Journal of Infection (2005) **51**, e305–e308

www.elsevierhealth.com/journals/jinf

CASE REPORT

Reactivation of tuberculosis after apparently adequate chemoprophylaxis

Graeme P. Currie[a,*], Francis X.S. Emmanuel[b], David Ford[c], Graham Devereux[a]

[a]*Department of Respiratory Medicine, Aberdeen Royal Infirmary, Foresterhill, Aberdeen AB25 2ZN, Scotland, UK*
[b]*Scottish Mycobacteria Reference Laboratory, Royal Infirmary of Edinburgh, Little France, Edinburgh EH16 4SA, Scotland, UK*
[c]*Department of Respiratory Medicine, Scarborough Hospital, Woodlands Drive, Scarborough YO12 6QL, England, UK*

Accepted 21 February 2005
Available online 11 April 2005

KEYWORDS
Tuberculosis;
Contact;
Chemoprophylaxis

Abstract Screening of the close contacts of patients with pulmonary tuberculosis remains an important component in the control and prevention of the disease. It is carried out to identify active and latent infection, and those requiring BCG vaccination. Guidelines suggest giving chemoprophylaxis to asymptomatic contacts with a positive Heaf test (grades 2–4) and normal chest radiograph [Control and prevention of tuberculosis in the United Kingdom: code of practice 2000. Joint Tuberculosis Committee of the British Thoracic Society. *Thorax* 2000;**55**:887–901]. We report a case involving a close contact where current guidelines were followed, but failed to prevent subsequent development of active disease from the same strain of *M. tuberculosis*.

Case report

In 2004, a 17 year old woman presented with a 3 month history of productive cough, weight loss, night sweats and dyspnoea. Her chest radiograph is shown in Fig. 1. A sputum smear was positive for acid fast bacilli (AFB) and *Mycobacteria tuberculosis* complex was confirmed by direct molecular probing for an insertion sequence (IS6110) unique to organisms of the *M. tuberculosis* complex. Culture confirmed the organism was *M. tuberculosis* and that it was fully susceptible to isoniazid, rifampicin, ethambutol and pyrazinamide. HIV testing was negative. Treatment with rifampicin, isoniazid, pyrazinamide and ethambutol for 2 months followed by rifampicin and isoniazid for 4 months resulted in symptomatic and chest radiographic resolution.

Three years previously in 2001, the 42 year old mother of this case had presented to a distant

* Corresponding author. Tel.: +44 1224 681818.
E-mail address: graeme.currie@nhs.net (G.P. Currie).

0163-4453/$30.00
doi:10.1016/j.jinf.2005.02.021

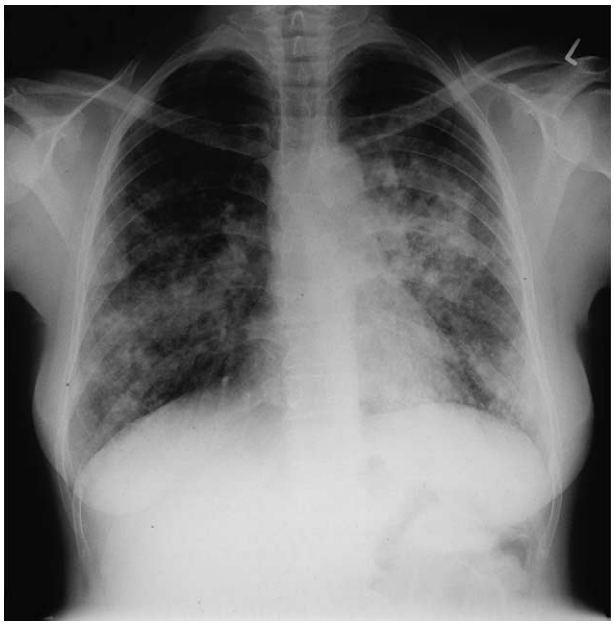

Figure 1 Chest radiograph of the daughter of the index case showing changes at presentation (3 years following chemoprophylaxis).

hospital with a 6 week history of increasing breathlessness, dry cough, night sweats and lethargy. There was no suspicion of illicit drug use or immunodeficiency. Her chest radiograph on presentation is shown in Fig. 2. A diagnosis of pulmonary tuberculosis was made after histological examination of transbronchial biopsies demonstrated AFB and caseating granulomata with multinucleate giant cells. Culture of bronchoalveolar lavage fluid yielded *M. tuberculosis* fully sensitive to first line anti-tuberculous drugs. Treatment with rifampicin, isoniazid, pyrazinamide and ethambutol for 2 months followed by rifampicin and isoniazid for 4 months was associated with clinical and chest radiographic improvement.

The son and daughter (then aged 14 years) were Heaf tested as part of the mother's routine contact tracing. The 6 year old son had recently developed a cough and exertional breathlessness and his Heaf test result was grade 4. Primary tuberculosis was confirmed by the demonstration of a small left-sided pleural effusion and left hilar lymphadenopathy on chest radiography. In accordance with current guidelines,[1] he was commenced on 2 months of rifampicin, isoniazid and pyrazinamide, followed by 4 months of rifampicin and isoniazid and this was associated with an improvement of his respiratory symptoms. The asymptomatic daughter's Heaf test result was grade 4, but a chest radiograph was normal. In accordance with guidelines,[1] she received 3 months of chemoprophylaxis with rifampicin and isoniazid. Despite mild nausea on initiation of treatment, her concordance (confirmed by both mother and daughter) was good.

Molecular typing of the *M. tuberculosis* isolates from the daughter (2004) and mother (2001) demonstrated identical MIRU-VNTR profiles (225 323 153 223) suggesting that the same genotype of the organism was responsible for infection in both individuals. Mycobacterial interspersed repetitive unit (MIRU) variable number tandem repeat (VNTR) typing is a PCR-based molecular subtyping method based on the number of copies of repeated units at 12 independent loci located throughout the genome.[5] It yields highly discriminatory genetic profiles, and the utility of this method for the investigation of apparently clustered cases of tuberculosis has been recently demonstrated.[6] Our report, therefore, indicates that the daughter's tuberculosis was a consequence of reactivation of organisms acquired from her mother 3 years previously, despite standard anti-tuberculous chemoprophylaxis.

Discussion

This report describes a case of pulmonary tuberculosis developing in a 17 year old female who had been a close contact of a case of pulmonary tuberculosis 3 years earlier. When initially contact traced she was asymptomatic, and because she had exhibited a grade 4 Heaf test she was given standard chemoprophylaxis. The genotypes of the *M. tuberculosis* strains from the patient and her mother were identical, confirming suspicions that this was as the result of reactivation of the initial infection from her mother 3 years previously, and not reinfection. This was despite 3 months of chemoprophylaxis with rifampicin and isoniazid as recommended by the British Thoracic Society, and the organism being fully sensitive to these drugs.[1]

Following the identification of a person infected with *M. tuberculosis*, early contact tracing is required to facilitate prompt detection of potentially affected individuals. Close contacts generally consist of those sharing the same household or who spend considerable time together. More casual contacts are not considered to be at significant risk of contracting tuberculosis unless the index case is smear positive or if contacts are susceptible to infection. The British Thoracic Society produced updated guidelines in 2000 in which an algorithm advises clinicians on how to manage close contacts of patients with pulmonary tuberculosis.[1] These recommendations propose that isoniazid