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Extensive nosocomial transmission of tuberculosis in a low-incidence country

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SUMMARY

Background: This paper describes a nosocomial outbreak of tuberculosis in a hospital ward where the number of cases with active tuberculosis among contacts was unexpectedly high. The outbreak was not revealed until the *Mycobacterium tuberculosis* genotyping results from the first two secondary tuberculosis cases were available.
Aim: To highlight the importance of correct infection control measures when tuberculosis is suspected.
Methods: A retrospective review of the contact investigations following the diagnosis of the index case admitted to the ward.
Findings: Seven contacts including three healthcare workers (HCWs) developed tuberculosis within 10 months after the death of a HIV positive patient from pulmonary tuberculosis. Six out of seven cases were verified by culture and all six *M. tuberculosis* isolates were confirmed by restriction fragment length polymorphism to cluster with the *M. tuberculosis* isolate from the index case. For the HCWs there was a correlation between number of working hours and risk of acquiring tuberculosis infection and disease.
Conclusions: It is essential that infection control guidelines regarding tuberculosis are followed, and that HCWs should continuously be informed about current tuberculosis control measures. All staff members at clinics treating tuberculosis cases should be screened for latent tuberculosis infection in order to have a reference, in case of future contact-tracing after accidental exposure to tuberculosis.

Introduction

The annual incidence of tuberculosis in Sweden is low with an overall incidence of six or seven per 100,000 inhabitants resulting in around 500 cases per year during the 1990s and early 2000s. Since 2005 the total number of tuberculosis cases has increased, reaching 680 cases in 2010. The majority of patients with tuberculosis in Sweden have their origin in high-incidence countries whereas the incidence for tuberculosis cases with Swedish origin only is one per 100,000 inhabitants. Most of the latter individuals are elderly or have parents from a high-incidence country. In 1996, genotyping of drug-resistant strains of *Mycobacterium tuberculosis* was initiated using restriction fragment length polymorphism (RFLP), and, since the year 2000, ~85% of all *M. tuberculosis* strains found in Sweden have been genotyped. RFLP is useful to detect clusters of *M. tuberculosis* isolates, which could indicate recent and ongoing transmission within a specific setting or within

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a country.[1–3] General bacillus Calmette–Guérin (BCG) vaccination in Sweden was discontinued in 1974 and since then has been offered only to children from high-risk groups, i.e. children with parents from countries with a tuberculosis incidence of >25 per 100,000. It is also offered to unvaccinated, tuberculin skin test-negative nursing and medical students and to medical staff working with infectious or lung diseases.

The objective of this outbreak investigation was to analyse the reasons for its spread and to identify shortcomings in local control measures.

Methods

This ward belongs to the clinic of infectious diseases in a large referral university hospital specializing in infectious diseases in patients with drug misuse, and has a capacity of 16 patients allocated in 12 rooms with one or two beds. Social contacts, patients on the ward and healthcare workers (HCWs) were all part of the contact-tracing. Patients admitted to the ward were identified through the hospital database and ward logs. HCWs were categorized as direct-care providers and as those assigned to the same ward but not directly involved in the care of the index case. Major exposure was defined as nursing the index case for >8 h, in accordance with Swedish and European guidelines.[4]

Contacts were tested with tuberculin skin test. Two units of purified protein derivative (Tuberculin PPD RT23; Statens Serum Institut, Copenhagen, Denmark) were injected intradermally and cutaneous induration was measured after 72 h. If the tuberculin skin test reaction was ≥10 mm or the contact had symptoms suggestive of tuberculosis, chest X-ray and an examination by a specialized physician were performed. In cases of a concomitant HIV infection or other immunosuppressive conditions, the lower limit for a positive tuberculin skin test reaction was 6 mm. In some cases, an additional interferon-gamma release assay using the commercially available QuantiFERON-TB Gold in tube (QFT) was performed according to the manufacturer's instructions.

A case of active tuberculosis was defined as a patient with clinical symptoms and radiological findings compatible with tuberculosis, later confirmed by mycobacterial culture or by response to tuberculosis treatment.

A confirmed secondary case was defined as a case with an identical isolate of *M. tuberculosis* as compared with the *M. tuberculosis* isolate of the index case, determined by RFLP analysis. The isolates were cultured on Löwenstein Jensen medium, DNA was extracted and RFLP typing was performed using the insertion sequence IS*6110* as a probe and *Pvu*II as the restriction enzyme.[5] Visual bands were analysed using the BioNumerics version 6.6 software. Strains with identical RFLP patterns (100% similarity) were judged to belong to a cluster.

This investigation was undertaken as a public health response, not as human subject research. No additional investigation besides contact-tracing was performed. For this reason we have not applied for ethical permission.

Results

At the end of July in 2008 the county medical officer in Stockholm was informed about two recently diagnosed cases of tuberculosis in which *M. tuberculosis* isolates analysed with RFLP were identical with an *M. tuberculosis* isolate from a case diagnosed in January the same year. All three cases were known intravenous drug users and HIV carriers.

Index case

A 50-year old male intravenous drug user was admitted on 28 December 2007 with a six-week history of coughing and weight loss. He was diagnosed with HIV in 2003 but had no treatment with antiretroviral drugs and his most recent CD4 count was 400/mL. On admittance pulmonary tuberculosis was considered a possibility and the patient was isolated. He was subsequently misdiagnosed as suffering from *Pneumocystis jiroveci* pneumonia and isolation was discontinued before any sputum for mycobacterial analysis had been obtained. The treatment for *P. jiroveci* pneumonia included high-dose steroids and initially the patient improved. After a week of *P. jiroveci* pneumonia treatment his condition deteriorated. A bronchoscopy was performed on 14 January and on 17 January the laboratory reported a positive polymerase chain reaction (PCR) for the *M. tuberculosis* complex in bronchoalveolar lavage. The patient was isolated and started on tuberculosis treatment. The patient's clinical condition deteriorated despite tuberculosis treatment and he died on 22 January 2008.

Family and friends

The results of contact-tracing are shown in Table I. Contact-tracing among the index case's friends and family was initiated directly after his tuberculosis diagnosis. Seven individuals were identified as possibly exposed. Four of them were intravenous drug users, three of whom were HIV-infected. Of these, one was diagnosed with latent tuberculosis infection (LTBI) (tuberculin skin test: 8 mm) and all four contacts who were HIV negative had possible LTBI (tuberculin skin test: from 10 to 30 mm). They were followed at the tuberculosis polyclinic for two years after exposure, and so far have not developed active tuberculosis even though only one has received prophylactic treatment.

Healthcare workers with major exposure

During March 2008, 18 of the HCWs with major exposure to the index case were screened and seven of them diagnosed with possible LTBI (tuberculin skin tests: from 13 to 36 mm). Most of them had been working at the ward for years and it was difficult to judge whether they were recently infected or not. Results of previous tuberculin skin tests were not known. Only one of 18 was definitely not BCG-vaccinated and this person had a negative tuberculin skin test. Nine were BCG-vaccinated and data for the remaining eight HCWs were lacking. Out of seven diagnosed with possible LTBI at least five were definitely

Table I
Result of contact investigation by type of contact

	Active TB	Latent TB	Not infected	Total
Family/ friends	0	5 (1 HIV^+)	2 (2 HIV^+)	7 (3 HIV^+)
Fellow patients	4 (2 HIV^+)	4	7 (3 HIV^+)	15 (5 HIV^+)
Healthcare workers	3	15	18	36

TB, tuberculosis; HIV, human immunodeficiency virus.