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Case Report

Nontuberculous Mycobacterium Arthritis and Spondylitis in a Patient with Lupus

Nayoung Park[1], Sunjoo Lee[2], Chisook Moon[3], Dongyook Kim[1], Heuichul Gwak[4], Minyoung Her[1]

Divisions of [1]Rheumatology and [3]Infection Disease, Department of Internal Medicine, Departments of [2]Radiology and [4]Orthopedic Surgery, Busan Paik Hospital, Inje University College of Medicine, Busan, Korea

Approximately 90% of nontuberculous mycobacterium (NTM) infections involve the pulmonary system; NTM infections involving areas of the musculoskeletal system such as the joints or spine are uncommon. This report describes a case of refractory knee swelling in a patient with systemic lupus erythematosus (SLE). Indolent arthritis of the knee eventually progressed to spondylitis and a paraspinal abscess requiring surgical incision and drainage. The cause of the infectious arthritis and spondylitis was diagnosed as NTM infection, specifically *Mycobacterium kansasii*. This case emphasizes the importance of a high index of clinical suspicion for mycobacterial infection, as well as repeated attempts to isolate the organism, in patients with SLE who present with atypical chronic arthritis. **(J Rheum Dis 2016;23:66-70)**

Key Words. Nontuberculous mycobacteria, Systemic lupus erythematosus

INTRODUCTION

Arthritis is a common manifestation of systemic lupus erythematosus (SLE) and is one component of the 1982 American College of Rheumatology (ACR) SLE classification criteria. It is not unusual for physicians to see SLE patients with arthritis. SLE-associated arthritis generally presents as intermittent polyarthritis involving the hands, wrists and knees [1]. If pain persists in one joint, especially the knee or hip, avascular necrosis should be suspected in SLE patients.

Nontuberculous mycobacterium (NTM) species are typically environmental and poorly pathogenic for humans; they can, however, be responsible for opportunistic diseases in subjects with various predisposing conditions. Approximately 90% of NTM infections involve the pulmonary system; the rest involve the lymph nodes, skin, soft tissues, bones and joints, which are also important targets of NTM infection [2,3]. *Mycobacterium kansasii*, *M. marinum*, and *M. avium* are common forms of NTM and can involve musculoskeletal tissues [4]. There is a well-known and steadily increasing risk of disseminated infections in immunocompromised patients, such as organ transplant recipients and patients with autoimmune diseases, including SLE [5-7].

In this paper, an SLE patient who presented with refractory knee arthritis progressed to spondylitis and a paraspinal abscess caused by NTM infection, specifically *M. kansasii*. This case highlights the importance of a high index of clinical suspicion for mycobacterial infection in patients with atypical chronic arthritis.

CASE REPORT

A 73-year-old woman presented with a 1-month history of left knee pain and swelling; 4 months prior, she was diagnosed with SLE based on the presence of leukopenia, thrombocytopenia, oral ulcers, pleuritis, high antinuclear antibody titers, and positive anti-Ro antibodies. She was treated with hydroxychloroquine, danazol and inter-

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Corresponding to : Minyoung Her, Divisions of Rheumatology, Department of Internal Medicine, Busan Paik Hospital, Inje University College of Medicine, 75 Bokji-ro, Busanjin-gu, Busan 47392, Korea. E-mail : bettyboomboo@hanmail.net

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mittent prednisone.

A physical exam showed tenderness, swelling and heatness of the left knee joint. Synovial fluid analysis showed a neutrophil count of approximately 5,000/mm^3; gram staining, cultures and acid-fast bacilli (AFB) staining were all negative. A knee radiograph showed underlying osteoarthritis. Magnetic resonance (MR) images of the knee showed joint effusion with intense synovial enhancement. The probable diagnosis was inflammatory arthritis associated with SLE. Methotrexate, nonsteroidal anti-inflammatory drugs (NSAIDs), and intra-articular steroid injections were prescribed.

Three months later, the patient returned in a wheelchair with marked knee swelling and intractable pain. Physical examination of the left knee was remarkable for severe swelling, heatness, erythema and a limited range of motion. A joint fluid analysis still indicated an inflammatory pattern, with 11,000/mm^3 white blood cells and 98% polymorphonuclear cells. However, new bone erosions were visible on the knee radiograph (Figure 1). MR images of the knee showed a peripherally enhancing fluid collection in the suprapatellar pouch and the lateral gastrocnemial bursa (Figure 2A). Furthermore, multifocal bone erosions of the lateral femoral condyle and tibial plateau were observed (Figure 2B). Infectious arthritis and bursitis were suspected, and the patient underwent surgical incision and drainage. A synovial tissue biopsy was performed, which showed fibrinosuppurative inflammation. The patient was empirically started on 1 g intravenous cefazedone twice daily for 1 month, which was followed by oral therapy with 100 mg cefixime twice a day for 4 months. Gram stain and culture of the knee fluid and synovial tissue showed no definite evidence of bacterial infection. However, the patient's left knee joint symptoms persisted, and her C-reactive protein level never reached the normal range but instead remained between 3 and 5 mg/L.

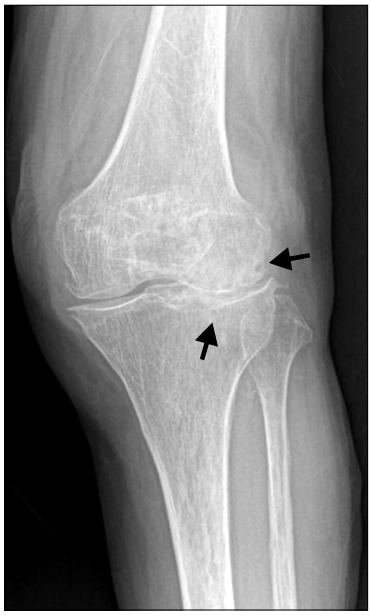

Figure 1. A knee radiograph shows bone erosions of the lateral femoral condyle and tibial plateau (arrows).

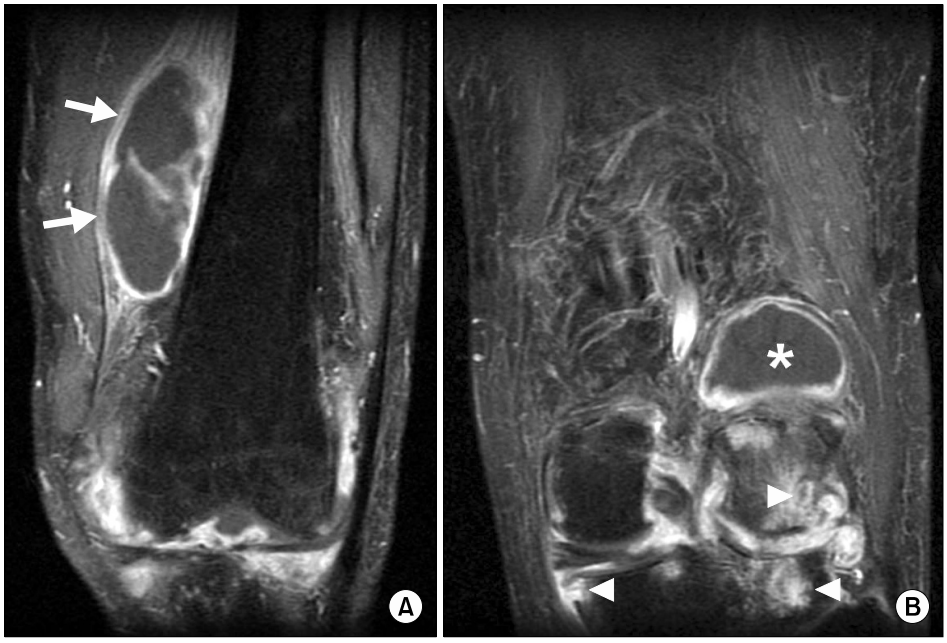

Figure 2. Gadolinium-enhanced coronal fat-suppressed T1-weighted magnetic resonance images show a peripherally enhancing fluid collection in the suprapatellar pouch (arrows) and lateral gastrocnemial bursa (asterisk). Note the intense enhancement of the synovium of the knee joint and bone erosions of the lateral femoral condyle and tibial plateau (arrowheads).

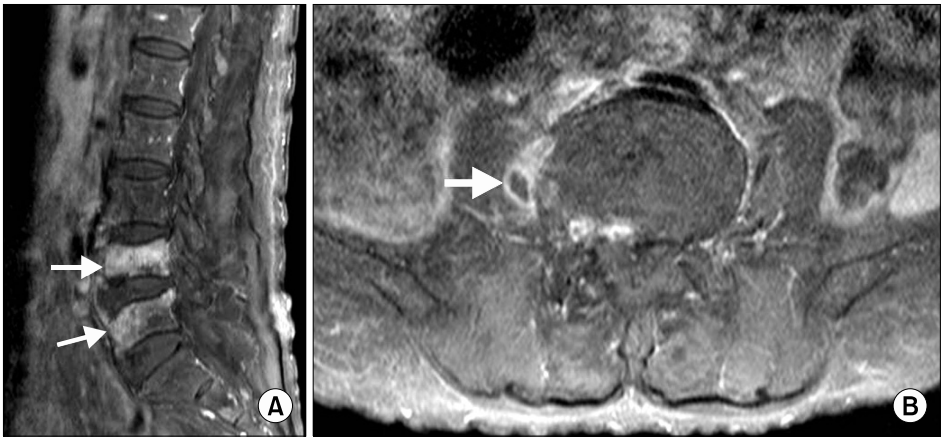

Figure 3. (A) A gadolinium-enhanced sagittal fat-suppressed T1-weighted magnetic resonance (MR) image shows heterogeneous enhancement of the L4 and L5 vertebral bodies, suggesting spondylitis (arrows). (B) A gadolinium-enhanced axial fat-suppressed T1-weighted MR image shows peripheral enhancement of a fluid collection in the right psoas muscle (arrow).

While she remained on antibiotics, she gradually developed back pain that was refractory to analgesics. Physical examination revealed tenderness with gentle percussion in the lumbar region, a limited range of motion in the back, and marked swelling of the left popliteal fossa. An ultrasonographic examination of the left knee was performed, which showed a large cystic lesion in the left popliteal fossa with internal debris. Gram stain, cultures, tuberculosis polymerase chain reaction (Tb-PCR), and AFB stain of the Baker's cyst were all negative. MR images of the lumbar spine showed heterogeneous enhancement of the L4 and L5 vertebral bodies (Figure 3A). A small abscess (5×12 mm) was observed in the right psoas muscle at the L4-5 level (Figure 3B). Infectious spondylitis with a right psoas abscess was diagnosed, and decompression with surgical incision and drainage of the abscess were performed. Routine cultures with gram staining of the abscess showed negative results. AFB positive strain was cultured on egg-based solid media from the abscess and this was presumptively reported as NTM by negative results for Tb-PCR. This strain was finally identified as *M. kansasii* using GenoType Mycobacterium assay (Hain Life science GmbH, Nehren, Germany). *M. kansasii* was also detected in the Baker's cyst fluid using this assay.

The final diagnosis was NTM knee arthritis, an infected Baker's cyst, spondylitis, and a paravertebral abscess caused by NTM infection, specifically *M. kansasii*. The human immunodeficiency virus (HIV) antibody was negative, and a chest X-ray was normal. Treatment with anti-mycobacterial medications including isoniazid (300 mg/d), rifampin (450 mg/d) and ethambutol (800 mg/d) was initiated, but the patient developed nausea and vomiting. She was therefore treated with clarithromycin (500 mg/d), rifampin (450 mg/d) and ethambutol (800 mg/d) for more than one year, and her symptoms finally improved with these medications.

DISCUSSION

NTM are widely distributed in nature and usually have low pathogenic potential. More than 140 NTM species have been reported in the literature; only 25 species have been strongly associated with atypical mycobacterial diseases, and the rest are environmental organisms [7,8]. Approximately 90% of NTM cases involve the pulmonary system, and NTM infections involving the musculoskeletal system are uncommon [2]. Musculoskeletal mycobacterium tuberculosis (MTB) infection mostly occurs via hematogenous spread from a primary focus, such as a lung, kidney, or lymph node, and rarely via direct inoculation from adjacent tissues [9]. In contrast, musculoskeletal NTM infection is usually acquired through direct inoculation from penetrating trauma, injuries, needle injections or surgical procedures.

Clinically, osteoarticular NTM infections are indistinguishable from MTB infections. Signs and symptoms of both types of infections include localized pain, joint swelling, stiffness, low grade fever, sweating, chill, fatigue, anorexia and weight loss [2]. Shu et al. (2009) reported about mycobacterial arthritis of large joints. Relative to patients with MTB large-joint arthritis, patients with NTM large-joint arthritis tend to be younger and have longer symptom duration and more delayed diagnosis. In cases of NTM arthritis, systemic symptoms such as fever are more common, synovial fluid analysis has a higher leukocyte counts, there is a relatively specific histological finding of non-caseating granulomatous inflammation, and the clinical course is generally more in-

dolent and less toxic. However these differences in clinical characteristics are statistically insignificant [10].

Patients with NTM-related vertebral osteomyelitis generally have various degrees of immunosuppression, such as acquired immunodeficiency syndrome, SLE, or a history of organ transplantation [2,8]. *M. kansasii* and the *M. avium* complex are the most common causes of NTM diseases in the United States [3,4].

In cases of atypical monoarthritis in immunocompromised patients, mycobacterial infections should be considered [4-6]. However, due to their rarity, clinical diversity, the lack of specific imaging findings, and the difficulty in isolating and culturing the infectious organism, heightened clinical suspicion is needed to diagnose cases of NTM arthritis [11-13]. The clinical features are often indistinguishable from those of pyogenic osteomyelitis. *M. kansasii* infections are generally indolent, and a delay in diagnosis is common [11]. In our case, the delayed diagnosis of knee arthritis led to spondylitis and a paraspinal abscess that required surgical treatment. Despite accumulating data regarding NTM, its diagnosis and treatment remain challenging. If mycobacteria are not present in sufficient numbers to be observed under the microscope, an AFB smear may be negative despite mycobacterial infection [3,12]. Therefore, an AFB culture must be performed in conjunction with an AFB smear to rule out the possibility of mycobacterial infection.

There are no established guidelines for the treatment of NTM infections. Antimicrobial treatment is poorly effective when not combined with surgical treatment [13,14]. Once an NTM infection is diagnosed, a combination of surgical and antimicrobial therapy is often required to completely eradicate the lesions. In addition, the optimal duration of therapy has not been established because antibiotics penetrate more poorly into the bones than into the respiratory tract. Therefore, bone NTM infections require a longer duration of antibiotic treatment (usually more than 12 months) than do respiratory NTM infections, and medications should not be discontinued until symptoms resolve and erythrocyte sedimentation rate (ESR) normalizes [11].

It is important for the physician to recognize NTM infections, in addition to *M. tuberculosis*, in patients presenting with musculoskeletal symptoms. Physicians should include NTM as well as *M. tuberculosis* in the differential diagnosis of organisms that can cause indolent infectious arthritis in patients with atypical chronic arthritis, especially in the setting of immunocompromised conditions.

SUMMARY

NTM infections involving the musculoskeletal system are uncommon but need to be considered in the appropriate circumstances, or an important diagnosis may be missed. Due to their rarity, as well as the lack of systematic epidemiologic studies, standard case definitions, accurate mycobacterial identification and specific imaging findings, a definitive diagnosis of NTM diseases is often delayed or even impossible. Therefore, a heightened clinical suspicion for NTM in patients with arthritis is needed when routine gram stains, cultures or histopathological findings do not identify the organism. In cases of atypical monoarthritis in patients with SLE or other rheumatic diseases with recent-onset inflammation of any part of the musculoskeletal system, mycobacterial infection should be considered as a possible causative agent, especially when the patient is receiving immunosuppressive drugs.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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