Mycotic Septic Arthritis of the Ankle Joint

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Abstract
Septic arthritis is a debilitating acute orthopedic emergency. Unfortunately, the diagnosis can be delayed or missed in immunocompromised patients with diabetes mellitus, and the result can be catastrophic. These patients are also at risk for atypical infections, including mycotic subtypes, which are more insidious than their more aggressive, more common Staphylococcus counterparts. The result is increased morbidity. In this article, we report a case of Candida albicans septic arthritis in a patient with diabetes mellitus and rheumatoid arthritis. Her case highlights the complexities of this specific disease entity. With early diagnosis, treatment is multimodal, involving surgical débridement and prolonged antifungal therapy.

Case Report
A 52-year-old woman with type 2 DM (requiring subcutaneous insulin analogue therapy) and RA presented to a local emergency department with a 3-day history of right ankle pain after having the subtalar joint injected with steroid by a rheumatologist 4 weeks earlier. For about 2 weeks, there was purulent discharge from the peroneal sheath. The patient’s RA was being treated with prednisolone (maintenance therapy). Physical examination revealed low-grade pyrexia (37.8°C) and difficulty bearing full weight on the ankle. Clinically, the joint was not erythematous, but active and passive movements were painful. Blood tests revealed a C-reactive protein level of 98 mg/dL and a white blood cell (WBC) count of 11.3 × 10^9/L. Erythrocyte sedimentation rate (ESR) was not checked. The ankle underwent magnetic resonance imaging (Figures A-D). The subtalar joint was aspirated under ultrasound guidance, and specimens were sent for identification of organisms and sensitivities. More aspirate was obtained 1 week later. Both aspirates grew mycotic organisms.

Mycotic screening of the fluid was positive for C. albicans. The patient was referred to the orthopedic team, which performed urgent arthroscopic surgical débridement, biopsy, and washout of the subtalar joint. After surgery, a 6-week course of antifungal therapy with anidulafungin was started, per specialist microbiology advice.

The septic ankle was successfully managed with arthroscopic surgical débridement followed by treatment with anidulafungin. The patient continued to make good progress and was weight-bearing when discharged home from the orthopedic unit.

Discussion
Worldwide, about 1 in 6 people has arthritis, which affects daily lifestyle and reduces quality of life. Degenerative, inflammatory, and septic arthritis each has its management challenges.1

Septic arthritis is an acute infection of the joint, usually of bacterial etiology. It can present as a polyarticular arthropathy (~15% of cases),2,3 but a monoarthritis of the hip, knee, or ankle is more common.4

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The Kocher criteria are often applied to cases of suspected septic arthritis of joints, even though they were initially used to distinguish septic arthritis from transient synovitis in pediatric hip joints. Kocher and colleagues reported 4 key clinical criteria: inability to bear weight, WBC count over $12 \times 10^9/L$, ESR over 40 mm/h, and temperature over 38.5°C. When all 4 criteria are met, the predictive value is 99.6%. These criteria are now widely applied to adult joints, and not only the hips.

In septic arthritis, the most common causative pathogen is \textit{S. aureus}. \textit{Streptococcus}, \textit{Neisseria}, and \textit{Pseudomonas} also are common. Although much rarer, \textit{Candida} variants and other mycotic pathogens have been implicated as well. \textit{C. albicans} is a well-known fungus that colonizes mucosal surfaces. Research indicates increased oral \textit{C. albicans} colonization in rheumatoid patients. Although most \textit{Candida} septic arthritis cases are caused by \textit{C. albicans}, there is no large body of data showing the true incidence of fungal pathogens in septic arthritis.

Our literature search yielded 2 case reports on \textit{Candida} septic arthritis involving the ankle, but the causative organisms were \textit{Candida parapsilosis} and \textit{Candida glabrata}. Cases of \textit{Candida} septic arthritis involving the knee or shoulder have also been reported. Case reports demonstrate that \textit{Candida} fungal arthritis is extremely rare. Etiology reportedly includes direct intra-articular inoculation by surgery or secondary to hematogenous seeding, particularly in immunocompromised patients. Risk factors include immunosuppression and joint suppression. DM and RA are common comorbidities in patients with septic arthritis. The pathophysiology of RA is inflammatory pannus formation of the periarticular surface with subsequent articular cartilage destruction and erosion, as well as progressive deformity and functional debilitation.

Patients with DM are at increased risk for developing fungal and other infections. Factors increasing this risk include disruption of skin-barrier integrity; reduced peripheral oxygen and blood supply, which also disrupts antibiotic delivery; and hyperglycemia-induced reduction in antibody function and disruption of phagocytosis and chemotaxis.

Fungi are eukaryotic, and infections caused by these organisms are difficult to treat. As fungal infections are more prevalent among immunosuppressed patients, they often result in prolonged treatment without guarantee of eradication, as spores may persist subclinically.

Literature on \textit{C. albicans} septic arthritis is lacking in general but especially in rheumatoid patients. Delayed diagnosis and suboptimal treatment may result in fungal osteomyelitis. There is little evidence on treating this rare fungal complication, and outcomes historically have been poor.

In an animal model, Marijnissen and colleagues found that \textit{C. albicans} infection can increase destruction in an arthritic joint by cytokine environment modification. The result was advanced destruction of the joint and debilitation. For disease management, the authors considered these essential: early diagnosis, prompt treatment, and, as indicated, surgical débridement.

Treatment of \textit{Candida} septic arthritis largely involves use of antifungal medication, either with surgical débridement, as in our patient’s case, or without. Which antifungal medication to use should be based on sensitivities, identified from wound aspirate, and microbiology advice about treatment duration. The antibiotic should be a broad-spectrum antifungal cover, in keeping with local antibiotic prescribing guidelines, which can be refined once definitive organism culture and sensitivity results are known. However, early aggressive treatment is essential. Periprosthetic fungal infection is rarely resolved without implant removal.
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Conclusion
This case reflects the complexities of septic arthritis caused by atypical pathogens and highlights the need for clinical vigilance in the setting of comorbidities, such as DM and RA. Failure to consider the diagnosis early on might result in delayed and inadequate treatment, increased joint destruction, and, potentially, osteomyelitis with subsequent increased morbidity. Early diagnosis (based on joint aspirate findings), surgical débridement, and prolonged aggressive treatment with antifungal medication are the mainstays of treatment.

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