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Eur Respir J 2014; 44: 1082–1085 | DOI: 10.1183/09031936.00064014 | Copyright ©ERS 2014

Human-to-human transmission of *Mycobacterium kansasii* or victims of a shared source?

To the Editor:

Nontuberculous mycobacteria (NTM) are ubiquitous in the environment [1] and can cause opportunistic infections in humans with either an immunological deficit or structurally abnormal lungs, such as in cystic fibrosis, bronchiectasis or chronic obstructive pulmonary disease (COPD) [2]. Unlike *Mycobacterium tuberculosis*, human-to-human transmission of NTM is generally thought to be uncommon [2–4], although there is evidence that transmission of certain NTM is possible in certain circumstances [5]. Domestic plumbing has also been suggested as a potential source of infection [6].

We describe what we believe to be the best evidence to date of human-to-human transmission of *Mycobacterium kansasii* in a husband and wife living in East London, UK, an area with a high incidence of tuberculosis (~112 cases per 100 000 per year) [7]. A recent survey suggested a UK isolation rate for NTM of around three cases per 100 000 per year with no data available for true disease incidence [8].

The first of the couple to be seen in chest clinic was a 69-year-old Caucasian lady who reported a 6-month history of weight loss, reduced appetite and a cough productive of 30 mL sputum twice daily. Her past medical history was of an episode of severe pneumonia aged 6 years and COPD, having smoked 10 cigarettes per day until 2 years previously. All routine blood tests were unremarkable, including a normal erythrocyte sedimentation rate (ESR) of 11 $mm \cdot h^{-1}$ (normal range 10–15 $mm \cdot h^{-1}$). Chest computed tomography (CT) was ordered, and demonstrated emphysema, right lower lobe bronchiectasis and a calcified granuloma. Three sputum samples were smear negative, but two of her three sputum samples proved culture positive for mycobacteria and she was commenced on standard antituberculous chemotherapy. After the mycobacteria in both samples had been identified as *M. kansasii*, isoniazid and pyrazinamide were discontinued. She continued on rifampicin and ethambutol for a total of 12 months, and converted to negative cultures after 2 months of treatment. It should be noted that this regimen is not that advocated by the American Thoracic Society [2] but was administered at the discretion of her treating physician.

Within a month of this woman being diagnosed with *M. kansasii* disease, her husband was referred to the same chest clinic by their general practitioner (GP). This 75-year-old Caucasian male presented with a history of 20 kg weight loss over 3 years, on a background of 60 pack-years of smoking. He was known to

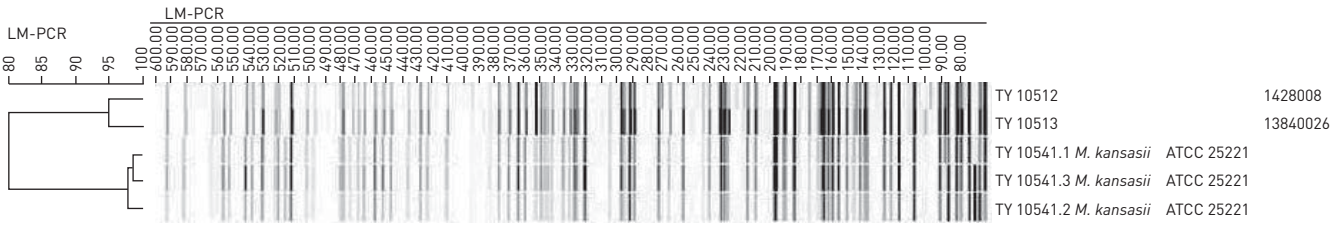

FIGURE 1 Amplified fragment length polymorphism (AFLP) typing result of the patients' *Mycobacterium kansasii* strains (isolates TY 10512 and 10513). With >95% similarity in the AFLP patterns, the strains of both patients are to be interpreted as identical. *M. kansasii* ATCC 25221 was used, in triplicate, as an outgroup. LM-PCR: ligation-mediated PCR.

suffer from stage 3 chronic kidney disease (CKD) and a thoracoabdominal aortic aneurysm. Chest radiography demonstrated apical shadowing. Blood tests demonstrated mildly raised inflammatory markers (C-reactive protein 33.6 $mg \cdot mL^{-1}$, normal range <10 $mg \cdot mL^{-1}$; ESR 21 $mm \cdot h^{-1}$) and confirmed the CKD. Chest CT demonstrated a large, thick-walled cavity in the left upper lobe with adjacent bronchiectatic changes. On bronchoscopy, bronchial washings were smear positive for mycobacteria and he was commenced on standard antituberculous chemotherapy. When cultures yielded *M. kansasii*, pyrazinamide was discontinued. After 4 months of isoniazid, rifampicin and ethambutol treatment, he died of complications of his aortic aneurysm.

When the husband was first referred to clinic, the couple's GP raised the question as to whether his symptoms might be the result of transmission of his wife's infection. To investigate this case further, amplified fragment length polymorphism typing [9] was performed on samples cultured from both patients, finding them to have identical strains of *M. kansasii* (fig. 1). Additionally, filtered water and biofilm samples taken from the patients' shower, bathroom and kitchen taps were cultured on Middlebrook 7H11 solid media; all distinct colony morphologies were subcultured and identified using the Inno-LiPA Mycobacteria v2 (Innogenetics, Ghent, Belgium) molecular assay, which includes specific probes for *M. kansasii*. From all these samples *Mycobacterium gordonae*, *Mycobacterium chelonae* and various *Mycobacterium fortuitum* complex members were successfully cultured, but not *M. kansasii*.

While long since first hypothesised [10], we propose that these cases provide, to date, the most convincing evidence of human-to-human transmission of *M. kansasii*, as the *M. kansasii* isolates obtained from both patients were genetically identical and we were unable to prove a shared domestic exposure. With his prolonged period of ill health, cavitary disease and smear positivity, it appears highly plausible that the husband could be considered the index case. Both patients were frail with bronchiectatic changes on their CT scans, with COPD confirmed in one and suspected in the other. It is likely that this provided the ideal environment of structurally abnormal lungs with possibly a degree of immune suppression, provided by their general frailty, for the *M. kansasii* to replicate.

Alternatively, it is possible that they had a shared exposure outside of the home, that their water supply had transiently been contaminated with *M. kansasii* but that this had cleared by the time our investigations were commenced, or that culture of *M. kansasii* was hindered by the plethora of more rapidly growing mycobacteria.

We propose that this case suggests that human-to-human transmission of *M. kansasii* is possible given the ideal circumstances. As this is the first reported case, the risk is likely to be so low as not to require any changes in standard infection control practices.

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Best evidence to date of human-to-human transmission of *M. kansasii* or are the patients victims of shared exposure? http://ow.ly/xx4Dp

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Received: April 07 2014 | Accepted after revision: May 26 2014 | First published online: June 25 2014

Conflict of interest: None declared.

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Eur Respir J 2014; 44: 1085–1087 | DOI: 10.1183/09031936.00066614 | Copyright ©ERS 2014

Early BCG vaccination is unrelated to pulmonary immunity against *Mycobacterium tuberculosis* in adults

To the Editor:

Vaccination with *Mycobacterium bovis* bacille Calmette–Guérin (BCG) is performed for the prevention of tuberculosis. *M. bovis* BCG vaccination is among the most commonly applied of all vaccines worldwide [1]. *M. bovis* BCG vaccination efficiently reduces the morbidity and mortality of tuberculosis in children, especially miliary tuberculosis and meningitis [2].

Although recent investigations of *Mycobacterium tuberculosis*-specific immune responses by interferon-γ release assays (IGRAs) provide evidence on the effect of *M. bovis* BCG vaccination on the prevention of primary infection with *M. tuberculosis* [3–5], it has been suggested that this effect diminishes during adolescence [2, 6]. Consequently, adults are probably not protected from pulmonary tuberculosis by BCG vaccination.

To date, no study has investigated the impact of *M. bovis* BCG vaccination performed in childhood on pulmonary immune responses in adults. The objective of this study was to assess the effect of childhood *M. bovis* BCG vaccination on systemic and pulmonary immune responses to *M. tuberculosis* in healthy adult individuals exposed to patients with acid-fast bacilli (AFB)-positive sputum smear-positive tuberculosis in Germany.

An observational, cross-sectional, multicentre study was conducted by the German Ministry of Education and Research-funded research consortium on ''Pulmonary Tuberculosis – Host and Pathogen Determinants of Resistance and Disease Progression (TB or Not TB)''. Healthcare workers (HCWs) with 1) ongoing professional contact with patients with AFB sputum smear-positive tuberculosis, 2) a cumulative professional exposure of at least 2 years, and 3) no clinical signs and/or symptoms of active tuberculosis were recruited at 18 German pulmonary medicine centres (centres are listed in the Acknowledgements section).

Furthermore, household contacts (HHCs) without evidence of active tuberculosis were enrolled at three urban municipal healthcare centres (*i.e.* Frankfurt, Hamburg and Hannover); their enrolment required 1) the absence of clinical signs and/or symptoms of active tuberculosis, and 2) cumulative exposure of >40 h to an AFB sputum smear-positive patient with culture-proven pulmonary tuberculosis. Individuals with a history of pulmonary tuberculosis who completed a standard course of tuberculosis treatment >6 months before enrolment and did not experience a relapse were recruited in a control group.

Epidemiological, clinical and demographic data, including BCG vaccination status, were captured using an *ad hoc* standardised questionnaire. An unblinded physician verified *M. bovis* BCG vaccination by clinical