Short Communication

Management of a Nosocomial Outbreak of *Mycobacterium tuberculosis* Beijing/W Genotype in Taiwan: an Emphasis on Case Tracing with High-Resolution Computed Tomography

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SUMMARY: A nosocomial outbreak of *Mycobacterium tuberculosis* Beijing/W genotype infected 15 healthcare workers (HCWs) in a medical center in Taiwan, where there is a high prevalence of tuberculosis and a high rate of positive tuberculin skin tests. An index patient with laryngeal cancer and a lung abscess was identified by epidemiological investigation and it was found that an *M. tuberculosis* isolate from his lung tissue sample had an identical IS6110 restriction fragment length polymorphism pattern to the isolates from 3 HCWs. Confirmation of the identity of this strain as Beijing/W genotype was made using spoligotyping. Seven hundred and eighty-five HCWs potentially exposed to the probable index patient received contact investigation and chest X-ray screening. We used chest high-resolution computed tomography (HRCT) to clarify trivial lesions in chest X-rays. Nine HCWs with smear-negative pulmonary tuberculosis were diagnosed by HRCT. Fifteen of the 35 (42.9%) HCWs with documented exposure to the index patient developed pulmonary tuberculosis within 11 months after exposure. The outbreak was successfully controlled by active case finding and enforcement of infection control strategies. Intervention to detect the potential tuberculosis source is helpful in the prevention and control of a nosocomial tuberculosis outbreak. HRCT can be a useful tool for tuberculosis diagnosis of contacts in an outbreak situation.

The hazard that tuberculosis (TB) poses to healthcare workers (HCWs) and patients in hospital settings is a serious concern in infection control. The tuberculin skin test (TST) is widely used as the standard procedure in TB contact investigation during a nosocomial TB outbreak in accordance with the guidelines of the US Centers for Disease Control and Prevention (1). However, it is difficult to apply the TST routinely in Taiwan due to the high prevalence of positive tuberculin skin tests. A recent study showed that TST was reactive in 84.6% of HCWs and even as high as 92.3% in TB-ward nurses; these tests were considered false positive when compared to Quantiferon-TB Gold (Cellestis Ltd., Melbourne, Australia) (3). Instead of using TSTs, contact history tracing, risk assessment, and regular chest X-ray (CXR) screening are performed in most hospitals in Taiwan for conducting TB contact investigation. However the use of CXR for diagnosing pulmonary TB dose not provide a high level of sensititvity and may be interpreted differently between doctors. High-resolution computed tomography (HRCT) is currently the most accurate noninvasive tool for the evaluation of lung structure and has proven useful in the diagnosis of pulmonary TB (4–6), however its application in outbreak investigation is rarely reported.

An outbreak of *Mycobacterium tuberculosis* among HCWs in a 1,600-bed medical center in southern Taiwan occurred during July and August 2005. Three nurses who worked in the chest medicine ward were diagnosed with pulmonary TB between June and August 2005 (Table 1). Because these HCWs worked in the same ward and the infections occurred within an unusually close interval, a series of investigations into this event was conducted by the Department of Infection Control. A detailed TB-contact history was obtained...
Table 1. Characteristics of infected health care workers

<table>
<thead>
<tr>
<th>HCW/position</th>
<th>Detection date</th>
<th>Symptom</th>
<th>Chest X-ray</th>
<th>HRCT</th>
<th>AFB/MTB</th>
<th>Adverse drug reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>A Nurse</td>
<td>Jun 2005</td>
<td>Fever in April 2005</td>
<td>LT UL lesion</td>
<td>—</td>
<td>Neg/Neg</td>
<td>Itching 3 × LFT</td>
</tr>
<tr>
<td>B Nurse</td>
<td>Jun 2005</td>
<td>Fever, chest pain</td>
<td>Pleural effusion</td>
<td>—</td>
<td>Neg/Neg</td>
<td></td>
</tr>
<tr>
<td>C Intern</td>
<td>Jul 2005</td>
<td>Mild cough</td>
<td>RT UL lesion</td>
<td>—</td>
<td>Neg/Neg</td>
<td>Rash 2 × LFT</td>
</tr>
<tr>
<td>D Nurse</td>
<td>Jul 2005</td>
<td>Fever, cough, dyspnea</td>
<td>RT side pleural effusion</td>
<td>RT pleural effusion</td>
<td>Neg/Pos</td>
<td></td>
</tr>
<tr>
<td>E Nurse</td>
<td>Aug 2005</td>
<td>Cough, dyspnea</td>
<td>Bil lung pneumonia</td>
<td>Consolidation (RLL, RUL)</td>
<td>Neg/Neg</td>
<td></td>
</tr>
<tr>
<td>F Nurse</td>
<td>Aug 2005</td>
<td>Mild afternoon fever</td>
<td>RT UL lesion</td>
<td>—</td>
<td>Neg/Neg</td>
<td></td>
</tr>
<tr>
<td>G Nurse</td>
<td>Aug 2005</td>
<td>Mild dry cough and dyspnea</td>
<td>RT LL lesion</td>
<td>Centrilobular and acinar nodules (RLL, both apex)</td>
<td>Neg/Neg</td>
<td>GI upset Itching</td>
</tr>
<tr>
<td>H Nurse</td>
<td>Aug 2005</td>
<td>Dry cough and mild fever in June 2005</td>
<td>Bil UL pneumonia</td>
<td>Centrilobular and acinar nodules (RUL, LUL)</td>
<td>Neg/Neg</td>
<td>Optic neuritis Itching</td>
</tr>
<tr>
<td>I Nurse</td>
<td>Aug 2005</td>
<td>Dry cough and fever, cough in April 2005 (s/p moxifloxacin)</td>
<td>Bil UL lesion</td>
<td>Consolidation (RML, RLL)</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>J Nurse</td>
<td>Aug 2005</td>
<td>Mild cough</td>
<td>LT UL lesion</td>
<td>Consolidation (Left lingual segment)</td>
<td>Neg/Neg</td>
<td>Itching</td>
</tr>
<tr>
<td>K Nurse</td>
<td>Sep 2005</td>
<td>Fever and cough in July 2005 (s/p azithromycin)</td>
<td>LT LL lesion</td>
<td>Centrilobular and acinar nodules (RUL, LUL, LLL) Tree-in-bud appearance (RUL)</td>
<td>Neg/Neg</td>
<td></td>
</tr>
<tr>
<td>L Nurse</td>
<td>Nov 2005</td>
<td>Cough</td>
<td>Bil UL lesion</td>
<td>Consolidation (LUL, LLL) Tree-in-bud appearance (LUL, LLL)</td>
<td>Neg/Neg</td>
<td>Rash 7 × LFT Jaundice 2 × LFT</td>
</tr>
<tr>
<td>M Nurse</td>
<td>Dec 2005</td>
<td>Mild cough</td>
<td>Bil UL lesion</td>
<td>Centrilobular and acinar nodules (RUL) Cavitation (RUL)</td>
<td>Neg/Neg</td>
<td></td>
</tr>
<tr>
<td>N Nurse</td>
<td>Jan 2006</td>
<td>Chest pain and mild dyspnea</td>
<td>RT side pleural effusion</td>
<td>RT pleural effusion (Pleura)</td>
<td>Neg/Neg</td>
<td></td>
</tr>
<tr>
<td>O Intern</td>
<td>Jan 2006</td>
<td>Mild cough</td>
<td>LT UL lesion</td>
<td>Centrilobular and acinar nodules (LUL) Tree-in-bud appearance (LUL)</td>
<td>Neg/Neg</td>
<td></td>
</tr>
</tbody>
</table>

HCW, healthcare worker; HRCT, high-resolution computed tomography; AFB, acid-fast bacilli; MTB, M. tuberculosis culture; LT, left; RT, right; UL, upper lung field; LL, lower lung field; Pos, positive; Neg, negative; LFT, fold increase over upper limit of normal aminotransferase level.

from every employee who worked in the Department of Internal Medicine for 1 year preceding the 2005 outbreak who might have been exposed to infectious TB. The employees received a serial CXR examination in August 2005 to detect any parenchymal abnormalities compared to previous records, after obtaining their informed consent. If any lesion was apparent upon CXR or any respiratory symptoms were found, sputum specimens were collected for acid-fast bacillus (AFB) stain and mycobacterial culture. HRCT was arranged for trivial or inconclusive pulmonary lesions identified by CXR to further clarify the lesions. To identify the index case, we reviewed all records of pulmonary TB cases among the patients who had been housed in the chest medicine ward instead of the negative-pressure isolation ward in the year preceding the 2005 outbreak.

In August 2005, 785 HCWs who worked in the Department of Internal Medicine were screened by CXR and their contact histories were investigated. All 785 HCWs had been vaccinated with BCG. A total of 15 HCWs, including 11 nurses, 3 interns, and one resident physician, developed pulmonary TB (Table 1). None of the 15 HCWs had positive results for HIV antibody testing, conditions known to cause an immunocompromised condition, or abnormal CXR findings 6 months previously. The risk of infection was the highest for nurses (11 of 18, 61.1%), followed by interns (3 of 7, 42.9%), with the lowest risk for resident physicians (1 of 8, 12.5%) among the documented contacts with the index patient. Neither of the two attending physicians that were exposed became infected. The isolates from the 3 HCWs with culture-proven TB were susceptible to all first-line anti-TB drugs including rifampin, isoniazid, pyrazinamide, ethambutol, and streptomycin. Nine smear-negative HCWs with inconclusive CXR findings received HRCT to clarify the pulmonary lesions. All
HRCT revealed characteristic findings of active pulmonary TB (4–6), including 8 centrilobular and acinar nodules, 4 tree-in-bud appearances, 4 consolidations, 2 pleural effusions, and others with ground glass opacity, cavitation, and bronchial wall thickening. All 15 HCWs received anti-TB medications by Directly Observed Therapy (DOT), with subsequent resolving of symptoms and CXR indicated pulmonary improvement, without any relapses among any of the subjects during the 3-year follow-up. However, adverse drug reactions occurred in 8 HCWs (8/15; 53%), including anti-TB agent-associated hepatitis in 6 HCWs (6/15; 40%) (Table 1). We followed up these HCWs with both CXR and microbiological or radiological evidence in any of the other 770 HCWs with normal initial symptoms and CXR indicated pulmonary improvement.

From August 2004 until the appearance of infected HCWs, 22 patients (in whom a diagnosis of active pulmonary TB had not been suspected initially and who had been admitted to the chest medicine ward rather than to isolation rooms) were later diagnosed to have pulmonary TB by either a positive-culture result or positive AFB (Table 2). Use of the chi-square test to compare the relative risk (the frequency of contact) among the HCWs who developed pulmonary TB to patterns of contact with these patients narrowed the list of the probable index patients to four for whom the P value was <0.05.

Patient 4, the index case, had laryngeal cancer and had been admitted to the chest medicine ward because of a right lower lung abscess. The patient had severe cough, and three sputum specimens collected at the time of admission were negative for AFB. During this patient’s hospitalization, he received neither radiotherapy nor chemotherapy, but various procedures were performed, such as sputum suction, chest percussion, intubation with laryngoscopy, and echo-guided lung tissue biopsy. As documented in his chart, patient 4 had direct contact with 35 HCWs. The patient died of respiratory failure and septic shock 1 month after admission, and M. tuberculosis complex was later identified from his lung biopsy tissue 2 months after admission. When genotyping was performed on isolates available from 17 of the patients, only the specimen from patient 4 produced an RFLP pattern identical to those available from 17 of the patients, only the specimen from patient 4 produced an RFLP pattern identical to those from the 3 HCWs from whom isolates were available. Spoligotyping determined that the isolate belonged to the M. tuberculosis Beijing/W genotype family.

To contain the TB outbreak, the ventilation in the chest medicine ward, outpatient department, and bronchoscopy room was enhanced (from 2 to 6 air changes per hour), which was recommended by the US Centers for Disease Control and Prevention and the American Institute of Architects (7), and daily ultraviolet germicidal irradiation was used in these areas. Procedures to generate aerosols were conducted only in the negative-
pressure ward for suspected TB patients. A cough screening program for unexplained prolonged cough and TB education program were also arranged. Strict regulations were established for the microbiological laboratory to provide AFB-staining results within 24 h, and for the radiologists to report immediately when active pulmonary TB was suspected.

Our report illustrates the difficulty of rapidly identifying index patients and infected contacts in a region with a high prevalence of positive TST. Furthermore, there is a lack of consensus over whether TST is a reliable diagnostic method and whether isoniazid prophylaxis should be applied in Taiwan. Under the circumstances, most Taiwanese hospitals use serial CXR surveillance to identify possible pulmonary TB patients for contact investigation, but sensitivity for the diagnosis of TB is not good enough (8,9). Our result revealed chest HRCT is useful as a supplementary tool to diagnose pulmonary TB for equivocal lesions in the CXR images in an outbreak. HRCT is currently the most accurate noninvasive tool for the evaluation of lung structure and has good diagnostic value in detecting active pulmonary TB when the sputum smear is negative for AFB (8,9). There is a good correlation between HRCT findings with pulmonary TB activity and positive-AFB smears (10,11), especially for centrilobular and acinar nodules, tree-in-bud appearance, cavitation, and consolidations, which significantly indicate active pulmonary TB (8–12). The presence of large nodules, tree-in-bud appearance, lobular consolidation, and the location of the main lesion in segments 1, 2, and 6 on HRCT were significantly associated with active pulmonary TB. The specificity and sensitivity of HRCT were 88–93% and 83–88%, respectively. The presence of at least 3 of the above findings results in a positive likelihood ratio of 13.3 (8,9,11). Consolidations and cavitations are more common in active than in inactive disease. In this outbreak, 9 HCWs had HRCT exams and all revealed active pulmonary TB with the most common HRCT features of centrilobular and acinar nodules (88.9%), followed by tree-in-bud appearance (44.4%) and consolidations (44.4%). We used HRCT to supplement CXR screening in identifying an additional 7 HCWs who had mild respiratory symptoms and trivial abnormalities in CXRs, and negative results from AFB smears and mycobacterial cultures. These patients can be missed without HRCT. Our results are in agreement with the view that HRCT is useful in visualization of subtle findings in plain CXR and is able to play a role in assisting CXR in outbreak investigations. There are two Japanese reports of using HRCT in contact investigations during an outbreak; these reports also showed close correlation with ambiguous symptoms and suggested using HRCT for detecting TB cases among contacts (13,14).

In an area with a high prevalence of TB, the level of suspicion should be increased accordingly, especially in patients with malignancies and chronic lung diseases (15). The index patient with laryngeal cancer was admitted for lung abscess; pulmonary TB was not diagnosed initially, and the patient was not placed in isolation. TB bacilli were transmitted rapidly and efficiently to HCWs by the patient’s coughing and aerosol production. TB can coexist in laryngeal cancer patients and can easily be misdiagnosed (16). Although the pulmonologists and infectious disease physicians were alert for TB (17), the index patient was still overlooked. Efforts to rapidly identify patients with TB may include exploiting a rapid mycobacterial culture system to reduce incubation time and to enhance yield; newer technologies, such as HRCT and rapid assays for TB, can also be used so that infected patients may be placed in isolation rooms more quickly.

The *M. tuberculosis* Beijing/W genotype caused serious concern because it has been associated with several nosocomial TB outbreaks (18,19). Members of the Beijing/W genotype family have emerged as prevalent strains worldwide and have exacted considerable morbidity and mortality (20–22). This Beijing/W genotype may be the reason for the high transmissibility and rapid progression to pulmonary TB diseases in this outbreak. The high rate (42.9%), 15 of 35 HCWs who were exposed to the index patient) of HCWs to develop pulmonary TB within 1 year by this Beijing/W genotype suggested this genotype has a high transmissibility.

With the challenges of infection control in regions with a high prevalence of TB and positive TSTs, our study suggests that HRCT can be a helpful supplement to CXR during contact investigations. Furthermore, implementation of the effective infection control measures described in this report, and prompt treatment of infected individuals as a result of the contact investigation, contributed to the containment of this outbreak.

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**Conflict of interest** None to declare.

**REFERENCES**


