CASE REPORT

Pulmonary Alveolar Proteinosis: A Rare Cause of Respiratory Failure

Zeeshan Munir, Muhammad Zeeshan Khosa and Muhammad Yaqoob Qazi

Abstract

Pulmonary Alveolar Proteinosis (PAP) is a rare syndrome in the paediatric age group and characterized by intra-alveolar accumulation of proteinaceous phospholipid-laden material called surfactant. The diagnosis is made by High Resolution Computed Tomography (HRCT) chest which shows characteristic crazy paving appearance and diagnosis confirmed by Bronchoalveolar Lavage (BAL). We report two cases. First was a 9-month old infant who presented with respiratory distress and peripheral cyanosis since birth. He was diagnosed on High Resolution Computed Tomography (HRCT) chest as a case of pulmonary alveolar proteinosis and broncho-alveolar lavage confirmed his diagnosis. Second case was a 10-year old female child who had a history of repeated chest infections for 5 years and now presented with cough and respiratory distress for 45 days. She was also diagnosed on HRCT chest but unfortunately she died before broncho-alveolar lavage.

Key Words: *Pulmonary alveolar proteinosis. Surfactant. Crazy paving appearance.*

INTRODUCTION

Pulmonary Alveolar Proteinosis (PAP) is an uncommon cause of respiratory failure in infants and children. In this condition, surfactant, (a phospho-lipo-proteinaceous material), accumulates in alveoli that result in gas exchange impairment leading to dyspnea and respiratory failure.[1,2]

Children usually present with dyspnea, cough, failure to thrive and respiratory failure. Examination of the respiratory system reveals inspiratory crackles and cyanosis. High-Resolution Computed Tomography (HRCT) of the chest is diagnostic and typically demonstrates a crazy-paving appearance. Diagnosis is confirmed by broncho-alveolar lavage which is also a therapeutic modality and mainstay of treatment but it is a highly invasive procedure.[3,4] The mainstay of treatment is lung transplantation. Currently, pulmonary transplantation of macrophage progenitors is also used as effective and long-lasting therapy for pulmonary alveolar proteinosis.[5]

The purpose of this report is to describe this rare condition in 2 paediatric cases with fatal outcome.

CASE REPORT

Case 1: A 9-month male infant was admitted with complaints of cough and respiratory distress. He was born by normal vaginal delivery with normal birth events, product of consanguineous marriage and had previous history of hospital admissions multiple-times due to same complaints and was treated on the lines of bronchopneumonia. He was pale, tachypneic, having peripheral cyanosis and failure to thrive. On auscultation, he had bilateral coarse inspiratory crackles in the chest with sub-costal recessions. His arterial blood gas showed hypoxemia with compensated respiratory alkalosis. Complete blood count showed leucopenia with monocytosis and eosinophilia on differential count. Chest X-ray showed diffuse bilateral pulmonary infiltrates. Patchy alveolar opacities with interlobular septal thickening leading to crazy paving appearance were apparent on HRCT chest (Figure 1).

Bronco-alveolar lavage showed an opaque, milky fluid appearance. It contained large and foamy alveolar macrophages with proteinaceous background and increased number of lymphocytes. The aspirated material stains strongly positive for Periodic Acid-Schiff (PAS) stain and pathologic finding were granular, proteinaceous, fluid-filled alveolar spaces. Whole lung lavage was planned as treatment modality for that patient but the patient died due to respiratory failure before whole lung lavage.

Case 2: A 10-year girl was admitted with history of repeated chest infection for 5 years and now presented with cough and respiratory distress for 45 days. She had already taken Anti-Tuberculosis Therapy (ATT) for a period of one year and remained admitted multiple times in different hospitals due to chest infections. She was an emaciated, sick-looking girl, cyanosed in room air with obvious respiratory distress and clubbed. Moreover, she had bilateral crepitation in chest associated with intercostal and subcostal recessions. Rest of examination was normal. Her serum immunoglobulin levels and sweat chloride test were normal. Delta F-508 was negative and lung function test showed mild restriction and moderate airway obstruction. Chest X-ray showed reticulo-nodular interstitial opacities and HRCT showed typical crazy paving appearance (Figure 2).

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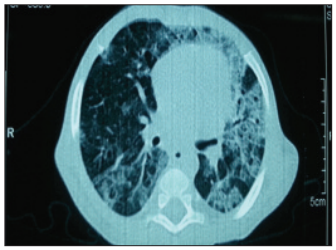

Figure 1: HRCT chest shows patchy alveolar opacities with interlobular septal thickening leading to crazy paving appearance.

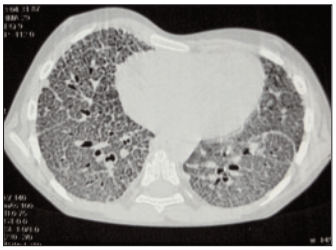

Figure 2: HRCT chest shows patchy alveolar opacities with interlobular septal thickening leading to crazy paving appearance.

Diagnosis of pulmonary alveolar proteinosis was made on the basis of history, clinical examination and characteristic findings on HRCT. Broncho-alveolar lavage was planned for that patient but she died due to respiratory failure before broncho-alveolar lavage.

DISCUSSION

Three clinically distinct forms of PAP have been described congenital, secondary and autoimmune (primary or idiopathic). Congenital PAP is seen in children, while adult forms are usually autoimmune or secondary. Congenital PAP has an autosomal recessive pattern and it usually presents shortly after birth. Congenital (genetic) PAP represents a group of disorders caused by mutations in the genes that encodes for surfactant protein B or C, ATP-binding cassette 3 (*ABCA3*), NK2 home box 1 (*NKX2-1*), or the beta chain of the receptor for granulocyte-macrophage colony-stimulating factor (GM-CSF). Secondary pulmonary alveolar proteinosis occurs due to functional impairment and reduced number of macrophages. Such condition occurs due to inhalation of inorganic dust or toxic fumes, in certain infections and hematologic cancers. In primary PAP anti-GM-CSF antibodies are present which prevent uptake of surfactant proteins by alveolar macrophages resulting in their accumulation.[1,2]

The diagnosis of pulmonary alveolar proteinosis can be made with confidence on the basis of the appearance of the lung on the HRCT scan of the thorax. HRCT typically demonstrates a ground-glass appearance or consolidation, combined with interlobular and intralobular septae thickening, a pattern termed crazy-paving. Crazy-paving appearance on HRCT is said to be characteristically strong enough to suggest the diagnosis in the appropriate clinical setting but the condition can be further confirmed on Bronco-alveolar Lavage (BAL). Classic findings in diagnostic BAL include a milky or opaque aspirate with large foamy alveolar macrophages (2 - 3 times their normal size) containing eosinophilic granules and increased lymphocytes. The aspirated material stains strongly positive for Periodic Acid-Schiff (PAS) stain and pathologic findings are granular, proteinaceous, fluid-filled alveolar spaces. Cholesterol crystals are sometimes observed. The serum LDH level may be elevated and polycythemia may be found as a consequence of chronic hypoxia. Arterial blood gas analysis may reveal a low partial pressure of oxygen and a compensated respiratory alkalosis secondary to hyperventilation. Pulmonary function tests can be normal but typically shows a restrictive ventilatory defect with a disproportionate and severe reduction of the carbon monoxide diffusing capacity. The impairment of gas exchange is secondary to filling of the alveoli with surfactant leading to ventilation and perfusion mismatch.[6,7]

Treatment of congenital (genetic) PAP is often difficult. Mechanical ventilation is sometimes necessary in children with congenital PAP. The mainstay of therapy in PAP is whole-lung lavage. Patients who undergo lavage during the course of their illness have improved survival rates. The mechanism of improvement is unknown but is presumed to be the removal of surfactant from alveoli or minimizing the effect of macrophage dysfunction. Complications include invasive procedure, respiratory failure and multiple procedures for whole lung lavage, superadded infection, pulmonary fibrosis and secondary amyloidosis. Without lung transplantation, mortality is almost inevitable in infancy.[8,9]

The latest treatment modality used on experimental basis in some centres for congenital PAP is intra-pulmonary transplantation of macrophage progenitors. The transplanted macrophage progenitors then differentiate into functional alveolar macrophages. These alveolar macrophages reduce alveolar proteinosis, normalize lung densities in HRCT and improve lung function.[5]

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