Pulmonary Alveolar Proteinosis Presenting as Pneumothorax — A Case Report

Char-Wen Chen, Han-Yu Chang, Tzuen-Ren Hsiue

Pulmonary alveolar proteinosis (PAP) is a rare disease in which lipoproteinaceous material accumulates within alveoli. Variable clinical presentations, from asymptomatic to dyspnea, have been reported. Herein, we present the case of a patient who was about 10 weeks pregnant and suffered from spontaneous pneumothorax without any trauma history. Video-assisted thoracoscopic surgery was performed and pulmonary alveolar proteinosis was diagnosed. Pulmonary alveolar proteinosis complicated with spontaneous pneumothorax is very rare and should be considered in patients with diffuse lung disease complicated with pneumothorax. ***(Thorac Med 2007; 22: 327-331)***

Key words: pulmonary alveolar proteinosis, pneumothorax

Introduction

Pulmonary alveolar proteinosis (PAP) is a rare disease in which periodic acid-Schiff stain positive lipoproteinaceous material accumulates within alveoli. It was first described in 1958 [1]. There are 3 distinct forms: congenital, secondary and acquired. More than 90% of cases are acquired, and auto-antibodies targeting granulocyte-macrophage colony-stimulating factor (GM-CSF) play an important role [2]. Congenital PAP was believed to be related to the mutation of the surfactant B, C and GM-CSF receptors [3]. Secondary PAP develops due to the decreasing numbers of macrophages or impaired function secondary to hematological malignancy, infection, or drug or inhalation-related factors. Variable clinical presentations and courses have been reported. The most common presentations in symptomatic patients are progressive dyspnea and cough, and less common presentations include fever, chest pain, and hemoptysis [3-5]. However, pulmonary alveolar proteinosis complicated with spontaneous pneumothorax is very rare: only 1 case report was found [6].

Case Report

A 20-year-old female patient suffered from intermittent chest discomfort and dyspnea for about 1 month before admission. She was about 10 weeks pregnant, and no other systemic disease had been noted before. She presented to another hospital with the complaint of a sudden onset of

Department of Internal Medicine, National Cheng Kung University Hospital, Tainan, Taiwan
Address reprint requests to: Dr. Han-Yu Chang, Department of Internal Medicine, National Cheng Kung University Hospital, No 138, Sheng-Li Rd, Tainan, 704, Taiwan

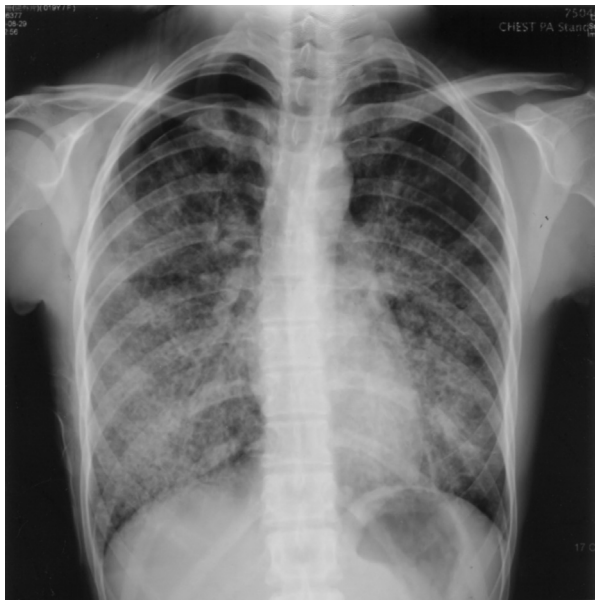

Fig. 1. Chest roentgenogram showing right-side pneumothorax with bilateral mixed alveolar and interstitial patterns.

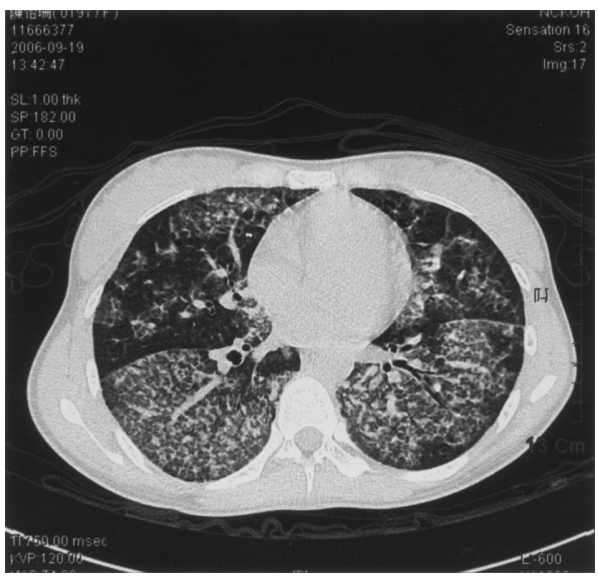

Fig. 2. CT of the chest demonstrating ground-glass opacification of the lung parenchyma with thickening interlobular septa: the distribution of infiltrates was patchy in geography, especially in the left upper lung field, which produced a "crazy paving" pattern.

severe chest pain followed by dyspnea for 1 day. The chest radiography showed right-side pneumothorax with a bilateral mixed alveolar and interstitial pattern (Figure 1). Chest tube insertion was performed and removed after resolution of the pneumothorax. She denied fever, cough or any trauma history. She was referred to our hospital due to the bilateral lung infiltration with poor response to antibiotic therapy. On physical examination, she was not febrile. Her breathing sounds were decreased in the bilateral lung fields with mild inspiratory crackles. Both the initial complete blood count and chemistry were normal. After artificially terminating the pregnancy, she received a chest computed tomography (CT) examination, and a "crazy paving" pattern was found (Figure 2). Open lung biopsy specimens, obtained by video-assisted thoracoscopy, showed pulmonary alveolar proteinosis (Figures 3A and 3B). There was no clinical evidence of hematological malignancy and no occupational exposure. She denied smoking and using any drug.

Secondary PAP was surveyed, but the results were all negative. The pulmonary function test showed a mild restrictive ventilatory defect with moderate impairment of diffusion capacity. The patient's total lung capacity was 71% predicted, and diffusing capacity for carbon monoxide (DLCO) was 49% predicted. Arterial blood gas in room air was normal. After consulting with the patient, she was followed up at the outpatient department because she did not meet the criteria for whole lung lavage.

Discussion

Many diseases present with bilateral lung infiltration complicated with pneumothorax, such as lymphangioleiomyomatosis, histiocytosis X and *pneumocystis jirovecii* pneumonia in HIV patients [7-8]. But the same presentation in pulmonary alveolar proteinosis is very rare. Chronic obstructive pulmonary disease and *P. jirovecii*

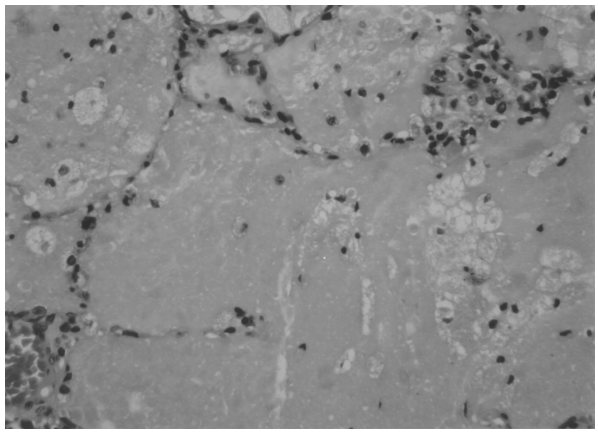

Fig. 3A. Lung histopathology section obtained from open lung biopsy. High power view of H&E-stained section showing eosinophilic material that completely fills the alveolar spaces.

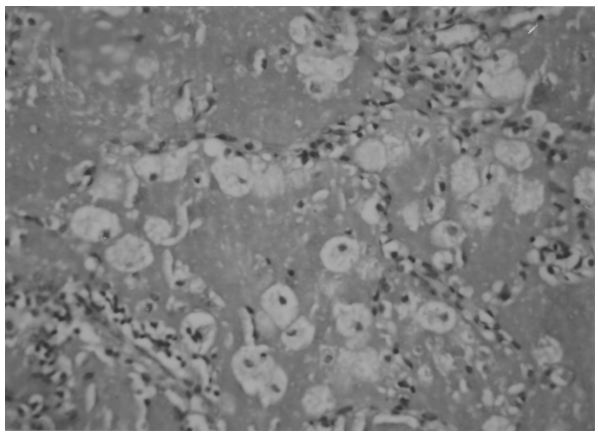

Fig. 3B. High power view showing eosinophilic material present within the alveolar spaces that stained strongly positive with periodic acid-Schiff after diastase digestion.

pneumonia related to infection with HIV are the most common conditions associated with secondary spontaneous pneumothorax [7]. Patients with a forced expiratory volume in 1 second (FEV1) of less than 1 liter, or a forced vital capacity (FVC) of less than 40% are at greatest risk. Pneumothorax develops in 2-6% of HIV-infected patients and is associated with *P. jirovecii* pneumonia in 80% of those cases. This is associated with a high mortality rate [7].

The diagnosis of PAP can be difficult to make due to the nonspecific symptoms and physical signs. Dyspnea and cough are the most common presenting symptoms. Some patients do not present until they develop a supervening infection. A low-grade fever may also occur as a consequence of pulmonary alveolar proteinosis without secondary infection [9]. Complications of PAP primarily are related to infections and relapse. All PAP patients have an increased risk of developing unusual forms of pneumonia [10]. Several rare associations with PAP have been reported to exist, including interstitial fibrosis, bronchiectasis with amyloidosis, bronchogenic carcinoma, Fanconi anemia, psoriasis, and lymphocytic interstitial pneumonia [11-13].

Actual lung tissue, obtained via transbronchial biopsy or open lung biopsy remains the gold standard for diagnosis [3]. High resolution computed tomography (HRCT) is superior to both conventional CT and chest radiography in demonstrating the morphologic characteristics of PAP. “Crazy paving” is the characteristic PAP finding on HRCT, and consists of patchy, ground-glass opacity associated with interlobular septal thickening [14]. However, other conditions, such as lipoid pneumonia and bronchio-alveolar carcinoma, can mimic the CT features. Whole lung lavage is still the standard treatment. Spontaneous improvement or remission of PAP was noted in some patients. Observation was suggested if the patient‘s shunt fraction was less than 10-12% and PaO_2 > 60 mmHg at room air, and there was no limitation of the patient’s daily activity [15].

The published literature regarding PAP presenting with pneumothorax is limited: only 1 case report was found. We have reported herein the case of a pregnant woman whose initial presentation was pneumothorax, but whether this

complication of PAP was associated with pregnancy is still unclear. Although it is rare, clinicians should always keep in mind that in a patient with bilateral lung infiltration complicated with spontaneous pneumothorax, pulmonary alveolar proteinosis should be considered.

References

1. Rosen SH, Castleman B, Liebow AA. Pulmonary alveolar proteinosis. N Engl J Med 1958; 258: 1123-42.
2. Kitamura T, Uchida K, Tanaka N, *et al.* Serological diagnosis of idiopathic pulmonary alveolar proteinosis. Am J Respir Crit Care Med 2000; 162: 658-62.
3. Trapnell BC, Whitsett JA, Nakata K. Pulmonary alveolar proteinosis. N Engl J Med 2003; 349: 2527-39.
4. Goldstein LS, Kavuru MS, Curtis-McCarthy P, *et al*. Pulmonary alveolar proteinosis: clinical features and outcomes. Chest 1998; 114: 1357-62.
5. Wang BM, Stern EJ, Schmidt RA, *et al*. Diagnosing pulmonary alveolar proteinosis: a review and an update. Chest 1997; 111: 460-6.
6. Anton HC, Gray B. Pulmonary alveolar proteinosis presenting with pneumothorax. Clin Radiol 1967; 18: 428-31.
7. Sahn, SA, Heffner, JE. Spontaneous pneumothorax. N Engl J Med 2000; 342: 868.
8. Sepkowitz, KA, Telzak, EE, Gold, JW, *et al*. Pneumothorax in AIDS. Ann Intern Med 1991; 114: 455.
9 . Davidson JM, Macleod WM. Pulmonary alveolar proteinosis. Chest 1969; 63: 13-28.
10. Shah PL, Hansell D, Lawson PR, *et al*. Pulmonary alveolar proteinosis: clinical aspects and current concepts on pathogenesis. Thorax 2000; 55: 67-77.
11. Bakhos R, Gattuso P, Arcot C, *et al*. Pulmonary alveolar proteinosis: an unusual association with Mycobacterium avium-intracellulare infection and lymphocytic interstitial pneumonia. South Med J 1996; 89(8): 801-2.
12. Ganguli PC, Lynne-Davies P, Sproule BJ. Pulmonary alveolar proteinosis, bronchiectasis and secondary amyloidosis: a case report. Can Med Assoc J 1972; 106(5): 569.
13. Kaplan AI, Sabin S. Case report: interstitial fibrosis after uncomplicated pulmonary alveolar proteinosis. Postgrad Med 1977; 61(5): 263-265.
14. Johkoh T, Itoh H, Muller NL, *et al*. Crazy-paving appearance at thin section CT: spectrum of disease and pathologic findings. Radiology 1999; 211: 155-60.
15. Kavuru MS. Pulmonary alveolar proteinosis In: Murray JF, Nadel JA, eds. Textbook of respiratory medicine. Fourth ed. Philadelphia: Elsevier Saunders, 2005; 1716-31.

肺泡蛋白質沉積症以氣胸來表現—病例報告

陳佳文　張漢煜　薛尊仁

肺泡蛋白質沉積症是一種罕見的疾病，其特色為酯蛋白類的物質會沉積在肺泡中。各式各樣的臨床表現，從沒有症狀到呼吸困難都被報告過。我們在此報告一個病例：一位懷孕的年輕女性在沒有任何的外傷情況下，引起自發性氣胸，經過外科切片檢查證實為肺泡蛋白質沉積症。肺泡蛋白質沉積症合併自發性氣胸極為罕見，如果病人有兩側的肺部浸潤合併氣胸，則肺泡蛋白質沉積症應該要列入鑑別診斷。*(胸腔醫學* ***2007; 22: 327-331)***

關鍵詞：肺泡蛋白質沉積症，氣胸

成大醫學院內科部　胸腔內科
索取抽印本請聯絡：張漢煜醫師，成大醫院內科部　胸腔內科，台南市勝利路 138 號