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Case report

Successful treatment of pulmonary alveolar proteinosis with whole lung lavage and subcutaneous GM-CSF

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ABSTRACT

Introduction: Pulmonary alveolar proteinosis (PAP) is a rare lung disease characterized by the accumulation of a periodic acid-Shiff-positive lipoproteinaceous material (surfactant) in the distal airways. The standard treatment is whole lung lavage (WLL), however, not all patients respond well to WLL.

Aim: We present an exciting case report on the successful treatment of the rare disease PAP with WLL and subcutaneous granulocyte macrophage colony-stimulating factor (GM-CSF) therapy for 12 weeks.

Case study: A 20 year-old woman with a 7-month history of progressive shortness of breath was referred to us. Computed tomography of the chest revealed typical geographic ground-glass opacity combined with interlobular septal thickening (crazy paving). Pulmonary function tests showed restriction with severe impairment of diffusion capacity (DL_{CO} 20%). Milky bronchoalveolar lavage fluid (BALF) was detected during bronchoscopy. The cytology of the BALF was consistent with PAP. WLL was performed and subcutaneous GM-CSF was started immediately and continued for 12 weeks. At the end of treatment, the patient's lung function was clearly improved (DL_{CO} 62%).

Results and discussion: One year after the withdrawal of treatment, the patient remains in good health, with no recurrence of hypoxemia and respiratory symptoms. Different treatment modalities have been applied since PAP was first defined, and WLL has been the preferred first line of treatment. Although our patient's condition improved after WLL, her respiratory insufficiency persisted. Consequently, we initiated treatment with subcutaneous GM-CSF.

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Conclusions: WLL significantly improved our patient's condition, and GM-CSF was effective at prolonging pulmonary washout from excess surfactant.

1. Introduction

Pulmonary alveolar proteinosis (PAP) is a rare lung disease characterized by the accumulation of a periodic acid-Shiff (PAS)-positive lipoproteinaceous material (surfactant) in the distal airways, resulting in various degrees of impaired gas transfer. The clinical manifestations of PAP range from asymptomatic to severe respiratory failure. Three forms of PAP are recognized: congenital – due to mutations in the surfactant or the granulocyte macrophage colony-stimulating factor (GM-CSF) receptor; secondary – related to myeloid malignancy, bone marrow transplantation, infection, and pneumoconiosis; and acquired or autoimmune – related to anti GM-CSF antibodies.[1] Autoimmune PAP covers approximately 90% of all PAP cases. The prevalence of PAP varies from 4 to 40 cases per 1 million, and the incidence is estimated at nearly 0.2 cases per 1 million.[2] The most common symptoms of PAP are dyspnea and cough. Radiographic imaging typically reveals centrally located bilateral symmetric alveolar opacities in the mid and lower lung zones, and bronchoalveolar lavage fluid (BALF), which typically has a milky appearance. For patients with moderate to severe symptoms, the standard treatment is whole lung lavage (WLL), wherein large quantities of saline are instilled into the lungs to remove the proteinaceous material. However, not all patients respond well to WLL; therefore, numerous therapies that enhance the clearance of the surfactant have been investigated. These therapies either target alveolar macrophages with exogenous GM-CSF or reduce the levels of anti-GM-CSF antibodies with plasmapheresis or rituximab.[3]

2. Aim

We present a case report of the successful treatment of alveolar proteinosis by subcutaneous GM-CSF after WLL.

3. Case study

A 20-year-old woman with a 7-month history of progressive shortness of breath without clinical signs of infection or obstruction was referred to us. The patient was a nonsmoker with no prior environmental or occupational organic/inorganic dust exposure. The chest radiographs showed bilateral air space consolidation. Computed tomography (CT) of the chest revealed typical geographic ground-glass opacity combined with interlobular septal thickening (crazy paving) (Fig. 1a and b). Pulmonary function tests showed restriction with severe impairment of diffusion capacity (DL_{CO} 20%), and arterial blood gas analysis confirmed severe hypoxemia (pO_2 44.5 mmHg, sO_2 81.7%, pCO_2 23.9 mmHg). Milky BALF was detected during bronchoscopy. The cytology of the BALF was consistent with PAP (positive PAS staining). Based on these findings, PAP was diagnosed.

Due to the severity of the patient's condition, WLL was performed (left lung on August 6, 2014; right lung on August 12, 2014) (Figs. 2 and 3). Five days after right lung lavage, pulmonary function was slightly improved (DL_{CO} 31%), and a CT image showed decreased ground glass opacity, with the exception of the superior left lobe, where crazy paving

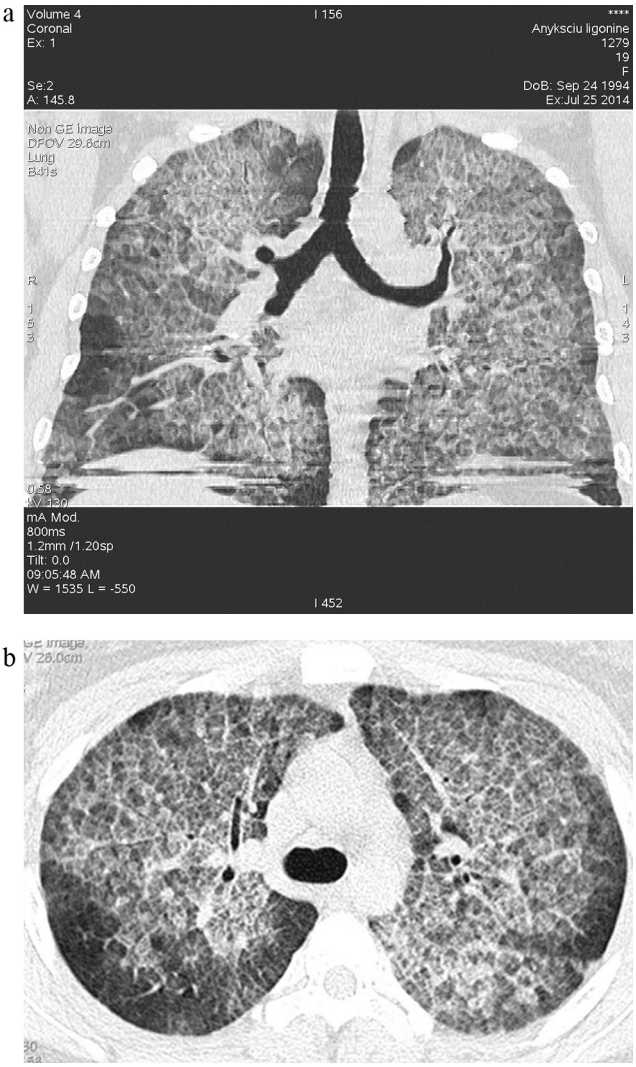

Fig. 1 – (a and b) CT scan (axial and coronal reformatted image, lung window) demonstrating widespread ground-glass opacity, thickened interlobular septa and intralobular lines (crazy-paving pattern).

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