In-hospital Airborne Tuberculous Infection from a Lesion of Calcified Pleural Thickening during Thoracic Surgery in a Patient with Lung Cancer

Kentaro Akata¹, Toshinori Kawanami¹, Kazuhiro Yatera¹, Takashi Tachiwada², Masaru Takenaka³, Shingo Noguchi³, Kei Yamasaki¹, Chisatsu Nishida¹, Takeshi Orihashi¹, Hiroshi Ishimoto¹, Chiharu Yoshii², Fumihiro Tanaka³ and Hiroshi Mukae¹

Abstract

A 75-year-old Japanese man underwent thoracic surgery to treat a large lung cancer lesion in the left upper lobe with calcified pleural thickening. Postoperatively, viable *Mycobacterium tuberculosis* was detected in the margin of the resected thickened calcified pleural lesion. Therefore, an infection control investigation of medical staff who had come in contact with the patient was conducted. Consequently, two of the 14 healthcare professionals who had been in the operating room were diagnosed with latent tuberculous infections. Therefore, strict precautions against airborne infections are required to prevent the in-hospital transmission of *M. tuberculosis* in such cases.

Key words: *Mycobacterium tuberculosis*, old tuberculous pleurisy, calcified pleural lesion, surgical procedure, nosocomial infection, airborne infection

(DOI: 10.2169/internalmedicine.54.4317)

Introduction

*Mycobacterium tuberculosis* (TB) can be isolated and live for a long period of time in granulomas, even in patients with clinically-suspected inactive tuberculosis (1, 2). Calcification of the pleura is associated with chronic tuberculosis (3). TB can be present as a latent infection even in intra- and extrapulmonary lesions suggestive of old pulmonary and/or pleural tuberculosis, and the surgical procedures used to remove these tissues may result in infectious airborne transmission. We herein report what may be the first reported case of a thoracic surgery-related nosocomial transmission of TB to healthcare professionals during surgery for primary lung cancer in a patient who had pleural thickening and calcification suspected to be a latent tuberculosis infection.

Case Report

A 75-year-old Japanese man was referred to our university hospital for surgery for a large lung cancer lesion in the left upper lobe. He had a medical history of left tuberculous pleurisy treated without antituberculous agents (only bed rest in a hospital) at 18 years of age, a gastric ulcer, silent cholelithiasis, and bilateral cataracts. He also had a history of smoking for 35 pack-years, but reported no history of exposure to asbestos or other mineral or toxic dust. He had previously been in good health without febrile episodes or symptoms, with the exception of the development of bloody sputum for a couple of days before visiting a hospital.

Chest computed tomography (CT) performed at the local hospital revealed a mass involving the left parietal pleura and mediastinum in the left upper and lingular lobes with
left calcified pleural thickening. Bronchoalveolar lavage fluid (BALF) and a transbronchial lung biopsy (TBLB) that were diagnostic for squamous cell lung cancer were obtained from the left S5 using fiber optic bronchoscopy. However, an acid-fast smear and polymerase chain reaction (PCR) analysis for TB in the BALF specimen were negative. A systemic investigation confirmed a diagnosis of primary pulmonary squamous cell carcinoma (c-T3N2M0, Stage IIIA), so the patient was admitted to our hospital to undergo surgery for lung cancer.

Upon admission, the patient’s height and body weight were 152 cm and 54 kg (body mass index: 23.4), respectively, and his body temperature was 36.3°C. No abnormal respiratory or cardiac sounds were audible, and no other abnormal physical findings were noted. However, the laboratory data obtained on admission (Table 1) revealed increased serum levels of C-reactive protein (CRP), squamous cell carcinoma antigens (SCC), the cytokeratin 19 fragment (CYFRA), and carcinoembryonic antigen (CEA), and a chest X-ray film (Fig. 1) demonstrated a large mass shadow in the left middle lung field with left pleural calcification. In addition, chest CT performed on admission (Fig. 2) showed a large tumor (62×42 mm in size) involving the left upper and lingular lobes, with a relatively clear margin, as well as enlarged mediastinal lymph nodes. Left calcified pleural thickening was also noted, suggesting old tuberculous pleurisy. Furthermore, preoperative ¹⁸F-fluorodeoxyglucose-positron emission tomography/computed tomography (FDG-PET/CT) showed the accumulation of FDG in the large tumor in the left upper lobe, with a maximum standardized uptake value (SUVmax) of 20.0, while the SUVmax in the calcified and non-calcified areas of the left pleura were 1.0 and 2.8, respectively.

Surgical treatment for the left lung cancer was performed. Initially, left upper lobectomy was scheduled; however, severe adhesion of the pleura was observed, and left pleuropneumonectomy with pleural decortication, as a result, pericardiectomy and mediastinal lymph node dissection were ultimately performed due to the marked pleural adhesion. The areas of left thickening and calcified pleura were also resected using a rib shear, and the fluid contents of the pleural thickening accidentally spilled into the intrathoracic space. The operation time was 5 hours and 5 minutes.

Ziehl-Neelsen staining of a smear of the left calcified pleura showed acid-fast bacilli (equivalent to a Gaffky score of 2), with positive results on TB-PCR reported three days

---

Table 1. Laboratory Findings on Admission.

<table>
<thead>
<tr>
<th>Hematology</th>
<th>Tumor markers</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC 8,900 /µL</td>
<td>CEA 3.9 ng/dL</td>
</tr>
<tr>
<td>Neu 75.8 %</td>
<td>CYFRA 11 ng/dL</td>
</tr>
<tr>
<td>Lym 13.2 %</td>
<td>SCC 32.6 ng/dL</td>
</tr>
<tr>
<td>Mon 8.5 %</td>
<td>ProGRP 35 pg/dL</td>
</tr>
<tr>
<td>Eos 1.9 %</td>
<td></td>
</tr>
<tr>
<td>Bas 0.6 %</td>
<td></td>
</tr>
<tr>
<td>RBC 425×10⁴ /µL</td>
<td></td>
</tr>
<tr>
<td>Hb 13.3 g/dL</td>
<td></td>
</tr>
<tr>
<td>Hct 38.9 %</td>
<td></td>
</tr>
<tr>
<td>Plt 25.9×10⁴ /µL</td>
<td></td>
</tr>
<tr>
<td>Biochemistry TP 7.2 g/dL</td>
<td></td>
</tr>
<tr>
<td>Alb 3.9 g/dL</td>
<td></td>
</tr>
<tr>
<td>T-Bil 0.7 mg/dL</td>
<td></td>
</tr>
<tr>
<td>AST 15 IU/L</td>
<td></td>
</tr>
<tr>
<td>ALT 12 IU/L</td>
<td></td>
</tr>
<tr>
<td>ALP 244 IU/L</td>
<td></td>
</tr>
<tr>
<td>γ-GTP 17 IU/L</td>
<td></td>
</tr>
<tr>
<td>LDH 192 IU/L</td>
<td></td>
</tr>
<tr>
<td>BUN 10 mg/dL</td>
<td></td>
</tr>
<tr>
<td>Cr 0.57 mg/dL</td>
<td></td>
</tr>
<tr>
<td>Na 139 mEq/L</td>
<td></td>
</tr>
<tr>
<td>K 4.1 mEq/L</td>
<td></td>
</tr>
<tr>
<td>Cl 104 mEq/L</td>
<td></td>
</tr>
<tr>
<td>CRP 2.26 mg/dL</td>
<td></td>
</tr>
</tbody>
</table>

Figure 1. Chest X-ray film taken on admission showed a mass in the left middle lung field with calcified pleural thickening. The left lung field had shrunk.
The patient was isolated to control airborne infection after the surgery, and treatment with antituberculous agents [isoniazid (INH): 300 mg/day, rifampicin: 450 mg/day, ethambutol: 750 mg/day, pyrazinamide: 1.2 g/day] was initiated. The patient’s postoperative clinical course was favorable. The thoracic drainage tube was subsequently removed, and the patient was released from isolation six days after the operation after confirming the negative results of sputum acid-fast smears on three consecutive days. Seven days after the surgery, the culture results for the BALF specimen obtained from the left B' at the previous hospital one month before the current operation were found to be positive for TB. In addition, the histopathological findings of the resected left upper lung included an epithelioid granuloma at the periphery of the squamous cell carcinoma, consistent with a diagnosis of pulmonary tuberculosis, and TB was cultured from the resected pleura. There were no carcinomatous involvements of the hilar or mediastinal lymph nodes; therefore, a final diagnosis of primary squamous cell lung carcinoma in the left upper lobe (p-T2aN0M0, Stage IB) complicated by pulmonary tuberculosis and left latent tuberculous pyothorax was made. The risk of transmission of TB was not considered before or during the thoracic surgery; thus, no strategies to control airborne infection were implemented, and only standard surgical masks were used in this case. A total of 14 medical personnel [four surgeons, two anesthesiologists, five nurses, and three medical engineers (MEs)] had been in the operating room during the surgery. Health checkups, including T-spot TB testing, were carried out on the medical personnel postoperatively just after the surgery and two months later. Two MEs subsequently demonstrated positive findings for T-spot TB two months after the surgery. Chest X-ray films and CT scans of these two individuals showed no radiological abnormalities, and they each received INH (300 mg/day) for six months for latent tuberculosis infection, as the cultured TB was sensitive to INH. The treatment protocol was completed without side effects, and chest CT scans obtained 6 months after the end of the INH therapy did not disclose any abnormal findings.

**Discussion**

This case report described the spread of a hospital-acquired airborne TB infection in the operating room during thoracic surgery for lung cancer in a patient with a latent tuberculous calcified pleural lesion. Viable TB was subsequently detected in the left calcified and thickened pleural lesion. Radiologically, a chest CT scan of the patient demonstrated no cavitary lesions or granular, nodular or branching shadows suggestive of active TB infection in the lung field. In addition, an acid-fast smear and TB-PCR analysis of a preoperative BALF sample were both negative. In addition, a mild degree of accumulation of FDG on FDG-PET/CT in the non-calcified areas of the left pleura might be
Table 2. Reports on Nosocomial Transmission of Extrapulmonary TB with Surgical Procedure.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Country</th>
<th>Year (years)</th>
<th>Sex</th>
<th>Underlying disease</th>
<th>Medical history</th>
<th>Primitive diagnosis</th>
<th>Specimen</th>
<th>Acid-fast smears</th>
<th>TB PCR</th>
<th>Culture</th>
<th>Final diagnosis</th>
<th>Days until diagnosis of TB from admission</th>
<th>Days until diagnosis of TB from surgical procedure</th>
<th>Surgical procedure</th>
<th>Incidence of LTBI in exposed HCWS</th>
<th>Incidence of active TB in exposed HCWS</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>USA</td>
<td>67, M</td>
<td></td>
<td>Unknown fever</td>
<td></td>
<td>Abscess of the hip and thigh</td>
<td>Smear of the abscess</td>
<td>+</td>
<td>Not analyzed</td>
<td>Not analyzed</td>
<td>Tuberculous subcutaneous abscess</td>
<td>8 days</td>
<td>4 days</td>
<td>Drainage, irrigation, debridment, and dressing change</td>
<td>Employees during or after surgical procedure 44/80(55%), others 2/35(6%)</td>
<td>1/115(0.9%) (prophylaxis was unknown)</td>
</tr>
<tr>
<td>5</td>
<td>USA</td>
<td>84, F</td>
<td></td>
<td>Deep venous thrombosis</td>
<td>Skin ulcer of upper anterior thigh</td>
<td>Tissue of the skin ulcer from autopsy</td>
<td>+</td>
<td>Not analyzed</td>
<td>Not analyzed</td>
<td>Cutaneous tuberculosis</td>
<td>31 days</td>
<td>Not described</td>
<td>Debridment and dressing change</td>
<td>Employees during surgical procedure 10/56(18%), others 1/13(8%)</td>
<td>2</td>
<td>A nurse was skin-test negative. Another nurse of skin-test converter refused prophylaxis because of pregnancy</td>
</tr>
<tr>
<td>6</td>
<td>The Netherlands</td>
<td>84, M</td>
<td>HT†, DM‡, RA§, and bursitis in his left bursa trochanterica</td>
<td>Hip abscess</td>
<td>Culture of the abscess</td>
<td>+</td>
<td>Not analyzed</td>
<td>+</td>
<td>Tuberculous subcutaneous abscess</td>
<td>23 days</td>
<td>20 days</td>
<td>Drainage, irrigation, and debridement</td>
<td>17/372(5%), 17: hospital employees, 372: hospital contact, details unknown</td>
<td>1</td>
<td>A nurse who was skin-test converter refused prophylaxis because of pregnancy</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>USA</td>
<td>71, M</td>
<td></td>
<td>Nothing</td>
<td>Epididymo-orchitis</td>
<td>Tissue¶ from autopsy</td>
<td>+</td>
<td>Not analyzed</td>
<td>+</td>
<td>Disseminated tuberculosis¶</td>
<td>27 days</td>
<td>3 days</td>
<td>Orchietomy, drainage, irrigation, and dressing change</td>
<td>Employees during or after surgical procedure 12/95(13%)</td>
<td>0/23(0%)</td>
<td></td>
</tr>
<tr>
<td>This case</td>
<td>Japan</td>
<td>75, M</td>
<td></td>
<td>Old tuberculosis pleurisy</td>
<td>Old tuberculosis pleurisy</td>
<td>Smear of tissue from the pleura</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Pulmonary tuberculosis and tuberculous pleurisy</td>
<td>2 days</td>
<td>0 day</td>
<td>Extrapleural pneumonectomy</td>
<td>Surgical suite employees 2/14(14%)</td>
<td>Nothing</td>
<td></td>
</tr>
</tbody>
</table>

* Intramuscular injection of the antibiotic into the left gluteal area
† HT: hypertension
‡ DM: diabetes mellitus type II
§ RA: Rheumatoid Arthritis: treated with corticosteroids
¶ a corticosteroid injection for bursitis in his left bursa trochanterica
†† prostate, lungs, liver, spleen, kidneys, adrenals, and brain

This case Japan 75, M Old tuberculosis pleurisy Old tuberculosis pleurisy Smear of tissue from the pleura + + + Pulmonary tuberculosis and tuberculous pleurisy 2 days 0 day Extrapleural pneumonectomy Surgical suite employees 2/14(14%) Nothing
suggested weak inflammatory lesions.

Postoperatively, T-spot TB \(^6\) tracking with chest radiology was performed among the clinical staff who came into close contact with the patient in the operating room, and 2 MEs were subsequently found to have acquired latent tuberculosis infections during the surgery. TB may be latent, even in calcified pleural or pulmonary lesions that are generally suggestive of old tuberculosis, and surgical procedures may open closed infected lesions, as occurred in the present case. To our knowledge, this is the first report of a clinical case involving the nosocomial transmission of TB to healthy medical staff during thoracic surgery for a calcified pleural lesion.

In the present case, the TB may have been spread to the air when the calcified pleural lesion was resected using a rib shear during surgery in the operating room. Extrapulmonary tuberculosis generally does not become airborne if the infected lesion remains closed to the air. However, exposure of the lesion to the air during surgical treatment carries a risk of airborne transmission of the microbe. There have been only four reported cases of nosocomial transmission to medical professionals during surgical treatment for extrapulmonary tuberculosis (Table 2) (4-7). In these four cases of unexpected infection with extrapulmonary tuberculosis on admission (two patients with gluteal subcutaneous abscesses, one patient with a femoral ulcer, and one patient with orchitis/epididymitis caused by TB), the diagnosis of TB was made after surgery (3 episodes of drainage from infectious foci, three episodes of debridement, 3 episodes of gauze exchange, and two episodes of wound washing). Tracking of the contacts in the hospital (69-372 medical staff members) was conducted in all four of these cases, revealing positive conversions in tuberculin skin tests (TSTs) two months after exposure in 11-17 (4.6-10.2%) of those with negative TST findings immediately after exposure.

Aerosolized particles measuring 1 to 5 μm may be deposited in the alveoli when inhaled as droplet nuclei (8). In the above 4 cases of nosocomial transmission of extrapulmonary tuberculosis (4-7), the inhalation of droplet nuclei of TB aerosolized into the air by the surgical procedure may have led to transairway infection. In particular, the number of medical professionals with infections related to exposure during surgical treatment was markedly higher than that observed before surgery in three of the above reports (4, 5, 7). In the present patient, the patient was mechanically ventilated with under-tracheal intubation during surgery, and bacterial/viral filters that could decontaminate over 99.9% of particles less than 0.02 μm in size were used in intake and output of the air from the ventilator so that air-born infection by exhaust contamination of TB could be avoided. The two infected MEs were only in the operation room during mechanical ventilation; therefore, resection of the left calcified tuberculosis pleural lesion may have induced the aerosolization of TB, with subsequent airborne infection. The two MEs were in the operation room to assist to set up and to help operate thoracoscopy. The reason why only two MEs showed latent tuberculosis infection is unknown. Because the four surgeons and nurses who were close to the operative field wore both a surgical mask and a mask attached to their surgical gown, use of two masks might therefore better prevent TB infection than a surgical mask alone. In addition, used thoracoscopy equipment was checked before the cleaning process by MEs wearing only a surgical mask, which may be the reason why two MEs were infected by TB.

As demonstrated by this report, when thoracic operation involves surgical procedures opening calcified old tuberculous pleural thickening in patients with previously untreated tuberculosis, the operation should be performed in a negative pressure operating room with high efficiency particulate air (HEPA) filter, and all medical staff should wear an N95 mask.

In conclusion, TB may be spread via surgical procedures, even in patients with latent or old TB infections with calcified pulmonary or pleural lesions. Precautions against airborne infections, including TB, must be taken for medical professionals during surgery, with greater attention paid in cases with such findings, especially when the calcified pulmonary or pleural lesions show a high accumulation of FDG.

The authors state that they have no Conflict of Interest (COI).

References


© 2015 The Japanese Society of Internal Medicine
http://www.naika.or.jp/imonline/index.html