Respiratory Medicine Case Reports 21 (2017) 135–137

Contents lists available at ScienceDirect

Respiratory Medicine Case Reports

journal homepage: www.elsevier.com/locate/rmcr

Tuberculous pleural effusion occurring concurrently with asbestos-related pleural disease

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ARTICLE INFO

Article history:
Received 11 November 2016
Received in revised form
11 April 2017
Accepted 22 April 2017

Keywords:
Tuberculosis (TB)
Tuberculous pleural effusion (TBPE)
Asbestos-related pleural disease (ARPD)

ABSTRACT

An eighty-four-year-old man presented with progressive exertional dyspnea, productive cough and weight loss for two months. His physical exam was notable for diminished breath sounds at the right base, with dullness to percussion. Chest-x-ray showed moderate right-sided pleural effusion and bilateral calcified pleural plaques as well as diaphragmatic plaques consistent with asbestos-related pleural disease (ARPD). Pleural fluid was exudative with predominantly mononuclear cells, negative acid fast bacilli stain, negative cultures, and negative cytology for malignant cells. Due to recurrence of the effusion, 4 weeks after drainage, thoracoscopic pleural biopsy was planned but pleural fluid cultures came back positive for mycobacteria tuberculosis. Patient was started on anti-tubercular therapy but treatment had to be stopped due to liver toxicity. Patient subsequently developed pneumonia and deteriorated despite antibiotic therapy and expired.

1. Introduction

Tuberculosis (TB) is one of the most common causes of pleural effusion in the world [1]. Benign asbestos pleural effusion, usually unilateral, is the most common manifestation of asbestos-related pleural disease [2]. Both are exudative and a pleural biopsy is needed for diagnosis as TB and malignancy need to be ruled out in patients with suspected asbestos-related pleural effusion [3]. The association between pulmonary TB and asbestosis of the lung has been reported, with the prevalence of pulmonary tuberculosis in patients with asbestosis ranging from 3.8% to 36% [4,5]. Poor immunogenicity along with decreased defensive capacity of the lung due to asbestosis has been hypothesized to make these patients more prone to mycobacterium infections 95). The association between TB pleural effusion with asbestos-related pleural disease has not been reported. We report a case of TB pleural effusion occurring concurrently with asbestos-related pleural effusion.

2. Case report

An eighty-four-year-old man presented with progressive exertional dyspnea, productive cough and weight loss for two months. He denied fever and hemoptysis. Past medical history was significant for hypertension, atrial fibrillation and diabetes mellitus. His medications included warfarin, metoprolol, glipizide, lisinopril, and simvastatin. The patient was a Korean War veteran and a retired machinist. He had never smoked in his life. He denied any known direct exposure to asbestos.

The patient was afebrile with normal vital signs. His physical exam was notable for diminished breath sounds at the right base, with dullness to percussion. Blood work showed stable normocytic anemia; serum chemistries were normal. Chest-x-ray (Fig. 1) showed moderate right-sided pleural effusion and bilateral calcified pleural plaques as well as diaphragmatic plaques consistent with asbestos-related pleural disease (ARPD).

Thoracentesis revealed serous fluid, with glucose 130 mg/dL, LDH 884 mg/dL, protein 4.8gm/dL, pH 8, Albumin 2.39gm/dL, WBC 2100 (7% neutrophils and 93% mononucleated cells), RBC 64000. Fluid culture showed no organisms on gram stain and subsequently no growth. Cytology was negative for malignant cells. AFB stain was negative. Three weeks later, on outpatient follow-up, a chest CT scan (Fig. 2) showed a loculated right-sided pleural effusion, pleural-based nodular density left lower lobe with pleural plaques compatible with ARPD. A thoracoscopic pleural biopsy was planned but before this could be performed, the patient was hospitalized again, 5 weeks after his initial presentation, with worsening

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http://dx.doi.org/10.1016/j.rmcr.2017.04.018

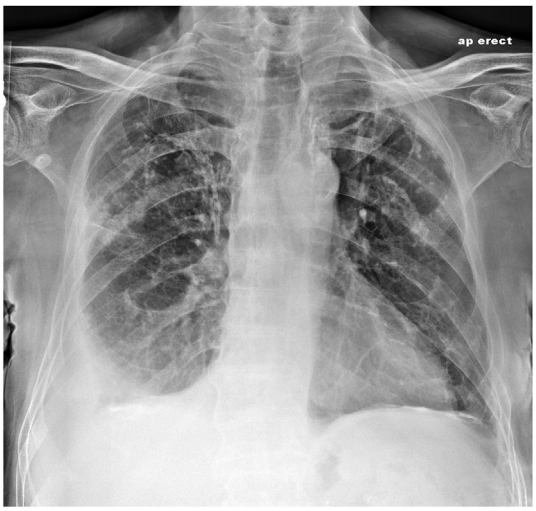

Fig. 1. Chest-X-Ray showing moderate right-sided pleural effusion and bilateral calcified pleural plaques as well as diaphragmatic plaques.

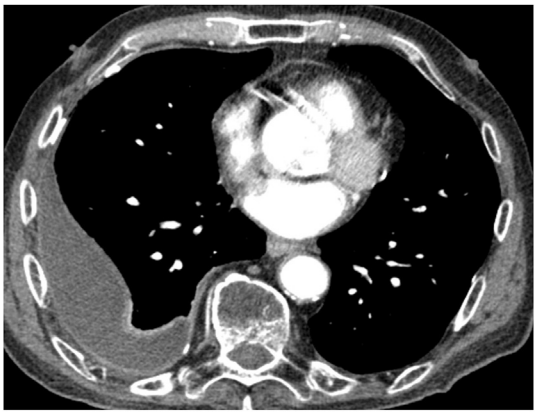

Fig. 2. Chest CT scan showing a loculated right-sided pleural effusion with calcified pleural plaques.

symptoms of shortness of breath. Chest x-ray revealed a recurrent right-sided pleural effusion. A repeat thoracentesis revealed glucose 42 mg/dL, LDH 746 mg/dL, protein 5.2 gm/dL, pH 7.5, albumin 2.19gm/dL, WBC 79, with 58% neutrophils, 42% mononucleated cells, RBC 2000. Cytology was negative for malignant cells. Acid fast bacilli (AFB) stain and Gram stain were negative. At that time, pleural fluid AFB culture from the first thoracentesis turned positive for mycobacterium tuberculosis and a diagnosis of tubercular pleural effusion, superimposed on ARPD, was made.

The patient was started on isoniazid, rifabutin and ethambutol. Treatment was stopped two weeks later due to development of liver toxicity. The patient subsequently developed health-care associated pneumonia and deteriorated clinically despite treatment with broad-spectrum antibiotics. Per the patients previously expressed wishes, comfort measures were instituted and he expired soon after.

3. Discussion

Although tuberculosis (TB) mainly affects the lungs, in 25% of cases extra-pulmonary TB can be the initial presentation of the disease [6]. After lymph node involvement, the pleura is the second most common affected extra-pulmonary site [6]. TB is one of the most common causes of pleural effusion (30–60%) in the world [7]. In the United States, tuberculous pleural effusion (TBPE) accounts for 2–5% of all pleural effusion, with incidence of approximately 1000 cases per year [1,6].

TBPE can occur as a result of a primary infection, especially in young adults. The fluid has very few organisms and pleural tissue has granulomata [8]. TBPE can also occur in reactivation pulmonary TB and military TB. In these cases, a longer duration of symptoms and lower glucose levels in pleural fluid have been reported as compared to primary TBPE. In addition, tuberculin skin test (TST) was positive in over 80% of primary TBPE and 61% in reactivation TBPE. The yield of acid-fast bacilli (AFB) in smear and culture of pleural fluid was statistically higher in reactivation TB, while no such difference was noted in the pleural tissue [8].

The inhalation of asbestos may lead to various pulmonary diseases including lung cancer, pneumoconiosis, pleural plaques, benign pleural effusion, and malignant mesothelioma [9]. Most patients with asbestos-related lung disease have a strong exposure history; however, significant disease can occur with minimal exposure and, rarely, with an unknown exposure. Benign asbestos pleural effusions, usually unilateral, are the most common manifestation of asbestos-related pleural disease, usually occurring within ten to twenty years after exposure [2]. Asbestos pleural effusions are exudative. However, in cases of exudative pleural effusions, a pleural biopsy may be needed to evaluate for tuberculosis (TB) and malignancy [10]. When followed over time, these effusions may wax and wane. The development of any new pleural effusion in the setting of asbestos -related pleural disease mandates a thorough evaluation, including tuberculosis skin testing and diagnostic thoracentesis.

The frequent association between silicosis and tuberculosis is well known. Though there have been reports of the occurrence of pulmonary TB in asbestosis, the relationship between the two is not entirely clear. Reports on the subject are contradictory [4,5]. The only study on the relationship between asbestosis and pulmonary TB determined the incidence of TB in 2846 workers [4]. This study did not find statistically significant difference in the incidence of tuberculosis in patients with asbestosis (3.87%); in those exposed to asbestos but without asbestosis (3.45%) and healthy people (3.93%). The authors of this study concluded that asbestosis was not a risk factor for tuberculosis. However, asbestosis cannot be deemed not to be a risk factor for pulmonary TB based on one study. A more recent historical cohort study [5] looked at the prevalence of pulmonary tuberculosis in workers with asbestosis in Hong Kong and found the prevalence of PTB infection was high (36.29%) in these subjects. Poor immunogenicity along with decreased defensive capacity of the lung due to asbestosis was hypothesized to make these patients more prone to mycobacterium infections [5]. These findings need to be confirmed by future studies.

The most important step in the approach to the diagnosis of the TBPE is to have a strong clinical suspicion of the disease [11]. A negative tuberculin test does not rule out TBPE because this test is negative in about one third of cases. In most cases, pleural fluid analysis usually leads to suspicion of TBPE. This effusion starts as a neutrophilic inflammatory response, followed by granuloma formation and release of Adenosine deaminase (ADA), a T-cell enzyme [12]. Within a week, the fluid develops lymphocytic predominance and is usually exudative in about 90% of cases. A pleural fluid protein concentration greater than 5 g/dl, a low pleural fluid glucose level (<60 mg/dl), and a low pH (<7.2) are found in more than 70, 25 and 10% of patients, respectively [11,12].

ADA in pleural fluid is a useful tool for early diagnosis of TBPE. In a meta-analysis of 63 studies (2796 patients) to determine the accuracy of ADA measurements in the diagnosis of tuberculous pleurisy, ADA had a sensitivity of 92% and specificity of 90% [13].

ADA may be elevated in other conditions (such as empyema and parapneumonic effusions). Of the two ADA isoenzymes, ADA2 is generally increased in TB effusions [14].

Interferon-γ, a cytokine released from $CD4^+$ lymphocytes, is elevated in TBPE [11,15]. A recent meta-analysis revealed that this has a sensitivity of 89% and a specificity of 97% when diagnosing TB [16]. Elevated Interferon-γ levels can also be found in pleural fluid in cases of malignancy and empyema. As there exists more data supporting the effectiveness of ADA in diagnosing tuberculous effusion, the use of interferon-γ remains limited. The gold standard for the diagnosis of TBPE remains the detection of M. tuberculosis in the sputum/pleural fluid culture or pleural biopsy [3,8]. M. Tuberculosis can be cultured from both the pleural fluid as well as the pleural tissue in 70% of the cases. Combining both pleural fluid and sputum cultures may increase the diagnostic yield up to 79% [3,8]. Ultrasound guided pleural biopsy has a diagnostic yield up to 90% for pleural TB and sensitivity increases with the number of biopsies taken [3].

The treatment for TBPE is the same as for pulmonary TB [1,8]. Resorption of the pleural effusion might take 2–4 months. Other additional treatment options include surgical intervention and the use corticosteroid in selected patients. The evidence behind these treatments is limited and controversial [1].

Whether patients with asbestosis may have a predisposition to developing pulmonary TB needs to be determined by further studies. This, to our knowledge, is the first reported case of a tubercular pleural effusion occurring concurrently with asbestos-related pleural disease.

4. Conclusion

Pleural effusion is a known manifestation of asbestos-related pleural disease but concurrent tubercular pleural effusion should be ruled out by appropriate microbiological and histopathological studies as there may be a likely association between the two conditions.

Acknowledgements

None.

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