Mycobacterium microti Llama-Type Infection Presenting as Pulmonary Tuberculosis in a Human Immunodeficiency Virus-Positive Patient

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A rare case of Mycobacterium microti infection in a human immunodeficiency virus-positive patient is described. Because of unusual morphological and cultural features, the pathogen was analyzed by spoligotyping and identified as the Mycobacterium microti llama type. Although culture of M. microti is difficult, drug susceptibility testing could be performed, which correlated with the clinical outcome.

CASE REPORT

A 48-year-old white male was admitted with a 3-month history of night sweats, productive cough, progressive dyspnea, and weight loss of 10 kg, which he attributed to dysphagia. The patient smoked 20 cigarettes a day and denied foreign travel and exposure to household, farm, or wild animals or to persons infected with tuberculosis (TB). Upon physical examination, the patient appeared chronically ill, but in no acute distress. There was an extensive oral thrush. Occasionally crackles were heard over the right upper chest.

A chest X-ray showed a right upper lobe infiltrate without cavitiation. Ziehl-Neelsen staining of the initial sputum specimen revealed sharply curved acid-fast bacilli (AFB) (Fig. 1A). The patient was isolated in a low-pressure chamber, and antituberculous treatment with isoniazid, rifampin, and pyrazinamide was initiated. Tests for human immunodeficiency virus type 1 (HIV-1) were positive. His CD4+ count was 104 × 10^6/liter, the CD4+/CD8+ ratio was 0.14, and the viral load as >750,000 copies/ml, indicating long-standing and advanced HIV infection. Oral thrush and dysphagia resolved after treatment with oral fluconazole. The patient was discharged after 31 days, when sputum samples were AFB smear negative. Mycobacterial cultures remained negative. After 3 months, the pulmonary infiltrate had almost completely resolved, and the treatment was changed to isoniazid and rifampin. Meanwhile, the CD4+ count had declined to 54 × 10^6/liter. Antiretroviral treatment with zidovudine, lamivudine, nelfinavir, and efavirenz was initiated. After 2 months of antiretroviral therapy, the CD4+ count increased to 256 × 10^6/liter, while the viral load decreased to 237 copies/ml.

A total of six mycobacterial isolates could be grown from sputum specimens (Table 1). Mycobacterial growth was first indicated in liquid medium (Bactec 12B; Becton Dickinson, Cocksveill, Md.). Growth of mycobacteria was also detected on Stonebrink medium (1), a solid medium which contains pyruvate instead of glycerol, but not on Loewenstein-Jensen medium (Table 1). The isolates were identified as M. tuberculosis complex with the ACCUProbe culture confirmation test (GenProbe, San Diego, Calif.).

FIG. 1. (A and B) Ziehl-Neelsen-stained sputum showing sharply curved AFB (arrows) (A) and spoligotype patterns of three sputum cultures (lanes 1 to 3) obtained from the patient, as well as those of a clinical M. bovis isolate (lane 4) and M. tuberculosis H37Rv (lane 5) as controls (B). All three sputum cultures showed a spoligotype pattern observed previously in an M. microti strain obtained from a zoo llama (4).
Due to the sharply curved appearance of the AFB, which is unusual for the _M. tuberculosis_ complex, and because of the slow growth on solid media, these mycobacteria were analyzed by spoligotyping, a technique based on the mycobacterial strain-dependent presence or absence of short nonrepetitive spacer sequences that intersperse the repetitive direct repeat sequences. The mycobacteria were identified as _M. microti_ type llama (4) by the characteristic spoligotype pattern (Fig. 1B). Drug susceptibility testing in liquid medium (Bactec 460TB; Becton Dickinson) revealed susceptibility to isoniazid, rifampin, pyrazinamide, ethambutol, and streptomycin.

_Mycobacterium microti_, which belongs to the _Mycobacterium tuberculosis_ complex, has been described to cause TB, mainly in small rodents, but has been considered to be nonpathogenic for humans (4–6). More recently, van Soolingen et al. (4) demonstrated different strains of _M. microti_ isolated from vole, hyrax, llama, pig, and ferret by molecular methods. In retrospective analyses, they additionally found four infections of humans in The Netherlands caused by _M. microti_ strains that showed a high degree of similarity to strains from a ferret and a pig (4; K. Kremer, D. van Soolingen, J. D. A. van Embden, S. Hughes, J. Inwald, and G. Hewinson, Letter, J. Clin. Microbiol. 36:2793–2794, 1998). We have reported the first _M. microti_ llama-type infection presenting as pulmonary TB in an HIV-positive patient in Germany.

To our knowledge, this is the first report of an _M. microti_ infection with the llama type presenting as a pulmonary TB in an HIV-positive patient. The only other case of an _M. microti_ llama-type infection in humans was not described in detail (Kremer et al., letter). The first four _M. microti_ isolates from humans (3 and 4 months, respectively) were significantly longer than those for our _M. microti_ llama-type isolate (Table 1).

Three of the four _M. microti_ isolates from humans (2, 4) were found in immunocompromised patients (two had experienced kidney transplantation, one was HIV infected). Only in two patients did empirical triple therapy with antituberculous drugs result in regression of the pulmonary symptoms and disappearance of the AFB. The pulmonary infiltrate of the HIV-infected patient, however, disappeared only when a six-drug therapeutic regimen including clarithromycin and ofloxacin was followed (2). However, in our patient, antituberculous therapy including isoniazid, rifampin, and pyrazinamide was successful, which indicates that regular TB therapy is sufficient for treatment of patients with _M. microti_ infection. These findings also correlated with results obtained by drug susceptibility testing in liquid media.

Contacts with mice by two patients with _M. microti_ infections were found to be suggestive for zoonotic transmission (4). However, a possible source of infection could not be identified in our patient.

In conclusion, the case presented here emphasizes the necessity to consider _M. microti_ as a relevant pathogen in immunocompromised patients. The prevalence and clinical importance of different types of _M. microti_ may have been underestimated so far because of difficulties with primary isolation and differentiation. Hence, further studies applying molecular methods are necessary to analyze the epidemiology of _M. microti_ more thoroughly.

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**REFERENCES**


