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Peritoneal dialysis (PD) catheter-related peritonitis from *Aureobasidium pullulans* caused by poor caregiver's hand hygiene

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ABSTRACT

Catheter-related peritonitis is common but rarely caused by fungal infection. We report the first case of PD patients with catheter-related peritonitis form *Aureobasidium pullulans*, a black yeast-like dematiaceous fungus, and reviewing the relevant literatures. A potential cause of this infection is poor hand hygiene and improper fingernail care. The infection could be prevented if patient and caregiver strictly follow hand-washing protocols.

1. Introduction

Aureobasidium pullulans is described as a black yeast-like fungus with melanin pigment cell wall and frequently isolated from environment [1]. *A. pullulans*-associated human infectious disease have been well described causing cutaneous infection, scleritis, splenic abscesses, and catheter-related infections which may occur during traumatic inoculation, surgery, or particularly catheter manipulation or insertion [2]. Despite few reports of *A. pullulans* peritonitis [1,3,4] and colonization inside peritoneal dialysis (PD) catheter [5], there is no report of causing catheter-related peritonitis defined as peritonitis that occurred simultaneously with exit-site infection (ESI) or tunnel infection from the same organism [6]. We therefore report a case of *A. pullulans* peritonitis via peri-catheter route. An identification of the fungus was confirmed by positive culture and DNA sequence analysis of the Internal Transcribed Spacer (ITS) region and D1/D2 portion of the 28S rRNA region. By root-cause analysis, an etiology of the infection was probably related to poor caregiver's hand hygiene and improper fingernail care. Thus hand and fingernail hygiene must be part of an integrated approach to prevent peritonitis and ESI.

2. Case

A 64-year-old Thai man with diabetic end-stage renal disease and cirrhosis had been on continuous ambulatory PD (CAPD, 1.5%D x 4 exchanges/day) with caregiver in PD exchange since 2016 presented with cloudy dialysate on 9 October 2017 (Day 0). The diagnosis of peritonitis was confirmed with dialysate leukocyte counts of 418 cells/μL and neutrophil predominance (82%). He had noticed asymptomatic black scab during daily exit-site dressing for 1 week (day −7) but did not report to his PD nurse. He had never experienced peritonitis and had no residual renal function (RRF). A combination of intraperitoneal (IP) cefazolin and ceftazidime at dosage 1 gm daily was prescribed resulting in partial resolution of the cloudy effluent. However, the leukocyte still persisted at more than 100/μL. The dialysate culture from day 0 later revealed a negative organism. On Day +5, PD fluid (PDF) were re-examined, again yielding a negative result; however, the IP antibiotics were escalated to meropenem 1 gm daily. On Day +11, a black purulent discharge was spilled out from exit site (Fig. 1A). Potassium hydroxide (KOH) examination of the discharge revealed dematiaceous yeast. Fungal peritonitis was suspected. The black purulent swab from exit-site and drained effluent were urgently submitted to Chulalongkorn University (CU) microbiology lab for a microorganism

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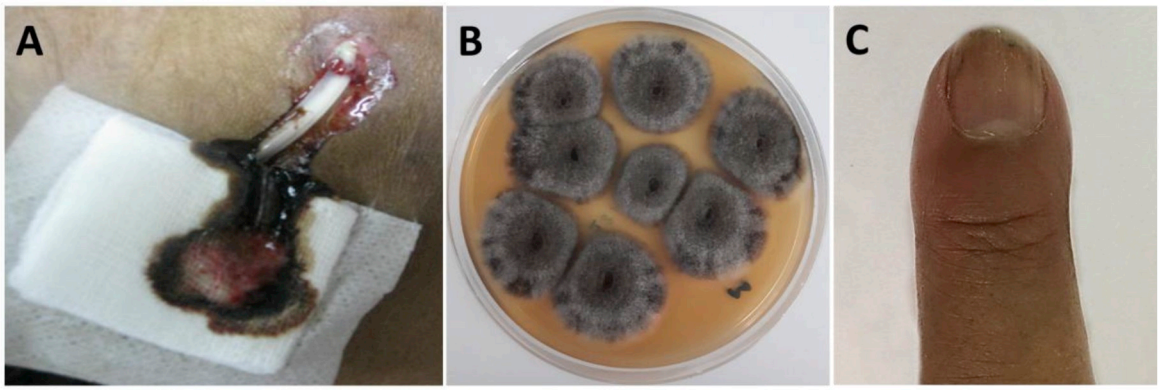

Fig. 1. (A) The black purulent discharge from his exit site. (B) *Aureobasidium pullulans* culture on SDA from pus culture for 17 days. (C) The black stain from fingernails of the caregiver.

identification. An intravenous liposomal amphotericin B, 5 mg/kg/day was early administrated on the same day for 14 days (Day +12 to Day +25). The PD catheter was removed on day +13 and then the dialysis mode was permanent shift to hemodialysis.

At the CU microbiology lab, the effluent and the swab were plated onto blood agar, chocolate agar, and Sabouraud dextrose agar (SDA). After 7 days of incubation, black colonies were presented on both blood agar and SDA isolated from both specimens. The pathogen harvested from the colonies was identified as *Aureobasidium* spp. using API20c AUX kit (bioM'erieux, Marcy l'Etoile, France) based on biochemical reactions (Fig. 1B). To identify species of the isolated pathogen, a standard fungal PCR and a DNA sequencing of the internal transcribed spacer (ITS) and D1/D2 regions using the universal fungal primer, ITS1/ITS4 (White et al., 1990) and 5.8SR/LR7 of the 28S rRNA (Vilgalys lab, Duke University) were performed. The sequencing results from both discharge and PDF of ITS region showed 99% (542/548) identity to *A. pullulans* (accession number MG333439.1) and 28s rRNA region showed 89% (887/1000) identity *to A. pullulans* (accession number DQ470956.1) (First BASE Laboratories, Singapore Science Park II, Singapore) by employing the BLASTN program (National Center for Biotechnology Information Internet homepage).

To identify an etiology of the infection, the attending physician performed a root-cause analysis. In July 2017 (Month −3), the patient's house was flooded for 2 months. He reported numerous black stains on surface of his bathroom door and sink. However, these strains were later isolated with standard fungal culture as numerous fungal species but not *A. pullulans*. Interestingly, his spouse, whom also is his caregiver and is a hairdresser, apparently had onychomycosis of her fingers and black dirt under her fingernails (Fig. 1C). She reported an improper hand washing sometimes. Fungal cultures from the disease nails and the nail dirt revealed negative culture and *Aureobasidium* spp., respectively. Touch contamination from caregiver's nail dirt was suspected as a major source of the infection. Thus, aseptic technique, nail care, and hand hygiene were reemphasized. Twelve weeks of oral itraconazole at dosage of 200 mg daily was prescribed in order to eradicate the onychomycosis, although the disease nail was cultured negative. The patient and the caregiver responded well to the above treatment and had a complete recovery of the infections.

3. Discussion

This is the case report of ESI and catheter-related peritonitis from *Aureobasidium pullulans*, which DNA sequencing confirmed the same pathogens from both exit-site discharge and dialysate. In the root cause analysis, caregiver's nail dirt was suspected as a source of this rare organism. From review of literatures, 24 cases of *A. pullulans* infection were previously described during year 1986–2018 (Table 1). The majority (11 cases) were presented with systemic infections, 10 cases with CAPD-associated peritonitis, 1 case with infected splenic abscess, 1 case with scleritis, and 1 case with superficial wound infection. Including the presenting case, there were 12 males, 6 females and 7 unknown genders. The mean age was 38.5 years. Apart from skin and orbital infections [10,13,15,17], 3 cases reported that *A. pollulans* were identified from Hickman catheters [8,14,16], 3 cases from central venous catheters [12,13], and 1 case from PD catheter [5]. These findings suggested that catheter was one of the important risk factor of this fungal infection. However, information regarding PD catheter removal and onset of the removal are not available for all reported case, thus the benefit of catheter removal cannot be concluded as recommended by ISPD Guideline 2016 [19].

There is no standard antifungal regimens for eradicating *Aureobasidium* infection, data from previous reports suggested that amphotericin B alone had been efficacious for treatment of peritonitis [4,5]. Other antifungal regimens had been reported to be effective such as amphotericin B combination with fluconazole [12,14,15], voriconazole [13], micafungin [16] or natamycin and fluconazole [10], as well as voriconazole alone [17], fluconazole alone [11] or in combination with flucytosine [1]. Unfortunately, 3 and 1 cases were unsuccessfully treated with amphotericin B [2,8,9] and with micafungin [18] resulting patient's dead subsequently. Due to lack of a standard treatment of *A. pullulans* peritonitis and its rarity, liposomal amphotericin B administration for 2 weeks with early catheter removal provided a good clinical outcome as presented here.

Despite of source of the infection are still inconclusive, an insufficient attention to aseptic technique during bag exchange combined with a hot-humid climate which promoted the rapid growth of the fungi is postulated. Patient's bathroom door and sink were considered but not been proven to be sources of fungi. Caregiver's hand hygiene is commonly overlooked by clinician as a potential source of the infection. Many microorganisms have been reported to convey by the caregiver, including bacteria (both Gram-positive and Gram-negative), *Candida*, and various types of virus such as rotavirus, adenovirus, and viral hepatitis. In our case, the caregiver with fungal contaminated nail dirt performed PD bag exchanges with her bare hands is proven to be a carrier of the infection. The organism isolated from caregiver's nail dirt was the same species of the pathogen identified from exit-site discharge and PD effluents. Although, hand hygiene and nail care is a simple, low-cost method to prevent the spread of many microbes but usually improper performance and inadequate attention.

In conclusion, we reported a case of catheter-related peritonitis from black yeast with a successful treatment by the standard antifungal therapy and early PD catheter removal. Good personal hygiene, particularly proper hand washing techniques during PD procedure and proper fingernail care of patients and caregivers performing PD, are necessary and reemphasized here for the prevention of the infection.

Table 1
Summary of patients with *Aureobasidium pullulans* infection reported in the literature.

No	Sex	Ages (years)	Underlying condition	Antifungal therapy	Catheter removal	Site of colonization	Site of infection	Outcome	Year (Ref)
1	M	67	Disseminated lymphoma	No treatment	No	–	Splenic abscess	Death	Salkin IF, 1986 [7]
2	M	28	AML	Amphotericin B	Yes	Hickman catheter	Systemic	Death	Kaczmarski EB, 1986 [8]
3–9	NA	NA	NA	NA	NA	PD	Peritonitis	NA	Pritchard RC, 1987 [3]
10	W	53	Ovarian carcinoma	Amphotericin B	NA	Broviac catheter	Systemic	Death	Girardi LS, 1993 [9]
11	M	34	CRF due to DM	Amphotericin B	Yes	PD	Peritonitis	PD	Clark EC, 1995 [4]
12	W	35	CRF due to DM	Amphotericin B	Yes	PD and catheter	Peritonitis	HD	Caporale NE, 1996 [5]
13	M	50	Keratoplasty	Amphotericin B, Natamycin and Fluconazole	No	–	Scleritis	Decreased vision	Gupta V, 2001 [10]
14	M	28	Severe trauma	Fluconazole	NA	NA	Systemic	Survive	Bolignano G, 2003 [11]
15	M	4 Mo	(TAPVD) with obstruction	Amphotericin B	NA	Gore-Tex patch	Systemic	Death	Hawkes M, 2005 [2]
16	M	37	Tubulointerstitial nephritis	Flucytosine and Fluconazole	Yes	PD	Peritonitis	HD	Mise N, 2008 [1]
17	W	61	Metastatic cerebral tumor	NA	Yes	CVC tip	Systemic	Survive	Huang YT, 2008 [12]
18	W	54	pleural-cutaneous fistula with empyema	Amphotericin B and Fluconazole	Yes	CVC tip	Systemic	Survive	Huang YT, 2008 [12]
19	M	11	Fanconi's anemia with bone marrow transplant	Amphotericin B and Voriconazole	Yes	CVC and skin	Systemic	Survive	Joshi A, 2010 [13]
20	M	11	Intestinal lymphangiectasia	Fluconazole and Amphotericin B	Yes	Hickman catheter	Systemic	Survive	Mershon-shier KL, 2011 [14]
21	W	28	HIV	Fluconazole and Amphotericin B	No	Blood, Arthritis, Pulmonary and skin	Systemic	Survive	Van Hougenhouck-Tulleken WG, 2016 [15]
22	M	66	Crohn's disease with a single kidney	Amphotericin B and Micafungin	Yes	Hickman catheter	Systemic	Survive	Mehta SR, 2017 [16]
23	W	16	Kidney transplant	Voriconazole	No	Wound at site of surgery	Superficial wounds	Survive	Nalcacioglu H, 2018 [17]
24	M	49	AIDS	Micafungin	No	Blood and Upper endoscopy	Systemic	Death	Mittal J, 2018 [18]
25	M	64	CRF due to DM	Liposomal Amphotericin B	Yes	Catheter exit-site	Peritonitis	HD	The present case

Abbreviations: Pt, patient; Mo, months; NA, not available; CRF, chronic renal failure; DM, diabetes mellitus; CVC, central venous catheter; TAPVD, total anomalous pulmonary venous drainage; ASD, atrial septal defect; AML, acute myelocytic leukemia.

Conflict of interest

The authors declare no conflicts of interest. The authors alone are responsible for the content of the study.

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