**Case Report**

**Isolation of an obscure fungus, *Parengyodontium album*, from the blood of a severely neutropenic patient: The first reported case from Malaysia**

Nurdiyana Mohamed¹, Chuan Hun Ding¹, Asrul Abdul Wahab¹, Mohd Nizam Tzar¹, Murniahayati Hassan²

¹ Department of Medical Microbiology and Immunology, Faculty of Medicine, Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia
² Infectious Diseases Research Centre, Institute for Medical Research, Ministry of Health, Malaysia

**Abstract**

*Parengyodontium album* is a very rarely encountered opportunistic fungal pathogen. A severely neutropenic 11-year-old boy with acute T-cell lymphoblastic leukemia/lymphoma was febrile and lethargic during his admission for elective chemotherapy. No cutaneous lesion or obvious source of infection was noted, and clinical examination was otherwise unremarkable. A blood specimen was sent for culture and fungal elements were visualized. Amphotericin B was administered empirically while awaiting fungal identification. Morphologically, a hyaline mould with thin septate hyphae plus smooth-walled conidiophores and conidiogenous cells arranged in whorls of up to four was cultured. Internal transcribed spacer region sequencing identified the fungus conclusively as *P. album*. Repeat blood culture was also positive for the same fungus. Following a two-week course of amphotericin B, fungemia clearance was attained.

**Key words:** Amphotericin B; *Engyodontium album*; internal transcribed spacer; *Parengyodontium album*.

*J Infect Dev Ctries* 2022; 16(10):1668-1670. doi:10.3855/jidc.17016

(Received 26 June 2022 – Accepted 19 August 2022)

Copyright © 2022 Mohamed et al. This is an open-access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

**Introduction**

Opportunistic mycoses have been increasing in tandem with the rise in the number of patients with compromised immune systems. Although published case reports on *Parengyodontium album* per se are astoundingly sparse in medical literature, the fungus has a global distribution. In the environment, it is a saprobe that can be isolated from soil, marine sediments, plant materials, and even wall paint [1]. It can also be found on a wide range of substrates such as jute, paper, and linen [2]. *P. album* secretes extracellular enzymes (namely proteinase and keratinolase), which cements its role as a pathogen [3]. Its significance as a human pathogen is further augmented by its propensity to be resistant to antifungal agents, most notably to fluconazole and flucytosine [1]. We report the isolation of *P. album* in an immunocompromised teenager with acute T-cell lymphoblastic leukemia/lymphoma.

**Case Report**

An 11-year-old boy with acute T-cell lymphoblastic leukemia/lymphoma with nasal tumour and renal infiltration was admitted to our healthcare facility for a scheduled chemotherapy. On the day of admission, a high body temperature of 38.3 °C was recorded, and a pre-chemotherapy laboratory assessment showed that his total white count was nearly zero (0.5 × 10⁹/L) – the absolute neutrophil count was indeed zero. Further history taking revealed that he had been feeling lethargic and feverish for the past four days. Clinical examination was otherwise unremarkable, with no cutaneous lesions or other potential sources of infection being apparent. A blood sample was taken aseptically for bacteriological and mycological cultures.

The presence of febrile neutropenia necessitated the administration of empirical antibiotics. Intravenous cefepime and amikacin were administered while awaiting culture results. Despite being on antibiotics, the fever did not abate, and a temperature spike of 39 °C was recorded on the third day of antibiotic therapy. On this same day, the laboratory informed the visualisation of fungal elements in the blood culture (Figure 1). The patient’s blood was negative for bacterial growth and his serum galactomannan antigen assay was likewise negative. Consequently, the antimicrobial regimen was switched to intravenous meropenem and intravenous amphotericin B (AmB).

After three days, the fungus grew on Sabouraud dextrose agar as floccose whitish colonies, with the reverse side of the colony being cream-coloured (Figure
2). Microscopically, thin septate hyphae, smooth-walled conidiophores, and conidiogenous cells in whorls of one to four were observed (Figure 3). Although we initially suspected *P. album*, due to the paucity of reported infections caused by this fungus, a molecular diagnosis was also sought.

The clinician resent a new blood sample after three days to exclude contamination during the previous blood taking and a mould with identical morphological features was isolated again. The administration of AmB (due to its broad-spectrum of activity against moulds) was continued while molecular identification was attempted. The isolate was sent to Malaysia’s Institute for Medical Research (IMR), which carried out a polymerase chain reaction targeting the internal transcribed spacer (ITS) regions. The primers used were 5’TCCGTAGGTGAACCTGCGG-3’ (for ITS1) and 5’TCTCCGCTTATTGATATGC-3’ (for ITS4). Following DNA sequencing, the fungus was identified as *Parengyodontium album* (GenBank accession no. MN947607.1). AmB was administered for a total duration of two weeks and by this time the mould was no longer culturable from the patient’s blood.

**Discussion**

Despite being touted as an emerging pathogen in modern medical literature, *P. album* is hardly a newcomer to the medical mycology scene [1]. *P. album* was initially placed in the *Beauveria* genus when it was first described more than a century ago in 1912 [4]. Since then, it was renamed *Tritirachium album* in 1940, placed back in the *Beauveria* genus in 1948, and reclassified as *Engyodontium album* in the early 1970s to accommodate hyaline fungi that produce white cottony colonies with whorled (i.e., verticillate) conidiophores [4-5]. Its current genus (*Parengyodontium*) was proposed barely just a decade ago in 2016 following matrix-assisted laser desorption ionisation-time of flight mass spectrometry analyses, and to date, *P. album* is the sole member of this genus [1]. Although we utilized ITS sequencing to authenticate our isolate’s identity, 28S nuclear ribosomal DNA and the β-tubulin gene may also serve as good DNA markers for molecular identification [1].

Thus, despite its rarity, *P. album* is not so ‘obscure’ after all, as it had already been wreaking havoc as *Engyodontium album*, by being implicated in, among others, infective endocarditis (in the USA), fungemia (in Brazil), mycotic keratitis (in India) and brain abscess (in Germany) [2-4]. To the best of our knowledge, we are the first to report a case of *P. album* infection from Malaysia. Although our patient was neutropenic (which in many instances can be a sole predisposing factor for fungemia), an immunocompromised state is not an absolute prerequisite for systemic *P. album* infections, as the fungus had been implicated as a cause of endocarditis in a seemingly immunocompetent patient [4].

![Figure 1. A Gram stain of the positive blood specimen showing fungal elements (1000× magnification).](image1)

![Figure 2. A. The fungus grew as floccose whitish colonies; B. with the reverse side of the colony being cream-coloured.](image2)

![Figure 3. A lactophenol cotton blue stain of the colony showing thin septate hyphae, smooth-walled conidiophores, and conidiogenous cells in whorls of one to four were observed (600× magnification).](image3)
Currently designated as a zoonotic fungus, its zoonotic potential cannot be discounted because it has been reported to cause infections in dolphins and has been isolated from giant pandas and mares [6]. Our patient had no recent exposure to animals and did not keep pets.

We did not perform antifungal susceptibility testing on our P. album isolate because a guideline dictating this has yet to be published by a relevant authority (namely the Clinical and Laboratory Standards Institute). However, from the published in-vitro data, posaconazole was found to have the highest activity against clinical P. album isolates, as evidenced by minimal inhibitory concentration (MIC) values between 0.015 to 2 μg/mL [1]. Voriconazole has also been proposed as a suitable antifungal, albeit with slightly higher MIC values ranging from 0.03 to 4 μg/mL [1,7]. Fluconazole and fluconazole fared the worst, with all tested isolates demonstrating fluconazole MICs surpassing 64 μg/mL, and more than half had fluconazole MICs of at least 128 μg/mL [1]. AmB (which we administered to our patient), and agents from the echinocandin class appears to be somewhat “in between” in terms of MIC values, between 0.5 and 2 μg/mL [1,7]. Nonetheless, the clearance of fungemia recorded in our patient lends support for AmB usage in P. album infections. There was a case of mycotic keratitis from India that was successfully managed with AmB (although it was co-administered with fluconazole) [3].

Conclusions

When dealing with a neutropenic patient with a systemic fungal infection, we should be especially mindful that the ‘usual suspects’, such as Candida spp. and Aspergillus spp may not be the causative pathogen. Even if resources are limited, the diagnostic laboratory in developing countries should endeavour to secure molecular confirmation (through DNA sequencing) of obscure or rarely encountered pathogens such as P. album. An early clue would be the occurrence during the culture of a hyaline mould with thin septate hyphae plus smooth-walled conidiophores and conidiogenous cells arranged in whorls. Although AmB may be administered at the outset, the threshold to switch to either voriconazole or posaconazole should be low.

Acknowledgements

We are grateful to the Dean of the Faculty of Medicine, Universiti Kebangsaan Malaysia, for his motivation and permission to publish this article. We would also like to thank the staff from the Infectious Diseases Research Centre, Institute for Medical Research, Malaysia, for assisting with the molecular identification of our isolate.

References


Corresponding author

Chuan Hun Ding, MB BS, DrPath
Associate Professor of Medical Microbiology,
Department of Medical Microbiology & Immunology,
Level 16, Preclinical Building, Faculty of Medicine,
Universiti Kebangsaan Malaysia, 56000 Kuala Lumpur, Malaysia
Tel: +603-91459531
Fax: +603-91459524
Email: dingch@ppukm.ukm.edu.my

Conflict of interests: No conflict of interests is declared.