieux Vitek, Marcy l'Etoile, France) (bionumber 6102544061305370, 99% probability). An oligonucleotide array system targeting the internal transcribed spacer 1 and 2 region of the rRNA genes and sequence analysis of the amplified internal transcribed spacer region using the BLAST program confirmed that the isolates were indeed *C. dubliniensis* (GenBank accession no. HQ457430.1, 99% identity).[6] The MIC values of nine antifungal agents against the two *C. dubliniensis* isolates were determined by a commercial system with the broth microdilution method (Sensititre YeastOne, SYO; Trek Diagnostic Systems, West Sussex, UK). The two isolates were susceptible to fluconazole, voriconazole, itraconazole, caspofungin, micafungin, anidulafungin, and 5-flucytosine (Table 1).[7]

Discussion

C. dubliniensis can cause invasive infections, especially in immunocompromised patients. This rare pathogen has been reported to cause human infection in the United States, Australia, Europe, and Argentina. The prevalence of *C. dubliniensis* as the causative agent of candidiemia ranges from 0.96% in Argentina to approximately 2% in the United States and the United Kingdom.[8—12] To the best of our knowledge, these are the first two cases of fungemia due to *C. dubliniensis* in Taiwan. Both cases occurred in the same 2500-bed medical center during the period 2009—2010.

In this study, both cases were classified as healthcare-associated catheter-related bloodstream infections, and one of the patients had cancer during the episode of infection. In a study reported by Chen et al,[13] the majority of patients (19 of 22, 86%) with *C. dubliniensis* fungemia had healthcare-associated infections, and 79% of them had vascular access devices.

The clinical outcomes of patients with *C. dubliniensis* fungemia have not been well defined because of the limited number of cases. In one series of four patients with *C. dubliniensis* fungemia, one patient died as a consequence of this infection.[11] In another study, the 30-day crude mortality rate was 27.7% (5/18).[13] In the present study, both patients survived for 5 and 8 days, respectively, without any antifungal therapy and had favorable responses after antifungal treatment and removal of the catheters. These findings might indicate the potential low virulence of the organism. However, further large-scale studies are needed to better understand the clinical manifestations and prognosis of *C. dubliniensis* fungemia.

We tested the *in vitro* activity of nine antifungal agents against the two *C. dubliniensis* isolates. The MICs of the tested echinocandins were highest for capsofungin, and the MICs of the tested azoles were in the order voriconazole $<$ itraconzaole $<$ posaconazole $<$ fluconazole. The MIC values were in agreement with those reported previously[13] against 22 *C. dubliniensis* isolates. In that study, the MIC_{90} values of the tested azoles were in the order voriconazole (0.016 μg/mL) $<$ itraconzaole $=$ posaconazole (0.125 μg/mL) $<$ fluconazole (1.0 μg/mL). Based on the above-mentioned *in vitro* studies, azoles remain the drugs of choice to treat *C. dubliniensis* infections.

In conclusion, *C. dubliniensis* is an emerging pathogen that causes invasive infections, and it may play an important role in the clinical setting of bloodstream infections.[14] Healthcare-associated catheter-related bloodstream infections due to this pathogen may respond well to appropriate antifungal agent and catheter removal. The *in vitro* studies showed there was no resistance to antifungal agents but that azoles are effective against *C. dubliniensis*.

Table 1 Susceptibilities of two *C. dubliniensis* isolates causing catheter-related candidemia to nine antifungal agents

Antifungal agents	MIC (μg/mL)								
	Anidulafungin	Micafungin	Caspofungin	5-Flucytosine	Posaconazole	Voriconazole	Itraconazole	Fluconazole	Amphotericin B
Isolate 1 (Case 1)	0.03	0.015	0.06	≤0.06	0.03	≤0.008	0.03	0.25	0.25
Isolate 2 (Case 2)	≤0.015	0.03	0.12	≤0.06	0.03	≤0.008	≤0.015	0.5	≤0.12

Conflicts of interest

All contributing authors declare that they have no conflicts of interest.

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