Case Report

Pulmonary tuberculosis due to *Mycobacterium microti*: a study of six recent cases in France

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Human tuberculosis caused by *Mycobacterium microti* is rare, but its prevalence and clinical significance may have been underestimated. To the best of our knowledge, 21 cases have been reported in the literature in the last decade. We report six recent pulmonary cases caused by *M. microti* over a period of 5 years detected in French clinical mycobacteriology laboratories of the hospital network. Our data confirm the potential of *M. microti* to cause clinical illness in immunocompetent patients. *M. microti* grew slowly from specimens, delaying the final microbiological diagnosis. Therefore, patients with tuberculosis caused by *M. microti* could benefit from the use of rapid diagnostic molecular techniques directly on clinical samples. From a review of the literature and this study, a classical antituberculous therapy seems effective in treating patients with *M. microti* disease.

Introduction

Mycobacterium microti belongs to the *Mycobacterium tuberculosis* complex (MTBC), a group that includes *M. tuberculosis*, *Mycobacterium bovis*, *Mycobacterium africanum*, '*Mycobacterium canettii*', *Mycobacterium pinnipedii* and *Mycobacterium caprae*, the main agents of human and animal tuberculosis. *M. microti*'s natural hosts and reservoirs are small rodents such as voles, shrews and wood mice. Sporadic cases of infection by *M. microti* have also been reported in other animals, such as cats, llamas, dogs,

Abbreviations: HIV, human immunodeficiency virus; MIRU-VNTR, mycobacterial interspersed repetitive unit–variable-number tandem repeat; MTBC, *Mycobacterium tuberculosis* complex.

pigs, ferrets, badgers and a cow (van Soolingen *et al.*, 1998). *M. microti* was considered an unimportant pathogen for humans until 1998, when the first case of human pulmonary tuberculosis was reported (Foudraine *et al.*, 1998). During the last decade, 20 additional cases of human infection have been reported in 10 other publications (de Jong *et al.*, 2009; Emmanuel *et al.*, 2007; Foudraine *et al.*, 1998; Frank *et al.*, 2009; Geiss *et al.*, 2005; Horstkotte *et al.*, 2001; Jenkins *et al.*, 2006; Kremer *et al.*, 1998; Niemann *et al.*, 2000; van Soolingen *et al.*, 1998).

Case reports

Here we report for the first time 6 cases of human pulmonary tuberculosis caused by *M. microti* in France and review the other 21 cases from the literature. Six clinical strains of *M. microti* were isolated from the respiratory specimens of six patients over a period of 5 years (2002–2007) in French clinical mycobacteriology laboratories of the university hospital network, non-university hospitals and a specialized private laboratory (Biomnis, Lyon, France). All these strains were referred to the Mycobacteria Reference Laboratory at the Pasteur Institute (Paris, France). Diagnosis of pulmonary tuberculosis due to *M. microti* was established when mycobacteria were identified as *M. microti* by two complementary molecular methods, GenoType MTBC (Hain Lifescience) and spoligotyping (Brudey *et al.*, 2006). The genetic diversity of the isolates was also explored by 24-locus mycobacterial interspersed repetitive unit–variable number tandem repeat (MIRU-VNTR) typing. The medical records of the six patients were recovered retrospectively. Patient data included demographic characteristics, clinical symptomology, co-morbidities, treatment and outcome. Microbiological documentation of *M. microti* was abstracted as follows: presence of acid-fast bacilli on smears, time of growth detection of mycobacteria on both solid (Coletsos) and liquid media (MGIT BACTEC 960; Becton Dickinson), and antibiotic susceptibility.

We performed a comprehensive search of the literature in the Medline database from 1966 to 2009 using the following key terms: '*Mycobacterium microti*', '*Mycobacterium microti* pulmonary tuberculosis' and '*Mycobacterium microti* human infection'. A second search was performed using the references included in the articles found from the initial search. We identified a total of 10 articles reporting 21 cases of human infection due to *M. microti* (de Jong *et al.*, 2009; Emmanuel *et al.*, 2007; Foudraine *et al.*, 1998; Frank *et al.*, 2009; Geiss *et al.*, 2005; Horstkotte *et al.*, 2001; Jenkins *et al.*, 2006; Kremer *et al.*, 1998; Niemann *et al.*, 2000; van Soolingen *et al.*, 1998).

During the 5 year period under study, six patients were diagnosed with pulmonary tuberculosis caused by *M. microti* in France. The median age of patients was 40.3 years (range 29–61 years). There were four males and two females, all born in France. For the six patients, tuberculosis in their childhood or among their friends and family could not be proved. None of the patients was particularly exposed to pets, especially cats or small rodents. Two patients had underlying conditions such as diabetes mellitus.

The median time between the onset of clinical symptoms and the diagnosis of tuberculosis was 24.8 weeks (range 24–32 weeks). Presenting symptoms were a productive cough in six patients, night sweats in two, weight loss in five, fever in one and haemoptysis in one. Chest radiographs revealed upper-lobe cavitating pulmonary lesions in all six patients (four unilateral and two bilateral).

For the six patients, sputum smear microscopy showed acid-fast bacilli, and *M. microti* was isolated from at least one respiratory sample. *M. microti* grew on solid egg media only for one patient, in liquid medium only for two patients and in both media for three patients. The mean time of culture positivity was 48 days (range 42–58 days). All the isolates were sensitive to isoniazid, rifampicin, ethambutol and streptomycin by the proportion method in liquid medium (MGIT BACTEC 960). Three of the six isolates were sensitive to pyrazinamide, one was resistant and the results were inconclusive for two. A commercial reverse hybridization and multiplex line probe assay, GenoType MTBC (Hain Lifescience), identified the six strains as *M. microti*. Additionally, all the strains showed *M. microti*-specific signatures by spoligotyping. The spoligotype of two strains has already been described as ST641 in the international spoligotyping database SpolDB4 (Brudey *et al.*, 2006), whereas the spoligotypes of four strains were not found to have been described (Table 1). Four patients were initially treated with a combination of four antituberculous drugs (rifampicin, isoniazid, ethambutol and pyrazinamide) and one patient with a triple therapy (rifampicin, isoniazid and pyrazinamide) for a mean duration of 10 months. All six patients were cured on completion of the regimen and no relapse had been reported as of May 2010.

Discussion

M. microti tuberculosis is uncommon in humans. To the best of our knowledge, this description of six pulmonary cases is the first and largest series ever reported in the literature and brings to 27 the number of reported cases in both human immunodeficiency virus (HIV)-positive and -negative patients. Overall, the location of tuberculosis was predominantly pulmonary (19 cases) and uncommonly extrapulmonary (2 intra-abdominal and 1 osteomyelitis of the hip) (de Jong *et al.*, 2009; Emmanuel *et al.*, 2007; Foudraine *et al.*, 1998; Frank *et al.*, 2009; Geiss *et al.*, 2005; Horstkotte *et al.*, 2001; Jenkins *et al.*, 2006; Kremer *et al.*, 1998; Niemann *et al.*, 2000; van Soolingen *et al.*, 1998). The location was not indicated in five cases (de Jong *et al.*, 2009; Emmanuel *et al.*, 2007; Foudraine *et al.*, 1998; Frank *et al.*, 2009; Geiss *et al.*, 2005; Horstkotte *et al.*, 2001; Jenkins *et al.*, 2006; Kremer *et al.*, 1998; Niemann *et al.*, 2000; van Soolingen *et al.*, 1998). Most of the patients with

Table 1. Summary of clinical, radiological and microbiological features of human infection with *Mycobacterium microti*

Study and country	Year	Patient no.	Age (years), sex, immune status	Infection site	Symptoms at presentation	Chest X-ray	Animal contact	Antibiotic therapy/ duration (months)	Outcome	Microbiological result			Spoligotype*
										Direct AFB result for specimen	Culture results, culture duration (days), liquid culture, solid culture	Drug susceptibility	
This study, France	2002	1	30, M, diabetic	Lung	Cough, weight loss, night sweats	Cavitation right upper lobe	No	INH, Rif, PZA/6	Cured	+	+, 52, liquid +, solid −	S=Rif, Eth, INH, Stm, PZA	ST641
	2002	2	40, M, normal	Lung	Cough, weight loss	Cavitation right upper lobe	No	INH, Rif, PZA/6	Cured	+	+, 48, liquid +, solid −	S=Rif, Eth, INH, Stm, PZA	ST641
	2005	3	61, M, diabetic	Lung	Cough, weight loss	Cavitation bilateral upper lobe	No	INH, Rif, PZA, Eth/12	Cured	+	+, 48, liquid +, solid +	S=Rif, Eth, INH, Stm; R=PZA	Spacers 4–7, 23, 25, 32–38
	2005	4	40, F, normal	Lung	Cough, weight loss	Cavitation bilateral upper lobe	No	INH, Rif, PZA, Eth/12	Cured	+	+, 48, liquid −, solid +	S=Rif, Eth, INH, Stm; PZA=not interpretable	Spacers 4–7, 23, 25, 32, 35–38
	2007	5	29, F, normal	Lung	Cough	Cavitation right upper lobe	No	INH, Rif, PZA, Eth, Mox/8	Cured	+	+, 42, liquid +, solid +	S=Rif, Eth, INH, Stm; PZA=not interpretable	Spacers 37, 38
	2007	6	42, M, normal	Lung	Weight loss, fever, night sweats, haemoptysis	Infiltrate upper lobe, cavitation right upper lobe	No	INH, Rif, PZA, Eth/6	Cured	+	+, 42, liquid +, solid +	S=Rif, Eth, INH, Stm, PZA	Spacers 25, 37
Foudraine *et al.* (1998); van Soolingen *et al.* (1998), The Netherlands	1998	7	39, M, HIV+	Lung	Weight loss, fever, night sweats	Infiltrate in the left lower lung lobe	NA	INH, Rif, Eth, PZA, Ofl, Clar/ 48	Cured	+	−, NA, NA	NA	No
Foudraine *et al.* (1998); van Soolingen *et al.* (1998), The Netherlands	1998	8	12, M, kidney transplantation	Lung	Cough	NA	No	NA/NA	Cured	+	NA	NA	No
	1998	9	41, M, kidney transplantation	Peritoneal	Fever, weight loss	No	Mice	NA/NA	Died	+	NA	NA	No
	1998	10	34, M, NA	Lung	Cough	Cavernous in the right apical segment of the upper lobe	No	NA/24	Cured	+	NA	NA	No
Kremer *et al.* (1998), England and Wales	1998	11	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	1998	12–15	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Niemann *et al.* (2000), Germany	2000	16	53, M, normal	Lung	Weight loss, cough	Bilateral upper infiltrate without cavitation	No	INH, Rif, PZA/24	Cured	+	+, NA, liquid+ (Bactec 460), solid −	S=INH, Rif, PZA, Eth	No
	2000	17	58, M, diabetic	Lung	Weight loss, cough, fever, night sweats	Bilateral lesions infiltrate	No	INH, Rif, PZA, Eth/NA	Cured	+	+, NA, liquid +, solid −	No	No

Table 1. cont.

Study and country	Year	Patient no.	Age (years), sex, immune status	Infection site	Symptoms at presentation	Chest X-ray	Animal contact	Antibiotic therapy/ duration (months)	Outcome	Microbiological result			Spoligotype*
										Direct AFB result for specimen	Culture results, culture duration (days), liquid culture, solid culture	Drug susceptibility	
Horstkotte *et al.* (2001) Germany	2001	18	48, M, HIV+	Lung	Weight loss, cough, night sweats	Right upper infiltrate without cavitation	No	INH, Rif, PZA, Eth/24	Cured	+	+, NA, liquid + (Bactec 460), solid −	S=INH, Rif, PZA, Eth	No, *M. microti* on culture
Geiss *et al.* (2005), Germany	2005	19	69, NA, normal	Abdominal (milary)	NA	NA	NA	NA	Died	+	+, 58, liquid +, solid −	NA	No
Jenkins *et al.* (2006), England	2006	20	33, M, HIV+	Lung	Weight loss, haemoptysis	Left upper lobe shadowing	NA	INH, Rif, PZA, Eth, Clar/24	Cured	+	+, NA, NA, NA	S=Rif, Eth, INH; R=PZA	NA
Emmanuel *et al.* (2007), Scotland	2007	21	41, F, normal	Lung	NA	NA	Farmer	INH, Rif,, PZA, Eth/24	Cured	+	+, NA, liquid −, solid +	Failed	ST641
	2007	22	39, M, HIV+	Lung	NA	NA	No	INH, Rif, PZA, Eth/24	Died	+	+, NA, liquid −, solid +	Failed	ST641
	2007	23	76, F, normal	Lung	NA	NA	No	INH, Rif, PZA, Eth/24	Cured	+	+, NA, liquid +, solid −	S=Rif, Eth, INH; R=PZA	No
	2007	24	45, F, normal	Lung	NA	NA	Pets (cat, dog)	INH, Rif, PZA, Eth/24	Cured	+	+, NA, liquid −, solid +	Failed	Spacers 4–7, 23, 24
Frank *et al.* (2009), Germany	2009	25	68, M, diabetic	Lung	Fatigue, chronic cough	Cavitation left upper lobe	Raccoon dog	INH, Rif, PZA, Eth/NA	Cured	+	+, 56, liquid+ (Bactec 960TBH), solid +	Failed: S=Rif and INH by molecular method	No
de Jong *et al.* (2009), The Netherlands	2009	26	60, M, diabetic	Lung	Weight loss, night sweats, high fever	Infiltrate left upper lobe	No	INH, Rif, PZA, Eth, NA/6	Cured	+	−, liquid −, solid −,	No	NA
	2009	27	58, M, normal	Osteomyelitis, hip	Night sweats, pain in hip, weight loss	Normal	No	INH, Rif, Eth, Amik, Moxi/9	Cured	+	−, liquid −, solid −	No	NA

AFB, Acid-fast bacilli; Amik, amikacin; Clar, clarithromycin; Eth, ethambutol; F, female; INH, isoniazid; M, male; Moxi, moxifloxacin; NA, not available; Ofl, ofloxacin; PZA, pyrazinamide; R, resistant; Rif, rifampicin; S, sensitive.

*The ST number designations are from the International Spoligotyping Database (www.pasteur-guadeloupe.fr).

pulmonary tuberculosis caused by *M. microti* (12/18) presented clinical symptoms similar to typical cases caused by *M. tuberculosis*, including a cough in 11 cases, weight loss in 13, night sweats in 7, fever in 5 and haemoptysis in 2 (Table 1).

Our data may suggest the potential of *M. microti* to cause clinical illness in immunocompetent patients. Among the 27 cases, 10 patients did not present any known immunological deficiencies (for which relevant clinical details were available). Among 11 other patients, tuberculosis was associated with HIV infection (4 cases), kidney transplantation (2 cases) and diabetes (5 cases). Indeed, recently, Restrepo *et al.* (2008) suggested that diabetes could be associated with an altered immune response to *M. tuberculosis*.

Specimen smear-microscopy was positive in most of the patients (22/27), and 7 presented cavitating lung lesions with positive direct smears. However, *M. microti* grew slowly from specimens (median 50.30 days; range 42–58), delaying the final microbiological diagnosis. Therefore, patients with tuberculosis caused by *M. microti* with specimens rich in acid-fast bacilli could benefit from the use of rapid diagnostic molecular techniques (such as spoligotyping or GenoType MTBC) directly on clinical samples. This rapid diagnosis could help prevent erroneous clinical diagnoses, inadequate treatments and movement of potentially contagious patients.

The ecological niche of *M. microti* remains unclear, although it is a recognized pathogen for wild rodents and occasionally for pets such as dogs or cats. Little is known about the incidence and ecology of *M. microti* infection in farm and other domestic animals (van Soolingen *et al.*, 1998). Several studies have described a high prevalence of *M. microti* infection in wild rodents, suggesting that these animals could be its reservoir. Zoonotic transmission could occur directly from rodents to humans, via domestic hosts such as cats or pet ferrets (van Soolingen *et al.*, 1998), or by contact with animal-contaminated environmental samples. However, zoonotic transmission investigations in most of the human cases were unsuccessful in tracing back the patient's potential infection source. Human-to-human transmission of *M. microti* has been suggested from secondary cases based on purified protein derivative skin testing (van Soolingen *et al.*, 1998), but it has never been proven by DNA fingerprinting. Therefore, the source of human infections remains unknown. Based on MIRU-VNTR fingerprinting (data not shown), our results indicate a lack of a genetic link between the six strains of *M. microti* isolated from patients in France, which excludes an epidemiological link among these patients.

Successful treatment of *M. microti* lung disease included several weeks of triple or quadruple antituberculous therapy. Among 19 patients with pulmonary tuberculosis, only 1 with a background of full-blown AIDS had a fatal outcome. Among the 27 cases of *M. microti* infection from the literature, death due to lethal Landouzy septicaemia was also reported in an elderly immunocompetent patient (Geiss *et al.*, 2005). Among the cases reviewed here, *M. microti* was susceptible to isoniazid, rifampicin, ethambutol and streptomycin. However, drug resistance and *in vitro* susceptibility interpretation problems were noted for pyrazinamide in three and two isolates, respectively, in this series. From a review of the literature, antituberculous therapy including isoniazid, rifampicin and ethambutol was successful, which indicates that regular antituberculous therapy with or without associated pyrazinamide is effective in treating patients with *M. microti* disease.

Comparative genomics has demonstrated that the genome of *M. microti* partially or completely lacks several genes of the RD1 region that are essential for virulence in other members of the MTBC (Brodin *et al.*, 2002). Indeed, in the past, several trials of *M. microti* as a vaccine led to the conclusion that it had a lack of virulence in immunocompetent humans. Although human pulmonary tuberculosis caused by *M. microti* is uncommon, our report together with the literature review suggest that the natural deletion of the RD1 region alone does not appear to alter the pathogenic capacity of *M. microti*. Its prevalence and clinical importance may have been underestimated, either because of the difficulties of primary isolation and differentiation of *M. microti* within the MTBC, or because of a lack of clinical differences between *M. microti* and *M. tuberculosis* pulmonary tuberculosis. However, other than in known immunocompromised patients developing *M. microti* infection, we cannot exclude that other genetic or immunological factors were predisposing the patient to mycobacterial infections. Additional studies using molecular methods remain necessary to clarify the real impact of *M. microti* in the epidemiology of human tuberculosis: (i) systematic molecular identification of MTBC species from human, wild (small rodents) and domestic animal (cats) strains in France; (ii) study and comparison of the genetic diversity of *M. microti* in animal (wild and domestic) and human compartments, and identification of the transmission within and between compartments (e.g. generalist and specialized genotypes).

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References

Brodin, P., Eiglmeier, K., Marmiesse, M., Billault, A., Garnier, T., Niemann, S., Cole, S. T. & Brosch, R. (2002). Bacterial artificial chromosome-based comparative genomic analysis identifies *Mycobacterium microti* as a natural ESAT-6 deletion mutant. *Infect Immun* **70**, 5568–5578.

Brudey, K., Driscoll, J. R., Rigouts, L., Prodinger, W. M., Gori, A., Al-Hajoj, S. A., Allix, C., Aristimuño, L., Arora, J. & other authors (2006).

Mycobacterium tuberculosis complex genetic diversity: mining the fourth international spoligotyping database (SpolDB4) for classification, population genetics and epidemiology. *BMC Microbiol* **6**, 23.

de Jong, E., Rentenaar, R. J., van Pelt, R., de Lange, W., Schreurs, W., van Soolingen, D. & Sturm, P. D. J. (2009). Two cases of *Mycobacterium microti*-induced culture-negative tuberculosis. *J Clin Microbiol* **47**, 3038–3040.

Emmanuel, F. X., Seagar, A.-L., Doig, C., Rayner, A., Claxton, P. & Laurenson, I. (2007). Human and animal infections with *Mycobacterium microti*, Scotland. *Emerg Infect Dis* **13**, 1924–1927.

Foudraine, N. A., van Soolingen, D., Noordhoek, G. T. & Reiss, P. (1998). Pulmonary tuberculosis due to *Mycobacterium microti* in a human immunodeficiency virus-infected patient. *Clin Infect Dis* **27**, 1543–1544.

Frank, W., Reisinger, E. C., Brandt-Hamerla, W., Schwede, I. & Handrick, W. (2009). *Mycobacterium microti* – pulmonary tuberculosis in an immunocompetent patient. *Wien Klin Wochenschr* **121**, 282–286.

Geiss, H. K., Feldhues, R., Niemann, S., Nolte, O. & Rieker, R. (2005). Landouzy septicemia (sepsis tuberculosa acutissima) due to *Mycobacterium microti* in an immunocompetent man. *Infection* **33**, 393–396.

Horstkotte, M. A., Sobottka, I., Schewe, C. K., Schäfer, P., Laufs, R., Rüsch-Gerdes, S. & Niemann, S. (2001). *Mycobacterium microti* llama-type infection presenting as pulmonary tuberculosis in a human immunodeficiency virus-positive patient. *J Clin Microbiol* **39**, 406–407.

Jenkins, N. E., Beadsworth, M. B., Anson, J. J., Nye, F. J., Martlew, V. J. & Beeching, N. J. (2006). Immune restoration disease in HIV patient. *Emerg Infect Dis* **12**, 689–691.

Kremer, K., van Soolingen, D., van Embden, J., Hughes, S., Inwald, J. & Hewinson, G. (1998). *Mycobacterium microti*: more widespread than previously thought. *J Clin Microbiol* **36**, 2793–2794.

Niemann, S., Richter, E., Dalugge-Tamm, H., Schlesinger, H., Graupner, D., Konigstein, B., Gurath, G., Greinert, U. & Rusch-Gerdes, S. (2000). Two cases of *Mycobacterium microti* derived tuberculosis in HIV-negative immunocompetent patients. *Emerg Infect Dis* **6**, 539–542.

Restrepo, B. I., Fisher-Hoch, S. P., Pino, P. A., Salinas, A., Rahbar, M. H., Mora, F., Cortes-Penfield, N. & McCormick, J. B. (2008). Tuberculosis in poorly controlled type 2 diabetes: altered cytokine expression in peripheral white blood cells. *Clin Infect Dis* **47**, 634–641.

van Soolingen, D., van der Zanden, A. G., de Haas, P. E., Noordhoek, G. T., Kiers, A., Foudraine, N. A., Portaels, F., Kolk, A. H., Kremer, K. & van Embden, J. D. (1998). Diagnosis of *Mycobacterium microti* infections among humans by using novel genetic markers. *J Clin Microbiol* **36**, 1840–1845.