Lung (2009) 187:51–54
DOI 10.1007/s00408-008-9104-8

OCCUPATIONAL LUNG DISEASE

An Association between *Mycobacterium malmoense* and Coal Workers' Pneumoconiosis

Emmet E. McGrath · Philip Bardsley

Received: 31 March 2008 / Accepted: 9 June 2008 / Published online: 30 August 2008

Abstract An association between *Mycobacterium malmoense* and underlying lung disease has been described. The purpose of this study was to further explore this relationship and in particular to identify any relationship between Coal Workers' Pneumoconiosis (CWP) and *M. malmoense* infection. Patient charts were reviewed of all patients who had a positive sputum or bronchoalveolar lavage for *M. malmoense* from 1999 to 2006 in a large district general hospital in South Yorkshire, UK. We also performed a literature review in search of this association; one case report was found. Four patients had positive sputum cultures for *M. malmoense* but only three of these fulfilled the ATS 1997 criteria for diagnosis of disease. Of these three patients, all had clinical and radiologic evidence of CWP. This study strengthens the evidence of a link between nontuberculous mycobacteria and underlying lung disease but more importantly highlights an association between *M. malmoense* and CWP which has been rarely reported and is poorly understood.

Keywords Nontuberculous mycobacteria · *Mycobacterium malmoense* · Pneumoconiosis · ATS/IDSA guidelines 2007

Abbreviations

NTM	Nontuberculous mycobacteria
ATS	American Thoracic Society
IDSA	Infectious Diseases Society of America
BAL	Bronchoalveolar lavage
AFB	Acid fast bacilli
COPD	Chronic obstructive pulmonary disease
CT	Computed tomography
CFA	Cryptogenic fibrosing alveolitis

E. E. McGrath (✉) · P. Bardsley
Department of Respiratory Medicine, Rotherham District General Hospital, Moorgate Road, Rotherham South Yorkshire S60 2UD, UK
e-mail: e.mcgrath@sheffield.ac.uk

P. Bardsley
e-mail: P.Bardsley@gmail.com

Introduction

Mycobacterium malmoense was first described by Schroder and Juhlin [1] in four patients from Malmo in 1977. Since then, cases have been reported in the United States, England, and Wales. *M. malmoense* has been isolated from animals, water, dust, food, and soil [2]. It can cause severe infection in patients with reduced host defences, although infection can also occur in immunocompetent patients with underlying pulmonary disease. Its incidence and prevalence are increasing along with other NTM family members, as was described by Henry et al. [3], who demonstrated an increase in the incidence of NTM in Leeds, UK, from 0.8 to 3.07 per 100,000 between 1995 and 1997. Rushton et al. [4] demonstrated a *M. malmoense* prevalence rate of 1/42,500 in the north of England in 2007.

Study Parameters

Hospital records of all patients who had a positive sputum or brochoalveolar lavage culture from a large district general hospital between 1999 and 2006 were consecutively reviewed along with the associated radiology. Of these, four patients had positive culture data for *M. malmoense* but one of these four did not fulfill the ATS 1997 guidelines on the diagnosis of NTM [5]. This

patient's positive culture data were treated as contamination. The patient was subsequently treated for community-acquired pneumonia and recovered well. The three infected patients came from the hospital's catchment area of Rotherham (where it is the only hospital), in South Yorkshire, which has a population of 248,000.

A Medline search was performed by entering the words "Mycobacterium malmoense" or "malmoense" along with "coal worker pneumoconiosis" and only one result was obtained, a case report from 2001.

Patients

Patient 1

A male ex-miner in his seventies presented to the outpatients department with a recent history of dyspnoea, fatigue, and a productive cough. He had a past medical history of pneumoconiosis and had a 20-pack-year history of cigarette smoking. His chest X-ray revealed vast fibrotic changes in both lungs in keeping with coal workers' pneumoconiosis (Fig. 1). CT thorax confirmed pneumoconiosis but a right upper lobe cavity was also detected (Fig. 2). Sputum culture was negative for AFB and tuberculin skin test was normal. *Aspergillus precipitins* and total IgE levels were normal. He had further sputum samples sent for culture and a bronchoscopy and bronchoalveolar lavage gave no immediate diagnosis. A sputum sample was reported positive for AFB and he was commenced on standard antituberculous treatment of rifampicin, isoniazid, ethambutol, and pyrazinamide. Five weeks later we received a report that his more recent sputum samples had grown a nontuberculous mycobacterium known as *Mycobacterium malmoense* which was resistant to pyrazinamide and isoniazid but sensitive to ethambutol, rifampicin, and clarithromycin. We adjusted his therapy, continuing with rifampicin and ethambutol and clarithromycin for 2 years. There were no further smear-positive samples documented while on therapy. His treatment was stopped after 12 months of culture-negative sputum samples were obtained and demonstrated. He had a very good response to therapy and attends the outpatient clinic for regular follow-up.

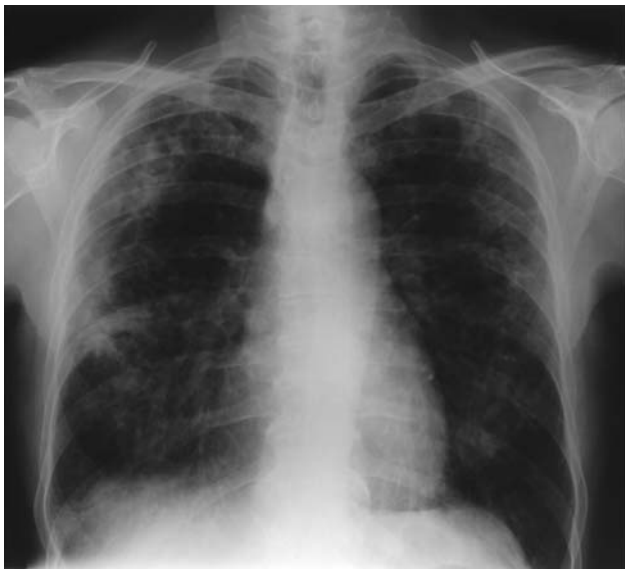

Fig. 1 An X-ray demonstrating chronic fibrotic changes in keeping with coal workers' pneumoconiosis. This patient's underlying lung disease predisposed him to an *M. malmoense* infection which can be seen as consolidation in the right upper lobe

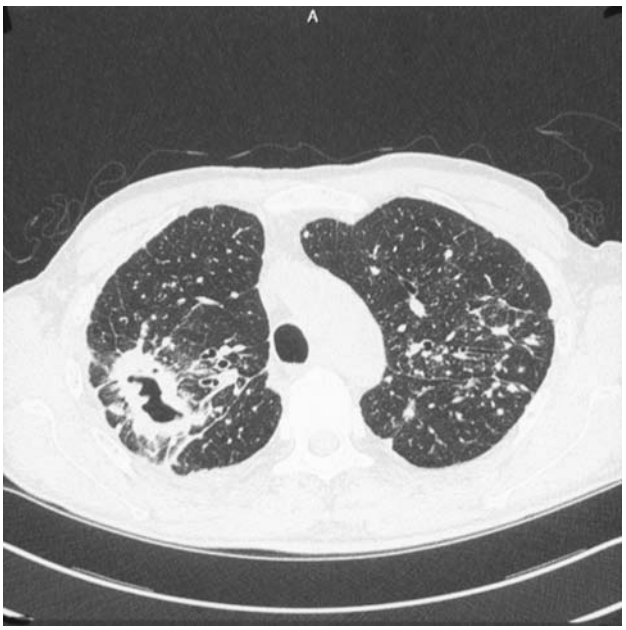

Fig. 2 CT thorax demonstrating a cavitating thick-walled cyst in the right upper lobe

Patient 2

A 69-year-old male ex-miner presented to the outpatients department with a 4-month history of cough productive of yellow sputum. He had experienced four episodes of haemoptysis over a 2-month period. He had a past medical history of pneumoconiosis and his FEV_1 was 1.35 L/min (45% predicted) with an FVC of 2.5 L/min (64% predicted). He had a 5-pack-year smoking history. Chest X-ray revealed chronic changes related to pneumoconiosis and an infiltrate in the right base. Tuberculin skin test was negative. His sputum cultures were negative and bronchoscopy and BAL were performed. The BAL cultured *M. malmoense* over the next few months and second and third sputum cultures confirmed the diagnosis. He was commenced on clarithromycin, ethambutol, and rifampicin and responded well to therapy. He attends clinic for regular follow-up and has had no further positive sputum cultures.

Patient 3

A 76-year-old ex-miner presented to the outpatients department with a 6-month history of dypsnoea, cough productive of green sputum, and poor appetite. He denied night sweats, fever, or haemoptysis. He had a history of pneumoconiosis and had never smoked cigarettes. His chest X-ray again revealed evidence of pneumoconiosis with consolidation in the right upper lobe. *Aspergillus precipitins* and IgE levels were normal. His FEV_1 was 47% predicted. Tuberculin skin test was negative. Sputum cultures revealed *M. malmoense*. He was treated with ethambutol, rifampicin, and clarithromycin for 2 years and his treatment was stopped after 12 months of culture-negative sputum samples were obtained. He had a good response to therapy but has recently died from a major cerebrovascular accident.

Discussion

M. malmoense is not an obligate pathogen and therefore generally does not cause disease in humans (unlike TB). Person-to-person spread has not been described. As with all opportunistic organisms, damage to the skin barrier or disruption to immune defence is required for infection. In immunocompetent patients, pulmonary infection tends to occur in patients with architectural abnormalities such as cystic fibrosis, bronchiectasis, previous tuberculosis, oesophageal motility disorders, COPD, and pneumoconiosis due to silica [6]. Henry et al. [3] demonstrated in their study of 71 patients with NTM disease that in the case of *M. malmoense* infection, eight patients were predisposed with COPD, two patients with previous TB disease, one patient with bronchiectasis, one patient with CFA, and one patient with lung cancer. A study in 2006 [7] demonstrated that patients with nontuberculous mycobacterial infection and bronchiectasis have a higher prevalence of coexisting aspergillus-related lung disease than patients with bronchiectasis who are not infected with nontuberculous mycobacteria. This emphasised the importance of identifying aspergillus-related lung disease because prognosis among undetected cases is extremely poor.

In 2003, a study on *M. malmoense* published by the British Thoracic Society [8] revealed that most patients with pulmonary infection were male and had underlying lung disease. The average age was 58 years with less than half of the patients showing bilateral disease. Twenty-six percent of patients had involvement of more than three lung zones and infection was confined to the upper zones in 30%. The study revealed a very high 5-year mortality ($\sim$33%); however, only 4% of the deaths were attributed to *M. malmoense* infection with the other 96% attributed to concomitant illnesses.

Lung infection due to *M. malmoense* is almost impossible to distinguish from tuberculosis both radiologically and clinically, but findings such as existing pneumoconiosis, volume loss, larger cavities, and air fluid levels are seen more frequently on chest radiographs of patients with *M. malmoense* than on those with *M. tuberculosis* [9].

M. malmoense can be very difficult to identify as it is very similar to other slow-growing nonpigmented mycobacterial species. Differences such as its low catalase activity and its marked ability to hydrolyse Tween 80 help differentiate it from other species [10]. With the introduction of more sensitive laboratory techniques, *M. malmoense* has been increasingly detected without clinical disease [11]. Correct identification is essential and the introduction of DNA probes has made this increasingly possible.

M. malmoense is sensitive to rifampicin and ethambutol, and despite being said to be microbiologically resistant to isoniazid, clinical response has been seen with this agent [3]. In 2001, another study by the British Thoracic Society demonstrated that *M. malmoense* was as responsive to rifampicin and isoniazid as it was to rifampicin, isoniazid, and ethambutol. The same study demonstrated that *M. malmoense* had the best outcome of all the NTM with a 42% 5-year survival rate [12]. Optimal treatment remains elusive but improvement has been documented with combinations of rifampicin, isoniazid, ethambutol, macrolides, and quinolones [13]. The ATS/IDSA 2007 guidelines should be consulted when this organism is suspected as they lay down criteria for the investigation, diagnosis, and treatment of this organism (Table 1) [6].

Table 1 ATS/IDSA guidelines on the diagnosis of NTM; both clinical criteria and microbiological criteria must be met for diagnosis

Microbiological criteria (only one of the following required)	Clinical criteria (both required)
A. Positive culture results from at least two separate sputum samples	A. Appropriate exclusion of other diagnoses including tuberculosis
B. Positive culture result from at least one bronchial wash or lavage	With
C. Transbronchial/lung biopsy with features of granulomatous inflammation or AFB and positive culture for NTM or biopsy with histopathologic features of NTM with one or more sputum or bronchial washings culture positive	B. Pulmonary symptoms, nodular or cavitary opacities on chest radiograph, or a high-resolution computed tomography scan that shows multifocal bronchiectasis with multiple small nodules

ATS = American Thoracic Society; IDSA = Infectious Diseases Society of America; AFB = acid fast bacilli; NTM = nontuberculous mycobacteria

We expected a higher prevalence of *M. malmoense* in our study given that Rushton et al. [4] had a prevalence rate of 1/42,000 in their study in the north of England. However, on reviewing their paper we found three major differences. First, they included all culture-positive laboratory samples, both pulmonary and a significant number of extrapulmonary samples. We reviewed only pulmonary samples. Second, they included the juvenile population in their study, whereas our hospital is an adult hospital and no juvenile data were included. The juvenile sample contribution was significant. Lastly, Rushton et al. found that when they analysed the case distribution data, the vast majority of their cases occurred in very large metropolitan areas in the north of England. Our catchment area is a relatively small town and not on the same scale as the large metropolitan boroughs in Rushton's study.

It is important to remember that the small number of prevalence studies that have been performed around the world have shown wide variability in prevalence rates. This may be the result of the use of different laboratory techniques and expertise, combined with different degrees of clinical suspicion for NTM that vary throughout the world. Now, with increasing awareness of these pathogens, combined with improved laboratory techniques and definitive guidelines, the next few years will provide some very interesting and important data on the incidence and prevalence of nontuberculous mycobacteria. It is predicted that NTM incidence and prevalence are set to increase in the coming years due to an increase in infection rates combined with increased organism detection by improved microbiological techniques [14].

In summary, we described three patients with coal workers' pneumoconiosis who developed *Mycobacterium malmoense* infection of the lungs. We believe that coal workers' pneumoconiosis is a risk factor for the development of this infection. Further prospective studies would help define the exact nature of this relationship and give it statistical power. While associations with pneumoconiosis due to silica dust have been described previously, this is one of the very few reports highlighting a link between CWP and *M. malmoense.*

References

1. Schroder KH, Juhlin I (1977) *Mycobacterium malmoense* sp nov. Int J Syst Bacteriol 27:241–246
2. Falkinham JO III (1996) Epidemiology of infection by nontuberculous mycobacteria. Clin Microbiol Rev 9:177–215
3. Henry MT, Inamdar L, O'Riordain D, Schweiger M, Watson JP (2004) Nontuberculous mycobacteria in non-HIV patients: epidemiology, treatment, and response. Eur Respir J 23:741–746
4. Rushton SP, Goodfellow M, O'Donnell AG, Magee JG (2007) The epidemiology of atypical mycobacterial diseases in northern England: a space-time clustering and Generalized Linear Modelling approach. Epidemiol Infect 135(5):765–774
5. Society American Thoracic (1997) Diagnosis and treatment of disease caused by nontuberculous mycobacteria. Am J Respir Crit Care Med 156:S1–S25
6. Griffith DE, Aksamit T, Brown-Elliott BA, Catanzaro A, Daley C, Gordin F, Holland SM, Horsburgh R, Huitt G, Iademarco MF, Iseman M, Olivier K, Ruoss S, von Reyn CF, Wallace RJ Jr, Winthrop K, ATS Mycobacterial Diseases Subcommittee, American Thoracic Society, Infectious Diseases Society of America (2007) Diagnosis, treatment and prevention of nontuberculous mycobacterial diseases. Am J Respir Crit Care Med 175:367–416
7. Kunst H, Wickremasinghe M, Wells A, Wilson R (2006) Nontuberculous mycobacterial disease and Aspergillus-related lung disease in bronchiectasis. Eur Respir J 28(2):352–357
8. British Thoracic Society (2003) Pulmonary disease caused by *M. malmoense* in HIV negative patients. 5-year follow-up of patients receiving standardised treatment. Eur Respir J 21:478–482
9. Evans AJ, Crisp AJ, Colville A, Evans SA, Johnston ID (1993) Pulmonary infections caused by *Mycobacterium malmoense* and *Mycobacterium tuberculosis*: comparison of radiographic features. AJR Am J Roentgenol 161:733–737
10. Warren NG, Body BA, Silcox VA, Matthews JH (1984) Pulmonary disease due to *Mycobacterium malmoense*. J Clin Microbiol 20:245–247
11. Buchholz UT, McNeil MM, Keyes LE, Good RC (1998) *Mycobacterium malmoense* infections in the United States, January 1993 through June 1995. Clin Infect Dis 27:551–558
12. British Thoracic Society (2001) First randomised trial of treatment for pulmonary disease caused by *M. avium intracellulare*, *M. malmoense* and *M. xenopi* in HIV negative patients: rifampicin, ethambutol and isoniazid-v-rifampicin and ethambutol. Thorax 56:167–172
13. Enzensberger R, Hunfeld K-P, Krause M, Rüsch-Gerdes S, Brade V, Böddinghaus B (1999) *Mycobacterium malmoense* infections in immunocompetent patients. Eur J Clin Microbiol Infect Dis 18:579–581
14. McGrath EE, Anderson PB (2007) Increased prevalence of nontuberculous mycobacteria infection. Lancet 370(9581):28