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The First Case of Prosthesis-related Infection Caused by *Quambalaria cyanescens* in Korea

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Dear Editor,

Quambalaria cyanescens (formerly *Sporothrix cyanescens*) is a plant pathogen that has rarely been isolated from clinical specimens; only two cases have been identified using sequence analysis [1, 2]. We report the first case of prosthesis-related human infection caused by *Q. cyanescens* in Korea. The Institutional Review Board of Seoul National University Hospital approved the study (2105-096-1219) and waived the need for informed consent.

In December 2020, a 61-year-old man with spinal metastases of renal cell carcinoma was hospitalized for pain, warmth, and redness at the surgical site. The patient had undergone multiple surgeries for tumor removal, spinal metastases, and spinal fixation 17 months prior. The patient's body temperature was 36.2°C; laboratory tests showed a white blood cell count of 9.28×10^9/L (reference interval, RI: 4.0–10.0×10^9/L), neutrophil count of 7.43×10^9/L (RI: 1.8–7.0×10^9/L), and C-reactive protein (CRP) level of 87.5 mg/L (RI: 0.0–5.0 mg/L). On hospitalization day 2, magnetic resonance imaging revealed an abscess around the thoracic spine. Cefazolin was used as empirical antimicrobial therapy due to the prior methicillin-susceptible *Staphylococcus aureus* infection. On day 5, tissue debridement was performed, and abscess specimens were collected.

The specimens were cultured on blood agar and Brucella agar at 35°C and Sabouraud dextrose agar (SDA) at 30°C. Atypical yeast-like colonies were observed on the blood agar after 48 hours of incubation. The colonies were subcultured on SDA and incubated at 30°C for 72 hours. The colonies were smooth, butyrous, and white (Fig. 1A). Microscopic examination revealed pseudohyphal budding patterns with sympodial conidiogenesis (Fig. 1B). Gram-positive rods also grew on Brucella agar.

Matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS; MALDI Biotyper, Bruker Daltonics GmbH, Bremen, Germany) was unreliable for identification of the fungi. The 28S rRNA gene D1/D2 region was sequenced using the NL1/NL4 primer pair and searched against GenBank [3]. The results showed 100.0% identity with *Q. cyanescens* (MN_162210.1) and *Q. simpsonii* (MH_874927.1). Because the identification was ambiguous, the internal transcribed spacer (ITS) region was sequenced using the ITS5/ITS4 primer pair [3]. The results revealed 100.0% identity with *Q. cyanescens* (KX_674666.1) and 96.12% identity with *Q. simpsonii* (MT_879594.1). Phylogenetic analysis using MEGA X (https://www.megasoftware.net) confirmed the isolate as *Q. cyanescens* (Fig. 1C).

The gram-positive rods were identified as *Cutibacterium* sp. using MALDI-TOF MS. *Cutibacterium acnes* was specifically identified by 16S rRNA amplicon sequencing of the abscess specimen using a MinION sequencer (Oxford Nanopore Technolo-

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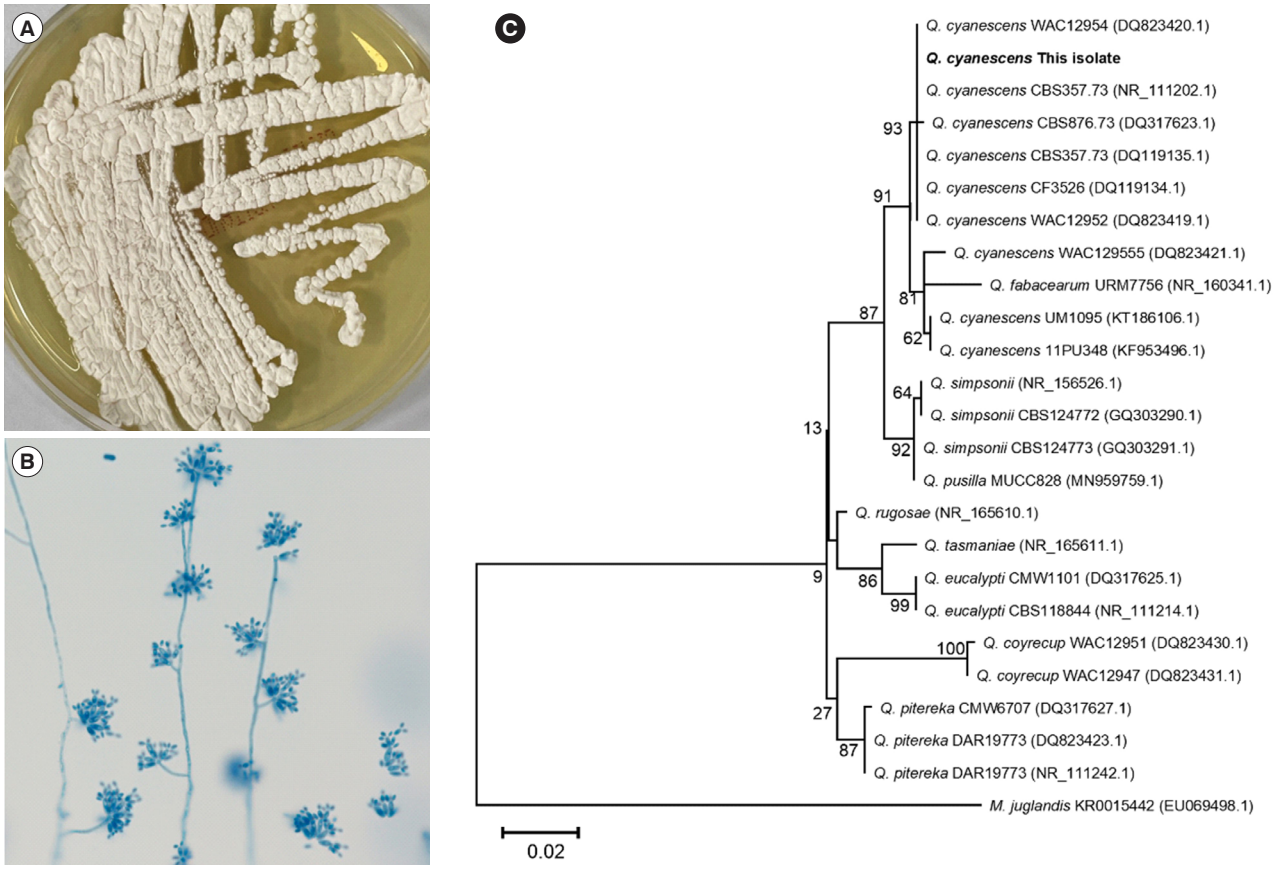

Fig. 1. Colony morphology, microscopic examination, and phylogenetic analysis of the *Quambalaria* isolate. (A) Colonies on a Sabouraud dextrose agar incubated at 30°C for 72 hours. (B) Microscopic examination of lactophenol cotton blue-stained *Quambalaria* isolate (400×). (C) Phylogenetic analysis of *Quambalaria* isolates (23 type and reference strains) based on the internal transcribed spacer region (619 nucleotide positions). The tree was constructed using the maximum-likelihood method and the GTR + I + G model, with *Microstroma juglandis* KR 0015442 (EU069498.1) considered as the outgroup. Bootstrap values are expressed as percentages of 1,000 replications, and the scale bar indicates the estimated number of substitutions per base. GenBank accession numbers are provided within parentheses.

gies, Oxford, UK) [4].

Antifungal susceptibility testing (AST) of the *Q. cyanescens* isolate was performed using a Sensititre YeastOne YO10 panel (TREK Diagnostic Systems Inc., Independence, OH, USA). The results showed high minimum inhibitory concentrations (MICs) for 5-flucytosine and echinocandins and low MICs for amphotericin B and azoles (Table 1). Seven days post debridement, the patient's serum CRP level had decreased to 33.9 mg/L. Follow-up cultures of tissue and wound specimens collected on day 36 during additional spinal fixation yielded negative results. No antifungal agents were administered during the 44 days of hospitalization. The abscess did not recur within six months of discharge.

Table 1. MIC values for the *Quambalaria cyanescens* isolate

Antifungal agent	MIC (μg/mL)
Anidulafungin	>8
Micafungin	>8
Caspofungin	8
5-Flucytosine	>64
Posaconazole	≤0.008
Voriconazole	≤0.008
Itraconazole	≤0.015
Fluconazole	≤0.12
Amphotericin B	0.12

Abbreviation: MIC, minimum inhibitory concentration.

Since being first described in 1973, the taxonomic classification of *S. cyanescens* has been changed several times, first to the genus *Cerinosterus* and then to the genus *Fugomyces*. The current genus classification of *Quambalaria* is based on phylogenetic analysis of ribosomal large subunit sequences and ul-

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trastructural characteristics [5]. Several *S. cyanescens* infections (e.g., skin infections, nosocomial pneumonia, and fungemia) have been reported; however, their diagnoses may be inaccurate as they were based only on morphological and physiological results [6, 7]. The current case is the third reported human infection caused by *Q. cyanescens* and confirmed using ITS sequence analysis. The sequence analysis was important for identifying the isolate as using morphological phenotypes and MALDI-TOF MS was challenging and ambiguous. The AST results for the isolate were consistent with those published previously [1, 2].

Postoperative spinal infection can be a significant complication of spinal surgery [8]. *C. acnes* appeared to be a contamination of the normal skin flora, considering that prosthesis-related infection by *C. acnes* is associated with low CRP levels and usually requires long-term antibiotic treatment [9, 10]. The current patient had an increased risk of infection due to his advanced age and immunocompromised status. As in the case of breast implant-related infection, *Q. cyanescens* can cause prosthesis-related infection with the patient improving only after debridement [1].

This is the first case of *Q. cyanescens* human infection in Korea. *Q. cyanescens* should be considered a potential pathogen causing prosthesis-related infections, and ITS region sequence analysis may be required to definitively identify *Q. cyanescens*.

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AUTHOR CONTRIBUTIONS

Conceptualization: Kwon SR and Park JH. Data curation: Kwon SR and Park JH. Formal analysis: Park JH. Methodology: Kim TS and Park JH. Investigation: Kwon SR and Park JH. Writing—original draft: Kwon SR; Writing—review and editing: Kwon SR, Kim TS, Park H, and Park JH.

CONFLICTS OF INTEREST

No potential conflicts of interest relevant to this article were reported.

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REFERENCES

1. Fan X, Xiao M, Kong F, Kudinha T, Wang H, Xu YC. A rare fungal species, *Quambalaria cyanescens*, isolated from a patient after augmentation mammoplasty--environmental contaminant or pathogen? PLoS One 2014;9:e106949.
2. Kuan CS, Yew SM, Toh YF, Chan CL, Lim SK, Lee KW, et al. Identification and characterization of a rare fungus, *Quambalaria cyanescens*, isolated from the peritoneal fluid of a patient after nocturnal intermittent peritoneal dialysis. PLoS One 2015;10:e0145932.
3. CLSI. Interpretive criteria for identification of bacteria and fungi by targeted DNA sequencing. 2nd ed. MM18: Wayne, PA: Clinical and Laboratory Standards Institute, 2018.
4. Moon J, Kim N, Lee HS, Shin HR, Lee ST, Jung KH, et al. *Campylobacter fetus* meningitis confirmed by a 16S rRNA gene analysis using the MinION nanopore sequencer, South Korea, 2016. Emerg Microbes Infect 2017;6:e94.
5. de Beer ZW, Begerow D, Bauer R, Pegg GS, Crous PW, Wingfield MJ. Phylogeny of the *Quambalariaceae* fam. nov., including important Eucalyptus pathogens in South Africa and Australia. Stud Mycol 2006;55:289-98.
6. Sigler L, Harris JL, Dixon DM, Flis AL, Salkin IF, Kemna M, et al. Microbiology and potential virulence of *Sporothrix cyanescens*, a fungus rarely isolated from blood and skin. J Clin Microbiol 1990;28:1009-15.
7. Tambini R, Farina C, Fiocchi R, Dupont B, Guého E, Delvecchio G, et al. Possible pathogenic role for *Sporothrix cyanescens* isolated from a lung lesion in a heart transplant patient. J Med Vet Mycol 1996;34:195-8.
8. Parchi PD, Evangelisti G, Andreani L, Girardi F, Darren L, Sama A, et al. Postoperative spine infections. Orthop Rev (Pavia) 2015;7:5900.
9. Grossi O, Lamberet R, Longis PM, Touchais S, Boutoille D, Corvec S, et al. Risk factors for *Cutibacterium acnes* spinal implant-associated infection: a case-case-control study. Clin Microbiol Infect 2020;26:743-7.
10. Shiono Y, Ishii K, Nagai S, Kakinuma H, Sasaki A, Funao H, et al. Delayed *Propionibacterium acnes* surgical site infections occur only in the presence of an implant. Sci Rep 2016;6:32758.