Fungal Musculoskeletal Infections

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KEYWORDS

• Fungi • Osteomyelitis • Septic arthritis • Prosthetic joint infection • Candida • Aspergillus

KEY POINTS

- Fungal osteoarticular infections are complex infections that are seldom encountered in routine clinical practice.
- The clinical presentation is often subacute and diagnosis requires a high index of suspicion.
- Delayed diagnosis can lead to considerable morbidity.
- The treatment approach depends on the type of fungus present, the immune status of the host, the presence of foreign bodies, and the site of the infection.

INTRODUCTION

Fungal osteoarticular infections (OAI) are unusual but often destructive infections requiring surgery and prolonged antifungal therapy. These infections involve bone, joints, muscle, and connective tissue, such as ligaments and tendons, and can involve contiguous structures. The severity of these infections is related to the immune function of the host, the presence of foreign bodies, and the inherent pathogenicity of the organism. Over the past decade, there have been increasing reports of fungal musculoskeletal infections in both immunocompromised and immunocompetent hosts.[1]

PATHOGENESIS AND PRESENTATION

Fungal OAIs are caused by a wide variety of commensal, zoonotic, and environmental yeasts and molds. Although most of these infections occur in immunocompromised

Disclosure: Dr T.J. Walsh has received research grants in mycological research from Astellas, Pfizer, Merck, and Novartis. He has served as consultant to Astellas, Pfizer, Novartis, and Methylgene. The other authors have nothing to disclose.

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Infect Dis Clin N Am 31 (2017) 353–368
http://dx.doi.org/10.1016/j.idc.2017.01.006
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hosts, healthy hosts can also develop these infections as well. *De novo* infections in immunocompetent hosts with environmental dimorphic fungi, such as *Coccidioides immitis* and *Blastomyces dermatitidis*, arise following hematogenous spread from their site of entry or via direct inoculation.[2] Healthy hosts can also develop fungal musculoskeletal infections from nosocomial exposures, such as prior surgery or placement of indwelling foreign bodies. Fungal infections can be introduced via direct implantation, as seen in the intravenous drug use community, in trauma victims, and as a complication of parenteral treatment, such as was seen with the recent *Exserohilum rostratum* outbreak in the United States, which stemmed from the contamination of preservative-free steroids used for local spinal or paraspinal injections.[3] Immunocompromised patients are susceptible to a wide range of yeast and mold musculoskeletal infections, both endogenous and from the environment. The mostly commonly reported genera are *Candida* and *Aspergillus*, but a wide array of other opportunistic fungi, including *Fusarium* spp, *Scedosporium* spp, Mucorales, and dematiaceous molds, have been reported.[4]

The basic underlying pathophysiology of fungal musculoskeletal infections mirrors that of more common bacterial infections. These infections can occur in isolation or as part of a systemic infection with multiple organ involvement. The site of infection can be reached hematogenously, by contiguous spread or by direct inoculation.[5,6] In the setting of hematogenous spread, involvement of more than 1 noncontiguous bone or joint is common. Any bone or joint can be a site of infection, although the large, weight-bearing joints and bones, vertebrae, and ribs are most commonly involved.[2,5,6] Contiguous spread can occur from adjacent bone or joints, as well as from infected soft tissue in close proximity, as is seen in skull-base osteomyelitis in the setting of untreated otogenic infections[7] or in the setting of eumycetoma.[8] Infection can also be introduced at the time of surgery. Given the delayed onset of infection in many cases, taking a careful history of prior procedures, including intra-articular injections, and of penetrating trauma to the site of infection, can help establish a route of direct inoculation. Increasingly, invasive fungal infections related to trauma sustained in combat or in natural disasters have been reported.[9,10] Many medically important fungi, including *Candida*, *Aspergillus*, *Cryptococcus*, *Coccidioides*, and *Trichosporon*, have been shown to form biofilm, which decreases the efficacy of antifungal treatment and may lead to intractable infections.[11,12]

Owing to their rarity and generally subacute presentation, the most important aspect of the diagnosis of these infections is their inclusion in the differential diagnosis, particularly in immunocompetent patients. Microbiologic and histologic detection of fungal infections can require specialized culture media and stains, which may not be used routinely during evaluation for an osteoarticular infection. Diagnoses can be delayed when positive cultures are assumed to be contaminants. Fungal OAI can present in a broad array symptoms and time of onset, depending on the pathogenicity of the underlying organism, the site of infection, and the underlying health of the patient. Local pain, swelling, and other typical signs of inflammation are the most common presenting symptoms and signs; with chronicity, sinus drainage and extension into soft tissue may develop.[6,13] These infections can mimic other processes, including malignancy, tuberculosis, and more routine bacterial infections.[14]

TREATMENT

The overall approach to treatment involves surgical debridement of necrotic and nonviable tissues, in combination with prolonged courses of antifungal therapy. In addition to debridement, surgical management also involves irrigation, removal of infected hardware when possible, fixation and/or grafting of bone, and use of