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Case Report

Candida arthritis in a patient diagnosed with spondyloarthritis

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Abstract

Candida arthritis is an unusual manifestation that usually affects the knees. A 35-year-old man presented with a 2-month history of pain and swelling in the right knee. Swelling persisted after anti-inflammatory treatment. Peripheric spondyloarthritis was considered, but methotrexate, sulfasalazine, and methylprednisolone did not reduce the swelling. Direct examination of synovial fluid and a culture were positive for *Candida albicans*. Intravenous and intra-articular amphotericin-B were administered. The arthritis regressed and a culture and direct staining showed negative results. *Candida* arthritis should be considered in patients with arthritis that is resistant to treatment and prolonged, even if risk factors are absent.

Keywords: *Candida*. Arthritis. Spondyloarthropathy.

INTRODUCTION

Septic arthritis is a common rheumatological emergency that requires immediate investigation and treatment to prevent permanent cartilage destruction. While fungal arthritis caused by *Candida* species is very rare, *Candida albicans* is the form that is isolated most frequently from fungus-infected joints. *Candida* arthritis usually affects large joints – most often the knees – and particularly involves patients who have risk factors[1] [2]. Here, we have presented a case of *Candida* arthritis in a patient who was diagnosed with and treated for peripheral spondyloarthritis.

CASE REPORT

A 35-year-old man presented with pain and swelling in his right knee that had started 2 months previously. On examination, he was febrile at 38.2°C and had swelling, warmth, and tenderness in his right knee. Five months previously, he had undergone brain surgery after trauma from a cerebrovascular accident. He had stayed in an intensive care unit for about 2 weeks.

Two months before he presented at our institution, swelling, pain, and tenderness began first in his shoulder and then in his right knee. Arthrocentesis was performed and increased white blood cell and neutrophil counts were observed in the synovial fluid, while cultures were negative. Seronegative spondyloarthritis was considered and methotrexate and sulfasalazine were prescribed. Although swelling decreased in his shoulder, it persisted in his knee. Despite performing arthrocentesis several times, administering intra-articular steroid injection, and providing medication, the swelling and tenderness of the right knee continued.

The erythrocyte sedimentation rate (ESR) was 48mm/h, the C-reactive protein (CRP) level was 10.8mg/dL, and rheumatoid factor and anti-cyclic citrullinated peptide test results were negative. The patient consulted the Department of Infectious Disease and Clinical Microbiology, and his synovial fluid was examined for a possible infectious agent. Direct examinations of synovial fluid with Gram and hematoxylin-eosin stains showed positive findings for fungal infection. Inoculation into BACTEC™ culture bottles (Becton, Dickinson and Company, Franklin Lakes, USA) led to the isolation of a *C. albicans* two times (**Figure 1**). Arthrocentesis revealed 52,000 cells/mm^3 (91% neutrophils). Magnetic resonance imaging showed intensive synovial tissue hypertrophy; increased synovial fluid; soft tissue edema expanding to the suprapatellar, infrapatellar, and popliteal areas surrounding the knee; and post-contrast enhancement (**Figure 2A**).

In an arthroscopic examination of the knee, synovial hypertrophy was detected (**Figure 2B**). During the procedure, articular debridement was performed and 50-mg lipossomal amphotericin-B was administered intra-articularly only once. Subsequently, intravenous lipossomal amphotericin-B was prescribed at 350mg/day for 38 days. After treatment, progressive clinical regression of the arthritis was observed. Further, direct examination of synovial fluid and inoculation

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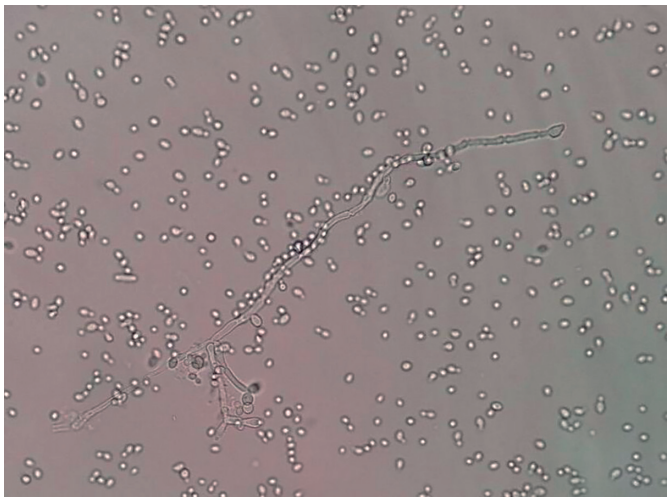

FIGURE 1. Germ tubes of *Candida albicans* detected in the synovial fluid.

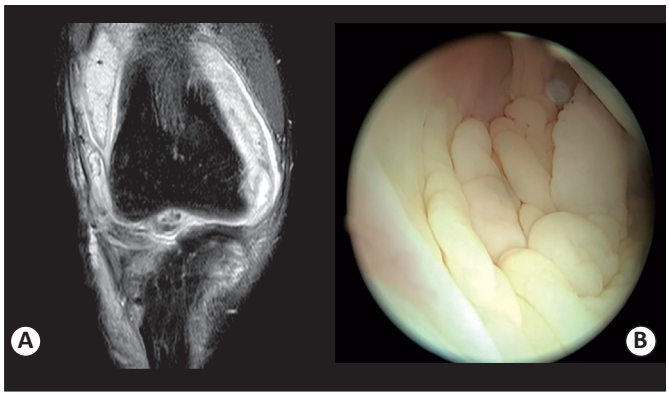

FIGURE 2. **(A):** Intensive synovial tissue hypertrophy; increased synovial fluid; soft tissue edema expanding to the suprapatellar, infrapatellar, and popliteal areas located around the knee; and post-contrast enhancement in magnetic resonance imaging. **(B):** Atypical synovial and septal thickening and white villous formation in the knee during arthroscopic examination.

for fungal infection both showed negative results. His ESR was 17mm/h and his CRP level was 0.84mm/dL. Synovial inflammation and effusion also decreased on magnetic resonance imaging.

DISCUSSION

Although *Candida* species are an uncommon cause of infectious arthritis, the of *Candida* arthritis has increased in recent years. *Candida* arthritis can be a consequence of either hematogenous dissemination or direct inoculation due to trauma, surgery, or intra-articular injections. Invasive candidiasis is mostly associated with immunosuppressed conditions and is very uncommon in immunocompetent patients. *C. albicans*, the causative agent in our patient, has been the predominant *Candida* species documented in joint infections[1] [2].

In the present case, *Candida* infection may have been acquired in the intensive care unit after the patient's brain surgery, because of the use of broad-spectrum antibiotics. In the previously investigated intensive care units, 44.8% of patients were being treated for infection, of which 17.1% were associated with fungi[3] [4]. However, we could not rule out the possibility that the patient's arthritis may have first developed in an inflammatory form, both because the synovial analysis was negative for *Candida* infection and because his shoulder arthritis improved with methotrexate and sulfasalazine treatment. Nonetheless, arthrocentesis was performed several times, an intra-articular steroid injection was administered, and the immunosuppressive effects of the methotrexate and sulfasalazine medication may also have contributed to the fungal colonization. Fungal arthritis is most often attributable to hematogenous seeding, rather than to direct inoculation of fungi[5]. *Candida* arthritis following direct inoculation has been described, but appears to be rare and is linked with intra-articular injection, inoculation by surgery, and other underlying risk factors.

As in our patient, *Candida* arthritis usually affects large joints, most often the knees. Arthritis typically presents with pain or tenderness of the involved joint. The characteristic *Candida* septic arthritis often occurs without erythema and warmth of the involved joint, although most patients who have presented with affected joints that are more superficial (e.g., the ankle or knee) have reported warmth and swelling. Fever is often absent, but some febrile cases of candidal arthritis have been reported previously[5] [6], and our patient also had a fever.

When *Candida* arthritis occurs in patients with underlying chronic joint diseases, the diagnosis is commonly delayed because clinical findings are usually ascribed to the primary joint disease. Secondary destruction of articular cartilage and progressive bone deformity can occur; therefore, early detection and therapy are essential to prevent significant morbidity. Because there are no specific clinical or radiologic findings of *Candida* arthritis, only an appropriate culture permits diagnosis[7] [8]. Because of the persistency of the arthritis, despite conventional medical and interventional treatment for inflammatory arthritis, the synovial fluid is examined closely and repeatedly. Correct diagnosis is established through the isolation of *C. albicans* by positive Gram and hematoxylin-eosin stains, and appropriate culturing.

Candida arthritis is treated with joint debridement and antifungal medications. Prolonged systemic antifungals such as amphotericin, fluconazole, ketoconazole, and 5-flourocytosine (5FC) have been used in the treatment of *Candida* arthritis. Of these antifungals, amphotericin and 5FC can also be administered intra-articularly as an adjunctive treatment. Amphotericin has been used in most of cases, with encouraging results[6]. It has been recommended that the duration of medication-based therapy should be at least 6 weeks for *Candida* arthritis, despite the availability of little data[2].

In conclusion, in cases of arthritis that are resistant to treatment and prolonged, *Candida* arthritis should be considered, particularly for patients who have underlying risk factors. Early diagnosis and therapy are essential to prevent the establishment of joint deformity.

Conflicts of Interest

The authors declare that there is no conflict of interest.

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