Journal of Microbiology, Immunology and Infection (2019) 52, 833–835

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Correspondence

Fatal disseminated infection caused by *Prototheca zopfii* in a child with leukemia

Dear Editor,

Protothecosis is a rare infection caused by members of the genus *Prototheca*, an achlorophyllic algae ubiquitous in nature. Out of five species, only *Prototheca wickerhamii* and *Prototheca zopfii* are pathogenic in humans.[1]

A 13-year old male was admitted due to fever and foul discharge from his ileostomy for 1 day. He was diagnosed to have acute myeloblastic leukemia (AML) 8 months ago. His treatment course was complicated with typhlitis and enterovesical fistula necessitating an ileostomy creation 6 months ago. Due to advanced disease, he opted to receive palliative chemotherapy. Additionally, he had been receiving fluconazole, levofloxacin, and trimethoprim-sulfamethoxazole for recurrent bacteremia and fungemia for the past 3 weeks. The patient denied exposure to animals, farms, or natural water bodies.

On admission, the patient's temperature was 38.6 °C, heart rate was 175/min, respiratory rate was 26/min, and SpO2 was 97% on room air. Physical examination reveals normoactive bowel sounds, absence of tenderness or rigidity on palpation, liver margin locating at 3 cm below the right costal margin, palpable spleen tip, and an erythematous and indurated ileostomy on the right lower quadrant of his abdomen (Fig. 1A).

Complete blood count showed white cell count 16,160/μL, blasts and promyelocytes 92.4%, neutrophils 0%, lymphocytes 6.7%, hemoglobin 8.6 g/dL, platelets 72000/μL. Venous blood gas showed metabolic acidosis with pH 7.326, pCO2 39.4 mmHg, pO2 32.1 mmHg, HCO3 20.1 mmol/L, base excess −5.9. His C-reactive protein was 21.58 mg/dL. He was treated with teicoplanin, meropenem, micafungin, and prophylactic trimethoprim-sulfamethoxazole. The patient continued to be febrile with active ileostomy discharge.

Three weeks later, cream-colored colonies were cultured on CHROMagar (CHROMagar Company, Paris, France) on 2 separate blood culture and 1 ileostomy swab after 72 h of growth (Fig. 1B). Wet mount preparation showed asymmetrical morula-like structures (Fig. 1C). The species was identified as *P. zopfii* by Phoenix yeast ID panel (Becton Dickinson Diagnostics, Sparks, MD, USA) with 99% probability. Minimum inhibitory concentration value on susceptibility testing was not available.

By then, the patient had deteriorated to bed confinement. Amphotericin B was suggested for treatment, but was declined by the patient and his parents due to possible side effects. He died of sepsis and respiratory failure 2 days later.

This is the first reported disseminated *P. zopfii* infection in a pediatric AML patient, who are known to suffer high mortality with invasive fungal infections.[2] However, protothecosis may be more deadly as it is generally not suspected clinically, causing delayed diagnosis.[3] To date, there are 5 other reported cases of disseminated *P. zopfii* infection (Table 1).[1,3–6] Of note, all patients had various underlying diseases. Four patients received a transplant. All of the known reported cases died. All *P. zopfii* isolates obtained from positive blood cultures were identified using the Vitek 2 (bioMerieux, Marcy l'Etoile, France) or RapID Yeast Plus (Remel, Santa Fe, N.Mex.) systems. In contrast to previous series on *P. wickerhamii* infected patients,[4] the mortality rate with disseminated *P. zopfii* infection is much higher (14% vs 100%).[3,5] The source of *P. zopfii* in our patient may be the infected ileostomy. Treatment remains controversial because of limited experience. Polyenes and azole susceptibility is based on the presence of ergosterol in the lipid fraction of *Prototheca* cell membranes. However, the optimal dose and duration of antifungal therapy are unknown and treatment failures are common, High mortality could be attributed to poor host immunity and disseminated infection.[1,3]

In conclusion, disseminated protothecosis is a deadly opportunistic infection emerging in immunocompromised populations. Clinical awareness among such patients, as

https://doi.org/10.1016/j.jmii.2019.05.001

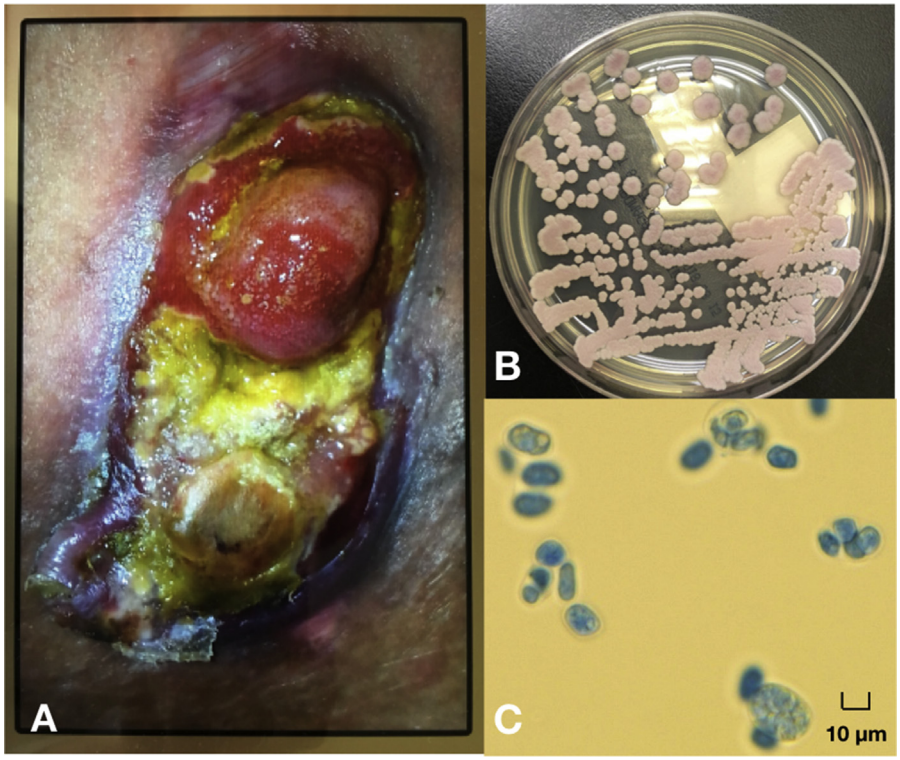

Figure 1. (A) Erythema, induration, and foul yellowish discharge from the ileostomy located on the right lower quadrant of the patient's abdomen. (B) Smooth, cream-colored, yeast-like colonies after 72 h of growth on CHROMagar *Candida* Medium, later identified as *Prototheca zopfii*. Previous reports indicate *Candida parapsilosis* and *Prototheca* spp. having a similar macroscopic appearances on CHROMagar *Candida* Medium.[1] (C) Wet mount preparation with lactophenol cotton blue shows *P. zopfii* with asymmetrical morula-like structures (10–15 µm) containing endospores or sporangiospores (magnification 400×).

Table 1 Overview of six fatal cases of disseminated *Prototheca zopfii* infection.

No.	Year of report	Age/sex	Underlying disease	Transplant received	Co-infection	Treatment	Reference
1	2003	59/F	ESRD, COPD, CAD	Lung	CMV viremia, *Serratia marcesens* pneumonia	Not treated	3
2	2004	58/M	Myelofibrosis, secondary AML	RIC MUD allogenic HSCT	None	L-ampB	1
3	2014	56/F	DLBCL	MUD allogenic HSCT	None	L-ampB	4
4	2014	62/F	Hairy cell leukemia	None	None	Itraconazole	5
5	2018	36/M	Alcoholic liver disease	Deceased donor liver transplant	*Klebsiella pneumoniae* bacteremia	L-ampB, fluconazole	6
6	2019	13/M	AML	None	*Candida lusitaniae*, *Wangiella dermatitidis* fungemia	Micafungin	Present report

AML, acute myeloid leukemia; CAD, coronary artery disease; CMV, cytomegalovirus; COPD, chronic obstructive pulmonary disease; DLBCL, diffuse large B-cell lymphoma; ESRD, end-stage renal disease; F, female; HSCT, hematopoietic stem cell transplantation; L-ampB, liposomal amphotericin B; M, male; MUD, matched unrelated donor; RIC, reduced-intensity conditioning.

well as microbiological expertise, could hopefully facilitate early diagnosis and improve treatment outcome in the future.

Conflicts of interest

The authors declare no conflicts of interest.

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18 February 2019
Available online 18 May 2019