Spondylitis Due to *Mycobacterium xenopi* in a Human Immunodeficiency Virus Type 1-Infected Patient: Case Report and Review of the Literature

Agnès Meybeck,1* Claude Fortin,1 Sophie Abgrall,1 Homa Adle-Biassette,2 Gilles Hayem,3 Raymond Ruimy,4 and Patrick Yeni1

Service de Maladies Infectieuses et Tropicales A,1 Service d’Anatomopathologie,2 Service de Rhumatologie,3 and Service de Bactériologie,4 Hôpital Bichat-Claude Bernard, Paris, France

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Nontuberculous mycobacterial infections are well known to occur in patients with human immunodeficiency virus infection. However, spondylitis due to mycobacteria other than *Mycobacterium tuberculosis* is uncommon. We report a case of biopsy- and culture-proven *Mycobacterium xenopi* spondylitis in an AIDS patient and discuss approaches to diagnosis and therapy. This case serves to highlight the potential pathogenic role of this usually environmental commensal organism in severely immunosuppressed AIDS patients and uncertainties in their management, given the scarce data on appropriate therapy for this organism.

CASE REPORT

A 42-year-old man was diagnosed with AIDS in 1998 when he presented with *Pneumocystis carinii* pneumonia. Over the next few years, he developed several other opportunistic infections, as he was not adherent to antiretroviral therapy. In August 2003, he was admitted for cellulitis on the right side of his face. On admission, neurological examination found static cerebellar syndrome associated with kinetic gait instability. No sensory or motor deficit was found. The rest of the physical results were normal. Laboratory studies revealed normal full blood count, except for lymphopenia. The CD4 T-lymphocyte count was 41/mm³. Renal function and hepatic biology were within the normal limits. Three blood cultures were negative. Cerebral computed tomography (CT) scan showed several bilateral cortical hypodensities of frontal and temporal regions without enhancing after contrast product injection. Cerebral magnetic resonance imaging (MRI) revealed T2-weighted images without enhancing after gadolinium injection in the same areas. Cerebrospinal fluid showed 1 white blood cell as well as a protein level of 0.62 g/liter and a glucose level of 3 mmol/liter (serum level, 5.8 mmol/liter), and cultures were negative. The blood count was 41/mm³. Renal function and hepatic biology were within the normal limits. Three blood cultures were negative. Cerebral computed tomography (CT) scan showed several bilateral cortical hypodensities of frontal and temporal regions without enhancing after contrast product injection. Cerebral magnetic resonance imaging (MRI) revealed T2-weighted images without enhancing after gadolinium injection in the same areas. Cerebrospinal fluid showed 1 white blood cell as well as a protein level of 0.62 g/liter and a glucose level of 3 mmol/liter (serum level, 5.8 mmol/liter), and cultures were negative. The patient received intravenous oxacillin and needed surgical drainage for a facial soft-tissue abscess. Oxacillin was continued for 10 days. A presumptive standard treatment regimen against *Toxoplasma gondii* encephalitis was started, considering neurological signs and intracerebral abnormalities during CT scan and MRI. Progress was satisfactory at first, but after 2 weeks our patient developed sudden flaccid paralysis of both legs with a T8 sensory level. MRI of the spine revealed signs of spondylitis at the T7 to T8 level, with a locally compressing paraspinal soft-tissue-associated inflammatory process. Transoesophageal echocardiography showed no signs of endocarditis. A CT-guided vertebral biopsy was performed. Gram and acid-fast stains showed no organism, and standard bacterial cultures were negative after 48 h. Histology of the specimen showed nonspecific inflammation. Supposing that *Staphylococcus aureus* could be responsible for T7 to T8 spondylitis given the recent history of facial cellulitis, rifampin (600 mg twice a day) and ofloxacin (400 mg twice a day) were started after oxacillin was discontinued. Retrospective studies with chest X-rays taken 2 months earlier showed loss of T7 to T8 vertebral disk height, and this suggested chronic installation of discovertebral abnormalities. Moreover, MRIs suggested a subacute to chronic process compatible with mycobacterial disease. No history of tuberculosis was found. A tuberculin skin test was negative. Nevertheless, quadruple antituberculous therapy was started, and isoniazid, pyrazinamide, and ethambutol were added to rifampin and ofloxacin. Complementary histologic studies performed on the earlier vertebral biopsy specimen revealed granulomatous inflammation with caseation. After 6 weeks, *Mycobacterium xenopi* was isolated from a vertebral biopsy specimen. The mycobacteria colony morphology was smooth, and growth characteristics disclosed a slow-growing mycobacterium with optimal growth speed at 42°C. Photoreactivity testing revealed a nonchromogen isolate. The suspicion of *M. xenopi* infection was confirmed with rRNA nucleic acid probe testing. Pyrazinamide and ofloxacin administrations were stopped. Treatment was changed from rifampin to isoniazid, ethambutol, clarithromycin, and rifabutin, considering eventual introduction of lopivir/ritonavir-based highly active antiretroviral therapy. The patient’s condition improved, with rapid regression of flaccid paralysis and disappearance of epidural mass on MRI 2 months after treatment was started.

*Corresponding author. Mailing address: Service des Maladies Infectieuses et Tropicales A, Hôpital Bichat-Claude Bernard, 46 rue Henri Huchard, 75018 Paris, France. Phone: 33 1 40 25 48 10. Fax: 33 1 40 87 10 81. E-mail: agnes.meybeck@caramail.com.

*M. xenopi* vertebral osteomyelitis is rarely reported in the medical literature, even for deeply immunodepressed human immunodeficiency virus type 1 (HIV-1)-infected patients. The signifi-
cance of the *M. xenopi* isolate in this case is confirmed by culture from a sterile site in the presence of histopathological findings compatible with mycobacterial infection. The evolution of illness was favorable after a treatment initially including classical quadruple antituberculous therapy (rifampin, isoniazid, pyrazinamide, and ethambutol) for presumed tuberculous osteomyelitis for 2 months and then changed to rifabutin, isoniazid, ethambutol, and clarithromycin after identification of *M. xenopi*.

*M. xenopi* was first described in 1959, when it was isolated from skin lesions of a toad (*Xenopus laevis*) (17). It is a slow-growing, nonchromogenic or scotochromogenic nontuberculous mycobacterium often considered to be a commensal or environmental contaminant. Improved culture techniques have led to an increasing number of *M. xenopi* isolates being identified in clinical specimens (4). Colonization of the respiratory tract is the most common explanation for isolation of *M. xenopi* (4, 6, 9). However, few cases of clinically significant infection due to *M. xenopi* have been reported, especially for patients with AIDS, generally with CD4 counts of less than 100 cells/mm$^3$ (8, 11). Lungs are the more frequent site of infection. Juffermans et al. (8) had reported 22 cases of HIV-infected patients from whom *M. xenopi* was isolated. Isolation of *M. xenopi* from a pulmonary specimen was found in 16 cases (8). However, extrapulmonary disease and disseminated disease have rarely been described. El-Helou et al. (5) had reported 28 cases of HIV-infected patients from whom one or more isolates of *M. xenopi* had been recovered. *M. xenopi* was thought to be of clinical significance in seven patients (25%): three with bacteremia, three with pulmonary disease, and one with lymphadenitis (5).

*M. xenopi* vertebral infections have been described after discovevertebral surgery, induced by contact with contaminated surgical instruments (2). In the absence of surgery, vertebral osteomyelitis has been reported for five non-HIV-infected patients and recently for one HIV-infected patient (3, 7, 10, 12, 14, 15). Clinical presentation is rather similar to that of *M. tuberculosis* vertebral infections, but clinical progression seems slower with *M. xenopi* infection. Astagneau et al. (2) reported 58 cases of *M. xenopi* spinal infections after discovevertebral surgery. The mean time between discetomy and diagnosis was 5.6 years (2). In the case of *M. xenopi* osteomyelitis in an HIV-infected patient reported by Kulasegaram et al., the backache history had continued for 2 years (10). Diagnosis confirmation always required invasive techniques: CT-guided vertebral biopsies.

Optimal treatment for *M. xenopi* infection is not well established. In vitro susceptibility tests do not correlate with clinical response. The American Thoracic Society guidelines recommend isoniazid, rifabutin, and ethambutol, with or without streptomycin or clarithromycin, for 18 to 24 months (1). This type of infection can be difficult to treat, with a high relapse rate reported despite prolonged courses of antibiotics. A recent randomized trial compared rifampin, ethambutol, and isoniazid to rifampin and ethambutol for treatment of pulmonary disease caused by *M. avium* subsp. *intracellulare*, *M. malmoense*, or *M. xenopi* in HIV-negative patients (16). *M. xenopi* was isolated in 42 cases. Failure and relapse rate comparison showed significant difference in favor of the association of rifampin, ethambutol, and isoniazid (11 versus 22%; *P* = 0.03). The relapse and failure rates found in this study indicated much worse outcomes than those for *M. tuberculosis*. A retrospective study conducted with HIV-infected patients with *M. xenopi* pneumonia or bacteremia showed a high rate of mortality (66%) (5). Better regimens are needed. Ongoing studies evaluating macrolides and quinolones may offer alternative treatments (13).

In conclusion, this case illustrates the importance of strain identification in the case of vertebral osteomyelitis, especially in immunodeficient HIV-infected patients, because atypical mycobacteria, *M. xenopi* in particular, can be implicated. Strain identification has prognostic and therapeutic implications. Treatment should be adapted and prolonged.