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Case report

Two rare cases of fungal bursitis due to *Phialemoniopsis pluriloculosa*

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ABSTRACT

Fungal infections due to *Phialemoniopsis* spp. are rarely reported in the medical literature. We report the first two cases of fungal bursitis of the knee by *Phialemoniopsis pluriloculosa*, which has not been previously reported. Both patients were successfully treated with a six-month course of posaconazole.

Introduction

Phialemoniopsis spp. are dematiaceous fungal organisms that cause a group of infections known as phaeohyphomycoses [1]. Previously thought to be related to *Phialemonium*, this genus is now known to be morphologically distinct as proposed by Perdomo et al. in 2013 [1]. These organisms are naturally found in the environment such as soil, sewage, and river water. Currently, six species are known—*Phialemoniopsis cornearis, Phialemoniopsis curvatum* (formerly *Phialemonium curvatum), Phialemoniopsis ocularis, Phialemoniopsis hongkongensis, Phialemoniopsis endophytica* and *Phialemoniopsis pluriloculosa* [1,2]. Phaeohyphomycosis due to these organisms is typically related to skin and soft tissue after trauma or injury [3]. Five total patients with skin infections have been reported previously due to *Phialemoniopsis* spp. Bursitis due to *Philemoniopsis* spp. has never been previously reported based on our literature review [4–8]. We present the first report of two cases of fungal bursitis by *Phialemoniopsis plurilocusa* in two patients.

Case 1

The patient was a 60-year-old male with type II diabetes mellitus and rheumatoid arthritis (managed with methotrexate 15 mg once per week and folic acid once per day). He had swelling of the right knee for one year, which was thought to be secondary to chronic rheumatoid arthritis. After starting his new occupation as a garbage truck driver, his right knee pain worsened over the course of a few weeks. He was evaluated at an orthopedics office on day 0, where he was found to have a large effusion along the medial right knee over the pes anserine insertion. The patient denied any known trauma, fever or chills at that visit but reported other chronic rheumatoid joint pain and myalgias without acute changes. At that visit, ultrasound-guided aspiration of the right infrapatellar bursa yielded 60 mL of yellow serous fluid. Cell count analysis of the fluid showed 2235 WBC/μL (63 % neutrophils, 13 % lymphocytes, 22 % mononuclear cells, 1% eosinophils). Although both the Gram stain and the fungal smear of bursal fluid were initially negative, routine cultures as well as fungal culture both grew a fungal isolate as "1+ mold," which was presumptively identified as 1+ *Sporothrix schenckii* on day 14. To confirm this isolate, he underwent a repeat diagnostic right knee bursal aspiration by orthopedics on day 29. Fungal culture of the repeat specimen was again positive and reported as two colonies of mold. MRI imaging of the right knee was also obtained on day 31, demonstrating a medial meniscal tear and a fluid collection anterior to the patellar tendon and the tibial tuberosity communicating with the medial knee. The patient was referred to infectious diseases and initiated on itraconazole 200 mg BID for treatment of presumptive *Sporthorix schenckii* on day 42. The fungal isolate was sent to the University of Texas Fungus Testing Laboratory (UTFTL) for complete identification and susceptibility testing.

The patient underwent irrigation and debridement of the right knee joint on day 45, during which two infected fluid pockets were noted measuring 8 × 10 mm and 10 × 12 mm. Straw-colored

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synovial fluid was encountered and necrotic subcutaneous tissue was debrided. The bursa was excised, and pathology demonstrated minimal inflammation and focal superficial fibrin deposition. On day 48, results from the initial aspiration returned from the UTFTL and reported the fungal isolate as *Phialemoniopsis pluriloculosa* identified by combined phenotypic characterization and DNA sequencing of the targets D1/D2 and ACT with susceptibilities as noted in Table 1. Fungal isolate from the second aspiration (from day 29) also resulted as *Phialemoniopsis pluriloculosa*, and subsequently four out of six total fungal cultures sent from surgically debrided specimens (from day 45) also resulted as *Phialemoniopsis pluriloculosa* per the UTFTL. The patient was switched to posaconazole 300 mg QD on day 52 due to concern for relative resistance to itraconazole and better tolerability. The patient was treated with posaconazole for a total of six months, which he tolerated well and returned to his baseline status.

Case 2

A 49-year-old male with a history of osteoarthritic joint pains and coronary artery disease presented with sporadic left knee pain and swelling in late June 2018. He was evaluated by his primary care physician on day 0, where he was diagnosed with prepatellar bursitis and underwent left knee arthrocentesis with removal of 6 mL of blood-tinged fluid demonstrating 1650 WBC/μL (neutrophils 49 %, lymphocytes 41 %). Routine cultures of this fluid were negative, and no fungal cultures were collected. At the same visit, he underwent intra-articular steroid injection at the site of inflammation with some relief of symptoms. Two days later, he presented to the emergency department (ED), with worsening symptoms and left knee erythema was also noted. Left knee aspiration was performed, from which 3 mL of clear yellow fluid showed 300 WBCs. The patient was presumptively diagnosed with left knee cellulitis, bursitis and empirically treated with oral cephalexin for 10 days.

He again returned on day 38 to the ED with worsening left knee erythema, swelling, pain and low-grade temperatures around 100.4 °F. Repeat CBC at this time showed mild leukocytosis (12,000/μl) with elevated CRP (4.19 mg/dL) and ESR (16 mm/hr). CT scan with contrast of the left knee demonstrated a ring-enhancing multiloculated fluid collection in the prepatellar region. On day 39, the patient underwent incision and drainage of the left knee prepatellar bursa abscess, during which purulence was encountered. Both routine as well as fungal cultures of this drained fluid rapidly grew 2+ mold. On day 44, the patient was initiated on posaconazole 300 mg QD. The fungal isolate was sent to the UTFTL for molecular identification and susceptibility testing. Subsequently on day 68, the identification returned as a *Phialemoniopsis* species closest to *Phialemoniopsis pluriloculosa,* identified by combined phenotypic characterization and DNA sequencing of the targets ITS and D1/D2 with susceptibilities as noted in Table 1. The patient was continued on a six-month course of posaconazole and had complete resolution of symptoms.

Table 1
Susceptibilities of isolated Phialemoniopsis pluriloculosa to antifungal agents (in μg/mL).

Antifungal agent	Case 1	Case 2
Amphotericin B	0.5	0.5
Fluconazole	>64	32
5-Fluorocytosine	>64	>64
Itraconazole	1	1
Voriconazole	2	1

All tests were performed by the Fungus Testing Laboratory at the University of Texas Health Science Center at San Antonio Department of Pathology.

Discussion

These two cases represent the first documented cases of fungal bursitis due to a new species of *Phialemoniopsis*—*Phialemoniopsis pluriloculosa,* identified by DNA sequencing and phenotypic characterization in both the patients. This organism has never been previously reported to be a human pathogen. Infections due to *Phialemoniopsis* spp. such as *curvatum, ocularis, endophytica* and *hongkongensis* have been reported. These infections were in immunocompromised patients and involved a prior history of trauma [4–8]. Our first patient was immunocompromised; however, he reported no trauma or injury preceding the infection. The source of his infection was not known. His occupation as a garbage truck driver could have possibly led to the exposure, considering this organism is found in the environment and the timing of onset of this patient's symptoms. Our second patient notably demonstrated no immunocompromising conditions nor a history of known trauma or injury. This patient had received a preceding steroid injection about one month prior to the diagnosis of left knee fungal prepatellar bursitis. The corresponding steroid production lot underwent evaluation for possible contamination, which was negative. The origin of his infection was unknown and possibly related to his occupation as a landscaper.

Since documented infections secondary to *Phialemoniopsis* spp. are rarely reported, there is a paucity of data regarding treatment for bursal and joint infections. Susceptibility studies of the closely related genus *Phialemonium* show that these organisms may be more susceptible to voriconazole and posaconazole. Some studies demonstrated noticeably higher MICs to amphotericin B deoxycholate and capsofungin, whereas fluconazole and itraconazole demonstrated intermediate MICs [9].

Based on above studies, oral itraconazole or voriconazole seemed reasonable oral treatment options, and both have also demonstrated consistent *in vitro* activity against organisms causing phaeohyphomycoses [10]. The susceptibility results demonstrated minimum inhibitory concentrations (MIC) of 1 μg/mL to itraconazole in both cases and MICs of 2 μg/mL and 1 μg/mL to voriconazole, in cases 1 and 2 respectively. As itraconazole usually reaches therapeutic levels around 1 μg/mL, this was not considered an ideal option. For voriconazole, our institution had extensive experience during a fungal meningitis outbreak in 2012 and observed lower tolerance to voriconazole. Therefore, a six-month course of 300 mg posaconazole QD was utilized in both patients, and they were treated successfully without any side effects [11,12].

Of note regarding the first case, the organism was presumptively misidentified as *Sporothrix schenckii*. Only after the isolate was sent to the UTFTL for DNA sequencing, the organism was specifically identified as *Phialemoniopsis pluriloculosa*. Therefore, physicians should consider the potential for misidentification of these isolates and should specifically request DNA identification in such cases.

Only one patient had an immunocompromising condition, and neither had a history of known trauma. Both were outdoor workers with frequent exposure to garbage and soil. Thus, occupational exposure could be proposed as a potential risk factor. Physicians evaluating such patients should consider *Phialemoniopsis* spp. as an etiology of routine culture-negative bursitis in the presence of appropriate risk factors.

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Consent

None.

Author contribution

Dr. Ekta Bansal provided care to the patients involved in this case as well as writing and preparing this manuscript.

CRediT authorship contribution statement

Harsh Patolia: Writing - original draft, Writing - review & editing. **Ekta Bansal:** Supervision, Writing - review & editing, Conceptualization.

Declaration of Competing Interest

The authors report no declarations of interest.

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