A Swollen Knee in a 77-Year-Old Lung Cancer Patient Receiving Antimicrobial Therapy for Pneumonia

(See page 1778 for the Photo Quiz.)

Diagnosis: Septic arthritis due to *Scedosporium apiospermum*.

A filamentous fungus was isolated from the specimen of the swelling knee, which showed whitish, downy, cottony colonies on blood and chocolate agar plates (Figure 1B) and grayish-white colonies on potato dextrose agar (Figure 2A). Microscopic morphology showed *Scedosporium* anamorph (conidiophores bearing single ovoid conidia) and *Graphium* synanamorph (a later stage at the edge of the colony, consisting of stiff, erect bundles of hyphae, terminating in a brush of club-shaped conidiogenous cells) (Figure 2B and 2C). These macroscopic and microscopic features were compatible with *Scedosporium* species. The organism was further identified as *Scedosporium apiospermum* with sequence analysis of internally transcribed spacer regions and ribosomal DNA D1/D2 domain sequence (a fragment of the nuclear gene calmodulin) [1].

*Scedosporium apiospermum* is a ubiquitous filamentous fungus originating in a wide variety of natural environments, such as soil, manure, dried vegetation, and contaminated waters. It had originally been considered as the asexual stage (anamorph) of *Pseudallescheria boydii* until advances in multi-locus phylogenetic studies revealed that the previously named *P. boydii* is a species complex which is comprised of at least 8 species. *Pseudallescheria boydii* and *S. apiospermum* are now considered to be 2 distinct species [2].

Invasive infections caused by *Scedosporium* species are emerging in critically ill and immunocompromised patients and are associated with high morbidity and mortality rates [3,4].

Figure 1.  A, Photograph of the left knee at presentation.  B, Multiple whitish, downy, cottony colonies on blood and chocolate agar plates.

Figure 2.  A, *Scedosporium apiospermum* on potato dextrose agar at 40 days of incubation at 25°C, showing grayish-white, suede-like colonies.  Wave-like spread of the colony on potato dextrose agar is characteristic of the fungus.  B, Lactophenol cotton blue stain showing 2 types of anamorphic forms: *Scedosporium* anamorph, oval conidia present singly or as small groups on elongated conidiophores (arrowheads), and *Graphium* synanamorph (arrows) (magnification, ×400).  C, *Graphium* synanamorph: long, erect conidiophores cemented together to form synnemata.  The apex of each synnema terminates in a brush of club-shaped conidia (magnification, ×1000).
The species cause a wide range of clinical symptoms, ranging from localized mycetoma to deep-seated disease and disseminated infections [3]. Our reported case, as a cancer patient, was under risk for opportunistic invasive fungal infections; however, joint and bone involvement is uncommon [5]. Patients with fungal osteoarticular infection often have a history of local trauma, surgery, or therapeutic joint steroid injection, or the infection is secondary to hematogenous spread in immunocompromised hosts [5]. Bone and joint involvement by S. apiospermum is often manifested with an indolent course [3]. Because the clinical course and histopathology of S. apiospermum joint infections are similar to those of other filamentous fungi such as Aspergillus species, Fusarium species, and Sporothrix schenckii, definitive diagnosis would necessarily be established through synovial culture. Molecular techniques could provide rapid and timely identification [6].

Our reported patient had received erlotinib treatment for 1 year with multiple follicular papules over seborrheic regions and extremities before the fungal arthritis episode. These inflammatory follicular papules, which impaired the cutaneous barrier, may provide an environment for colonization, proliferation, and invasion by microorganisms [7, 8]. Further studies are needed to evaluate whether erlotinib would increase the possibility of invasive fungal infection.

Therapeutic options for Scedosporium species infections are limited because they are nonsusceptible to a number of antifungal agents such as fluconazole and fluconosine, and possess variable susceptibility to amphotericin B,itraconazole, and ketoconazole [9]. In the largest case series study of S. apiospermum infection, 70 patients with S. apiospermum infection were treated with voriconazole. Sixty-four percent of patients achieved a successful response after a median of 103 days of therapy [4]. Early surgical intervention combined with adequate antifungal treatment is considered to be the essential management. Regressed swollen knee was observed after 10 days of voriconazole treatment in our patient; he later died due to severe ventilator-associated pneumonia.

Notes

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