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Case Report

The unexpected bilateral Tuberculous empyema: a case report in a child

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Abstract

Tuberculous pleurisy is characterised by unilateral exudates with predilection on the right side, whereas bilateral involvement is rarely encountered. A positive history of contact with tuberculous case and a negative Bacillus Calmette-Guerin (BCG) vaccination scar are usually seen. Here we illustrate a case of bilateral tuberculous lung empyema in a previously healthy child with a presence of BCG scar and an initial non-existence contact history with tuberculosis patient.

Keywords: *Bilateral lung empyema, tuberculous empyema, tuberculous pleurisy*

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Introduction

In developing countries where the incidence of tuberculosis (TB) is relatively high, pleural TB is the most frequent cause of exudative pleural effusion; it is important to differentiate between tuberculous and non-tuberculous causes. Tuberculous pleurisy typically occurs during primary infection and therefore affects younger populations. In developed countries, it is commonly a reflection of disease reactivation, affecting older patients. Tuberculous pleural effusion (TPE) can cause trapped lung or progress to tuberculous empyema. It is classically characterized by unilateral exudates with right-sided predilection, whereas bilateral effusions or empyema are rare. Here we report a case of bilateral tuberculous lung empyema with presence of BCG scar and initial non-existence contact history with tuberculosis patient.

Case report

A 4-year-old Malay girl presented with one-week history of fever and chesty cough; not associated with shortness of breath, wheezing or constitutional symptoms such as loss of appetite or weight. The only significant history in the past was an acute episode of gastroenteritis requiring hospitalisation at the age of one year. Her immunisation was completed up to age, including BCG. There was no history of contact with TB patient, and no known illnesses among her family members.

On admission she was febrile and mildly tachypnoeic. Tonsils were enlarged with no cervical lymphadenopathy. Chest examination revealed reduced air entry with minimal rhonchi and bibasal crepitations posteriorly. She also had hepatomegaly. Examination of other systems was unremarkable. At initial presentation, full blood count (FBC) was normal. Erythrocyte sedimentation rate (ESR) was 118 mm/hr. Chest radiograph showed haziness with loss of costophrenic angles at both lung fields (Figure 1). She was initially treated with penicillin (200 mg/kg/day) for 2 days and erythromycin (100 mg/kg/day) for 2 days.

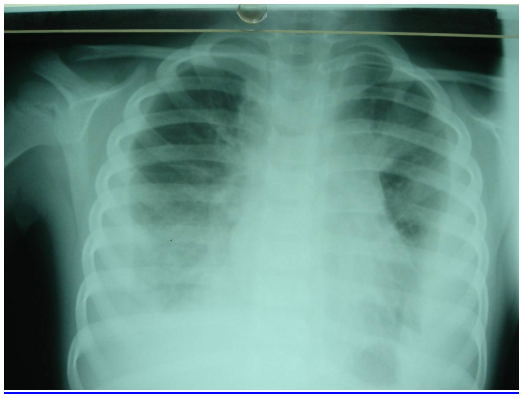

Figure 1: *Chest radiograph of the patient showing bilateral haziness of both lung fields with loss of costophrenic angles*

The following day, she became more tachypnoeic and feverish. Evaluation of respiratory system showed signs of respiratory distress with reduced bilateral chest expansion, stony dullness to percussion and reduced breath sound at bases with bronchial breathing and generalized crepitations. Chest drainage was performed on both lungs; thick, greenish yellowish pus was obtained on drainage. The antibiotics were changed to cloxacillin (200 mg/kg/day) and cefotaxime (200 mg/kg/day). For the next 3 weeks, her temperature remained spiking and the chest persisted to drain pus, especially more on the right as compared to the left.

Subsequent FBC yielded leukocytosis (WBC, $16.9x10^9$) with neutrophils predominant (74%) and thrombocytosis (platelet counts, $987x10^9$). Other blood chemistry was normal. Microscopic examination from pleural fluid showed numerous pus cells (>1000 cells/L) with elevated protein (43 g/L) and lactate dehydrogenase (LDH, 2240 IU/L) levels, while plasma LDH was 1238 IU/L (normal range for age 140–304 IU/L). Blood and pleural cultures for bacteria (including *Burkholderia pseudomallei*) and fungi were

negative. She was also seronegative for *Mycoplasma pneumoniae*, melioidosis, human immunodeficiency virus (HIV) and *Legionella pneumophila*. Immunoglobulin levels were normal. Serial gastric lavage for acid-fast bacilli (AFB) with Ziehl-Neelson staining and culture for *Mycobacterium tuberculosis*, as well as Mantoux test were all negative. Chest radiographs for both parents were normal. Pleural fluid sent repeatedly for AFB and *Mycobacterium* culture were consistently negative; however polymerase chain reaction (PCR) on four samples was positive for *M. tuberculosis*.

She was started on anti-tuberculosis therapy by the end of third week of hospitalization, comprising of two-month of an initial intensive daily dose of isoniazid (INH), rifampicin (RIF), pyrazinamide (PZA) and pyridoxine (INH 10 mg/kg/day; RIF 10 mg/kg/day; PZA 20 mg/kg/day; pyridoxine 5 mg daily)[14]. She unfortunately developed skin rash reaction thought to be due to rifampicin, and therefore was replaced with a low dose of ethambutol (15 mg/kg/day) for two months. Cloxacillin and cefotaxime were continued for a total of six weeks duration. A re-inquiry into the history revealed that maternal grandmother died due to pulmonary tuberculosis with bone dissemination in late 1990's. Her fever settled and appetite improved and she was more cheerful. However, the right chest tube continuously drained small amount of fluid and the left pleural fluid re-accumulated after chest tube was removed.

Computed-tomography (CT) of thorax demonstrated bilateral pleural loculated collections with thickened and enhancing wall at mid and lower zones, measuring 2.6cm x 5.5cm x 6.5cm on the right and 2.4cm x 5.0cm x 5.5cm on the left. There was associated bibasal consolidation and interstitial opacities; however no mediastinal lymphadenopathy was seen. She underwent right decortication with pleurodesis; intra-operative findings were thickened right pleural wall with collection of thick purulent materials. There was interlobular adhesions of the right lung and collection of pus at left mid-zone; hence left chest tube was reinserted. Subsequent histopathology examination of pleural biopsy showed chronic inflammatory changes without granulomatous reaction.

Prior to discharge, chest radiograph showed re-expanded lung fields bilaterally, with less pleural thickening. However, her lungs were still dull to percussion with reduced breath sounds; left more than right, and no crepitations heard. Two weeks after discharged, thoracic ultrasonography showed no obvious residual pleural fluid collections. She continued to receive anti-TB therapy, which was planned for a total of nine months. On follow-up she was well and gaining weight.

Discussion

Pleural tuberculosis is the most frequent cause of exudative pleural effusion in a region with high incidence of tuberculosis[1, 2]. In developing countries where the prevalence of TB is still high, tuberculous pleurisy typically occurs during primary infection and tends to affect younger populations (less than 45 years old)[1, 2]. In industrialized or developed country where tuberculosis is less common, pleural TB more commonly reflects disease reactivation, and is affecting older patients[3]. TPE is very uncommon in young children (15.4% of children with TPE are < 10 years of age)[4], and has been more prevalent in older children and adolescents[5]. A positive history of contact with tuberculous case and presence of BCG vaccination scar are not usually seen in children with TPE[4, 5].

In a developing country like Malaysia where the incidence of TB is relatively high, at 106 per 100,000 population (2005 annual report of the Tuberculosis Division of the Ministry of Health, Malaysia), it is important to differentiate the tuberculous and non-tuberculous causes of exudative pleural effusions. In children, TPE usually presents as an acute illness (high-grade fever,

thoracic pain and dyspnoea)[4, 5]. Most commonly reported symptoms are fever, cough, anorexia and malaise. Other constitutional symptoms: fatigue, low-grade fever, chills sensation, night sweats and weight loss are common complaints in older patients[6]. TPE is classically characterized by a unilateral exudate with a predilection for the right pleural space[1, 2, 6], whereas bilateral effusions, as in our case, are rare.

TPE is a delayed hypersensitivity reaction against mycobacterial antigens in the pleural space following rupture of a subpleural caseous focus. It can cause trapped lung or progress to a tuberculous empyema, which represents a chronic, active infection of pleural space. Bilateral pleural empyema is the most distinguishing feature of this patient. Apart from a short history of fever and cough, the absence of other constitutional symptoms, the initial negative history of contact with TB patient and the fact that she had received a BCG vaccination, initially had brushed away the possibility of TB pleurisy. The other possibility left was the diagnosis of other infections causing bilateral pleural empyema, classically *Staphylococcus aureus*[7, 8] which has accounted for the greatest proportion of cases; however, drug-resistant *Streptococcus pneumoniae* may now be the emerging pathogen[9]. Other agents include *Haemophilus influenzae, Streptococcus pyogenes,* Enterobacteriaceae, anaerobes, *Legionella, Histoplasma, Coccidioides, Aspergillus, Entamoeba, Nocardia, Mycobacterium tuberculosis,* and *Paragonimus.*

Throughout the course treatment with broad-spectrum antibiotics, patient's fever remained unabated and chest drainage continued to discharge pussy material. After nearly three weeks of hospitalization, pleural fluid PCR for *M tuberculosis* yielded positive results on four occasions, and following that anti-TB chemotherapy was commenced. In tuberculous pleurisy, bacteriological confirmation often not achieved since the mycobacterial populations in the effusion is generally small; bacilli are rarely seen in smears and pleural fluids will yield positive cultures in only 25-45% of cases[3, 4, 6]. However, pleural biopsy culture results were positive in 40-65% of the patients with the disease[3, 4, 6]. The diagnosis of tuberculous empyema in this patient was assured by the findings of bilateral loculated pleural fluid with thickened (> 2 cm) and enhancing wall on CT imaging. Empyema should be suspected if pleural thickening is in excess of 2 cm or if more than one linear shadow is visible running parallel to the inner chest wall on chest radiographs and CT shows a loculated pleural fluid collection in association with pleural thickening and calcifications[10].

Detection of mycobacterial deoxyribonucleic acid (DNA) by the PCR based on amplification of the organism is an interesting test. In lung specimens, PCR can be performed rapidly and has a diagnostic yield comparable to culture; it has also been used to detect mycobacterial DNA in pleural fluid, with sensitivities ranging from 20-80% and specificities of 80-100%, depending on the area of the genome that is amplified and the technique used for DNA extraction[11, 12]. A recent study by Lima et al showed the sensitivity of PCR was 31.3% and specificity was 96.6%[13].

The current recommended treatment for all pulmonary and extra-pulmonary TB (except bone and joint disease, miliary disease and meningitis) is a six-month regimen of isoniazid and rifampicin, with the addition of pyrazinamide in the first two months[14]. HIV patients may require a longer treatment. Our patient's condition was significantly improved with the anti-tuberculous treatment. However, with the persistence of empyema and the presence of pleural thickening, thoracic surgery was considered necessary for her. A number of different surgical approaches are available to treat empyema, which include the traditional thoracotomy followed by decortication, the increasingly popular video-assisted thoracoscopic surgery (VATS) and finally rib resection with open thoracic drainage[15].

Conclusion

In a developing country of high tuberculosis incidence like Malaysia, a diagnosis of TB should always be entertained when there is failure to respond to the conventional anti-microbial therapy. TB infection should also be borne in mind even when the patient presented with unusual manifestation, and in such cases, TB PCR is a useful adjunct for a definite diagnosis.

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