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A 36-Year-Old Woman with Cough, Dyspnea and Pulmonary Infiltration

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WHAT IS YOUR DIAGNOSIS?

*A 36-year-old female was admitted with cough and dyspnea. There was no history of prior cardiopulmonary disorder two years before the admission when the symptoms began and the patient has had a progressively aggravating course since six months ago. Family history and social history were unremarkable. No history of smoking or drug use was present. She was married, with two children; she was a housewife and no evident risk factors for human immunodeficiency virus (HIV) infection were detectable. She was diagnosed with hypothyroidism 8 years ago for which she was receiving levothyroxin 0.2 mg/ day. The patient was afebrile with blood pressure of 120/70 mmHg, heart rate 90 bpm, and respiratory rate of 28 per minute. On admission, she was oxygen dependent. Oxygen saturation was 85% while receiving 3 liters per minute of oxygen with nasal canula. Physical examination was unremarkable except for basilar fine crackles of both lungs. Complete blood cell count, erythrocyte sedimentation rate (ESR), biochemistry, electrolytes, liver and renal function tests all were in the normal limit. Arterial blood gas (ABG) while receiving 3 liter/min nasal O_2 demonstrated: pH: 7.38, PO_2: 43, O_2 saturation: 89, PCO_2:37, HCO_3: 26. Chest X-ray is shown in Figure 1. Echocardiographic study revealed normal left ventricular function, and enlargement of the right cardiac chambers. Pulmonary arterial pressure was estimated around 50 mmHg. Severe restrictive pattern was found in the pulmonary function test (Figure 2).A high-resolution computed tomography (HRCT) of the chest was performed (Figure 3).****(Tanaffos 2008; 7(1): 75-78)***

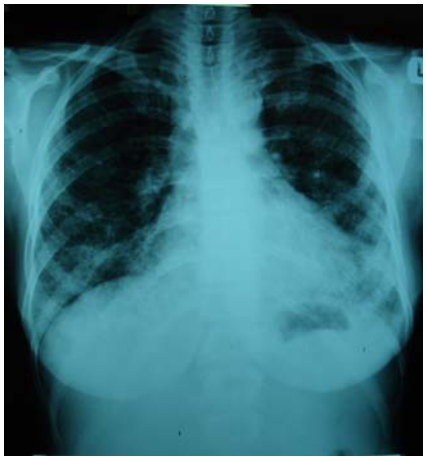

Figure 1. Chest x-ray of patient

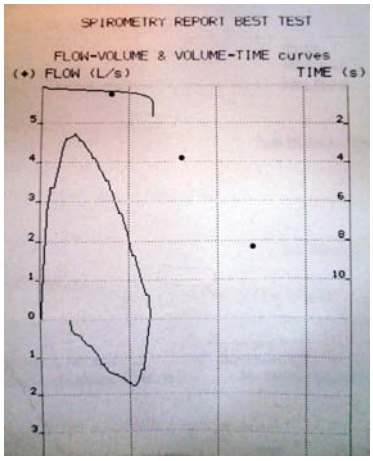

Figure 2. Restrictive pattern in the spirometry

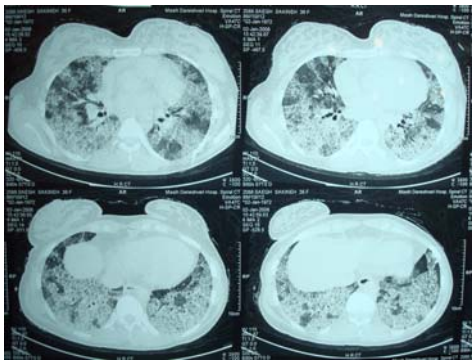

Figure 3. HRCT of patient

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Diagnosis: Pulmonary alveolar proteinosis

Bilateral symmetrical alveolar infiltration is seen on the chest x-ray (Figure 1). Lung HRCT also confirms bilateral ground-glass opacifications and thickened interlobular septa, (appearance referred to "crazy-paving", Figure 2); all findings are highly suggestive of pulmonary alveolar proteinosis.

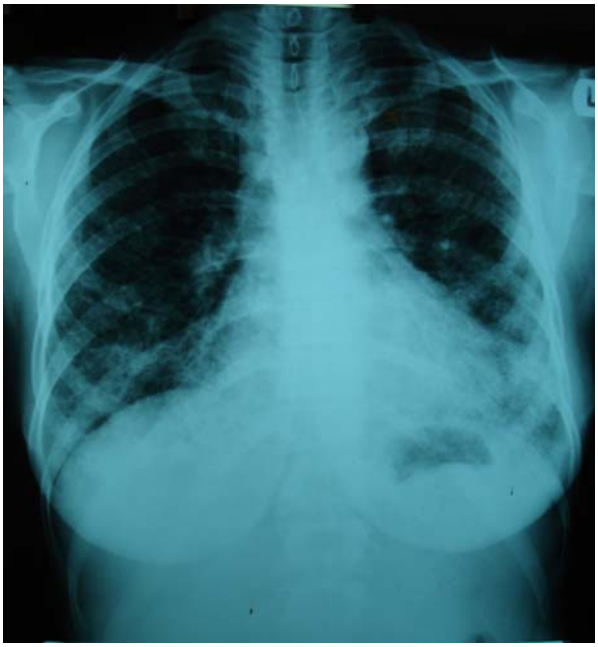


Figure 1. Chest x-ray of patient.

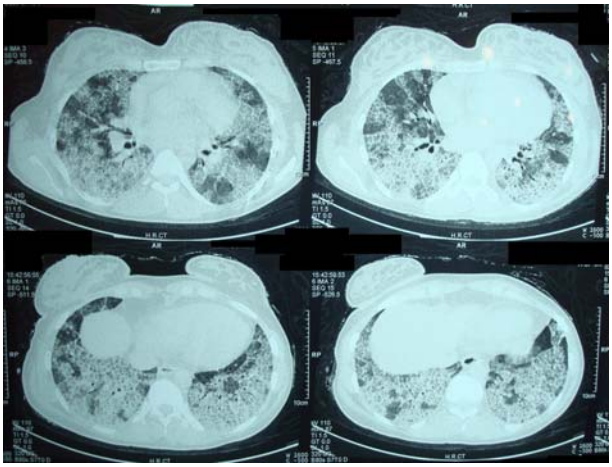
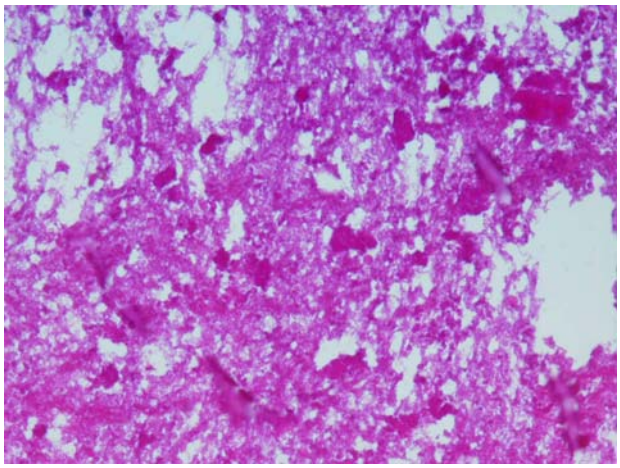


Figure 2. HRCT of patient.

Bronchoscopy and bronchoalveolar lavage (BAL) were performed due to patient's persistent hypoxemia. BAL fluid was grossly milky and opaque. Examination of the BAL fluid showed large amounts of granular acellular eosinophilic lipoproteinaceous periodic acid-Schiff (PAS) positive material (Figure 3). BAL fluid was negative for any pathogenic organism or malignant cell. Transbronchial lung biopsy was not performed due to severe hypoxemia.



Figures 3. Granular acellular eosinophilic lipoproteinaceous periodic acid-Schiff (PAS) positive material

Therapeutic lung lavage was performed for her right lung, and is planned to be performed one month later for the other side. After the first lavage, clinical improvement was significant and oxygen saturation increased to 92% without supplemental oxygen. Follow-up HRCT also showed considerable improvement (Figure 4).

Pulmonary alveolar proteinosis (PAP) is a rare idiopathic pulmonary disease characterized by the accumulation of amorphous, PAS positive

lipoproteinaceous material in the distal airspaces, with no pulmonary inflammation or architectural distortion (1).

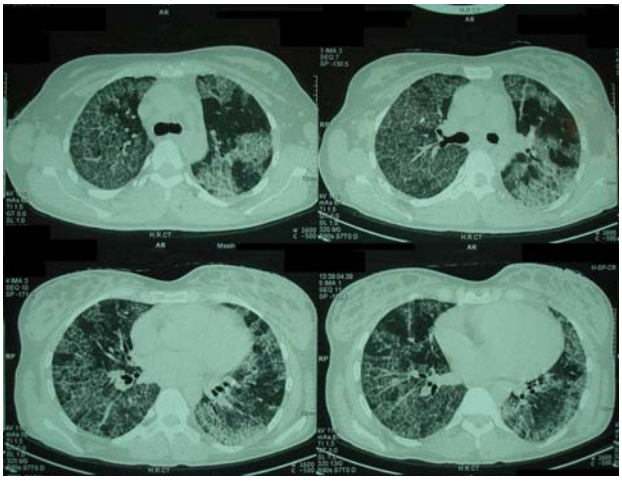


Figure 4. Follow-up HRCT after therapeutic lavage

PAP includes a heterogeneous group of disorders sharing the common feature of impaired surfactant clearance. PAP may be seen in various settings including as follows:

1) In the presence of circulating anti-granulocyte macrophage-colony stimulating factor (GM-CSF).
2) In the form of neonatal or congenital PAP
3) Following a systemic inflammatory process or malignancy (e.g. viral, bacterial, nocardial, mycobacterial, and fungal infection, pneumocystis pneumonia, hematological malignancies, and bone marrow transplantation).
4) PAP associated with specific exogenous or occupational exposures such as silicosis, aluminum dust or titanium exposure. (2)

Typical age at presentation for most patients with PAP is 30 to 50 years. There is a male to female ratio of 1:2. Clinical presentation is usually insidious. Major symptoms are progressive dyspnea on exertion, fatigue, weight loss, and low grade fever. On examination, crackles may be found in up to 50% of patients. Clubbing and cyanosis are rare in the course of PAP. On chest radiography, bilateral symmetric alveolar opacities located centrally in mid and lower lung zones are detectable while an HRCT reveals ground-glass opacifications with inter-lobular septal thickening (3).

Laboratory findings include polycythemia, hyper-gamma globulinemia and increased LDH level. Markedly elevated serum levels of lung surfactant proteins A and D have been found in PAP but are non-specific (4).

Pulmonary function tests show a restrictive pattern or sometimes an isolated decrease in DLCO (4).

Diagnosis: Although history, physical examination, radiographic studies and physiologic testing may suggest PAP, further evaluation is usually needed to confirm the diagnosis. Although the idea is that the impaired production or function of GM-CSF plays a role in the pathogenesis of PAP, our diagnostic approach is based on evaluation of tissue specimens. Examination of tissue obtained by transbronchial biopsy or fluid obtained by bronchoalveolar lavage has obviated the need for open or thoracoscopic lung biopsy (5).

BAL fluid is milky and alveolar macrophages are engorged with the PAS positive material. On histologic examination, the normal alveolar architecture is generally preserved with no inflammatory cell infiltration and terminal bronchioles and alveoli are filled with lipoproteinaceous material (5).

The most acceptable and effective form of treatment has been therapeutic whole lung lavage via a double lumen endotracheal tube. One lung is lavaged with warmed (37°C) saline while the other lung is ventilated. Bilateral sequential whole lung lavage is performed at the same time. After lung lavage, the patients often feel dramatically better with improvement in exertional dyspnea. Thirty to forty percent of patients require only one lavage; while others require repeated lung lavages at

intervals of 6 to 12 months (6).

Supra-physiologic doses of the growth factor have been employed in several cases. Preliminary data suggest that patients treated with GM-CSF have some improvements in pulmonary function but this appears to be less remarkable than whole lung lavage (7).

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