View Box - Case I

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History

A 43 year old woman, non-smoker, was referred to our hospital with 2 years history of gradually increasing dyspnea and non-productive cough. There was no history of fever, weight loss or chest pain.

Physical Examination

Vital Signs: Temperature 36.5° C; respiratory rate 20/minute; Pulse: 76 beats per minutes; BP 108/52 mm Hg. General: Healthy appearing womanwithout any signs of acute distress.

Chest: A few coarse crackles were audible posteriorly in the lower and mid lung fields.

Neck: No venous distension.

Cardiac: Nonnal heart sound with no mumurs. Extremities: No cyanosis, edema or clubbing.

Laboratory Findings

Total WBC count: 5000/uL (neutrophils 29, eosinophils 21, lymphocytes 45, monocytes 5). Hb: 8.lg/dl, RBC 3.64 x 10^4

Serum LDH: 539 mu/m (nonnal 202-43 5 mu/ml). With patient breathing room air, arterial blood gas values were as follows:

PH: 7.397, PaO2: 80 mrnHg, PaCO2: 34.8 mmHg. Pulmonary function test was as follows: VC: 1 .7L, %VC:

62%, FVC: 1.51L, FEV1: 1.51L, FEV1%: 89%, V50:

2.45L/S, V25: 0.93L/S, DLCONA: 2.76m1 min. mmHg/L. ESR. serum electrolytes and renal indices were normal.

Imaging

PA radiograph of the chest (Figure 1)

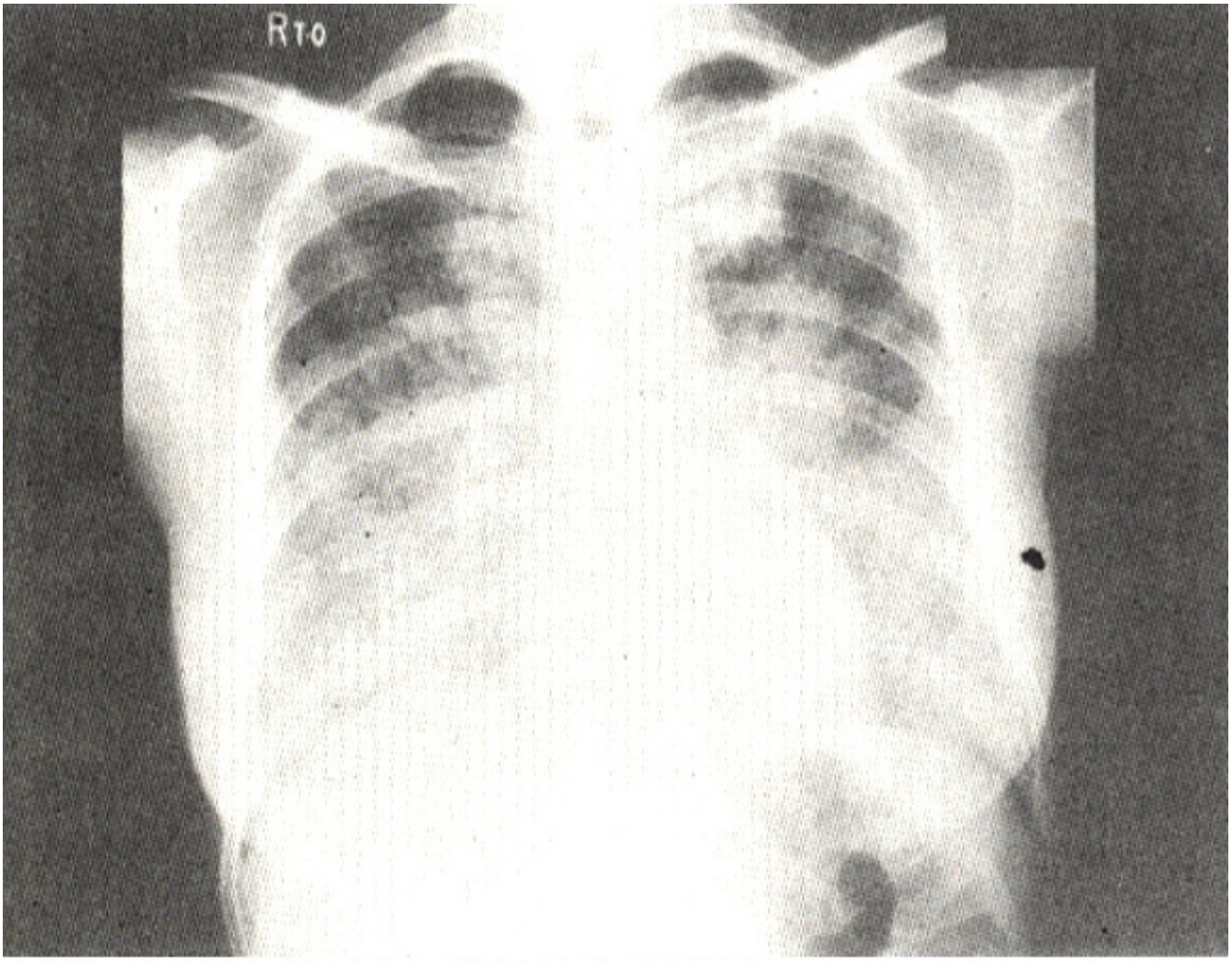

Figure 1. PA Radiograph of chest

showed diffuse confluent ill-defined opacities involving all the lung fields bilaterally. No canliomegaly or lymphadenopathy was seen. Computed tomography (CT) of the chest (Figure 2)

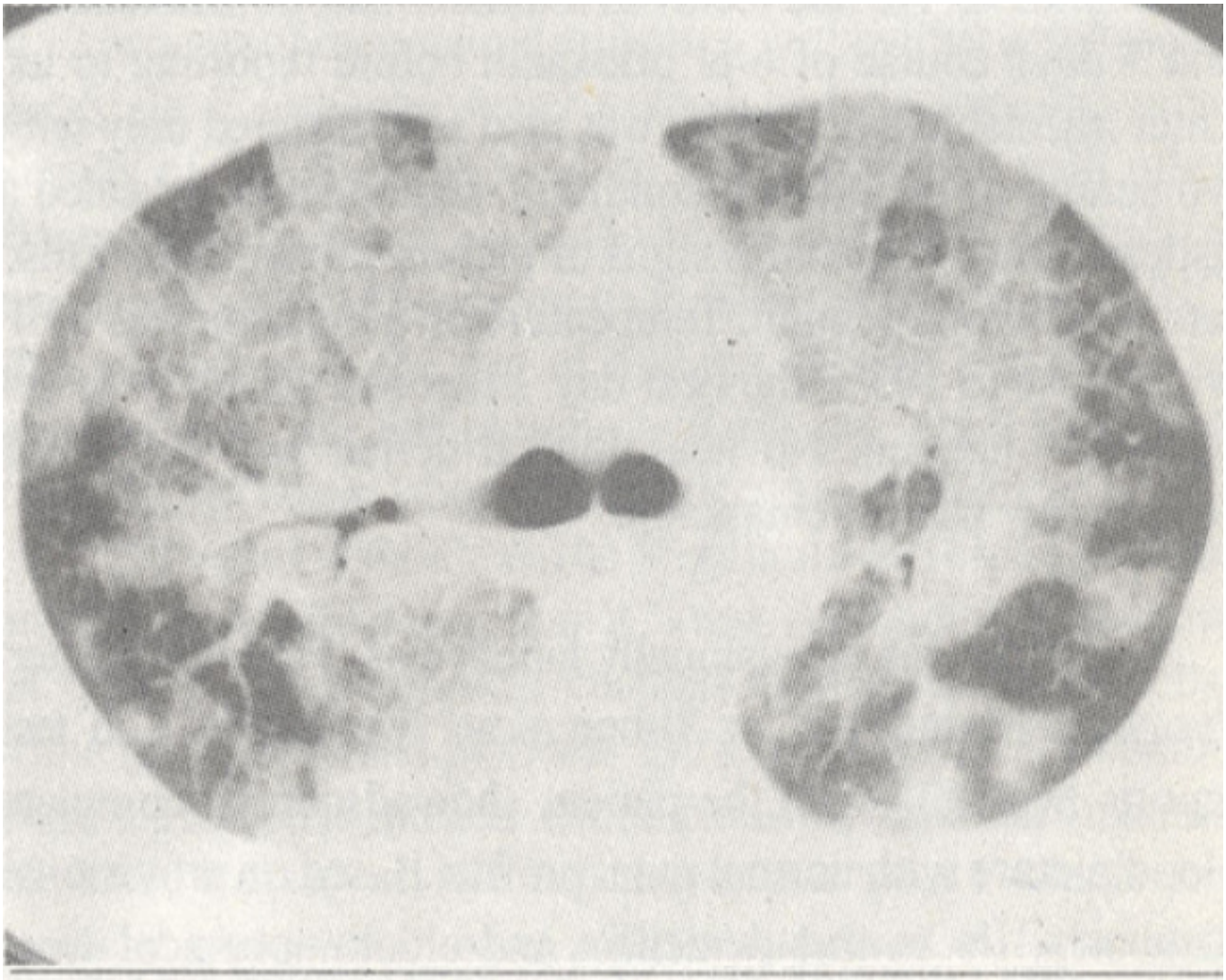

Figure 2. Computed tomography of the chest.

obtained[2] days later demonstrated wide spread ground-glass opacity bilaterally. A few small areas of sharply demarcated normal lungparenchymawere seenbetweenthe ground-glass opacity. Interlobular septa in the regions of ground glass opacity were thickened. No cavitation, effusion or lymphadenopathy was seen.Patient underwent bronchoalveolar lavage (BAL) and a diagnosis was made.

Diagnosis

Pulmonary alveolar proteinosis.

Discussion

Pulmonary alveolar proteinosis (PAP) is a rare disease of unknown origin, characterized by accumulation of periodic acid-Schiff (PAS) positive phospholipoproteinaceous material in alveolar spaces[1]. It usually occurs in patients between 20-50 years of age, although it has been reported in the children and elderly. Males predominate by a ratio of 2: ito 4:1.

PAP has been described in two forms; a “primary or idiopathic” form occurring in the absence of an identifiable associated disease or exposure and a “secondary” form provoked by orassociated with anothercondition[2]. Secondary PAP has been reported in three main categories of conditions:

(1) infections of the lung, (2) hernatological malignancies and other conditions altering patient’s

immune status, e.g., leukemia, lymphoma, HIV infection and (3) exposure to inhaled chemicals and minerals such as silica, aluminum dust and titanium.

Symptoms include mild dyspnea associated with a non-productive or minimally productive cough, weight loss, malaise and fatigue can also be present. Acute symptoms such as feverorpitgressive dy spnea suggest a complicating infection. Physical findings (e.g., fme crackles, clubbing of fmgers, etc.) occur ma minority of patients and are non-specific.

An elevated serum lactate dehydmgenase (LDH) level is most common associated laboratory abnormality. On arterial blood gas analysis, the PaO_2 and O_2 are typically reduced. Intrapulmonary shunt fraction while breathing 100% oxygen is typically elevated (average 20%). Patients also have elevated levels of lung surfactant proteins A and D in both the serum and bronchoalveolarlavage (BAL) fluid.

Typical radiograph shows a bilateral, diffuse, perihilar orcentral, ill-defined nodularorconfluent opacities, whichare usually worse at the bases. An interstitial pattern can also be present. As the abnonnalities are often more pronounced in the perihilar regions,, the radiographic appearance often resembles that of pulmonary edema except that cardiomegaly, Kerly B Lines and pleural effusion are not present. Patchy disease and peripheral predominance can also occur. The radiographic abnormality is often more dramatic than patient's symptoms.

The clinical and basic radiological features of PAP may be indistinguishable from otherconunon pulmonary disorders such as non-cardiogenic pulmonary edema, pulmonary infection (viral, fungal or pneumocystis carinii pneumonia), neoplasm (in particular, bronchioloalveolar carcinoma in patients with few symptoms), pneumoconiosis, sarcoidosis and pulmonary interstitial disease.

CT, especially the high resolution CT (HRCT), can be helpful in narrowing the differential diagnosis. HRCT features, in a proper clinical setting as in this case, often suggests the diagnosis of PAP. Routine CT scans in patients with PAP shows air space filling with variable and patchy distribution[3]. The air-space opacification is often sharply demarcated from the surrounding normal lung tissue, creating a "geographic" appearance. HRCT typically shows that this opacification is often more of a ground-glass appearance, reflecting the presence of the phospholipid/proteinaceous material of PAP within the alveoli[4]. It is associated with smooth thickening of the interlobular structures and interlobular septa, with no architectural distortion. The septal thickening is only seen in the areas of ground glass opacity. The combination of a geographic distribution of areas of ground-glass opacity with thickened interlobular septa within the areas of air-space disease results in a "crazy-paving" pattern that is strongly suggestive of PAP. However, similar appearance has also been reported in pneuinocystis, cytomegalovirus infections and mucin producing bronchioloalveolar carcinoma.

At present, BAL is the simplest way to diagnose PAP. Examination of the BAL fluid shows characteristic proteinaceous periodic acid-Scluff stain positive material on routine microscopy. This intra-alveolar material can be confirmed to represent lung surfactant material by electron microscopy or specific immunochemistry methods. Transbronchial or open lung biopsy, remains the "gold standard" but is not necessary except in problematic cases.

Whole lung BAL, performed under general anesthesia, is the only option for the therapy. The primary indications for therapeutic lavage are progressive dyspnea and deterioration in pulmonary function test The prognosis is generally good with eventual quiescence of the disease inmost patients after one or two therapeutic lavage. Relapses may occur requiring repeated lavage.

Acknowledgement

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References

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