Case Report

Serial bronchoscopic lung lavage in pulmonary alveolar proteinosis under local anesthesia

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ABSTRACT

Pulmonary alveolar proteinosis (PAP) is a rare disease, characterized by alveolar accumulation of surfactant composed of proteins and lipids due to defective surfactant clearance by alveolar macrophages. Mainstay of treatment is whole lung lavage, which requires general anesthesia. Herein, we report a case of primary PAP, successfully treated with serial bronchoscopic lung lavages under local anesthesia.

KEY WORDS: Pulmonary alveolar proteinosis, transbronchial lung biopsy, whole lung lavage

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INTRODUCTION

Pulmonary alveolar proteinosis (PAP) was first described in 1958 by Rosen *et al*.[1] It is an extremely rare disorder, occurring worldwide with an estimated prevalence of 0.1 per 100,000 individuals.[2] Arriving at the diagnosis of PAP can be a difficult task. The clinical manifestations are nonspecific, and high-resolution computed tomography (HRCT) scan findings in this disorder are not pathognomonic, though highly suggestive. A diagnosis of PAP can be confirmed by typical histopathological findings of lung biopsy specimens or the appearance of bronchoalveolar lavage (BAL). Whole lung lavage (WLL) introduced by Ramirez in the late 1960s, is the gold standard therapy.[3] Therapy with granulocyte macrophage colony-stimulating factor (GM-CSF) is another option. However, patients presenting with PAP are usually hypoxemic or in poor clinical condition, and WLL may be impossible to perform.

CASE REPORT

A 33-year-old female house wife from Manchery, Kerala presented with a one-year history of progressive shortness of breath and dry cough. She had no history of chest pain, haemoptysis, wheezing, abdominal pain, joint pain and skin rashes. She had history of surgery for bilateral carpel tunnel syndrome two years back. No other significant history or family history was reported. Symptoms aggravated over last three months and during admission, she was on non-invasive mechanical ventilatory support. She had received injectable steroids and multiple antibiotics during last six month, but had not shown any improvement.

On examination, she had dyspnea at rest, tachypnea, tachycardia, clubbing, bilateral pitting pedal edema and oxygen saturation was maintained only with non-invasive ventilator (NIV) support. On auscultation, bilateral end inspiratory crepititions were present without any post-tussive variation. Other systems were within normal limits.

On investigation, chest X-ray showed bilateral diffuse alveolar opacity [Figure 1]. Hemogram, blood sugar level, renal function, liver function, thyroid function, serum electrolytes and sputum examination were within normal limits. Anti-nuclear antibody (ANA) and viral markers were negative. Serum angiotensin converting enzyme (ACE) level was within normal limits. Serum lactate dehydrogenase (LDH) has increased (1194 U/L). Echocardiography was normal and arterial blood gas analysis (ABG) showed hypoxic respiratory failure. High-resolution computed tomography (HRCT) thorax showed extensive ground glass opacities with superimposed

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interlobular septal thickening producing a reticular pattern (crazy pavement) appearance involving upper and lower lobes of lung bilaterally [Figure 2]. Bronchoscopy showed secretions in bilateral bronchial tree. Periodic acid-Schiff (PAS) positive materials seen in broncho alveolar lavage (BAL) . Transbronchial lung biopsy (TBLB) histopathological examination was consistent with pulmonary alveolar proteinosis.

Treatment with daily injection granulocyte macrophage colony-stimulating factor (GM-CSF) 500 μg subcutaneously was given for 12 days. Clinico-radiologically no improvement was noted. Under local anesthesia using flexible fiberoptic bronchoscope therapeutic lung lavage was done. Total 2000-2500 ml of normal saline was instilled on one lung per sitting with the retrieval of about 1500-2000 ml of fluid. This procedure was done 6 times on alternate sides. There is no significant post procedure complication except for transient mild cough and oxygen desaturation. She was clinico-radiologically improved gradually with each lavage [Figure 3]. Oxygen status improved up to requirement of only two liter/min via nasal prongs (with stable ABG) at the time of discharge. During follow up she had stable ABG on room air. She was able to do routine activities for past one year.

DISCUSSION

PAP is a rare syndrome characterized by progressive accumulation of surfactant phospholipids and proteins within alveoli and terminal airways. Three main categories of PAP have been defined depending on the etiology: Congenital, auto-immune (primary or idiopathic), and secondary.

Congenital PAP is a heterogeneous group of disorders caused by mutations in surfactant proteins B or C, or the receptor for GM-CSF.[4]

Secondary PAP can develop in association with various conditions, such as immunodeficiency states, acute silicosis and other inhalational syndromes, hematologic malignancies and myelodysplastic syndromes.[1]

Primary PAP is an autoimmune disease, which produces neutralizing immunoglobulin G (IgG) antibodies against GM-CSF. All three forms of PAP share the feature of an impairment in the number and/or activity of alveolar macrophages leading to the alveolar accumulation of surfactant.[5-7]

The natural history of PAP can follow one of three pathways: Spontaneous improvement, stable with persistent symptoms, or progressive deterioration.[8]

More than 90% of all cases of PAP occur as the primary (idiopathic) form.[1] Primary PAP typically presents in previously healthy adults as progressive exertional dyspnea of insidious onset. Most individuals present were between the ages of 20 and 50 years.

Pulmonary function tests usually reveal a restrictive defect with a reduction in lung volume and diffusion capacity. The radiologically non-specific pattern of air space consolidation, which is usually bilateral and patchy, can be extensive. HRCT demonstrates patchy, ground-glass opacifications

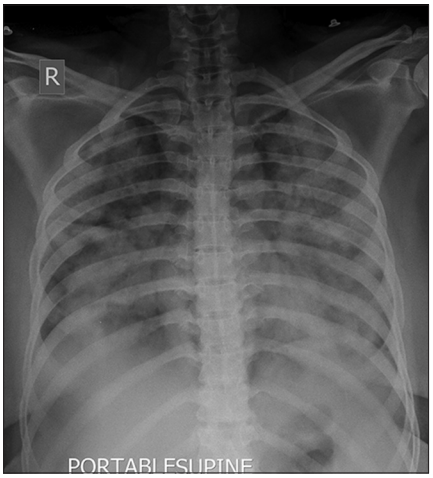

Figure 1: During admission

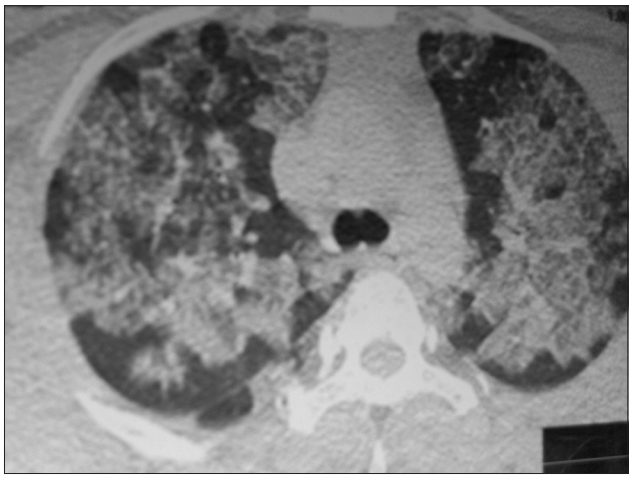

Figure 2: High-Resolution Computed Tomography Thorax

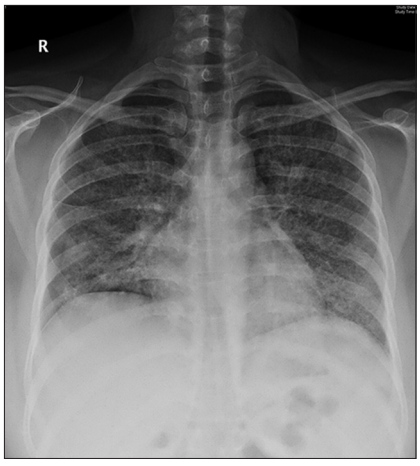

Figure 3: During discharge

with superimposed inter and intra lobular septal thickening, and this pattern is commonly referred to as 'crazy paving'.[8]

Open-lung biopsy is the gold standard for the diagnosis and reveals alveoli filled with granular, eosinophilic material that stains with PAS with preservation of the alveolar architecture, but in an appropriate clinical setting, a diagnosis can be confirmed by BAL and/or TBLB.[9] In this report, the diagnosis of PAP was made by TBLB.

Treatment of congenital PAP is supportive or lung transplantation and treatment of secondary PAP depends on the underlying cause or removal of offending agent. Primary pulmonary proteinosis has no specific treatment but improvement in pulmonary functions can be obtained with WLL.[10,11] However, WLL has complications such as endotracheal granuloma, stenosis, pleural effusion, hydropneumothorax and empyema. Also, severe hypoxemia restricts the applicability of the procedure.

Thus, in our case, instead of WLL with double-lumen endotracheal tube, we applied segmental lavage technique to all lobes with fiberoptic video bronchoscope (FOB) under local anesthesia. The patient's general condition, blood gases and chest radiography improved dramatically.

Even if a new alternative therapy to WLL has not yet emerged, modulation of the GM-CSF signaling pathway or novel biological approaches seem to be promising. Novel treatment approach to PAP is inhaled GM-CSF, plasmapheresis, and biological therapy (Rituximab - a monoclonal antibody directed against the CD20 antigen of B-lymphocytes).

CONCLUSION

In our case, getting a histopathological diagnosis from a hypoxic lung with NIV support was difficult. Secondly, giving general anesthesia to the patient surviving on FiO2 80% of NIV support debatable for WLL. Ultimately, a cure was obtained with segmental lavage technique with FOB, without using double-lumen tracheal tube, as it would be a safer treatment compared with WLL. This case report shows that serial bronchoscopic lung lavage is a simple, low cost and very safe treatment for PAP. It can be done under local anesthesia and does not require prolonged admission and ICU care, as compared with WLL.

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