Case Report

http://dx.doi.org/10.3947/ic.2012.44.6.530
Infect Chemother 2012;44(6):530-534
pISSN 2093-2340 eISSN 2092-6448

Infection & Chemotherapy

면역정상인에서 발생한 *Mycobacterium abscessus*에 의한 척추골수염

제동모 · 강철인 · 정지영 · 정혜민 · 조윤영 · 허경민 · 백경란

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Vertebral Osteomyelitis caused by *Mycobacterium abscessus* in an Immunocompetent Patient

Vertebral osteomyelitis caused by nontuberculous mycobacteria (NTM) is rarely reported, especially in an immunocompetent host. NTM are usually not susceptible in vitro to antituberculous drugs, and appropriate antimicrobial therapy for treatment of NTM infection is based on susceptibility results, which vary between different NTM species; therefore, treatment of vertebral osteomyelitis caused by NTM is challenging. We report on the first case of vertebral osteomyelitis caused by *M. abscessus* in an otherwise healthy individual, confirmed by cultures of bone tissue obtained during surgery. Clinical cure was achieved with a combination of antimicrobial therapy and surgery. We also review previous reports of vertebral osteomyelitis caused by NTM.

Key Words: Nontuberculous Mycobacteria, *Mycobacterium abscessus*, Vertebral Osteomyelitis, Immunocompetent Host

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Introduction

Nontuberculous mycobacteria (NTM) are free-living organisms that are ubiquitous in the environment. These organisms can also inhabit body surfaces or secretions without causing significant disease. Thus, occasional isolates of NTM are largely considered colonizers or contaminants. However, with the decreasing incidence of tuberculosis and development of new microbiological diagnostic methods, the importance of NTM in human disease has become increasingly evident. NTM cause distinct clinical syndromes, such as pulmonary disease, superficial lymphadenitis, skin and soft tissue infections, and disseminated disease in severely immunocompromised patients [1].

Rapidly growing mycobacteria (RGM) include three clinically relevant species, *Mycobacterium fortuitum*, *M. chelonae*, and *M. abscessus*. RGM are environmental organisms found worldwide; compared with other mycobacteria,

Submitted: July 19, 2012
Revised: October 1, 2012
Accepted: October 19, 2012
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RGM usually show rapid growth in subculture within one week. Among RGM, *M. abscessus* is the most pathogenic; RGM are likely to cause pulmonary infection, primarily in patients with underlying lung disease. RGM also cause infections of the musculoskeletal system from either hematogenous seeding or percutaneous inoculation due to trauma or surgery. The clinical course is indolent, slowly progressive, and destructive, due in part to delay in diagnosis. Herein, we report on a case of vertebral osteomyelitis caused by *M. abscessus* in an immunocompetent patient with no risk factors.

Case Report

A 55-year-old female patient presented with a ten-month history of progressive lower-back pain. She did not have a history of trauma, penetrating injury, or invasive procedure, such as acupuncture, immunocompromised status, diabetes, or steroid use. In another hospital, she was diagnosed with infectious spondylitis and was initially treated with cefazolin and then switched to ciprofloxacin for a total of two months.

However, her lower-back pain did not show improvement. Therefore, she was transferred to our hospital.

A physical examination showed diffuse tenderness over the mid-lumbar region, however, no other signs of neurological involvement were observed. She was afebrile and had a negative psoas sign.

Results of laboratory studies showed a WBC count of 6,700/mm^3 and a C-reactive protein (CRP) level of 6.04 mg/dL. A human immunodeficiency virus serology test showed a negative result, and the tuberculin skin test also showed a negative result. Findings on an initial CT scan showed infectious spondylitis of L2 and L3 and disc bulging with annular tears at L3-L4 and L5-S1. MRI of the spine showed enhancement of the L2, L3 vertebral bodies, the intervertebral disc space between L2-L3, as well as paraspinal abscesses (Fig. 1). She was diagnosed with vertebral osteomyelitis and underwent debridement and drainage of the paraspinal abscess, corpectomy of L2 and L3, total discectomy of L2 and L3, and anterior lumbar interbody fusion from L2 to L3 with an autologous iliac bone graft. A specimen obtained surgically showed acute osteomyelitis of the bone, chronic inflammation, and myositis of the soft tissue. Results of AFB stain, cultures, and NTM PCR (polymerase chain reaction) of the collected disc, muscle, and abscess indicated *M. abscessus*.

The patient was treated with an initial antimycobacterial regimen that included IV amikacin, IV imipenem, IV moxifloxacin, and oral clarithromycin. After the first month of treatment, by a drug sensitivity test of *M. abscessus* referred to the Korean Institute of Tuberculosis, *M. abscessus* isolated from the patient was found to be susceptible only to clarithromycin and was resistant to ciprofloxacin, doxycycline, and trimethoprim-sulfamethoxazole. The patient was discharged from the hospital, taking clarithromycin and rifampin.

At her two-month follow-up, she reported that her back pain had gradually subsided, her CRP level had normalized, and follow-up radiographs showed stabilization of the involved segments. The patient took clarithromycin and rifampicin for six months.

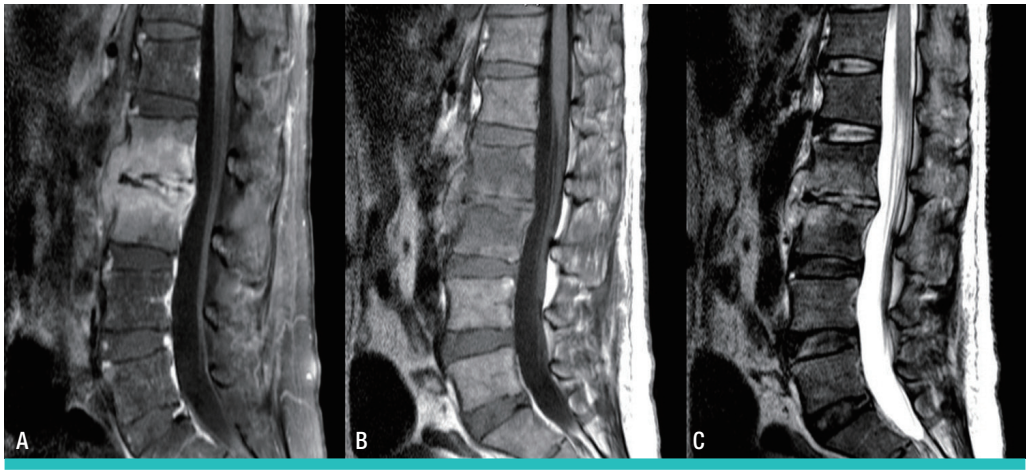

Figure 1. Spondylitis of the L2, L3 bodies with a prevertebral abscess is shown as low signal intensity on a T1-weighted image, high signal intensity on a T2-weighted image, and enhancement on a contrast media-enhanced T1-weighted image. (A) T1-weighted image, (B) T2-weighted image, (C) contrast media-enhanced T1-weighted image).

Discussion

NTM are an extremely rare cause of vertebral osteomyelitis. A MedLine review of the literature published between 1965 and June 2012 found only 53 case reports and one report on a nosocomial outbreak [2-15]. The NTM species identified most frequently was *M. avium* complex (n=17), followed by *M. xenopi* (n=12), *M. fortuitum* (n=9), *M. abscessus* (n=4), *M. chelonae* (n=2), and *M. kansasii* (n=3); single cases involving *M. bovis*, *M. flavescens, M. heckeshornense, M. simiae*, and two unidentified NTM were also reported (Table 1). Various degrees of immunosuppression (systemic lupus erythematosus with steroids, n=8; HIV infection, n=9; interferon receptor defect, n=1; carcinoma, n=1; diabetes, n=1; renal failure, n=1; liver cirrhosis, n=1; chronic granulomatous disease, n=1; rheumatoid arthritis with etanercept, n=1; and renal transplantation recipient, n=1) were reported in 25 (47.2%) of 53 patients with vertebral osteomyelitis caused by NTM. Seven patients (13.2%) developed vertebral osteomyelitis caused by NTM after blunt trauma or surgery to the back. Other reported causes of vertebral osteomyelitis were chronic lung disease (n=2) and intravenous drug abuse (n=2). Vertebral osteomyelitis caused by *M. abscessus* is none in an immunocompetent patient. We report on the first case of vertebral osteomyelitis caused by *M. abscessus* in an otherwise healthy individual.

Diagnosis of vertebral osteomyelitis, based on clinical, laboratory, and radiologic features, can be difficult. Due to the rarity of the disease, the insidious onset of symptoms, and the high frequency of lower back pain in the general population, it is often delayed or missed. In diagnosis, biopsy or culture of the vertebral lesion can provide important clues, and must be performed during the initial stages.

Diagnosis of NTM vertebral osteomyelitis can be easily missed in patients without risk factors. A high index of suspicion is required for prompt diagnosis in order to ensure improved long-term outcomes when the clinical course is indolent, slowly progressive, destructive, and not responsive to empirical antibacterial agents. Laboratory tests and imaging studies are not sufficient for diagnosis and differentiation from other infections. Organisms are isolated from sterile tissue or bony specimens for diagnosis of NTM vertebral osteomyelitis [16]. If the specimen shows a positive result for AFB stain, it will then be analyzed for *M. tuberculosis* using MTB-PCR. In the case of a positive result for MTB-PCR, it can be tentatively diagnosed as *M. tuberculosis*. However, the possibility of NTM should be considered in cases showing a negative result of MTB-PCR and the results of the AFB culture will be necessary in the final diagnosis.

RGM, in particular, are highly resistant to multiple antimycobacterial drugs. A previous study reported that that all isolates of *M. abscessus* and *M. chelonae* and approximately 80 percent of isolates of *M. fortuitum* are susceptible in vitro to the macrolide clarithromycin [17].

Because of these resistance patterns, routine susceptibility testing to antituberculosis drugs is not recommended for RGM [1]. Our results from antimicrobial susceptibility testing suggest that clarithromycin is the only effective agent against *M. abscessus*. Imipenem, cefoxitin, and amikacin may have a role in multiple drug regimens [18]. Monotherapy has proven disappointing for treatment of infections due to *M. abscessus*, and a combination of at least two to three active antibiotics is required.

No randomized controlled studies have evaluated the duration of antibiotic treatment for vertebral osteomyelitis. Previous experience suggests that in cases involving disseminated or deep-seated *M. abscessus* infection, antimicrobial treatment should be continued for a minimum of six weeks after clinical resolution of the primary infection; this usually requires six months of treatment [19]. A more prolonged course lasting years may be necessary in severely immunocompromised patients, and those with extensive bone destruction and/or paravertebral infection. A consensus on guidelines concerning treatment of spinal infections caused by NTM does not exist, however, limited clinical experience suggests that aggressive surgical debridement of all involved tissues is critical, and performance of sequential surgical procedures is often required. Indications for surgery in patients with pyogenic osteomyelitis include progression of disease despite adequate directed or empiric antimicrobial therapy, epidural or paravertebral abscess formation, and threatened or actual cord compression due to vertebral collapse and/or spinal instability [20]; because there is no consensus regarding indications for surgery in patients with vertebral osteomyelitis caused by NTM, these can be applied to patients with vertebral osteomyelitis caused by NTM. The best way to reduce the morbidity and mortality associated with vertebral osteomyelitis is to shorten the time between onset of symptoms and initiation of appropriate therapy.

Our case illustrates the unusual occurrence of vertebral osteomyelitis caused by one NTM, *M. abscessus*. Only four cases of vertebral osteomyelitis caused by *M. abscessus* have been reported in the literature; all patients had comorbid conditions, including steroid use, intravenous cocaine abuse, diabetes, and wounds from blunt trauma or surgery to the back. To the best of our knowledge, this is the first case of vertebral osteomyelitis caused by *M. abscessus* in an otherwise healthy individual. Owing to the negative AFB cultures and NTM PCR of the collected bony

Table 1. Clinical Characteristics of Patients with Vertebral Osteomyelitis Caused by NTM

Species	Underlying disease	Treatment	Treatment duration
M. abscessus	SLE, steroid therapy	Amikacin, clarithromycin	9 months
M. abscessus	Intravenous drug abuse	Clarithromycin, imipenem, cefoxitin	12 months
M. abscessus	Blunt trauma to the back	Clarithromycin	6 months
M. abscessus	Diabetes, surgery to the back	Clarithromycin-containing regimen	6 months
M. avium complex	None	Clarithromycin-containing regimen	12 months
M. avium complex	SLE, steroid therapy	Isoniazid, rifampin, ethambutol, streptomycin	NA
M. avium complex	SLE, steroid therapy	Amikacin, rifampin, ethambutol, ciprofloxacin, clofazimine	8 months
M. avium complex	None	Ciprofloxacin, erythromycin, ethambutol	6 months
M. avium complex	Blunt trauma to the back	Clarithromycin, ethambutol, clofazamine	18 months
M. avium complex	HIV infection	Clarithromycin, rifabutin, ethambutol	6 months
M. avium complex	Interferon receptor defect	NA	NA
M. avium complex	HIV infection	Ciprofloxacin, clarithromycin, ethambutol, rifabutin	NA
M. avium complex	HIV infection	Ciprofloxacin, azithromycin	NA
M. avium complex	HIV infection	Ciprofloxacin, clarithromycin, ethambutol, rifabutin	NA
M. avium complex	Renal failure	NA	NA
M. avium complex	HIV infection	Isoniazid, rifabutin, ethambutol, pyrazinamide, clarithromycin	NA
M. avium complex	Chronic lung disease	Clarithromycin, rifampin, ethambutol	NA
M. avium complex	Osteoporosis	Clarithromycin, rifampin, ethambutol	NA
M. avium complex	SLE, steroid therapy	NA	NA
M. avium complex	None	NA	NA
M. avium complex	None	Clarithromycin, rifampin, moxifloxacin	NA
M. bovis	Blunt trauma to the back	Isoniazid, rifampin, ethambutol	15 months
M. chelonae	Renal transplantation recipient	Ciprofloxacin, clarithromycin	15 months
M. chelonae	Intravenous drug abuse	NA	NA
M. chelonae	None	NA	NA
M. flavescens	None	NA	NA
M. fortuitum	Chronic granulomatous disease	Kanamycin, isoniazid, rifampin, ethionamide	24 months
M. fortuitum	Achalasia	NA	NA
M. fortuitum	Back injury	Isoniazid, rifampin, ethambutol, streptomycin, ethionamide, lincomycin	NA
M. fortuitum	Mental retardation	Rifampin, isoniazid, streptomycin, tetracycline	4 months
M. fortuitum	None	Gentamicin, ciprofloxacin	NA
M. fortuitum	SLE, steroid therapy	NA	NA
M. fortuitum	Chronic lung disease	NA	NA
M. fortuitum	None	NA	NA
M. heckeshornense	Rheumatoid arthritis with etanercept	Clarithromycin, rifampin, moxifloxacin	NA
M. kansasii	None	Isoniazid, ethambutol, streptomycin	36 months
M. kansasii	HIV infection	NA	NA
M. kansasii	None	NA	NA
M. simiae	Isoniazid prophylaxis for positive PPD	Isoniazid, rifampin, ethambutol, kanamycin	4 months
M. xenopi	SLE, steroid therapy	Isoniazid, rifampin, pyrazinamide, streptomycin	NA
M. xenopi	Breast cancer, tamoxifen therapy	Isoniazid, ethambutol, pyrazinamide, ciprofloxacin	24 months
M. xenopi	Hypertension	Isoniazid, rifampin, ethambutol, pyrazinamide, ciprofloxacin	24 months
M. xenopi	None	Clarithromycin-containing regimen	12 months
M. xenopi	None	Clarithromycin-containing regimen	12 months
M. xenopi	Liver cirrhosis	NA	NA
M. xenopi	SLE, steroid therapy	NA	NA
M. xenopi	HIV infection	NA	NA
M. xenopi	Discovertebral surgery	NA	NA
M. xenopi	HIV infection	NA	NA
M. xenopi	HIV infection	Isoniazid, rifabutin, ethambutol, clarithromycin	6 months
M. xenopi	SLE, steroid therapy	NA	NA
Unclassified NTM	Previous laminectomy	NA	NA
Unclassified NTM	Ankylosing spondylitis with interferon gamma	Meropenem, clarithromycin, amikacin	NA

NA, not available; SLE, systemic lupus erythematosus; PPD, purified protein derivative

specimens, the possibility of contamination by NTM cannot be completely excluded. However, we suppose that *M. abscessus* is the true pathogen because the clinical course of the patient showed improvement after treatment for NTM.

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