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LETTER TO THE EDITOR

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# Phaeohyphomycosis due to *Pleurostomophora richardsiae* in a Patient with a Hematological Malignancy

Dear Editor,

Phaeohyphomycosis is caused by dematiaceous fungi, such as *Exophiala*, *Cladosporium*, *Phialophora*, and *Wangiella*, which are found in soil, trees, and decaying vegetation [1]. The dematiaceous fungus *Pleurostomophora richardsiae* (previously known as *Phialophora richardsiae*) has rarely been implicated in human disease, and fewer than 30 human cases have been reported to date in the global literature written in English [2–9]. Herein, we present a rare case of cutaneous infection caused by *P. richardsiae* in a patient with a hematological malignancy. A 50-year-old man was admitted to Asan Medical Center with intermittent fever in October, 2022. He was diagnosed with myelodysplastic syndromes with excess blasts 2 (MDS-EB-2). The bone marrow (BM) examination revealed a markedly hypercellular marrow (cellularity, 95%) with an increased blast count (19.5%). The chromosomal analysis identified a monosomal complex cytogenetic aberration: 42,XY,del(5)(q13q35),der(7)t(7;17)(q22;q21),-12,-16,-17,-18,-20,+mar[16]/46,XY[4]. Following two cycles of decitabine treatment, the subsequent BM examination showed disease progression to acute myeloid leukemia. Considering the adverse feature of the disease biology, the patient was scheduled to receive induction treatment with azacitidine and venetoclax. Unfortunately, the disease persisted after two cycles of azacitidine and venetoclax, prompting intensive salvage chemotherapy. During the salvage treatment, a solitary plaque with crust was observed on the dorsum of the right hand (Figure 1(A)). He had a nodulous skin lesion following a previous injury and it was suddenly enlarged recently. A punch biopsy was performed on the lesion, followed by a fungus culture on the tissue sample. A plate culture yielded olive-green to dark-brown and velvety colonies after a 14-day incubation period (Figure 1(B)). A slide culture demonstrated septate hyphae, some forming bundles or loops. Two types of conidia were produced: hyaline conidia (oval to cylindrical) and brown, thick-walled spherical conidia (Figure 1(C)). The conidia were clustered at the apex of slender, tapering phialides (Figure 1(D)) with distinctive flared collarettes (Figure 1(E)). Grocott's methenamine silver stained tissue section of skin biopsy also showed fungal hyphae in the dermis (Supplemental Figure 1). Identification using matrix-associated laser desorption/ionization time-of-flight mass spectrometry (Biotyper; Bruker Daltonics, Billerica, MA, USA) with MBT Filamentous Fungi Library 4.0 was unsatisfactory, with calling several filamentrous fungi, such as *Curvularia lunata* (score 0.85), *Aspergillus fumigatus* (score 0.84), *Exophiala dermatitidis* (score 0.83), and *Nannizzia praecox* (score 0.82). Antifungal susceptibility testing using the Sensititre Yeast One system (Thermo Scientific, Cleveland, OH, USA) revealed the following minimum inhibitory concentrations: amphotericin B, 0.25 μg/mL; fluconazole, 32 μg/mL; voriconazole, 0.12 μg/mL; posaconazole, 0.12 μg/mL; itraconazole, 0.12 μg/mL; caspofungin, 8 μg/mL; anidulafungin, 8 μg/mL; micafungin, >8 μg/mL; and 5-flucytosine, >64 μg/mL, respectively. Further, sequencing of the internal ribosomal transcribed spacer and D1/D2 regions confirmed the identification of this fungi [10,11]. The amplified sequence was found to be 100.0% identical to that of *Pleurostoma richardsiae* (Accession No. MH869756) and was also deposited to GenBank (Accession no. OR073814). The phylogenetic tree of the internal ribosomal transcribed spacer and D1/D2 region genes showed that our *P. richardsiae* isolate was clustered with the other isolates of *P. richardsiae* from several countries, and differentiated from the other dematiaceous fungi including the other *Pleurostomophora* species also (Supplemental Figure 2). The patient received amphotericin B (200 mg/day) ampirically for 30 days, followed by caspofungin (50 mg/day) for 5 days, and then voriconazole (500 mg/day) for 10 days, with no evidence of recurrence. The current case presents phaeohyphomycosis rather than chromoblastomycosis, considering the localized lesion, irrespective of an immunocompromised status. Until now, the only six cases of *P. richardsiae* infection in immunocompromised patients have been reported (Supplemental Table 1) [4–9]. Almost of all were treated by surgical excision with or without antifungal therapy, and the only one case was recurred irrespective of surgical excision and topical injection of amphotericin B. The typical manifestation of *P. richardsiae* infection is believed to be a well-circumscribed subcutaneous cyst filled with pus [3], but scaly nodulous lesions have also been reported, similar to our present case [2]. A precise diagnosis of suspected

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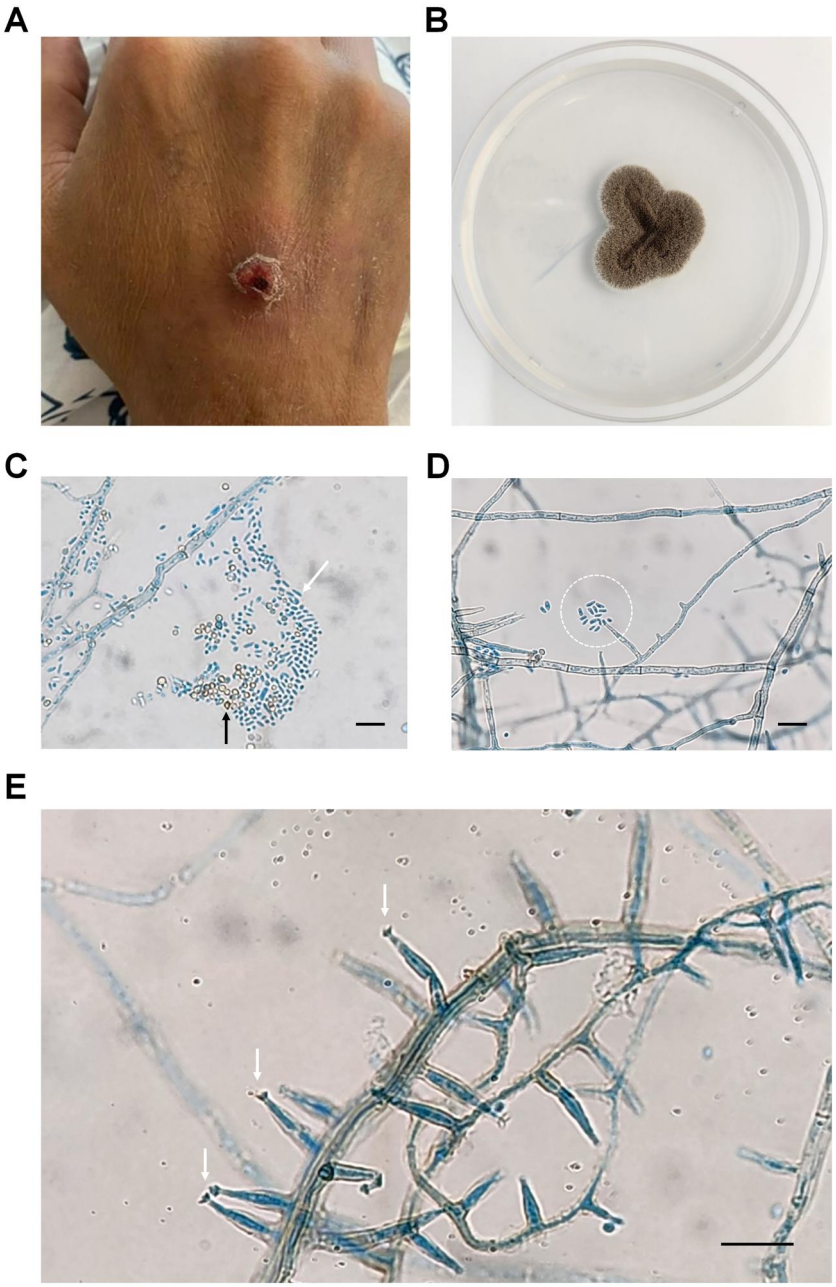


**Figure 1.** Clinical presentation of the patient and morphological findings for the infecting fungi. (A) Skin lesion on right hand dorsum; (B) Filamentous fungi grew as olive-green to dark-brown velvety colonies on potato dextrose agar incubated for 14 days; (C) Two types of conidia were produced: hyaline conidia which were oval to cylindrical (indicated by white arrow), and brown, thick-walled conidia which are spherical (indicated by black arrow) on lactophenol cotton blue stain (scale bar, 10 μm); (D) The conidia (within dotted circle) were clustered on the tip of slender and tapering phialides on lactophenol cotton blue stain (scale bar, 10 μm); (E) The phialides had flaring collarettes (indicated by white arrows) on lactophenol cotton blue stain (scale bar, 10 μm).

dematiaceous fungal infections is crucial, though not always easily achieved in a clinical laboratory. Of note, many laboratories employ MALDI-TOF for the routine identification of fungi. Numerous studies have investigated the performance of MALDI-TOF MS in accurately identifying yeast, non-dermatophyte filamentous fungi, and dermatophytes [12], but not darkly pigmented fungi. It is known that fungal melanin can suppress peptide and protein ion signals during the acquisition of MALDI–TOF mass spectra [13]. Above all, *P. richardsiae* was not included in our database of MALDI–TOF. With regard to microscopic examination, our present case showed *Phialophora*-like sporulation or conidiation [1,14]. This type of sporulation results in a flask-shaped phialide, with conidia forming and accumulating at the distal end of the flask, resembling "flowers in a vase" [14]. In this case, *P. richardsiae* was determined based on characterized phenotypical appearances and molecular evidence. Fortunately, *P. richardsiae* appeared to be susceptible to various antifungal agents in this case and the skin lesion exhibited a favorable course. There is still a lack of clinical evidence to recommend specific antifungal therapies for cutaneous *P. richardsiae* infection but surgical excision has been known to be usually curative and was typically recommended [3,4,6–9]. Several

antifungal agents were administered to our current patient in conjunction with his underlying hematological malignancy. In conclusion, we here describe a rare case of phaeohyphomycosis causex by *P. richardsiae* in an immunocompromised patient with hematological malignancy and give a suggestion for correct identification based on phenotypical and molecular evidence.

## Author contributions

Conceptualization: Kim MN and Won EJ. Data curation and experiment: Park S-J and U Jo. Funding acquisition: Won EJ. Investigation: Won EJ and Choi E-J. Supervision: Sung H and Kim MN. Writing—original draft: Won EJ. Writing—review and editing: U Jo, Choi E-J, Sung H, and Kim MN. All authors reviewed and approved the final version of the manuscript.

## Disclosure statement

No potential conflict of interest was reported by the author(s).

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## References

[1] Revankar SG. Dematiaceous fungi. Mycoses. 2007;50(2):91–101. doi:10.1111/j.1439-0507.2006.01331.x.
[2] Mohammed A, Rahnama-Moghadam S. Following the track to an unexpected diagnosis: phaeohyphomycosis. Am J Med. 2019;132(9):1047–1049. doi:10.1016/j.amjmed.2019.03.027.
[3] Levenstadt JS, Poutanen SM, Mohan S, et al. *Pleurostomophora richardsiae* – an insidious fungus presenting in a man 44 years after initial inoculation: a case report and review of the literature. Can J Infect Dis Med Microbiol. 2012;23(3):110–113. doi:10.1155/2012/406982.
[4] Ikai K, Tomono H, Watanabe S. Phaeohyphomycosis caused by *Phialophora richardsiae*. J Am Acad Dermatol. 1988;19(3):478–481. doi:10.1016/s0190-9622(88)70200-5.
[5] Tam M, Freeman S. Phaeohyphomycosis due to *Phialophora richardsiae*. Australas J Dermatol. 1989;30(1):37–40. doi:10.1111/j.1440-0960.1989.tb00406.x.
[6] Jumaa PA, Lightowler C, Baker LR, et al. Cutaneous infection caused by *Phialophora richardsiae* treated successfully by surgical excision in an immunocompromised patient. J Infect. 1995;30(3):261–262. doi:10.1016/s0163-4453(95)90877-3.
[7] Yehia M, Thomas M, Pilmore H, et al. Subcutaneous black fungus (phaeohyphomycosis) infection in renal transplant recipients: three cases. Transplantation. 2004;77(1):140–142. doi:10.1097/01.TP.0000107287.70512.E7.
[8] Tee LY, Tan BH, Tan AL, et al. Subcutaneous phaeohyphomycosis caused by *Pleurostomophora richardsiae* in a renal transplant recipient. JAAD Case Rep. 2020;6(1):66–68. doi:10.1016/j.jdcr.2019.10.027.
[9] Marples R, Micallef M, Whyte C. Ruxolitinib-associated phaeohyphomycosis: a case report. Cureus. 2021;13(11):e19335. doi:10.7759/cureus.19335.
[10] Chong E, Yu H, Kim TY, et al. Invasive *Hormographiella aspergillata* infection identified using DNA sequencing. Ann Lab Med. 2022;42(3):370–372. doi:10.3343/alm.2022.42.3.370.
[11] Won EJ, Choi MJ, Jeong SH, et al. Nationwide surveillance of antifungal resistance of *Candida* bloodstream isolates in South Korean hospitals: two year report from Kor-GLASS. J Fungi. 2022;8(10):996. doi:10.3390/jof8100996.
[12] Clark AE, Kaleta EJ, Arora A, et al. Matrix-assisted laser desorption ionization-time of flight mass spectrometry: a fundamental shift in the routine practice of clinical microbiology. Clin Microbiol Rev. 2013;26(3):547–603. doi:10.1128/CMR.00072-12.
[13] Buskirk AD, Hettick JM, Chipinda I, et al. Fungal pigments inhibit the matrix-assisted laser desorption/ionization time-of-flight mass spectrometry analysis of darkly pigmented fungi. Anal Biochem. 2011;411(1):122–128. doi:10.1016/j.ab.2010.11.025.
[14] Dixon DM, Polak-Wyss A. The medically important dematiaceous fungi and their identification. Mycoses. 1991;34(1–2):1–18. doi:10.1111/j.1439-0507.1991.tb00613.x.

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