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Case Report

Primary alveolar proteinosis – A report of two cases

Col D. Bhattacharyya^{a,*}, Brig M.S. Barthwal^b, Col C.D.S. Katoch^a,
Maj Gen S. Rohatgi, vsm^c, Col S. Hasnain^d, Col S.P. Rai (Retd)^e, Lt Col A. Arora^f

^a Senior Advisor (Medicine & Respiratory Med), MH CTC, Pune 411040, India^b Consultant (Medicine & Respiratory Med), MH CTC, Pune 411040, India^c DG (Org & Pers), Office of DGAFMS, New Delhi, India^d Senior Advisor (Anaesthesiology), MH CTC, Pune 411040, India^e Consultant, Pulmonary Medicine, Kokilaben Dhirubai Ambani Hospital, Andheri (West), Mumbai, India^f Classified Specialist (Pathology), MH CTC, Pune 411040, India

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Introduction

Pulmonary alveolar proteinosis (PAP) is a diffuse lung disease characterized by progressive accumulation of surfactant phospholipids and proteins in the distal air spaces. Three forms of PAP are recognized: (a) primary, (b) secondary – to dust exposures (aluminium, silica), and haematological malignancies, or after bone marrow transplantation, and (c) congenital.¹ More than 90% of cases of PAP are primary.² Whole lung lavage is the widely accepted form of treatment for primary PAP.³ We report two cases of primary pulmonary alveolar proteinosis who have been successfully managed with whole lung lavage.

Case report

Case 1

A 33-year-old soldier with history of smoking 15 cigarettes per day for 10 years, presented to a peripheral hospital with complaints of cough, breathlessness and 5 kg weight loss in 3 months. Chest X-ray revealed bilateral extensive alveolar opacities. Sputum was negative for AFB. He was empirically started ATT. He reported to our centre after 1 month as there was no response to ATT. His clinical examination was normal except resting hypoxaemia (SpO₂ 89% on room air), and bilateral infra-axillary crackles. His haemogram, liver and renal function tests were normal. Serum LDH was 540 IU/L (normal: 200–400). Chest X-ray revealed bilateral diffuse alveolar opacities. CECT chest revealed bilateral extensive ground-glass opacities with interlobular septal thickening within areas of ground-glass opacities resulting in a crazy pavement pattern (Fig. 1). Fiberoptic bronchoscopy (FOB) was normal. Bronchoalveolar lavage (BAL) was milky white in colour. BAL showed acellular proteinaceous debris with very few inflammatory cells, and periodic acid-Schiff positive material.

Transbronchial lung biopsy (TBLB) was inconclusive. His repeat FOB with BAL and TBLB also could not confirm the diagnosis. Open lung biopsy (OLB) revealed alveoli filled with amorphous, eosinophilic material showing cholesterol clefts with well-preserved alveolar structure and absence of

* Corresponding author.

E-mail address: dbhatta@rediffmail.com (D. Bhattacharyya).

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inflammatory cells (Fig. 2). He was diagnosed as a case of pulmonary alveolar proteinosis.

He was managed with whole lung lavage under general anaesthesia. Initially the left lung was lavaged while the right lung was isolated and ventilated by using a double lumen endotracheal tube. The lavaged lung was instilled with 1 L saline at 37 °C temperature each time. Dwelling time was 10 min and a change of position was carried out during this period. Vigorous manual percussion was done and the fluid was drained. A total of 9 L exchange was carried out till the effluent was clear (Fig. 3). Unilateral lung lavage of right side was done after 2 weeks. After 1 week of the procedure, there was marked improvement in his condition.

Case 2

A 28-year-old soldier, non-smoker, presented to a peripheral hospital with complaints of productive cough and breathlessness on exertion for 2 months. Clinical examination revealed no abnormality except crackles in bilateral infra-scapular regions.

Investigations revealed normal haematological and biochemical parameters. Sputum was negative for any organism. X-ray chest showed bilateral alveolar opacities. He was empirically started ATT to which he did not show any response. He was transferred to this hospital after 1 month. On examination, SpO₂ was 93% at room air. After 6 min walk SpO₂ fell down to 76%. Serum LDH was 590 IU/L. Sputum was negative for mycobacteria. HRCT chest showed evidence of

Fig. 2 – Alveoli are filled with granular, eosinophilic material showing cholesterol clefts suggestive of pulmonary alveolar proteinosis.

crazy paving pattern (Fig. 4). FOB was normal. BAL was milky in appearance. BAL cytology showed acellular amorphous eosinophilic PAS positive material. BAL was negative for any organism. TBLB showed preserved alveolar architecture with no inflammatory cell infiltration. The alveoli were filled with granular lipoproteinaceous material which stained pink with

Fig. 1 – HRCT chest demonstrates patchy, ground-glass opacification with superimposed inter- and intralobular septal thickening, giving rise to the pattern of 'crazy paving'.

Fig. 3 – Whole lung lavage fluid showing initial opaque appearance, followed by clear effluent.

PAS stain. He was diagnosed as a case of primary pulmonary alveolar proteinosis.

He was managed with therapeutic unilateral whole lung lavage. Initially the left lung was lavaged. A total 20 L exchange was carried out till the effluent was clear. Lung lavage of right side was done after 2 days. After 1 week of the procedure, there was marked improvement in his condition.

Discussion

Pulmonary alveolar proteinosis (PAP) is a rare disease with the annual incidence of about 0.36 per million individuals. In primary PAP there is a functional deficiency of GM-CSF.⁴ Age of presentation is around 20–50 years. Male to female ratio is 2.5:1. More than two thirds of the patients give history of smoking.⁵ The major symptoms of PAP are progressive

breathlessness on exertion, non-productive cough, low-grade fever, fatigue and weight loss. Clubbing, cyanosis and crackles may be present in 25–50% cases.

Routine blood counts are usually normal. There may be mild elevation of LDH. Anti-GM-CSF autoantibody is also elevated.⁶ Chest X-ray shows bilateral symmetric alveolar opacities. HRCT chest reveals patterns like ‘crazy paving’. Pulmonary functions tests show restrictive pattern, with reduction of DLCO. ABG shows hypoxia. FOB is usually normal. BAL fluid is milky in appearance.^{5,7} It stains with PAS. TBLB shows well-preserved alveolar wall and interstitial architecture. Alveoli and terminal air spaces are filled with fine eosinophilic material and minimal inflammatory cells. The vasculature is normal. If BAL and TBLB are inconclusive, open lung biopsy (OLB) is the gold standard in diagnosing primary PAP.

Treatment of primary PAP depends on the severity of disease. Asymptomatic patients require to be kept under observation. Patients with moderate to severe disease require treatment with whole lung lavage (WLL). WLL was first described by Ramirez–Rivera in 1963.⁸ Most patients experience clinical, physiological and radiological improvement following WLL. The course following WLL is variable. 30–40% patients require only one lavage. Others may require repeated lung lavages at interval of 6–12 months.⁹ GM-CSF has been used by both subcutaneous and by nebulization routes. Proportion of responders to GM-CSF is less than with WLL.¹⁰ There are limited data available on the use of rituximab, plasmapheresis and lung transplantation.

To conclude, though uncommon, cases of primary PAP are occasionally encountered in the practice of pulmonary medicine. Crazy paving in CT chest, characteristic BAL fluid and lung biopsy findings confirm the diagnosis. Whole lung lavage usually gives satisfactory result in most of the patients.

Conflicts of interest

All authors have none to declare.

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Fig. 4 – HRCT chest reveals geographical pattern of ground-glass opacification with thickened inter- and intralobular septae, giving the appearance of ‘crazy paving’.

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Journal Scan

P.J. Belmont Jr., B.J. McCrisky, R.N. Sieg, R. Burks, A.J. Schoenfeld, **Combat wounds in Iraq and Afghanistan from 2005 to 2009**, *Trauma Acute Care Surg*. 73 (2012) 3–12.

There have been no large cohort studies examining the wounding patterns and injury mechanisms in Iraq and Afghanistan from 2005 to 2009. This investigation sought to characterize the incidence and epidemiology of combat-related injuries for this period. Using the Joint Theatre Trauma Registry, a detailed description of the combat casualty care statistics, distribution of wounds, and injury mechanisms sustained by all US service members for wounds (DRG International Classification of Diseases-9th Rev. codes 800–960) during the Iraq and Afghanistan Wars from 2005 to 2009 was performed. Among the 1,992,232 military service members who were deployed, there were 29,624 distinct combat wounds in 7877 combat casualties. The mean age of the combat casualty cohort was 26 years old. The combat casualties were predominantly male (98.8%), Army (77.5%), and junior enlisted (59%). The distribution of combat wounds was as follows: head/neck, 28.1%; thorax, 9.9%; abdomen, 10.1%; and extremities, 51.9%. Explosive injury mechanisms

accounted for 74.4% of all combat casualties, which was significantly higher than those caused by gunshot wounds (19.9%) ($p < 0.0001$). From 2005 to 2007, explosive mechanisms of injury were significantly more common in Iraq than in Afghanistan ($p < 0.001$). The percentage of explosive mechanisms increased significantly in Afghanistan between the years 2007 (59.5%) and 2008 (73.6%) ($p < 0.0003$). The authors concluded that the wounding patterns observed in Iraq and Afghanistan from 2005 to 2009 differs from previous conflicts. Explosive mechanisms accounted for 74.4% of combat casualties, which is a higher percentage than in previous US conflicts. A progressive increase in the use of explosive mechanisms in Afghanistan, eventually equalling that in Iraq, was observed during the study period.

Contributed by:

Brig Man Mohan Harjai

Commandant, 166 MH, C/o-56 APO, PIN-900277, India

E-mail address: harjai101@hotmail.com.

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