SARCOIDOSIS VASCULITIS AND DIFFUSE LUNG DISEASES 2013; 30; 317-320

Transthoracic lung ultrasonography in pulmonary alveolar proteinosis – case report

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Abstract. A pulmonary alveolar proteinosis (PAP) is a rare disease characterized by an accumulation of surfactant components in lung alveoli. In diagnosis and monitoring of the disease high resolution computed tomography (HRCT) is usually used. Unfortunately, repeated exposure to CT scanning may be associated with an increased risk of radiation. We present a patient in whom repeated transthoracic lung ultrasonography (TLUS) brought parallel to HRCT data in assessing PAP extent. It may indicate that TLUS might be potentially a relevant tool in monitoring of PAP. *(Sarcoidosis Vasc Diffuse Lung Dis 2013; 30: 317-320)*

Key words: Pulmonary alveolar proteinosis, Lung ultrasonography, Monitoring

Introduction

A pulmonary alveolar proteinosis (PAP) is a rare disease characterized by an accumulation of phospholipids and proteins in lung alveoli due to defective surfactant clearance by alveolar macrophages. Clinical presentation of disease is heterogenous, however dyspnea is almost always a leading symptom. In some cases impaired gas exchange and progressive respiratory failure occurs (1, 2).

On high resolution computed tomography (HRCT) the pathological changes are seen as ground glass opacities (GGO) with superimposed interlobular septal thickening ("crazy paving" pattern). Lesions have a typical geographic distribution (3). Further, HRCT in combination with pulmonary function tests is usually used in the disease course monitoring (1, 2).

In recent years widely investigated technique in pulmonary disorders is transthoracic lung ultrasonography (TLUS) (4-7). To our knowledge till now it was not used in PAP monitoring. We present a repeated TLUS examination in monitoring a patient with PAP.

Received: 27 April 2013
Accepted after revision: 02 My 2013
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Case report

A 54 years old woodcutter, cigarette smoker, was transferred to the Pneumonology Department from a local hospital to diagnose an interstitial lung disease. The pulmonary changes were revealed in a chest radiogram a month earlier, and confirmed on a computed tomography. The patient complained of an exertional dyspnea and dry cough increasing for 10 weeks, without fever, weight loss, or hemoptysis. The only abnormality on physical examination was a tachypnea with a respiratory rate 16 per minute. In previous weeks he was treated with antibiotics, inhaled budesonide and formoterol, and in the last week with prednisone 1mg/kg per day without any clinical effect. A repeated chest X-ray showed bilateral opacities disseminated in both lungs, with predominance in hilar areas. The pulmonary function tests revealed restrictive pattern and decreased carbon dioxide diffusing capacity (DLCO). Arterial blood gas analysis confirmed respiratory insufficiency. Lactate dehydrogenase (LDH) level was elevated to 413 U/l, C-reactive protein (CRP) level was 5.2 mg/L (Table 1). Anti-nuclear antibodies ANA Hep2 and dsDNA were not present. A screening for extrinsic pneumonitis was obtained but no precipitins to the most common antigens triggering the disease were detected.

There were PAS positive masses on bronchoalveolar lavage (BAL) fluid smears, but there were no foamy macrophages, no lymphocytosis or eosinophilia. The predominant cells on BAL fluid smears were neutrophiles (53%). Abdominal ultrasonography was normal.

A diagnosis of PAP was made on a basis of open lung biopsy which revealed intraalveolar eosinophilic material with coarse granularity, few macrophages and lymphocytes. The substance was PAS positive and compatible with surfactant. The lung interstitial architecture was well preserved with no lymphocyte infiltration, granuloma or fibrosis of the alveolar septae. The picture was compatible with PAP.

This time HRCT examination was performed according to a standard protocol using GE HiSpeed CT 64 scanner. During the test the patient was in the supine position. Scans were performed at a full inspiration, from apex to the lung base with a thickness of 1mm and 10mm intervals. It revealed diffuse GGO

Table 1. Clinical manifestations and immunoglobulins in three patients with sarcoidosis

Variable	0	3 months	6 months
FEV1 (% pred.)	73,8	83,1	85,0
VC (% pred.)	72,8	82,8	88,9
FEV1% VC(% pred)	101	98,7	95,3
TLC (% pred.)	73,9	85,2	86,2
RV (% pred.)	61,2	88,3	84,3
RV%TLC (% pred)	79,0	99,5	93,2
DLCO SB (% pred.)	36,7	60,1	64,3
DLCO/VA (% pred.)	67,4	85,5	94,4
6MWT–distance (m)	520	465	720
Blood gas analysis	arterial		capillary
pH	7,47	-	7,399
pO2 (mmHg)	54,0	-	67,4
pCO2 (mmHg)	31,6	-	37,0
BE (mmol/L)	0,8	-	-1,7
SaO2 (%)	89,9	-	95,3
LDH (U/L)	413	-	291
CRP (mg/L)	5,5	<5	-

Pulmonary function tests results are showed as a percentage of a predicted value. FEV1 - forced expiratory volume in one second; VC - vital capacity; TLC - total lung capacity; RV - residual volume; DLCO SB - single-breath diffusing capacity of the lung for carbon monoxide; DLCO/VA - single-breath diffusing capacity of the lung for carbon monoxide corrected for alveolar volume; 6 MWT - 6 minute walking test; LDH - lactate dehydrogenase; CRP - C-reactive protein

Fig. 1. HRCT and TLUS in a patient diagnosed with PAP in a 0-3-6 months periods.
1.A – A' – A" - HRCT pictures show an extensive ground glass opacity with superimposed thickening of interlobular septae forming "crazy paving" pattern with its remission in consecutive scans.
1 B – B' – B" - convex probe - two-dimensional ultrasound image of the lungs presents an irregular pleural line and "white lung sign" with decreased number of changes in consecutives pictures.
1 C – C' – C" - linear probe - two – dimensional ultrasound images of the lungs show irregular pleural line and B lines with decreased number of changes in consecutives pictures.

in whole lungs with predominance in the middle, left lower and both upper lobes superimposed by massive thickening of interlobular septae along forming the "crazy paving" pattern (Figure 1A). At the same time TLUS was performed using CX50 Philips Healthcare scanner equipped with convex (1-5MHz) and linear (3-12Hz) probe. The patient was examined in the supine and sitting position. The probe was applied longitudinally and transversely to the intercostal space on the anterior, lateral and posterior walls of the chest. It showed an irregularity of a pleural line, B lines in a form of interstitial syndrome and extensive "white lung" sign corresponding with the areas of GGO (Figure 1 B, C).

Because of extensive changes in pulmonary function the patient was directed to the National Tuberculosis and Lung Diseases Research Institute in Warsaw considering the whole lung lavage but an evaluation after three months revealed clinical and functional improvement (Table 1). The HRCT scans showed partial remission of lung changes (Figure 1A'). TLUS performed at this time showed decreased extent of changes and partial re-aeration of a lung tissue (Figure 1B', C').

In the next three months the patient was assessed at our Department once again. He reported a progressive relief in symptoms. The pulmonary function tests showed maintained improvement (Table 1). HRCT showed succeeding remission, which was also seen in TLUS (Figure 1 A", B", C"). Moreover, LDH level was 291 U/L, blood gas analysis was normal.

Discussion

PAP is a rare disease characterized by alveolar accumulation of surfactant components in distal air spaces (1, 2). Surfactant, a mixture of lipids and proteins is synthesized and secreted onto alveolar surface by type II pneumocytes. It is recycled by the same cells or degraded by alveolar macrophages (1, 2, 8). A defective macrophage clearance leads to accumulation of surfactant in the alveolar lumen with a clinical manifestation ranging from an asymptomatic disease to life-threatening respiratory failure (1, 2).

In most cases the disease occurs as an auto-immune disorder in which antibodies against granulocyte-macrophage colony stimulating factor (GM-CSF) alter macrophages differentiation and function (1, 2, 9, 10). Less commonly it could have genetic background or be secondary to underlying disorders (1, 2, 9). Sometimes it could develop after inhalation of harmful particles, among them wood dust (1, 2, 11, 12).

HRCT is a traditional procedure to assess the pulmonary changes in PAP (2, 12). This technique typically shows a widespread bilateral GGO sharply demarcated from normal lung parenchyma with superimposed interlobular septal thickening forming a "crazy paving" pattern. The changes have geographical distribution and reflect an accumulation of surfactant material in lower respiratory tract. Although sometimes it could be found in other pathologies such pattern is characteristic for PAP and this technique is usually used in diagnosing and monitoring the disease course (1, 2, 12, 13, 14). However repeated many times it exposes the patient to high doses of radiation.

The radiation-free visualization of lung tissue could be offered by TLUS. In healthy individuals the acoustic impedance difference between chest wall and an aerated lung parenchyma results in almost total reflection of ultrasound beams at the pleura. In pathologies connected with increased density of the lung tissue sticking to the pleura the waves can penetrate a lung tissue. This phenomenon is used in growing number of publications regarding the usefulness of TLUS in diagnosing lung disorders, among them the interstitial lung diseases (5, 6, 7, 15). Nevertheless there is as yet no data on the monitoring these patients by TLUS. Our case presented such an opportunity.

We conducted TLUS simultaneously with HRCT examination in three consecutive occasions. It showed the irregularity of pleural line, B lines artifacts and extensive "white lung" sign, intense at the beginning of observation and receding in consecutive tests in parallel with HRCT remission. The observed ultrasound changes reflected pathologies traditionally visualized by HRCT. B line artifacts appear as vertical lines arising from the pleural line and extending to the edge of screen. They are formed by reflection of the ultrasound beams from thickened interlobular septae secondary to a presence of fluid in the compartment between the alveoli or as a result of lung fibrosis or other interstitial changes (4, 5, 7,

16). "White lung" sign appears as a result of fused multiple B lines. It reflects an accumulation of fluid in the alveoli and corresponds to the GGO areas in the HRCT (4, 16).

Additionally to our knowledge there was only one research concerning ultrasonography in PAP in which transoesophageal echocardiography was used in a monitoring of a lung recover after a whole lung lavage (17). In our study the comparison between both techniques HRCT and TLUS shows that TLUS might serve as a relevant monitoring tool in the assessment of changes in pulmonary parenchyma in the course of PAP.

Conclusions

TLUS could bring information similar to HRCT in assessing the extent of lung changes in PAP. This easy-to use technique could be used in monitoring PAP course. However, further studies are required to confirm this thesis.

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