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CASE REPORT

Subcutaneous phaeohyphomycosis caused by *Exophiala jeanselmei*

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Exophiala jeanselmei, a saprobe in the environment, is an opportunistic pathogen. We present a rare case of subcutaneous phaeohyphomycosis caused by *E jeanselmei* in a man aged 66 years with a 3-month history of a tender swelling on the dorsal area of the left middle finger. Purulent fluid was aspirated from the area, and the culture yielded black colonies composed of conidiophores, phialides, and yeast cells. After sequencing of the rDNA *ITS1-5.8S-ITS2* gene, the pathogen was confirmed as *E jeanselmei*. The patient was cured by surgical excision without any antifungal agents.

Introduction

Subcutaneous phaeohyphomycosis is an infection caused by pigmented, filamentous fungi with a cell wall containing melanin.[1] More than 100 species of fungi are associated with phaeohyphomycosis, including *Exophiala jeanselmei*, which exists worldwide in soil, on trees and rotting wood, and in decaying vegetation.[2] *E jeanselmei* is a black polymorphic fungal pathogen of humans. A common clinical presentation is a solitary, well-circumscribed, subcutaneous nodule that generally remains localized to the site of an initial injury.[3] Due to the rarity of this infection, no clinical trials exist to guide treatment decisions in the management of subcutaneous phaeohyphomycosis caused by *E jeanselmei*. Herein, we present an immunocompetent man aged 66 years with a 3-month history of a tender swelling on the dorsal area of the left middle finger caused

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by *E jeanselmei*. He was cured by surgical excision and required no antifungal medication.

Case report

A man 66 years of age visited our outpatient department due to a 3-month history of a painful swelling over the dorsal area of the left middle finger. He was a construction worker and did not have any systemic conditions, such as diabetes mellitus, alcoholism, cirrhosis, or immunodeficiency. Minor work-related trauma to his hands was not uncommon. Three months before this visit, a tender nodule appeared on the dorsal area of the left middle finger. The nodule enlarged and became even more tender. A local clinic prescribed oral cephalexin 500 mg every 6 hours for 2 weeks; however, the nodule continued to enlarge. In our outpatient department, the physical examination showed a 2 × 2 cm tender mass over the dorsal area of his left middle finger. The remainder of the physical examination was normal. A peripheral hemogram revealed a leukocyte count of 8140/μL. The C-reactive protein level was 2.56 mg/dL. Other data, including serum aspartate aminotransferase, alanine aminotransferase, blood urea nitrogen, creatinine, and glucose, were within normal limits. Chest radiography showed no specific lesions. Approximately 1 mL of purulent fluid was aspirated from the lesion and cultured on trypticase soy agar and brucella agar with 5% sheep blood.

After 10 days, olive-gray to brownish-black colonies grew on the brucella agar with the 5% sheep blood. These colonies were transferred to Sabouraud dextrose agar. After a week, black colonies with a jet-black reverse grew on the agar (Fig. 1). Lactophenol cotton blue staining showed conidiophores, phialides, and yeast cells (Fig. 1). The conidiogenous cells are annelides integrated with their supporting conidiophores. Based on the morphology, the lack of nitrate assimilation, and the ability to grow at 40°C, the organism was identified as *Exophiala* species.[4,5] After sequencing of the rDNA *ITS1-5.8S-ITS2* gene, the microorganism was identified as *E jeanselmei*.[6]

The patient underwent a surgical excision of the tender swelling 2 weeks later. The pathology showed a significant number of proliferating fungal hyphae and suppurative granulomas (Fig. 2). The tissue culture subsequently identified as *E jeanselmei*. The wound healed well, and no antifungal medications were required. The patient remained asymptomatic at the 12-month follow-up examination.

Discussion

Dematiaceous fungi are a group of pigmented, fungal forms found in the environment, which include the genera *Exophiala*, *Cladosporium*, *Phialophora*, *Xylohypha*, and *Fonsecaea*. *Exophiala* was previously considered as a contaminant microorganism; however, it has been increasingly reported in the literature as a clinical pathogens.[1,7,8] Infection with this organism can usually be traced to a traumatic inoculation. The injury may be as simple as a splinter or a prick from a thorn, and it may have occurred months or years before the lesion appears. Most infected patients had a history of working outdoors, usually with bare feet and/or in lightweight clothing.[1,7,8] Our case involves a construction worker who experienced direct seeding of the subcutaneous phaeohyphomycosis through minor wounds in his hands from outdoor work.

Diagnosis of phaeohyphomycosis caused by *E jeanselmei* involves both histopathologic evidence and the presence of positive cultures. Typical histopathologic changes involve a granulomatous tissue response with infiltration of polymorphonuclear leukocytes and occasionally microabscesses formation.[7] The growth of *Exophiala* is characterized by moist, brownish- to greenish-black yeast-like colonies that eventually become velvety due to the development of short, aerial, grayish hyphae. The front color is an olive black, and the reverse color is black in mature colonies. Microscopically, *Exophiala* initially appears as subspherical, budding yeast-like cells that often form long chains. As they mature, septate hyphae develop that give rise to numerous conidiogenous cells called annelides that are tubular and slender. These annelides usually taper to form narrow elongated tips, which help to distinguish *Exophiala* from other dematiaceous fungi.[3–5]

Identification of the various dematiaceous fungi responsible for black-grain mycetoma remains difficult with standard mycologic procedures and can be delayed up to

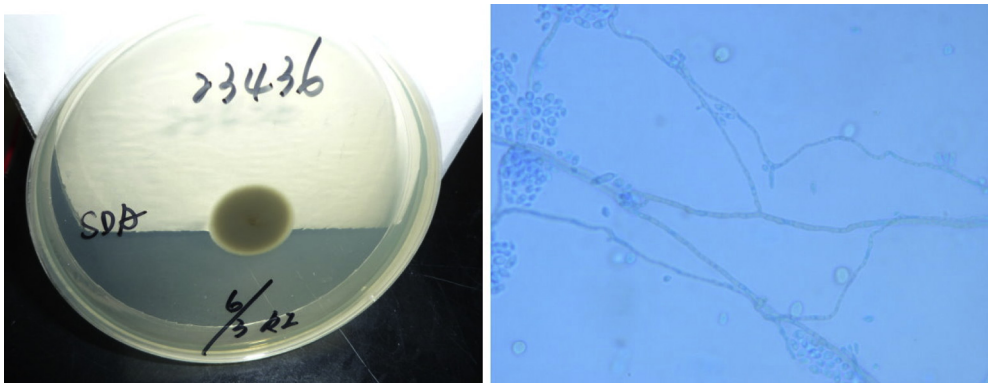

Figure 1. Sabouraud dextrose agar yielded a greenish black, velvety colony after an 8-day incubation at 30°C (left). Lactophenol cotton blue staining shows conidiophores, phialides, and yeast cells (right).

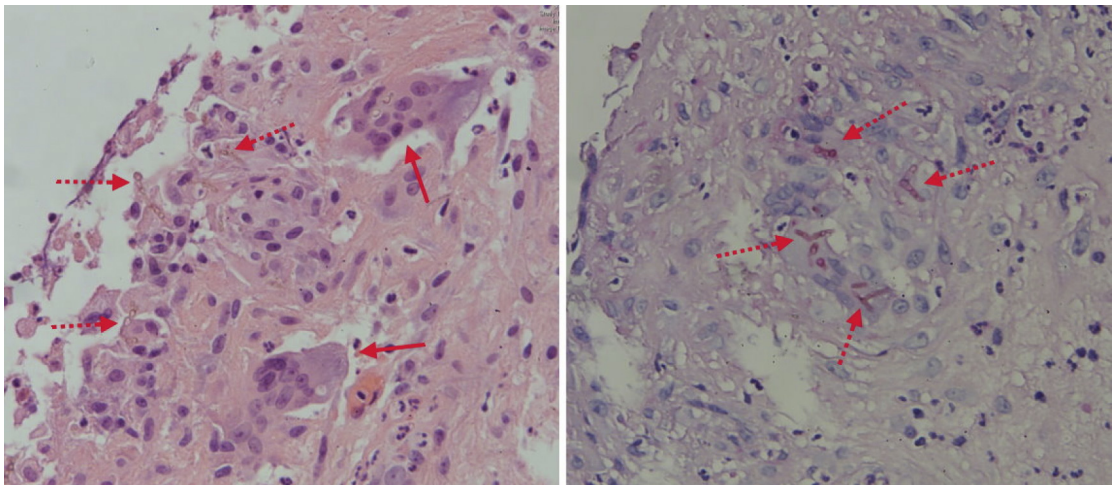

Figure 2. Hematoxylin and eosin staining shows granulomas with multinucleated giant cells and fungal hyphae (left). Periodic acid-Schiff staining shows multiple hyphae (right). An arrowhead with a dotted line indicates fungal hyphae. An arrowhead with a solid line indicates multinucleated giant cells.

12 weeks.[5] Phenotypic and biochemical methods cannot distinguish *E jeanselmei* from *E oligosperma*.[6,9] In addition, *E spinifera* may be confused with *E jeanselmei* due to similar early colony morphologic characteristics. Sequencing of the rDNA *ITS1-5.8S-ITS2* gene has proven to be a useful molecular tool for reliable and rapid identification of most black-grain mycetoma agents.[6,9]

Subcutaneous phaeohyphomycosis can occur in both immunocompetent and immunosuppressed patients, the latter being at greater risk of treatment failure and subsequent dissemination of the infection. Owing to the rarity of this infection, there are no clinical trials to guide the management of subcutaneous phaeohyphomycosis caused by *E jeanselmei*. The optimal antifungal agent in the treatment of *E jeanselmei* is still unknown. Historically, itraconazole and voriconazole have demonstrated the most consistent *in vitro* activity against *Exophiala* species.[10,11] Severe infections due to *E jeanselmei*, including pneumonia, fungemia, central nervous system infection, endocarditis, and peritonitis, have been reported in immunocompromised patients.[12,13] Antifungal therapy is recommended until all signs and symptoms of infection have resolved.[8] In Taiwan, three reported cases of subcutaneous phaeohyphomycosis caused by *Exophiala jeanselmei* were identified in the literature, and all three involved immunocompromised patients.[14,15] Two cases were treated successfully with itraconazole plus either debridement or cryotherapy. Our case showed that surgical excision alone was sufficient to treat and cure subcutaneous phaeohyphomycosis caused by *E jeanselmei* in an immunocompetent host. Although cryotherapy seems effective for treatment of subcutaneous phaeohyphomycosis, it is unknown whether cryotherapy alone is a sufficient treatment in immunocompetent hosts.

In summary, *E jeanselmei* should be suspected in immunocompetent patients presenting with chronic subcutaneous lesions. The diagnosis can be made by histopathologic and microbiologic evaluation of tissue and exudate. Surgical excision alone appears to be an efficacious therapy in immunocompetent hosts.

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