Vertebral Osteomyelitis Due to *Mycobacterium abscessus* in an HIV-Negative Patient: Case Report and Literature Review

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ABSTRACT

Atypical mycobacteria are an extremely rare cause of vertebral infection. Review of the English literature by use of MEDLINE from 1955 to 2012 revealed less than 50 cases of vertebral osteomyelitis due to atypical mycobacteria. Three of these cases were due to *Mycobacterium abscessus.* Infection of the musculoskeletal system with atypical mycobacterium usually involves tenosynovitis and occurs from either percutaneous inoculation or hematogenous spreading. The clinical course is indolent, slowly progressive, and destructive. Most cases were immunocompetent hosts. This presented case demonstrated vertebral osteomyelitis due to *M. abscessus* in an HIV-negative patient without history of any underlying diseases or trauma before having this infection. There are no consensus guidelines for the treatment of these infections. Treatment of these infections is difficult and requires a prolonged course of combination antimicrobial agents. Antimycobacterial treatments for infection due to *M. abscessus* are based on case series, in vitro susceptibility testing and the clinical experience of experts in patients with pulmonary diseases. Surgery is generally indicated with extensive cutaneous diseases, abscess formation or where drug therapy is difficult.

Keywords: Vertebral osteomyeltis, *Mycobacterium abscessus*

Siriraj Med J 2014;66:49-52
E-journal: http://www.sirirajmedj.com

BACKGROUND

Vertebral osteomyelitis due to infection with atypical mycobacterial organisms is rare. Direct inoculation following penetrating trauma, surgical incision or injections are important predisposing factors. Diagnosis is a major challenge that leads to the appropriate treatment. There are no consensus guidelines for treatment. Prolonged antimicrobial therapy in combination is recommended.

CASE REPORT

A 75 year-old Thai woman presented with a one-month history of progressive back pain and fever. She had mild weakness and numbness on both feet. She denied night sweats, chronic cough, weight loss and any skin lesions. She did not have any underlying disease. There was no history of trauma before the appearance of the symptoms. She did not have any history of drinking or smoking.

Physical examination revealed fever and tenderness over the lumbar spine. Abnormalities on neurological examination demonstrated weakness of extensor hallucis longus and impaired sensation on L5 to S1 dermatomes of both extremities. She did not have any skin lesions. No lymphadenopathy was detected. Other physical examinations were normal.

Laboratory studies found leukocytosis with neutrophil predominate. Her erythrocyte sedimentation rate (ESR) was 94 mm/hr. A test for antibodies to HIV was nonreactive. Blood tests for renal function, liver function and fasting sugar were normal. (Table 1) Chest x-ray was normal. Plain film of spine demonstrated diffused osteoporosis with moderate to marked collapse of L1-L5 bodies. Magnetic resonance imaging (MRI) found enhancing vertebral bodies and paravertebral soft tissue at L5-S1 levels. (Fig 1) Hemoculture demonstrated *Mycobacterium abscessus* that was susceptible to amikacin and clarithromycin. Commercial DNA probes (INNO-Lipa Line probes)

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Received 20 May 2013
Revised 19 June 2013
Accepted 24 July 2013

TABLE 1. Laboratory data.

Laboratory	Result
Completed blood count	Hb 11.3 g/dL, Hct 34%, WBC 10,400/mm^3 (N 72%, L 16%, M 9%, Eo1%), platelet 328,000/mm^3
BUN/creatinine	BUN 13 mg/dL, creatinine 0.7 mg/dL
Liver function test	Total/direct bilirubin 1.5/0.5 mg/dL, AST/ALT 32/22 U/L, alkaline phosphatase 94 U/L
Fasting blood sugar	FBS 93 mg/dL

were used for mycobacterial species identification. The susceptibility testing method was agar proportion method and reference of the minimum inhibitory concentration for amikacin, cefoxitin, ciprofloxacin, clarithromycin, doxycycline, imipenam and sulfamethoxazole-trimetroprim were 12, 4, 2, 3, 6, 16 and 36 mg/mL, respectively.

The patient's initial antimycobacterial regimen included intravenous amikacin, imipenam and ciprofloxacin as well as oral clarithromycin. After 2 weeks of treatment, she had no fever and less tenderness over the lumbar spine. The treatment was followed by oral ciprofloxacin and clarithromycin following the susceptibility results. The patient received antimycobacterial treatment for 18 months. She was pain free and able to walk with minimal assistance. The ESR was 42 mm/hr.

DISCUSSION

Atypical mycobacteria are an extremely rare cause of vertebral infection. Review of the English literature by use of MEDLINE from1955 to 2012 revealed only 34 cases reports and one nosocomial outbreak of vertebral osteomyelitis due to atypical mycobacteria. Three of these cases were due to *Mycobacterium abscessus*. The species identified most frequently was *Mycobacterium avium complex* (n= 14); this was followed by *Mycobacterium xenopi* (n=8) and *Mycobacterium fortuitum* (n=5). There were single cases involving *Mycobacterium kansasii*, *mycobacterium simiae, Mycobacterium chelonae* and one unidentified non-tuberculous mycobacterium.[1-16]

Mycobacterium abscessus is a rapidly growing mycobacteria (RGM). It is the most pathogenic of the RGM group to cause pulmonary infection, primarily in patients with underlying lung diseases.[17] In Thailand, most patients infected due to *M. chelonae/abscessus* had disseminated diseases followed by lymphadenitis. Three patients had osteomyelitis from hematogenous spreading in disseminated diseases.[18]

Infection of the musculoskeletal system with RGM usually involves tenosynovitis and occurs from either percutaneous inoculation (e.g., trauma or surgery) or hematogenous seeding. The clinical course is indolent, slowly progressive, and destructive. Most cases were immunocompetent hosts.[1-16] The presented patient had

TABLE 2. Clinical characteristics of patients with vertebral osteomyelitis due to *Mycobacterium abscessus.*

Case (ref)	Gender/ age(y)	Underlying condition	Country	Clinical manifestations	MRI	Treatment	Outcome
1 (1)	M/53	Intravenous drug abuse	USA	Low back pain, night sweat, weight loss	Destruction of L3-L5 vertebral bodies with paravertebral abscess	Clarithromycin+ imipenam+ cefoxitin for 12 months Debridement and fusion	Walks with aid
2 (3)	F/16	Skating accident	USA	Midthoracic back pain	Destruction of T9-T10 vertebral bodies with paravertebral abscess	Clarithromycin for 6 months No surgical treatment	Full range of activities
3 (17)	F/17	SLE, Steroid therapy	USA	Groin and leg pain, decreased Achilles reflex	Destruction of T12-L1 vertebral bodies	Amikacin for 2 months + clarithromycin for 7 months Debridement and fusion	Pain free
Presented case	F/75	No	Thailand	Back pain, fever	Destruction of L5-S1vertebral bodies	Amikacin (2 weeks)+ imipenam (2 weeks)+ ciprofloxacin (18 months)+ clarithromycin (18 months) No surgical treatment	Able to walk with minimal assistance

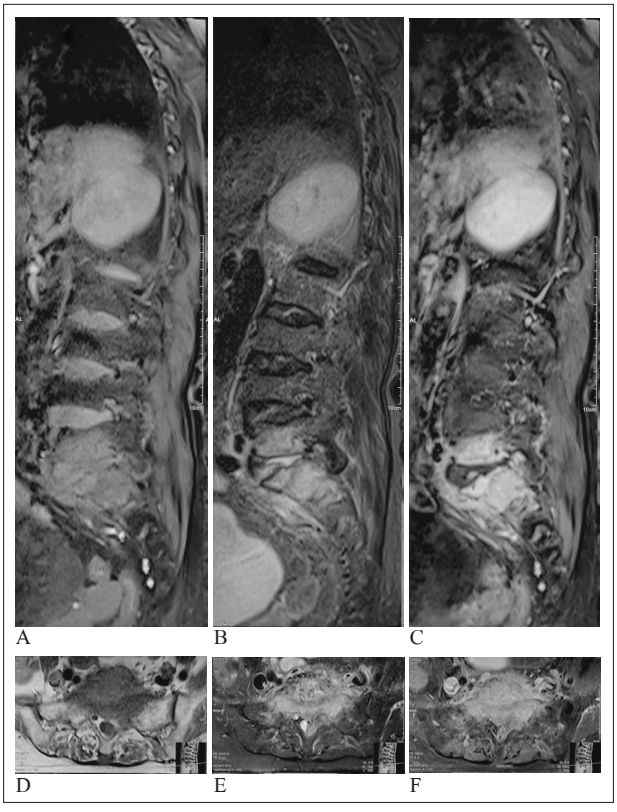

Fig 1. Magnetic resonance imaging with fat suppression in sagittal view A) T1-weighted B) T2 -weighted C) T1-weighted with gadolinium and in coronal view D) T1-weighted E) T2 -weighted F) T1-weighted with gadolinium demonstrated enhancement of L5-S1 vertebral bodies.

no history of any underlying diseases or trauma before having this infection.

The definite diagnosis of atypical mycobacterial vertebral osteomyelitis requires culture of a bone biopsy specimen.1 Although, the presented patient did not have culture from bone biopsy, but positive hemoculture without any other sites of infection other than her spine implied vertebral osteomyelitis with disseminated infection.

M.abscessus is highly resistant to multiple antimycobacterial drugs. Therapy includes both medical and surgical interventions. Antimycobacterial treatments are based on case series, in vitro susceptibility testing and the clinical experience of experts in patients with pulmonary diseases. The susceptibility pattern of isolates of *M. abscessus* is clarithromycin, amikacin, cefoxitin, imipenam and linezolid. The initial therapy for severe infections includes intravenous amikacinin, cefoxitin and imipenem combined with oral clarithromycin for 2-4 weeks. Therapy should be followed by an oral macrolide (clarithromycin or azithromycin) plus at least one other agent to which the organism is susceptible. The duration of therapy depends upon the site and severity of infection. A minimum of six months and twelve months of therapy were recommended for bone infection and for severe infections, respectively.[19,20] Previous study suggested that in disseminated or deep *M. abscessus* infections, antimicrobial treatment should be continued for at least 4-6 weeks after complete resolution, so this usually requires 6–12 months of treatment. However, more prolonged courses for years may be necessary in severely immunocompromised patients.[21] The presented patient received intravenous amikacin, imipenam and ciprofloxacin as well as oral clarithromycin for 2 weeks and followed by oral ciprofloxacin and clarithromycin for 18 months. Surgery is generally indicated with extensive cutaneous disease, abscess formation, or when drug therapy is difficult.[1] The presented case responded well to antimycobacterial agents and no abscess was seen on MRI, so surgery was not indicated for her.

This presented case demonstrated a rare occurrence of vertebral osteomyelitis due to *M. abscessus.* Treatment of these infections is difficult and requires a prolonged course of combination antimicrobial agents.

REFERENCES

1. Sarria JC, Chutkan NB, Figueroa JE, Hull A. Atypical mycobacterial vertebral osteomyelitis: case report and review. Clin Infect Dis. 1998 Feb;26 (2):503-5.
2. Igram CM, Petrie SG, Harris MB. Atypical mycobacterial vertebral osteomyelitis in an immunocompetent patient. Orthopedics. 1997 Feb;20(2):163-6.
3. Chan ED, Kong PM, Fennelly K, Dwyer AP, IsemanMD.Vertebral osteomyelitis due to infection with nontuberculous mycobacterium species after blunt trauma to the back:3 examples of the principle of locus minoris resistentiae.Clin Infect Dis. 2001 May 15;32(10):1506-10.
4. Danesh-Clough T, Theis JC, Vander Linden A. *Mycobacterium xenopi* infection of the spine: a case report and literature review. Spine (Phila Pa 1976). 2000 Mar 1;25(2):626-8.
5. Erard P, Robert-Grandpierre F, Kaeser P.Vertebral Osteomyelitis caused by *Mycobacterium avium–intracellulare* in a patient with AIDS. Clin Microbiol Infect. 1999 Oct;5(10):643-4.
6. Arend SM, Janssen R, Gosen JJ, Waanders H, de Boer T, Ottenhoff TH, et al. Multifocal osteomyelitis caused by nontuberculous mycobacteria in patients with a genetic defect of the interferon-c receptor. Neth J Med. 2001 Sep;59(3):140-51.
7. Aberg JA, Chin-Hong PV, McCutchan A, Koletar SL,Currier JS. Localized osteomyelitis due to *Mycobacterium avium complex* in patients with human immunodeficiency virus receiving high active antiretroviral therapy. Clin Infect Dis. 2002 Jul 1;35(1):E8-E13.
8. Otaki Y, Nakanishi T, Nanami M. A rare combination of sites of involvement by *Mycobacterium intracellulare* in a hemodialysis patient: multifocal synovitis, spondylitis, and multiple skin lesions. Nephron. 2002;92(3):730-4.
9. Telgt DS,Vanden Hoogen FH,Meis JF,Lemmens JA,Vanden Putte LB. Arthritis and spondylodiscitis caused by *Mycobacterium xenopi* in a patient with systemic lupus erythematosus. Br J Rheumatol. 1997 Sep;36(9):1025-6.
10. Kulasegaram R, Richardson D, Macrae B, deRuiter A. *Mycobacterium xenopi* osteomyelitis in a patient on highly active antiretroviral therapy (HAART). Int J STD AIDS. 2001 Jun;12(6):404–6.
11. Astagneau P, Desplaces N, Vincent V, Chicheportiche V,Botherel A, Mauqat S, et al. *Mycobacterium xenopi* spinal infections after discovertebral surgery: investigation and screening of a large outbreak. Lancet. 2001 Sep 1;358(9283):747-51.
12. Rahman I, Bhatt H, Chillag S, Duffus W. Mycobacterium chelonae vertebral osteomyelitis. South Med J. 2009 Nov;102(11):1167-9.
13. Pruitt TC, Hughes LO, Blasier RD, McCarthy RE, Glasier CM, Roloson GJ. Atypical mycobacterial vertebral osteomyelitis in a steroid-dependent adolescent. A case report. Spine (Phila Pa 1976). 1993 Dec;18(16):2553-5.
14. Pirofsky JG, Huang CT, Waites KB. Spinal osteomyelitis due to Mycobacterium avium-intracellulare in an elderly man with steroid-induced osteoporosis. Spine (Phila Pa 1976). 1993 Oct 1;18(13):1926-9.
15. Zvetina JR, Demos TC, Rubinstein H. Mycobacterium intracellulare infection of the shoulder and spine in a patient with steroid-treated systemic lupus erythematosus. Skeletal Radiol. 1982;8(2):111-3.
16. Petitjean G, Fluckiger U, Schären S, Laifer G. Vertebral osteomyelitis caused by non-tuberculous mycobacteria. Clin Microbiol Infect. 2004 Nov;10(11):951-3.

17. Griffith DE, Girard WM, Wallace RJ Jr. Clinical features of pulmonary disease caused by rapidly growing mycobacteria. An analysis of 154 patients. Am Rev Respir Dis 1993 May; 147(5):1271-8.
18. Phowthongkum P, Prasanthai V, Udomsantisook N, Suankratay C.Rapidly growing mycobacteria in King Chulalongkorn Memorial Hospital and review of the literature in Thailand. J Med Assoc Thai. 2005 Aug;88(8): 1153-62.
19. Griffith DE. The talking Mycobacterium abscessus blues. Clin Infect Dis. 2011 Mar 1;52(5):572-4.
20. Wallace RJ Jr, Swenson JM, Silcox VA, Bullen MG. Treatment of nonpulmonary infections due to Mycobacterium fortuitum and Mycobacterium chelonei on the basis of in vitro susceptibilities. J Infect Dis 1985 Sep; 152(3):500-14.
21. Ingram CW, Tanner DC, Durack DT, Kernodle GW, Corey GR. Disseminated infection with rapidly growing mycobacteria. Clin Infect Dis. 1993 Apr;16(4):463-71.