Chapter

Introductory Chapter: Whole Lung Lavage for Pulmonary Alveolar Proteinosis—The Challenges Remain

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1. Pulmonary alveolar proteinosis

Since its first description in 1958 by Samuel H. Rosen et al., understanding pulmonary alveolar proteinosis (PAP) (or pulmonary alveolar lipoproteinosis or pulmonary alveolar phospholipidosis) has made a tremendous advance [1].

Today, PAP remains a rare lung disease. Prevalence ranges from 3.7 to 40 cases per million, depending on the country, and the incidence has been estimated to be 0.2 cases per million. The main pathological mechanism behind the disease is the accumulation of lipoproteinaceous material in the alveoli due to dysfunctional clearance by alveolar macrophages or type II epithelial cells. There are three clinically distinct forms: (1) congenital, caused by mutations in the CSF2RA gene on chromosome Xp22.33 or impaired CSF2RB expression. The result is a dysfunctional α or β granulocyte-macrophage colony-stimulating factor (GM-CSF) receptor subunit. (2) Secondary pulmonary alveolar proteinosis develops in association with conditions involving functional impairment or reduced numbers of alveolar macrophages (hematologic cancers, pharmacologic immunosuppression, inhalation of inorganic dust or toxic fumes, and certain infections). (3) Finally, autoimmune PAP is initiated by immunoglobulin (Ig)-G anti-granulocyte-macrophage colony-stimulating factor (anti-GM-CSF) antibodies, which decrease functional alveolar macrophages [2].

Clinical presentation of PAP varies: dyspnea, cough, hemoptysis, fever, and chest pain appear in a different range, while signs of chronic respiratory failure (cyanosis, clubbing, inspiratory crackles) can be found in clinical examination.

Diagnosis demands appropriate serological, radiological, and bronchoscopic evaluation and opting out other interstitial lung diseases [3].

2. Therapeutic options

Unfortunately, apart from the conditions in which etiological therapy is available, therapeutic options remain limited. Supplementation of exogenous granulocyte-macrophage colony-stimulating factor (GM-CSF) or strategies aimed at reducing the levels of the autoantibodies, like plasmapheresis or rituximab—a monoclonal antibody directed against the CD20 antigen of B-lymphocytes and ameliorates PAP by decreasing anti-GM-CSF antibody concentration—are promising approaches. Other options like stem cell or lung transplantation have more limited use.

On the other hand, whole lung lavage (WLL) is the standard first-line therapy [4]. Theoretic concept behind WLL is simple. Clinical and physiological improvement is caused by the removal of lipoproteinaceous material and anti-GM-CSF antibodies from the alveolar space. Additional immunological effects on the effector cells (e.g., alveolar macrophages or type II epithelial cells) may also be included.

3. Whole lung lavage: the challenges

Due to the rarity of the disease, there are no guidelines regarding technical details about WLL. Usually, a dedicated team, which includes experienced anesthesia and respiratory nurses, anesthesiologist, respiratory physiotherapist, and a pulmonologist experienced in interventional pulmonology, is needed to perform the procedure [5].

Indications for WLL also vary. In general, dyspnea-induced limitation of daily activities is the rule, although decline in SpO_2 (>70% in room air), radiographic worsening, decline in DLCO or FVC, and other symptoms have also been used [6].

Thus, timing between diagnosis of PAP and WLL varies from 2 months to 17 years, although most of the patients need WLL within a year from diagnosis [5]. Time of repeating WLL depends on patient's condition [2]. Available literature reports an interval between 15 months and 3 years [7, 8]. Three (3) weeks interval between right and left lung WLL is considered safe and long enough for clinical improvement to arise [6]. However, bilateral WLL has also been performed without any problems [9].

Usually, the procedure is performed first in the most severely affected lung. Imaging techniques such as perfusion/ventilation scan can help in the final selection. Patient is positioned usually supine, although multiple positions, like lateral decubitus, Trendelenburg, and prone, have also been reported [10].

The procedure is carried out under general anesthesia. The preferred technique is total intravenous anesthesia, while volatile anesthetics has been used in cases of bronchospasm. After preoxygenation, a left double-lumen endotracheal tube (DLT) with minimum size 26 Fr is used for intubation and lung isolation. Right DLT is avoided due to risk of right upper lobe orifice block [6]. Recently, there also reports—still rare—of noninvasive ventilation (NIV) as alternative to intubation with DLT [11]. The same is valid also for anesthesia, as reports are published for WLL during local anesthesia and the use of fiber-optic bronchoscope [12].

Hypoxemia is common during WLL. Several strategies are suggested in order to cope with the problem: positive end-expiratory pressure (PEEP) application, manual ventilation of partially fluid-filled lung, intermittent double-lung ventilation, concomitant use of inhaled nitric oxide, ipsilateral occlusion of pulmonary artery of the non-ventilated lung via pulmonary artery catheter, hyperbaric oxygen therapy, and parallel use of veno-venous extracorporeal membrane oxygenation (ECMO) [6, 10, 13–16]. No guideline or data exist for the use of one method over the others.

In most of the literature warmed (to 37°C) NaCl 0.9% is reported as lung fluid. The total volume needed ranges from 30 to 50 liters [6]. The fluid can flow by gravitational force in 500–1000 ml or FRC equivalent volume aliquots for 10–30 cycles. The maximum pressure allowed should be below the sealing pressure of the ventilated lung (between 30 and 50 cm). In case of fiber-optic bronchoscopic lavage under local anesthesia, 50 ml aliquots are used [12].

The mechanism of protein transfer from the surfactant and blood into the lavage fluid during WLL has not been sufficiently studied. A recent report suggests a mathematical model—expressed with several differential equations—based on

diffusion for the transfer of most of the substances. However, there are still components of the alveolar proteinaceous material—mainly with low molecular weight—which do not follow the suggested model [17].

Chest percussion with a wraparound vest or manual percussion by a physiotherapist is applied for 3–5 minutes, in order to increase clearance of proteinaceous material. This can be performed throughout the procedure (from installation to removal of the fluid). Till now, there is no comparative study for the method of percussion; still, some authors claim that mechanical percussion with vest is best tolerated [10].

Intraoperative monitoring varies, yet it generally includes invasive arterial blood pressure for serial arterial blood gases examination. Recently, lung ultrasound has been also suggested as a promising method of monitoring the amount of saline used for lavage and pick-up complications like pleural effusion [18].

In the immediate post-procedure phase, diuretics can help clearing fluid from the lung [8], while follow-up is usually performed via chest X-ray or computer tomography imaging [6].

Complication rate ranges from 0.8% for pneumothorax to 18% for transient fever; other complications are hypoxemia, pleural effusion, pneumonia, wheezing, etc. [6].

Long-term efficiency of the procedure is generally good, though available literature is limited.

4. Conclusion: time for a consensus?

Almost 70 years after its first application and despite the lack of an alternative option, WLL performance and efficiency continues to rely mostly on local expertise and experience. Yet, as the available database knowledge is increasing (especially after 1990) and the indication for WLL include more and more conditions (i.e., pneumoconiosis, silicosis, lipoid pneumonia), it may be the time for a guideline or for a minimum consensus upon to improve future procedure's safety and efficiency and facilitate everyday clinical decision-making.

Conflict of interests

The author has no conflict of interest.

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