CASE REPORT

Phaeohyphomycotic pseudotumor of the right elbow caused by *Trematosphaeria grisea*

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INTRODUCTION

Dematiaceous fungi (DF) are ubiquitous saprophytic filamentous molds characterized by dark structures due to melanin deposition in their cell wall. The 3 clinical syndromes resulting from DF infection of the skin are eumycetoma, chromoblastomycosis, and phaeohyphomycosis. Cutaneous phaeohyphomycotic infections present as subcutaneous nodules or cysts and are histopathologically characterized by the presence of pigmented septate hyphae, pseudohyphae, or yeast in the absence of mycotic grains and medlar bodies. The latter are pathognomonic for eumycetoma or chromoblastomycosis, respectively, and may involve the bones, presenting as plaques (chromoblastomycosis) or deep draining sinuses (eumycetoma). The disease is endemic to tropical regions, affects patients regardless of immune status, and occurs after the introduction of the organism into the skin by minor trauma. Hence, acral areas are most often affected. Recent literature suggests that the type of clinical presentation (eumycetoma, chromoblastomycosis, or phaeohyphomycosis) may depend not only on virulence but also the type of induced host immune response.

*Trematosphaeria grisea* (*T. grisea*) is a dematiaceous fungus classically associated with eumycetoma and rarely implicated in phaeohyphomycosis. Herein, we present a case of a phaeohyphomycotic right elbow pseudotumor caused by *T. grisea* developing in an immunocompetent patient after treatment of long-standing fungal olecranon bursitis caused by the same organism.

CASE REPORT

A 49-year-old immunocompetent male truck driver from Chicago with an unremarkable medical history presented with a slow-growing painless soft-tissue mass on the right elbow after long-standing (4 years) olecranon bursitis. He could not recall any trauma to the site and denied travel to endemic areas, apart from staying in some of the southern states (Texas, Arizona, California, Florida) for work. He was otherwise in good general health.

On examination, he had an asymptomatic 4-cm nodule on posterior aspect of the right elbow with no overlying skin changes, warmth, or impairment in range of motion. The remaining skin exam was unremarkable, with no lymphadenopathy. He was HIV-negative, with otherwise normal complete blood count, blood chemistries, and CD4 count. He was originally referred by rheumatology who had treated him for olecranon bursitis prior to presentation at our clinic. Analysis of aspirated synovial fluid revealed brownish fluid with pigmented fungal hyphae. Genetic sequencing and culture revealed *T. grisea*. Imaging studies did not reveal dissemination, and the patient was initiated on itraconazole (100 mg twice daily) for 12 months per recommendation by infectious disease. Upon completion of therapy, the patient returned, complaining of a recurrent mass, which developed at the location of the prior bursitis.

Abbreviation used:

**DF**: dematiaceous fungi
Excisional biopsy demonstrated a mixed granulomatous infiltrate (Fig 2, A) consisting of giant cells, lymphocytes, and neutrophils. Special stains demonstrated septate fungal hyphae (Gomori methenamine silver stain; Fig 2, B) with production of melanin (Fontana-Masson stain; Fig 2, C). Growth of light gray colonies with central dark gray areas were obtained on Sabouraud dextrose agar (Fig 2, D), with no species-specific conidia or toruloid mycelia. Fungal ribosomal internal transcribed spacer region DNA sequencing was conducted using RipSeq Single software (Pathogenomix), which provided a 100% match to several CBS reference strains deposited in GenBank (PMID: 25737597). The organism was identified as \textit{T. grisea}.

To our knowledge, \textit{T. grisea} subcutaneous phaeohyphomycosis localized to the elbow subsequent to previously treated olecranon bursitis has not been reported. Eumycetoma localized to the elbow is also rare.\textsuperscript{1} While the olecranon region is prone to superficial injury, the development of fungal bursitis is exceptional and often associated with immunocompromised conditions.\textsuperscript{3} Moreover, our report confirms that, in addition to eumycetoma, \textit{T. grisea} can be a phaeohyphomycotic agent. Complex host-pathogen immune interactions determine the presenting clinicopathologic features of DF infection. Recent evidence suggests that different fungal cell wall lectins from the same species and their interaction with antigen-presenting cells may influence various T-helper cell immune responses.\textsuperscript{2} These varying responses may favor certain clinical presentations over another, even among infections with the same fungal organism.\textsuperscript{2} In fact, other species, such as \textit{Exophiala jeanselmei}, may also give rise to different DF syndromes (eumycetoma, chromoblastomycosis, or phaeohyphomycosis).\textsuperscript{6}

Although our patient denied staying in areas where \textit{T. grisea} is endemic (Latin and South America),\textsuperscript{7} he could have acquired the infection from a minor unrecognized trauma while traveling in Southern United States, close to the Mexican border. We speculate that the immune environment of the bursa, combined with long-term itraconazole treatment, prevented the formation of grains and full presentation of eumycetoma, resulting in the development of predominantly phaeohyphomycotic clinical and histopathologic features. Further research into the complex interplay between host factors, site of infection, and virulence of the fungal pathogen may yield more understanding as to this peculiar clinical presentation.

There is no standardized therapy for phaeohyphomycosis; however, surgical excision with or without antifungal therapy is a common approach.\textsuperscript{1} Itraconazole is preferred for most DF infections\textsuperscript{8} and is favored for \textit{T. grisea} with 200-400 mg per day.\textsuperscript{9} Antifungal treatment durations are individualized but often last for several months or longer.\textsuperscript{8}

In conclusion, the current case is unique in that it is the second \textit{T. grisea} subcutaneous phaeohyphomycosis and, likely, the first genetically confirmed report in the United States. Our report demonstrates that in addition to eumycetoma, \textit{T. grisea} can cause phaeohyphomycosis even in immunocompetent...
hosts. The possibility of infection with DF, including phaeohyphomycosis, should be considered when evaluating chronic subcutaneous masses especially after neoplastic, inflammatory, and other infectious etiologies have been excluded.

We wish to express our appreciation to the patient for providing consent for the publication of this case.

Conflicts of interest
None declared.

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Fig 2. Histologic and culture images from excisional biopsy. A, Mixed granulomatous infiltrate consisting of giant cells, lymphocytes, and neutrophils. (Hematoxylin-eosin stain; original magnification A, ×200). B, Septate fungal hyphae of variable sizes (Gomori methenamine silver stain; original magnification B, ×400). C, Tissue sample demonstrating positive, variable, patchy staining pattern (Fontana-Masson stain; original magnification C, ×400). Arrows indicate areas positive for melanin. D, Growth of light gray colonies with central dark gray areas on Sabouraud dextrose agar after 20 days of incubation at 30°C.
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