# Lobar flexible fiberoptic lung lavage: therapeutic benefit in severe respiratory failure in pulmonary alveolar proteinosis and influenza A H1N1 pneumonia

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## Abstract

Lobar fiberoptic lung lavage is a well-known procedure used in primary pulmonary alveolar proteinosis (PAP); the use of this procedure has increased in the recent years. This procedure has also been used in other pulmonary diseases such as desquamative interstitial pneumonia with good results. We describe a case of extremely severe respiratory failure due to concurrence of PAP and Influenza A H1N1 virus pneumonia which resolved with the help of this procedure. The patient, a 41-year-old woman, needed less mechanical ventilation after undergoing lobar fiberoptic bronchoscopic lavage. Moreover, a rapid and progressive improvement in the computed tomography of the lungs was observed. Flexibile fiberoptic bronchoscopic lobar lavage is a simple, safe procedure used not only in milder disease, but also in particular severe cases in which the physiological derangement of whole lung lavage would not be tolerated by patient or when extra-corporeal membrane oxygenation is not available.

## Introduction

Lobar or total lung lavage by flexibile fiberoptic bronchoscopy (FOB) is an alternative to whole lung lavage (WLL) in the treatment of pulmonary alveolar proteinosis (PAP).[1-4] Bronchopulmonary lavage was introduced by J. Ramirez and used not only in alveolar proteinosis but also in status asthmaticus[5] and in desquamative interstitial pneumonia[2] with good results.The use of multiple segmental or lobar lavage by FOB has been reported in English medical literature in less than 10 cases but often with interesting results.[1-4,6] Partial lung lavage, performed with bronchoscope has been considered a possibility when WLL is potentially harmful as in the case of severe hypoxemia and when extracorporeal membrane oxygenation is not feasible.[7] This option is also indicated for children. Since there is no pediatric-size double-lumen endotracheal tube available,unilateral lung lavage by bronchofiberscope and selective ventilation, with cuffed endotracheal tube, is an alternative.[7] Paquet and Karsli also utilized a two-cuffed endotracheal tube for the treatment of a pediatric patient.[8] Based on these experience we report a case of a patient with pulmonary alveolar proteinosis and presenting an influenza A H1N1 pneumonia treated and resolved with helping of FOB.

## Case Report

A 41-year- old woman, suffering from idiopathic alveolar proteinosis (biopsy confirmed) (PAP) was referred to Intensive Care Unit of the Hospital of Lavagna because of respiratory failure: $PaO_2/FIO_2$ (P/F) ratio 130, severe respiratory acidosis (pH 6.96 and $paCO_2$ 112) tachypnea (respiratory rate: 40 breaths per minute), tachycardia (pulse: 130 beats minute), fever (T 38.8°C) and stupor.

Prior to admission she was given a 7- day course of clarithromycin for an upper respiratory tract infection. In the week before the admission dyspnoea had been progressively increasing. The patient had been followed for five years at the Respiratory Diseases Department of Hospital of Sestri Levante for PAP. No therapy had been prescribed during the last two years because her condition had stabilized. She did not have a history of allergy. In the month prior to admission she complained of dyspnoea and mucous expectoration. In the week before admission dyspnoea was present also at rest.

Admission chest X-ray showed diffuse bilateral interstitial and alveolar infiltrates (Figure 1A); computed tomography (CT) scan of the thorax showed diffuse asymmetric alveolar infiltrates, ground-glass opacities associated with reticulo-nodular pattern (Figure 1B). Arterial blood gas performed by administering oxygen $FIO_2$ 60% by Venturi mask showed a severe acidosis ($PaO_2$ 44 mmHg, $PaCO_2$ 121 pH 6.96).

Thirty minutes after admission to the Intensive Care Unit, the patient was invasively ventilated by pressure-controlled ventilation: Inspiratory Positive Airway pressure (IPAP): 28 cm $H_2O$, Positive End Expiratory Pressure (PEEP):15 cm $H_20$, respiratory rate:16 per minute and $FIO_2$ 80% with a tidal volume of 290 mL. Arterial blood gas analysis revealed worsening parameters: pH 6.73, $PaCO_2$ 170 mmHg, $PaO_2$ 112 mmHg. The ventilation was modified (increasing PEEP to 20 $cmH_2O$). Improved blood gas values were noted twelve hours later. (pH 7.22, $PaCO_2$ 63.5, $PaO_2$ 112 with P/F ratio

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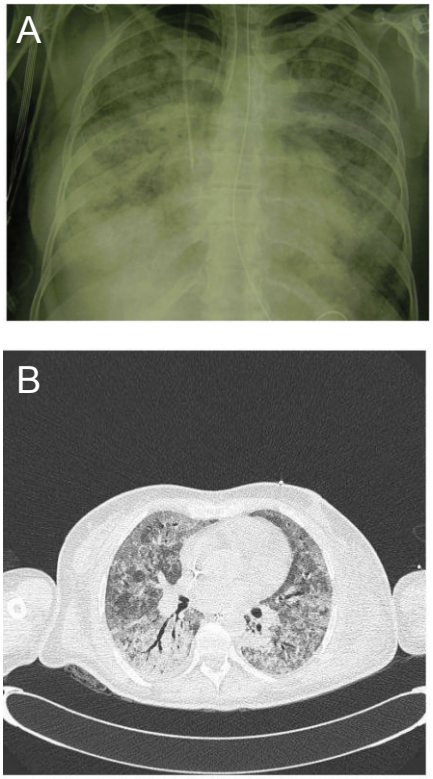


**Figure 1. (A) Chest x-ray: diffuse bilateral interstitial and alveolar infiltrates. (B) Computed tomography scan: diffuse asymmetric alveolar infiltrates, ground-glass opacities associated with reticulo-nodular pattern.**

234). Twenty-four hours later a normal pH was achieved (pH 7.35 $PaCO_2$ 50 $PaO_2$ 112 );PEEP was reduced (12 cm $H_2O$). Broad spectrum antibiotics (piperacillin +tazobactam 18 g in continuous infusion +levofloxacin 1000 mg every 24 hours) and antimycotical therapy associated with stress doses of Hydrocortisone 300 mg iv. were initiated at the admission. Over the next five days the clinical picture worsened and the PEEP was increased to 18 cm $H_2O$ and the patient remained hypercapnic ($PaCO_2$ 106 mm Hg with Ph 7.18). She underwent bronchoscopic aspiration and lavage which returned milky, thick fluid from the entire bronchial tree. The Real time polymerase chain reaction (PCR) of bronchoalveolar lavage sample resulted positive for Influenza A H1N1 virus. The biochemical analysis of bronchoalveolar lavage (a presence of *foamy* macrophages and elevated lipid index) and electronic microscopy of bronchoalveolar lavage (amorphous material with multi lamellated structure in concentric arrangement) confirmed the concurrence of influenza A H1N1 virus pneumonia with idiopathic alveolar proteinosis. The white blood cells (WBC) count was 3800 with 85% polymorphonuclear leukocytes with relative lymphopenia (3.2%); the hematocrit was 42%, haemoglobin 11.8 g/mL and C-reactive protein (CRP) 20.44 mg/L, lactate dehydrogenase (LDH) 2058 U/L. Antiviral therapy with Oseltamivir 150 mg twice a day started.

Urinary antigen test for Legionella pneumophila and Streptococcus pneumoniae were negative as were IgM antibodies for Mycoplasma pneumoniae.

PCR for the identification of Adenovirus, Human Coronavirus, Metapneumovirus, Chlamydia pneumoniae, Haemphilus influenzae, Legionella pneumophila, Mycoplasma pneumoniae and Streptococcus pneumoniae. antigens of Aspergillus and Ziehl-Neelsen stain for acid-fast bacilli and nucleoid acid amplification tests to identify Mycobacterium tuberculosis in blood and bronchoalveolar lavage were also negative.

A lobar lavage by bronchofibroscopy was performed seven days after admission using segmental lavage technique with instillation of 2000 mL of warm saline water.[1,8,9] After bronchopulmonary lavage tidal volume increased as did P/F ratio and blood gas analysis parameters improved. The bronchopulmonary lavage was repeated on 10th, 14th, 18th and 21st days .

The radiographic abnormalities gradually cleared (Figure 2), PEEP was progressively reduced, the laboratory data improved (WBC 7230, LDH 633 U/L,CRP 0.70) and the patient was transferred to the Division of Respiratory Diseases a week later .Pulmonary function tests showed a mild restrictive syndrome: forced vital capacity (FVC) 74.4% of predicted, forced expiratory volume in one second (FEV1) 78.5% of predicted, total lung capacity (TLC) 77.8% of predicted, Tiffeneau index 90.2) and a moderate-severe reduction of diffusion capacity for CO (40.5%) .

The clinical and radiologic picture improved progressively and the patient was discharged 42 days after admission to hospital. The patient continued follow-up and the functional respiratory parameters returned to the values present before the illness.

## Discussion

There are three clinically distinct form of PAP: congenital (2% of cases), acquired (also referred as primary or idiopathic 90% of cases) and secondary (5-10%). The clinical presentation of PAP varies from asymptomatic (31% of acquired cases) to a more chronic presentation with dyspnoea and cough sometimes accompanied by sputum described as *white and gummy* or *chunky*.[9] Pulmonary function test usually reveals restrictive lung disease, decreased carbon monoxide diffusion capacity and rarely hypoxemia. Chest CT scan findings are non-specific and often show smooth thickening of sepal lines superimposed on areas of ground-glass opacities, known as *crazy-paving*.[10] The gold standard for PAP diagnosis is open lung biopsy. Bronchoalveolar lavage is usually performed to exclude infection. The classic findings include a *milky* fluid containing large amounts of granular cellular eosinophilic (proteinaceous) material with morphologically abnormal *foamy* macrophages filled with PAS-positive intracellular inclusions. When electron microscopy is available, the presence of concentrically laminated phospholipid structures called lamellar bodies can confirm the diagnosis.[9,11] Associated infections have been reported in 5-20% of PAP cases. The infectious agents include Nocardia, Mycobacterium tuberculosis, Mycobacterium avium-intracellulare, Pneumocystis jirovecii, and cytomegalovirus.[11] An association with influenza A has not reported. Single lung lavage by FOB was performed in conscious patients as well as patients under general anaesthesia and mechanical ventilation;[7-10,12-14] in recent years the use of BAL lung lavage has increased; it seems to be effective as whole lung lavage.[7,8,12-14] It has similar long- term effects when compared with the latter. BAL lung lavage a is well-known and established procedure in primary pulmonary alveolar proteinosis.[1,3-5,7-8,12-14] BAL lung lavage was previously used in other pulmonary alveolar disorders.[2]The only effective treatment of PAP is bronchoalveolar lavage: the procedure is safe and does not require anesthetic support. It is recommended only in milder disease or conversely, in particular severe cases, in which the physiological derangement of WLL would not tolerated by patient or when extra-corporeal membrane oxygenation is not available. Our case report illustrates that extremely severe respiratory failure can be successfully managed with the alternative technique of lobar lung lavage by flexibile fiberoptic bronchoscopy.

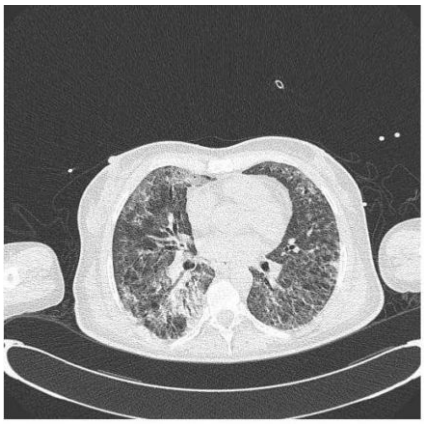

**Figure 2. After bronchoscopic lung lavage, a gradual clearing of the diffuse alveolar infiltrates and the ground glass opacities.**

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