

Caregiver skin infection causing peritoneal dialysis-associated peritonitis

Rutchanee Chieochanthanakit^a, Veerapat Wattanasatja^b, Panthira Passorn^a, Dhammika Leshan Wannigama^{c,d,e,f,g,h}, Talerngsak Kanjanabuch^{i,j,k,*}

^a Department of Internal Medicine, Sawanpracharak Hospital, Nakhon Sawan, 60000, Thailand

^b Department of Internal Medicine, Sunpasithiprasong Hospital, Ubon Ratchathani, Thailand

^c Department of Microbiology, Faculty of Medicine, Chulalongkorn University, King Chulalongkorn Memorial Hospital, Thai Red Cross Society, Bangkok, Thailand

^d Center of Excellence in Antimicrobial Resistance and Stewardship, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

^e Department of Infectious Diseases and Infection Control, Yamagata Prefectural Central Hospital, Yamagata, Japan

^f School of Medicine, Faculty of Health and Medical Sciences, The University of Western Australia, Nedlands, Western Australia, Australia

^g Biofilms and Antimicrobial Resistance Consortium of ODA Receiving Countries, The University of Sheffield, Sheffield, United Kingdom

^h Pathogen Hunter's Research Collaborative Team, Department of Infectious Diseases and Infection Control, Yamagata Prefectural Central Hospital, Yamagata, Japan

ⁱ Center of Excellence in Kidney Metabolic Disorders, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

^j Division of Nephrology, Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

^k CAPD Excellence Center, King Chulalongkorn Memorial Hospital, Bangkok, Thailand

ARTICLE INFO

Handling Editor: Dr Adilia Warris

Keywords:

Fungal peritonitis
Gibellulopsis nigrescens
Verticillium nigrescens
 Peritoneal dialysis
 Peritonitis
 Scalp infection

ABSTRACT

We present the first case report of peritoneal dialysis (PD)-associated peritonitis due to *Gibellulopsis nigrescens*, with the same pathogen detected in her caregiver's tinea capitis. This confirms that touch contamination from the caregiver's infection was the primary source of this rare organism. The species of pathogen causing peritonitis and her caregiver's scalp lesions were identified by DNA barcoding. The patient responded well to timely PD catheter removal and a 2-week course of systemic amphotericin B deoxycholate. Preventive strategies should prioritize hygiene practices, including maintaining adequate personal hygiene and practicing thorough hand washing, to mitigate the risk of touch contamination and subsequent infection with fungal pathogens.

1. Introduction

Fungal peritonitis represents a potentially life-threatening complication of peritoneal dialysis (PD), with associated high mortality rates [1–4]. *Gibellulopsis nigrescens* formerly known as *Verticillium nigrescens* [5] is typically a soil-borne filamentous mold that colonizes plant roots [5], causing vascular wilt in various plants, including potato, tomato, eggplant, hop, and peppermint [6,7].

Previously, *Verticillium* has been reported as human pathogen, causing periodontal infection [8], ophthalmic infections [9,10], sinusitis [11], onychomycosis [12] and triggering exacerbations of respiratory disease as aeroallergens [13]. Additionally, reports of fungemia [14] and hepatosplenic abscess [15] have been observed in immunocompromised hosts.

In 1994, a single report of this pathogen in a PD patient was documented, identified as *Verticillium* peritonitis, although the specific species name was not provided [16]. Therefore, we describe a case in which

a patient undergoing PD developed peritonitis caused by *V. nigrescens*, potentially linked to touch contamination from tinea capitis on the caregiver's scalp.

1.1. Case presentation

A 64-year-old Thai female, with a history of long-standing hypertension, dyslipidemia, type 2 diabetes mellitus, and kidney failure from diabetes kidney disease, had been undergoing continuous ambulatory PD (2Lx 4 exchanges daily) for 2 years, performed by her husband. She had multiple episodes of bacterial peritonitis. The latest episode involved a PD-related infection caused by *Escherichia coli*, which was successfully treated with appropriate antibiotics 3 months ago.

This time, she was admitted to Sawanpracharak Hospital with recurrent PD-related peritonitis. Her symptoms included generalized abdominal pain with cloudy effluent. On the first day of hospitalization (Day 1), the PD effluent (PDE) demonstrated a leukocyte count of 158

* Corresponding author. Division of Nephrology, Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand.
 E-mail address: Talerngsak.K@chula.ac.th (T. Kanjanabuch).

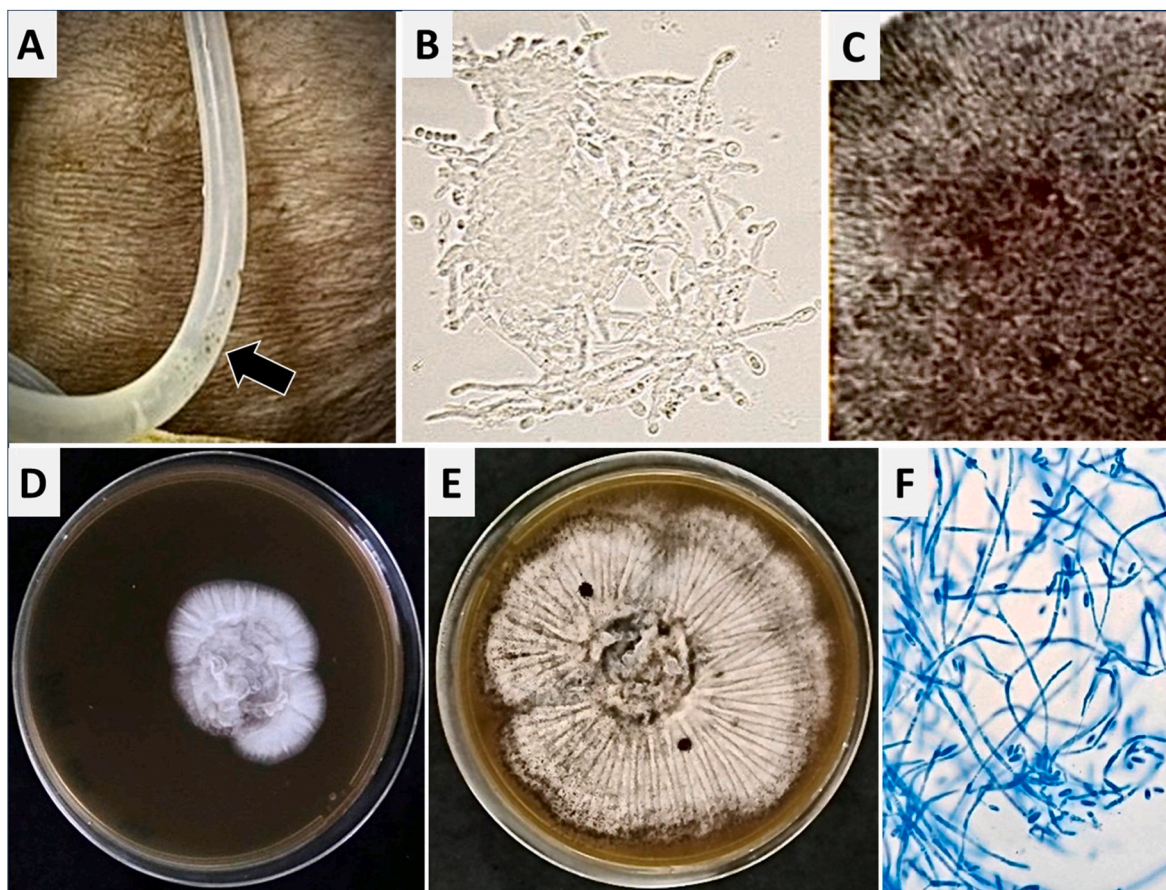


Fig. 1. White colonization (Black arrow) was observed inside the PD catheter lumen (A). Direct microscopic examination with a 20 % potassium hydroxide (KOH) mount from the catheter revealed multiple dark branching septate hyphae (B). Multiple crusted lesions, tinea capitis, on her caregiver's scalp (C). *Gibellulopsis nigrescens* colonies grown on Yeast and Mold agar (Oxoid, Hampshire, UK) day 3 (D) and day 7 (E) exhibiting a long, dark septate hyphae with multiple conidia when viewed under lactophenol cotton blue mounting (F). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

cells/mm³ with 64 % neutrophils, raising suspicion of bacterial peritonitis. Consequently, empirical treatment was initiated, consisting of intraperitoneal meropenem and vancomycin, 1 g each combination. On day 2, white particles were observed inside her PD-catheter lumen by the PD nurse (Fig. 1A). After a KOH stain revealing numerous septate hyphae with hyperpigmented conidia (Fig. 1B), PD-catheter was urgently removed and intravenous amphotericin B deoxycholate at dosage of 1 mg/kg/day for 2 weeks was added.

The PD transfer set, catheters, and PDE were submitted to a central laboratory, King Chulalongkorn Memorial Hospital, for microorganism identification. Using Yeast and Mold agar (Oxoid, Hampshire, UK) for inoculating PDE and PD catheter specimens, white colonies appeared and subsequently became off-white colored, finely floccose, with slight zonation (Fig. 1D and E). Lactophenol cotton blue staining of the colonies revealed numerous branched septate hyphae with dark elliptical conidia (Fig. 1F), morphologically consistent with *Trichosporon* spp. However, the species was eventually identified as *G. nigrescens* through molecular phylogeny using nucleotide sequences of internal transcribed spacer regions (ITS1/ITS4 primer), small subunit (NS1/NS4 primer), and large subunit (NL1/NL4 primer) of the nuclear ribosomal DNA gene complex with 60 %, 100 %, and 100 % query coverage and 99.6 %, 99.8, and 100 % identities, respectively.

Using the European Committee on Antimicrobial Susceptibility Testing (EUCAST) Antifungal Epidemiological Cutoff (ECOFF) referenced to a microbroth dilution value of ≥ 97.5 % of wild-type *Aspergillus flavus* populations [17], the pathogen was found to be susceptible to itraconazole (minimal inhibitory concentration 1 μ g/mL),

isavuconazole (MIC <0.125 μ g/mL), fluconazole (MIC 4 μ g/mL), posaconazole (MIC 0.5 μ g/mL), voriconazole (MIC <0.125 μ g/mL), and amphotericin B (MIC 1 μ g/mL) and undetermined to caspofungin and terbinafine with MICs 2 μ g/mL.

A root-cause analysis was conducted to determine the etiology of the infection. The patient had undergone PD exchanges performed by her husband. Upon thorough examination, multiple crusted and scaly plaques with scratching lesions (Fig. 1C) were observed on her husband's scalp. Both pruritic symptoms and inadequate hand washing, potentially leading to cross-contamination from the caregiver, were identified as sources of the infection. To establish the cause-effect relationship, the crusted lesions were scraped and examined. The examination revealed a fungal infection, tinea capitis, and the pathogen was eventually identified as the same organism, *G. nigrescens*, with DNA barcoding confirming the potential root cause. Additionally, the living area beneath the house, which had a wet floor without tiles and hosted domestic cows, was noted as another contributing factor. Hence, emphasis was placed on aseptic technique and a 2-week course of topical ketoconazole was provided to the caregiver. The caregiver responded well to the treatment, and the infections were completely resolved.

2. Discussion

In this report, we described a patient with PD-associated peritonitis infected by *G. nigrescens*, with the same pathogen detected in her caregiver's scalp lesions. This confirms that touch contamination from the caregiver infection was the primary source of this rare organism.

G. nigrescens is classified as a hyaline filamentous mold belonging to the Phylum Ascomycota, Class Sordariomycetes, Order Glomerellales and Family Plectosphaerellaceae [5]. Colonies usually grow medium fast, reaching 20–30 mm diameter in 10 days at 20 °C. They appear whitish with cream-colored reverses, finely floccose, slightly zonate, later becoming darker-colored [5]. Microscopic examination reveals hyaline-septate hyphae, branched conidiophores 1–2 times at the terminal position, and conidia elongate ellipsoidal to cylindrical, 1- or 2-celled, hyaline, smooth-walled, produced in slimy heads. Chlamydospores lateral, terminal or intercalary, singly or in chains, pale to dark brown, smooth- and thick-walled [5]. This fungus is primarily identified as a plant pathogen causing vascular wilt in various plants, including potato, tomato, eggplant, hop, and peppermint. It rarely presents as a human pathogen. However, there have been some reports causing human infections, including periodontal infection [8], ophthalmic infection [9,10], sinusitis [11], onychomycosis [12], and deep-seated infection [15].

According to the 2022 International Society for Peritoneal Dialysis (ISPD) Peritonitis Guidelines, prompt diagnosis, timely PD catheter removal, and administration of appropriate antifungal medication for a minimum of 2 weeks after PD catheter removal are crucial for the treatment of fungal peritonitis. There are no specific antifungal recommendations for the treatment of *G. nigrescens* in either the 2022 ISPD Guidelines [18] or the 2021 Global Guideline for the Diagnosis and Management of Rare Mold Infections [19]. Previous literature exhibits heterogeneity in treatment regimens such as amphotericin B [8,14,15], voriconazole [9] and fluconazole [10,16]. However, in this case, an *in-vitro* MIC was conducted using EUOFF referenced to a microbroth dilution value of *A. flavus* [17]. The pathogen was found to be susceptible to all available antifungal agents; however, the report was time-consuming. Consequently, amphotericin B was administered due to its broad-spectrum coverage, rapid time-kill rate, post-antifungal effect, and having action against biofilm formation [20], resulting in successful treatment.

Preventing peritonitis is paramount, especially in tropical regions where this fungus thrives in the environment. Prioritizing meticulous hand hygiene and providing comprehensive education to patients and caregivers regarding catheter care techniques is essential. Emphasis should be placed on personal hygiene and maintaining aseptic techniques and a sterile environment during PD exchanges. Patients and caregivers should receive thorough instructions on monitoring signs of infection and be encouraged to store supplies in a clean, dry area with adequate ventilation. Proper disposal of medical waste should be underscored, and measures should be taken to minimize direct pet contact with supplies, ensuring pets cannot access areas where PD exchanges are conducted.

In conclusion, we present the first documented case of fungal peritonitis caused by *G. nigrescens*, originated from the caregiver's infection. The case underscores the crucial role of personal hygiene in avoiding preventable infections.

CRedit authorship contribution statement

Rutchanee Chieochanthanakij: Writing – review & editing, Writing – original draft, Conceptualization. **Veerapat Wattanasatja:** Data curation. **Panthira Passorn:** Data curation. **Dhammika Leshan Wannigama:** Writing – review & editing, Writing – original draft. **Talerngsak Kanjanabuch:** Writing – review & editing, Supervision, Funding acquisition, Formal analysis.

Acknowledgements

We would like to acknowledge the physicians, nurses, technicians, and allied health professionals who are not listed as authors in this work and who provided care for the patient at Sawan Pracharak Hospital, Thailand. Special thanks are extended to Preeyarat Pavatung, B.Sc., and

Thunvarat Saejew, B.Sc., for their laboratory work at the Center of Excellence in Kidney Metabolic Disorders, Faculty of Medicine, Bangkok, Thailand. Informed consent, in accordance with the Declaration of Helsinki, was obtained from the patient. Chulalongkorn University does not require ethical approval for reporting individual cases or case series.

This research was funded by the Thailand Science Research and Innovation Fund at Chulalongkorn University (HEAF67300066 and CU_FRB65_hea [19]_026_30_07), the Ratchadapiseksompotch Fund at Chulalongkorn University (HEA663000115 and HEA663000116), the Ratchadapiseksompotch Fund - Graduate Affairs at Chulalongkorn University (GA66/047), the Kidney Foundation of Thailand (1205/2564), and the Royal College of Physicians of Thailand (02/66). TK has received consultancy fees from VISTERRA as a country investigator and is currently a recipient of the National Research Council of Thailand. Additionally, TK has received speaking honoraria from Astra Zeneca and Baxter Healthcare. The remaining authors have declared no commercial or financial relationships that could be perceived as potential conflicts of interest associated with this article.

References

- [1] T. Kanjanabuch, T. Nopsopon, T. Chatsuwan, S. Purisinsith, D.W. Johnson, N. Udomsantisuk, et al., Predictors and outcomes of peritoneal dialysis-related infections due to filamentous molds (MycopDICS), *PLoS One* 17 (5) (2022) e0268823.
- [2] M. Al Sahlawi, J. Zhao, K. McCullough, D.S. Fuller, N. Boudville, Y. Ito, et al., Variation in peritoneal dialysis-related peritonitis outcomes in the peritoneal dialysis outcomes and practice patterns study (PDOPPS), *Am. J. Kidney Dis.* 79 (1) (2022) 45–55, e1.
- [3] J. Perl, D.S. Fuller, B.A. Bieber, N. Boudville, T. Kanjanabuch, Y. Ito, et al., Peritoneal dialysis-related infection rates and outcomes: results from the peritoneal dialysis outcomes and practice patterns study (PDOPPS), *Am. J. Kidney Dis.* 76 (1) (2020) 42–53.
- [4] T. Thammathiwat, S. Tatiyanupanwong, U. Parinyasiri, D.L. Wannigama, T. Chatsuwan, T. Kanjanabuch, Peritoneal dialysis-associated peritonitis from pauci-septated mold: life-threatening but curable, *Med. Mycol. Case Rep.* 42 (2023) 100612.
- [5] R.G. Zare, Gibellulopsis, a suitable genus for *Verticillium nigrescens*, and *Musicillium*, a new genus for *V. theobromae*, *Nova Hedwigia* 85 (3–4) (2007) 463–489.
- [6] Melouk H, Horner C. *Verticillium nigrescens* from peppermint. *Phytopathology*. 64 (9):1267–1268.
- [7] G.H. Pethybridge, Notes on some saprophytic species of fungi, associated with diseased potato plants and tubers, *Trans. Br. Mycol. Soc.* 6 (1917) 104. IN5.
- [8] S. Habib, N. Naved, M.S. Awan, Oral mycotic infection caused by a rare *Verticillium* species - a case report, *BMC Oral Health* 23 (1) (2023) 441.
- [9] M.B. Nehemy, D.V. Vasconcelos-Santos, L. Torqueti-Costa, E.P. Magalhaes, Chronic endophthalmitis due to *verticillium* species after cataract surgery treated (or managed) with pars plana vitrectomy and oral and intravitreal voriconazole, *Retina* 26 (2) (2006) 225–227.
- [10] J.Y. Shin, H.M. Kim, J.W. Hong, Keratitis caused by *Verticillium* species, *Cornea* 21 (2) (2002) 240–242.
- [11] M. Twaruzek, E. Soszczyńska, P. Winiarski, A. Zwierz, J. Grajewski, The occurrence of molds in patients with chronic sinusitis, *Eur. Arch. Oto-Rhino-Laryngol.* 271 (5) (2014) 1143–1148.
- [12] P.D. Pukhrabam, Kh R. Devi, N.B. Singh, Pattern of onychomycosis—a RIMS study, *J. Comm. Dis.* 43 (2) (2011) 105–112.
- [13] A.A. Kwaasi, R.S. Parhar, F.A. al-Mohanna, H.A. Harfi, K.S. Collison, S.T. al-Sedairy, Aeroallergens and viable microbes in sandstorm dust. Potential triggers of allergic and nonallergic respiratory ailments, *Allergy* 53 (3) (1998) 255–265.
- [14] G. Bashir, M.A. Thokar, S. Ahmad, B.A. Pomda, R. Lone, T. Fazili, Fungemia caused by *Verticillium* species in an immunocompromised child, *Indian J. Med. Microbiol.* 24 (1) (2006) 65–66.
- [15] C.J. Wu, T.C. Chang, H.C. Lee, T.Y. Chen, N.Y. Lee, C.M. Chang, et al., *Verticillium* infection—a rare cause of hepatosplenic abscesses, *Diagn. Microbiol. Infect. Dis.* 62 (4) (2008) 427–429.
- [16] G. Amici, S. Grandesso, A. Mottola, G. Virga, T. Teodori, M.C. Maresca, et al., *Verticillium* peritonitis in a patient on peritoneal dialysis, *Am. J. Nephrol.* 14 (3) (1994) 216–219.
- [17] The European Committee on Antimicrobial Susceptibility Testing – EUCAST, Overview of antifungal ECOFFs and clinical breakpoints for yeasts and moulds [Internet] [cited 2024 Jan 11]. Available from: <https://www.eucast.org/astoffun/g/clinicalbreakpointsforantifungals>, 2023.

- [18] P.K.-T. Li, K.M. Chow, Y. Cho, S. Fan, A.E. Figueiredo, T. Harris, et al., ISPD peritonitis guideline recommendations: 2022 update on prevention and treatment, *Perit. Dial. Int.* 42 (2) (2022) 110–153.
- [19] M. Hoenigl, J. Salmanton-García, T.J. Walsh, M. Nucci, C.F. Neoh, J.D. Jenks, et al., Global guideline for the diagnosis and management of rare mould infections: an initiative of the European confederation of medical mycology in cooperation with the international society for human and animal mycology and the American society for microbiology, *Lancet Infect. Dis.* 21 (8) (2021) e246–e257.
- [20] G. Di Bonaventura, I. Spedicato, C. Picciani, D. D'Antonio, R. Piccolomini, In vitro pharmacodynamic characteristics of amphotericin B, caspofungin, fluconazole, and voriconazole against bloodstream isolates of infrequent *Candida* species from patients with hematologic malignancies, *Antimicrob. Agents Chemother.* 48 (11) (2004) 4453–4456.