

Case Report

©2013 NRITLD, National Research Institute of Tuberculosis and Lung Disease, Iran

ISSN: 1735-0344 Tanaffos 2013; 12(4): 48-52

TANAFFOS 

Segmental Lung Lavage with Fiberoptic Bronchoscopy in a Patient with Special Presentation of Pulmonary Alveolar Proteinosis

Hasan Allah Sadeghi

Department of Pulmonary Medicine, Rajaie
Cardiovascular Medical and Research Center, Iran
University of Medical Sciences, Tehran, Iran

Received: 11 January 2013

Accepted: 7 October 2013

Correspondence to: Sadeghi HA

Address: Rajaie Cardiovascular Medical and
Research Center, Iran University of Medical
Sciences, Tehran, Iran

Email address: sadeghi194@yahoo.com

Pulmonary alveolar proteinosis (PAP) is rare. It is characterized by the accumulation of proteinaceous materials in the alveoli. Typical appearance of BAL fluid (BALF) and positive PAS staining of BALF in conjunction with typical clinical and radiographic manifestations may be diagnostic of PAP. The current mainstay of treatment for PAP is whole-lung lavage. Therapy with granulocyte-macrophage colony stimulating factor is also an option. An alternative procedure is selective lobar/segmental lavage by fiberoptic bronchoscopy (FOB). Whole lung lavage with FOB for idiopathic PAP is currently a safe procedure in an experienced setting, and could be considered in patients with less severe lung involvement who cannot tolerate general anesthesia for the whole lung lavage. It provides long-lasting benefits. We report here our experiences with segmental lung lavage by FOB in a patient with very severe PAP since she could not undergo whole lung lavage under general anesthesia. The one year follow up results are also reported.

Key words: Fiberoptic bronchoscopy, Pulmonary alveolar proteinosis, Segmental lung lavage

INTRODUCTION

First reported by Rosen et al, in 1958, pulmonary alveolar proteinosis (PAP) is rare, with a prevalence rate of 0.37 per 100,000 population and a median age at diagnosis of 39 years (1). It is characterized by the accumulation of proteinaceous materials in the alveoli (1,2). The most common symptoms at presentation are dyspnea and cough, rales in 50% of patients, clubbing in 25%, and cyanosis in 21% (1).

Plain chest radiographs may show alveolar-filling pattern in 62.5% of patients (2,3). Infiltrates are mostly diffuse but sometimes show perihilar distribution (1,2,3). Spirometry and lung volumes may show a mild restrictive ventilatory defect. However, the diffusion capacity for CO

(DLCO) is disproportionately and severely reduced (2,3). Patients are mildly hypoxic with increased alveolo-arterial gradients (1,2,3). The serum lactate dehydrogenase (LDH) is mildly elevated (2,3). Typical HRCT scan findings for autoimmune PAP patients were ground glass opacities with a patchy geographic pattern, subpleural sparing, crazy-paving appearance, and more involvement of the lower lung field (4). These findings are rather infrequent for secondary PAP patients (4). More recently, levels of lung surfactant proteins A and D in both serum and BAL fluid of patients with PAP have been measured (3).

Open lung biopsy is the conventional tool for making the definite diagnosis of PAP, but BAL and transbronchial biopsies (TBLB) have largely supplanted this invasive

procedure, particularly in conjunction with CT scan (3,4). Typical appearance of BALF and positive PAS staining of BALF in conjunction with typical clinical and radiographic manifestations are diagnostic of PAP (4).

At present, the mainstay of treatment of PAP is whole-lung lavage (1,2,3). Therapy with granulocyte-macrophage colony stimulating factor is also possible; although its long-term safety has not been determined. An alternative procedure is selected lobar lavage by FOB (5). Whole lung lavage for idiopathic pulmonary alveolar proteinosis is currently a safe procedure in an experienced setting, and provides long-lasting benefits in the majority of patients (6). In patients and mouse models of PAP, deficient GM-CSF activity appears to result in defective alveolar macrophages that are unable to maintain pulmonary surfactant homeostasis and display defective phagocytic and antigen-presenting capabilities (7). Treatment with GM-CSF may have some place on treatment of patients suffering from PAP (1,2,7,8).

We report here our experiences of segmental lung lavage by FOB with a new technique in a patient with special presentation of very severe PAP. She could not undergo whole lung lavage under general anesthesia. The one year follow up results are also reported.

CASE SUMMARIES

A 43 year-old nonsmoker female with progressive dyspnea and hypoxic respiratory failure referred to our transplant center at Imam Khomeini General Hospital with a primary diagnosis of pathologically proven idiopathic interstitial lung fibrosis (IPF) and no response to classic treatment with high dose prednisolone and azathioprine.

She was healthy until 10 months before referral when she developed progressive dyspnea and cough with scant sputum. Primary evaluation at that time showed mild restrictive pattern on spirometry, and interstitial process in high resolution CT scan without honey combing suggestive of interstitial process like pulmonary alveolar proteinosis or nonspecific interstitial Pneumonitis (NSIP).

Further evaluation with FOB and TBLB was nondiagnostic. An open lung biopsy at that time showed interstitial process compatible with NSIP. Based on the diagnosis of IPF prednisolone one milligram/kg plus azathioprine 150 mg were administered for the patient. No improvement was observed after 3 months of therapy and she got worse. She was put on long term oxygen therapy (5 liters/min) by nasal prong. However, she got worse and became wheelchair bound during the 6 months period of treatment and her physician decided to transfer her to our center for lung transplant.

At the time of first visit she had dyspnea and tachypnea on bed despite 5 liters of O₂ by nose prong. She had a Cushingoid face with cyanotic lips. Thoracic examination showed no crackles on auscultation and a partial reduction in expansion. No other important findings were seen except for obesity. No clubbing was seen.

The patient was put on 12 liters of O₂ with mask to improve oxygenation and further evaluations were carried out.

Laboratory data showed normal CBC and differential count, hemoglobin = 16.5 mg/dl, hematocrit = 50.7 percent and normal ALT, AST, and Alkaline Phosphatase levels. LDH was minimally elevated. Other lab test results were within the normal range. ESR and CRP were also within the normal range. Antibody for HIV, HCV, and HBS and also HBS antigen were negative. Evaluation of pre-transplant viral and parasitic markers showed positive antibody of IgG type for Epstein-Barr virus, cytomegalovirus and toxoplasmosis with low titer of IgM antibodies.

New CT scan of the lungs showed interstitial process with crazy paving pattern and no honey combing despite clinical progression of disease. Plethysmography showed well preserved lung volumes and minimal restriction (Table 1). Diffusion of the lung for CO (DLCO) was severely decreased.

Table 1. Static and dynamic lung volumes and diffusion of lung for CO (DLCO) before bronchoalveolar washing, after complete washing and 12 months later.

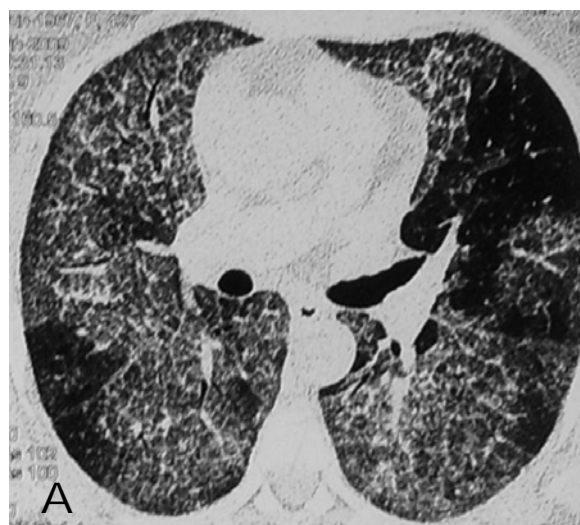
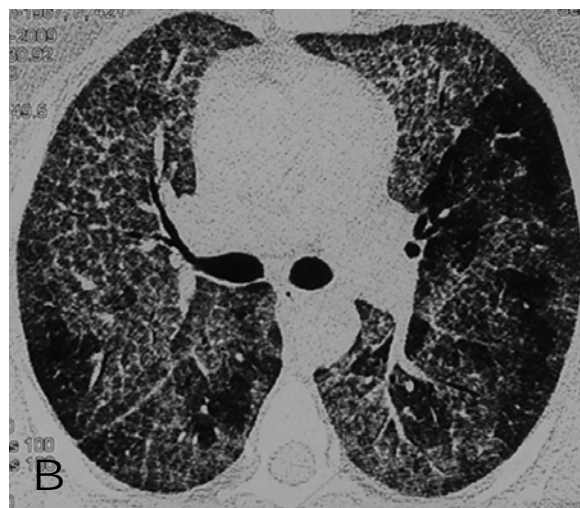
	FEV1 liter (%predicted)	FVC liter (%predicted)	TLC liter (%predicted)	RV liter (%predicted)	DLCO/mL/mmHg/min value (% predicted)	RV/TLC % (%predicted)
Before washing	2.16 (86)	2.36(81)	3.24 (72)	0.87 (58)	2.20(27%)	27(52)
After washing	2.20 (86)	2.52 (84)	4.81 (105)	2.29 (148)	5.48(70%)	49 (93)
One y later	1.98 (80)	2.18 (75)	4.46 (99)	2.29 (151)	5.46(69. 7%)	52 (101)

Reevaluation of the previous lung biopsy and new section of pathological block by the same and a new expert pathologist did not change the primary diagnosis of NSIP. Despite the pathologic report, re evaluation with FOB and bronchoalveolar lavage (BAL) ruled out PAP as a treatable cause. The patient was admitted to the hospital and FOB was done and BAL was obtained. BAL fluid had a completely turbid and milky appearance, highly suggestive of PAP. Positive PAS staining confirmed PAP and whole lung lavage was considered. Because of very severe hypoxia it was impossible to do the whole lung lavage with the usual technique under general anesthesia and therefore segmental bronchial washing with FOB was considered.

FOB was done under local anesthesia at the bronchoscopy unit. Midazolam and morphine sulfate were administered for sedation. Cardiac, blood pressure, and SPO2 monitoring was done at the time of bronchoscopy in the bronchoscopy unit. To preserve oxygenation throughout the procedure, the bronchoscope was passed through a small fit hole in the reservoir mask. Each time the bronchoscope was wedged into segmental bronchi 200 cc of warm saline was injected with 50 milliliter syringe and the fluids were then suctioned out. No balloon was used for blockage of bronchi. Both lungs were washed by warm (34°C) saline solution in 14 sessions, each time 3-5 segments with 3 liters of normal saline, based on the patient's tolerance. After the first 2 sessions, bronchoscopic washing was done as outpatient every 2-3 days.

She got better with progression of bronchoalveolar washing and no longer needed oxygen support and function class improved dramatically. At the end of therapy she was symptom free and six-minute walk test was 650 meter. New CT scan showed resolution of the interstitial process (Figures 1[A,B] and Figure 2 [A,B]) and

the new DLCO and plethysmography results were close to the normal range (Table 1); 12 months after lung washing she was still in good condition with no symptoms at rest or exertion and pulmonary function tests remained unchanged.

**Figure 1 A.** HRCT of the patient before segmental lung lavage at the level of the bronchus intermedius.**Figure 1 B.** HRCT of the patient before segmental lung lavage at the level of the carina

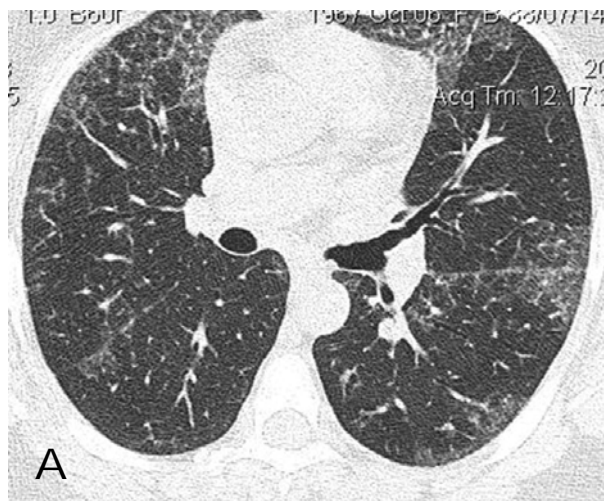


Figure 2 A. HRCT of the patient after segmental lung lavage at the level of the bronchus intermedius.

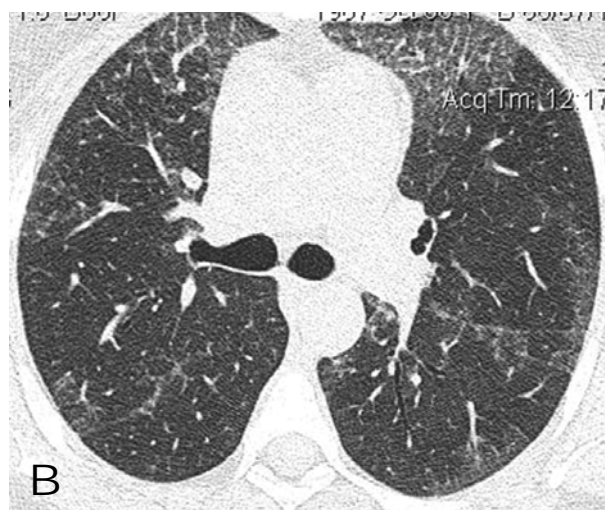


Figure 2 B. HRCT of the patient after segmental lung lavage at the level of the carina.

DISCUSSION

Pulmonary alveolar proteinosis is a rare disorder in which lipoproteinaceous materials accumulate in the alveoli (2). It is characterized by intraalveolar deposition of granular, eosinophilic, periodic acid-Schiff (PAS) positive proteinaceous materials resulting in cough and dyspnea (1,2,3). This material is composed primarily of lipoprotein and surfactant-like material and impairs gas exchange because of alveolar filling and alveolar membrane fibrosis and thickening (1,2,3).

The clinical presentation of PAP is nonspecific and most cases of acquired PAP present with progressive

exertional dyspnea of insidious onset and cough. Less commonly, fever, chest pain, or hemoptysis also occur, especially if secondary infection is present. As seen in our patient, clinical presentation of PAP is nonspecific, and the diagnosis is frequently missed, leading to inappropriate therapy and unnecessary morbidity (5). HRCT findings are highly specific for this disease (4).

If the results of PAS staining of BAL fluid are negative, TBLB is the next step of evaluation of patients suspicious of PAP (1,2,3). Diagnosis can be made effectively by transbronchial biopsy specimens obviating the need for an open lung biopsy in the majority of PAP patients (3). If the diagnosis is not proven by TBLB, open lung biopsy, video-assisted thoracoscopic surgery (VATS) and evaluation of lung parenchyma by a pathologist for PASS positive material is the final step in the diagnostic workup (1,2,3). Interestingly, OLB was misleading in this case and TBLB later proved PAP. Because of the non-homogenous involvement of the lungs, it may be misleading if biopsy tissue is taken from a non-involved area and or from lingula and right middle lobe tip which are more accessible for surgeons. Interstitial involvement and fibrosis may occur with further progression of disease. We suppose that misdiagnosis of our patient during evaluation at the other center, was due to improper selection of the site of open lung biopsy and probably the biopsy specimen in this case was obtained from the right middle lobe tip.

Acquired pulmonary alveolar proteinosis has been treated successfully by whole-lung lavage, and this procedure remains the standard of care (2).

Bronchoscopic washing of the lungs is an alternative treatment option. It has been done in reported cases with different techniques and good outcome (5). Major complications were reported to be severe coughs, tachycardia and hypoxemia during lavage (5). All the mentioned side effects occurred in this case. Our patient was also complicated with pneumothorax at the 4th session of FOB and lavage. She was treated with O₂ by nose prong for 3 days without further intervention. Pneumothorax was resolved within 10 days and segmental BAL was continued thereafter. This experience suggests that bronchoscopic

lobar lavage is safe although not simple. It may find application in patients in whom, severe lung involvement contraindicates a whole-lung lavage with generalized anesthesia. Another application of this method may be in patients with less advanced disease and less amount of proteinaceous substances that can be removed with a small volume of lavage fluid. This procedure has been used by others with different techniques (2,5). These studies involved either complicated procedures for preserving oxygenation, sedation and/or anesthesia, or use of trypsin as lavage fluid, which carries the potential danger of an allergic reaction and proteolytic damage (5). Shih-Lung Cheng et al. (5) used a very simple method. They used only xylocaine 2% spray for local anesthesia, but they did not use sedation or balloon during bronchoscopy.

We used midazolam and morphine sulfate for sedation of patient and partial control of cough, and xylocaine 10% for local pharyngeal, trachea and bronchial anesthesia without the presence of anesthesiologist. This technique of sedation was acceptable for the patient and allowed us to repeat FOB for several times.

There have been several reports regarding the therapeutic benefits of aeroGM-CSF in patients with PAP, manifested by clinical improvement in symptoms, disease markers, pulmonary function measurements, and radiographic imaging (chest CT scans or chest X ray) (7,8). We would have considered this option for our patient, if other methods of therapy had failed.

CONCLUSION

This experience suggests that bronchoscopic lobar lavage is simple and safe, and may find application in patients in whom a whole-lung lavage with generalized anesthesia is contraindicated, and also in those with less advanced disease in whom proteinaceous substances can be removed with a small volume of lavage fluid.

REFERENCES

1. Goldstein LS, Kavuru MS, Curtis-McCarthy P, Christie HA, Farver C, Stoller JK. Pulmonary alveolar proteinosis: clinical features and outcomes. *Chest* 1998; 114 (5): 1357- 62.
2. Trapnell BC, Whitsett JA, Nakata K. Pulmonary alveolar proteinosis. *N Engl J Med* 2003; 349 (26): 2527- 39.
3. Wang BM, Stern EJ, Schmidt RA, Pierson DJ. Diagnosing pulmonary alveolar proteinosis. A review and an update. *Chest* 1997; 111 (2): 460- 6.
4. Ishii H, Trapnell BC, Tazawa R, Inoue Y, Akira M, Kogure Y, et al. Comparative study of high-resolution CT findings between autoimmune and secondary pulmonary alveolar proteinosis. *Chest* 2009; 136 (5): 1348- 55.
5. Cheng SL, Chang HT, Lau HP, Lee LN, et al. Pulmonary alveolar proteinosis: treatment by bronchofiberscopic lobar lavage. *Chest* 2002; 122 (4): 1480- 5.
6. Beccaria M, Luisetti M, Rodi G, Corsico A, Zoia MC, Colato S, et al. Long-term durable benefit after whole lung lavage in pulmonary alveolar proteinosis. *Eur Respir J* 2004; 23 (4): 526- 31.
7. Robinson TE, Trapnell BC, Goris ML, Quittell LM, Cornfield DN. Quantitative analysis of longitudinal response to aerosolized granulocyte-macrophage colony-stimulating factor in two adolescents with autoimmune pulmonary alveolar proteinosis. *Chest* 2009; 135 (3): 842- 8.
8. Greenhill SR, Kotton DN. Pulmonary alveolar proteinosis: a bench-to-bedside story of granulocyte-macrophage colony-stimulating factor dysfunction. *Chest* 2009; 136 (2): 571- 7.