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Pulmonary Alveolar Proteinosis Treated with Oral Ambroxol Hydrochloride and Bronchoalveolar Lavage

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A 59-year-old man visited our hospital in June 1997 because of cough and dyspnea at rest. He was diagnosed as pulmonary alveolar proteinosis (PAP) by bronchoalveolar lavage (BAL) and transbronchial lung biopsy. The alveoli were distended with pink homogeneous material that showed staining with the periodic acid Schiff method. The concentration of surfactant protein A in BAL fluid was significantly increased. We treated the patient with oral ambroxol hydrochloride and therapeutic BAL. We believe that this combination of therapies is the first choice for the treatment of PAP.

Key words: ambroxol hydrochloride; bronchoalveolar lavage; flexible bronchofiberscope; pulmonary alveolar proteinosis; surfactant protein A

Pulmonary alveolar proteinosis (PAP) is characterized by the presence of copious eosinophilic, periodic acid Schiff (PAS)-positive material in the alveoli and by an excess of surfactant components (both lipids and proteins) in lung lavage. It may be present during the neonatal period or later in life. PAP is the consequence of a genetic defect involving the lungs, such as a mutation of the surfactant protein B (SP-B) gene, or it can represent an aspect of a different genetic disease, such as lysinuric protein intolerance. PAP may also be associated with infections, malignancies, exposure to dusts, or the use of certain drugs. In most cases, however, it occurs as an isolated entity with no apparent cause, and is known as idiopathic alveolar proteinosis (Antonella et al., 1996). The cause is likely related to either overstimulation of type II pneumocytes or an impairment of the mechanism for removal of alveolar phospholipids (Cesar et al., 1995). In the alveoli of patients with PAP, the alveolar clearance of proteinaceous materials is impaired. Many investigators have reported biochemical studies of bronchoalveolar lavage (BAL) fluid in the patients with PAP, including analyses of proteins and phospholipids (Sahu et al., 1976; Akino et al, 1978; Onodera et al., 1983; Honda et al., 1989). Amounts of protein and phospholipid were found to be significantly increased relative to those in contrast to normal subjects. Surfactant protein A (SP-A) is the predominant phospholipid-associated glycoprotein in pulmonary surfactant and is specific to the lung. The contents of SP-A in BAL fluid can be measured to diagnose PAP (Honda et al., 1993). We report a case of PAP diagnosed by an increase of SP-A in BAL fluid, and treated by oral ambroxol hydrochloride and BAL.

Patient report

A 59-year-old Japanese man who lives in Tottori Prefecture, Japan was admitted to our hospital in June 1997 because of cough and dyspnea at rest. His past medical history included 2 admissions for pneumonia in 1994 and 1995. He had smoked 20 cigarettes per day for over 30 years and had been employed as a garbage man of a building for over 18 years.

Abbreviations: BAL, bronchoalveolar lavage; PAS, periodic acid Schiff; PAP, pulmonary alveolar proteinosis; SP-A, surfactant protein A; SP-B, surfactant protein B; WLL, whole lung lavage

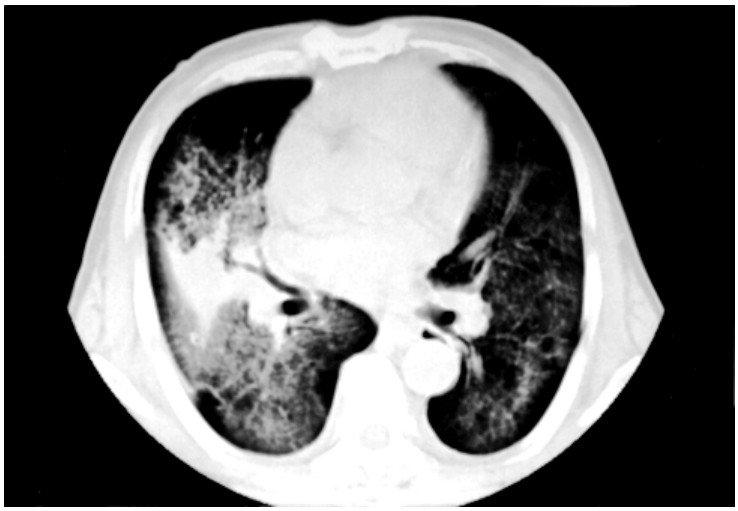

Fig. 1a. Computed tomogram of the chest on admission.

Although physical examination on admission showed respiratory distress, he complained only of mild dyspnea. He had a non-productive cough. Auscultation of the lung showed coarse inspiratory crackles in both lung fields. There was mild clubbing of the nail beds. The laboratory findings showed high levels of lactic acid dehydrogenase (421 IU/L), C-reactive protein (1.27 mg/dL) and carcinoembryonic antigen (7.3 ng/mL). Sputum cultures for bacteria, fungi and tuberculosis were negative. His chest radiograph showed diffuse bilateral interstitial reticular and alveolar densities of both lung fields. Computed tomography of the chest showed diffuse, non-segmental densities of various degrees, with a peripheral clear zone, primarily in the mid-lung field, and honeycombing shadows in the lower lung field (Fig. 1a). Analysis of arterial blood gases showed hypoxia (arterial oxygen pressure, 54.1 mm Hg). On the 3rd day after admission, the patient developed respiratory failure. BAL was performed on the right B^4 segment and a transbronchial lung biopsy was performed on the right B^4 and B^8 segments. The specimens were stained with hematoxylin and eosin. Light microscopy of the transbronchial lung biopsy showed distended alveoli with a pink homogeneous material that was PAS-positive, and slight thickening of the alveolar walls with minimal infiltration of lymphocytes (Fig. 2a). Immunostaining for SP-A of lung biopsy specimens resulted in positive staining (Fig. 2b). No atypical lymphocytes were detected in the infiltrating cells. The BAL fluid contained phospholipid and was sent to Sapporo Medical College, Sapporo, Japan to measure SP-A. The concentration of SP-A in the BAL fluid was significantly increased at 482.2 μg/mL (normal range, 1.3 to 5.2 μg/mL). Also the ratio of SP-A to phospholipid was 3.58 μg/nmol (normal range, 0.05 to 0.11 μg/nmol) (Honda et al., 1993). Therefore, we made a diagnosis of PAP, and treated the patient with oral ambroxol hydrochloride

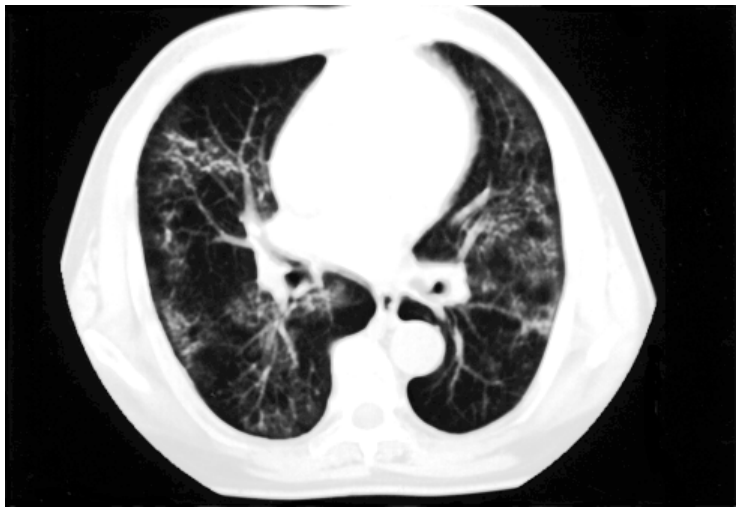

Fig. 1b. Computed tomogram of the chest obtained after oral administration of ambroxol hydrochroloride and therapeutic bronchoalveolar lavage (BAL).