Pulmonary alveolar proteinosis and successful therapy with combined lavage procedures: Case reports

NALAN DEMİR FIRAT¹, AYDIN ÇİLEDAĞ¹, PINAR AKIN KABALAK¹, DEMET KARNAK¹, BAŞAK CEYDA MECO², ZEKERİYYA ALANOĞLU² and NESLİHAN ALKIŞ²

Departments of¹Chest Diseases, ²Anesthesiology, Ankara University School of Medicine, Ankara, Turkey

Received February 2, 2011; Accepted March 16, 2011

DOI: 10.3892/etm.2011.230

Abstract. Pulmonary alveolar proteinosis (PAP) is a rare disease characterized by the accumulation of lipoproteinaeous material within alveolar spaces. Whole-lung lavage (WLL) has been the most common therapeutic intervention for this disorder. However, patients presenting with PAP are usually hypoxic or in poor clinical condition, and WLL may be impossible to perform. In such cases, multiple segmental lavage (MSL) may be advocated as a first-choice therapy prior to WLL. Herein, we present two cases with idiopathic PAP treated successfully with both lavage techniques consecutively. After the MSL procedure, WLL was performed, and both patients showed a marked clinical and physiologic improvement. Therefore, for patients who are not good candidates for general anesthesia, we recommend MSL (or ‘prewash’) before WLL to produce an increase in the blood oxygen level for long-duration general anesthesia. In the surgical room, close monitoring and repositioning of the patient as well as maintenance and inspection of the correct tube position, and manual chest wall percussion are extremely important for the safety and success of the procedure.

Introduction

Pulmonary alveolar proteinosis (PAP) is a rare disorder first described in 1958 by Rosen et al. (1). Alveolar spaces are progressively filled with a phospholipoproteinaceous material presumably caused by malfunction of the balance between surfactant production by type II pneumocytes and surfactant removal. The latter is affected primarily by alveolar macrophages. A diagnosis of PAP can be confirmed by typical histopathological findings of lung biopsy specimens or the appearance of bronchoalveolar lavage. Whole-lung lavage (WLL) introduced by Ramirez in the late 1960s, is still the gold standard therapy (2). Therapy with granulocyte macrophage colony-stimulating factor (GM-CSF) is another option, but its long-term safety has not yet been confirmed (3). The severity and natural history of alveolar proteinosis is variable, and severe hypoxemia may occur during the course of the disease. In patients with poor clinical condition and hypoxemia, WLL is difficult to perform due to possible complications involving general anesthesia. WLL often requires more than 4 hours per lung to perform (4). For surgery, the time is longer, and complication rates can be high. In these patients, multiple segmental lavage (MSL) with flexible bronchoscopy (FB) can be initially carried out to prepare the patient for the long-lasting general anesthesia required for WLL.

Materials and methods

Multiple segmental lavage. In our technique, FB is wedged as accurately as possible in all of the segments without error during the procedure. Before and during MSL, 2% xylocaine and low-dose parenteral sedation with midazolam and phen-tanyl are administered. In general, the lavage is preferably carried out on the lung part or lobe noted to have the most extensive accumulation as determined by radiology. In the surgical room, close monitoring and repositioning of the patient as well as maintenance and inspection of the correct tube position, and manual chest wall percussion are extremely important for the safety and success of the procedure.

Whole-lung lavage. In our technique, WLL of the preferred lung is performed under general anesthesia via isolation of the two lungs with a double-lumen endotracheal tube. Performance of single-lung ventilation lasts for a duration of 5 to 10 hours. The correct positioning of the tube is confirmed by fluoroscopy and fiberoptic bronchoscopy. Invasive arterial access for frequent blood gas analysis and continuous blood pressure monitoring should be carried out in addition to routine anesthesia monitoring which consists of O₂ saturation, CO₂ level and gas analysis and ECG. Two large bore (18-G)
IV access sites are initiated immediately after induction of anesthesia for rapid infusion of fluids. Central venous access is not preferred due to the risk of pneumo-hemothorax during the insertion of the catheter. Anesthesia induction can be performed with propofol 2 mg/kg, remifentanil 1 µg/kg, and rocuronium 0.6 mg/kg, and management is recommended to be continued with sevoflurane 2% in 50% oxygen/50% air, remifentanil 0.01 µg/kg IV bolus, when needed. Hemodynamic and respiratory parameters of the patient should be monitored throughout the procedure. Both lungs should be ventilated with 100% oxygen for 10 min for the denitrogenation process. The isolation of each lung is confirmed by water seal testing. Since the residual nitrogen bubbles can diminish the access of lavage fluid to the alveolar space and consequently the efficacy of WLL, after separation of the lungs, the lumen of the endotracheal tube leading to the lung to be lavaged is clamped proximally at the end of expiration (at functional residual capacity) for 5 min to achieve adequate degassing. Warmed isotonic saline solution at 37°C is then instilled by gravity 50 cm above the carina. After filling the lung with approximately 800 ml of saline, the lavage process consists of slowly instilling 500-ml aliquots in each cycle via a catheter. Manual chest percussion should be performed throughout the procedure as it has been noted that chest wall percussion enhances the removal of proteinaceous material. During the procedure, the position of the patient can be changed from supine to left or right lateral position intermittently. The average procedure lasts approximately 5-10 hours. An average range of 12 to 20 liters of warmed saline should be used, and lavage should be discontinued when the returning fluid becomes clear. The patient can be repositioned several times to a lateral decubitus position in relation to the non-lavaged lung. The major concerns which should be considered during repositioning of the patient include the possible malpositioning of the double-lumen tube and ischemic complications of the extremities. Extra precautions should be taken to prevent these complications by checking the positioning of the tube, monitoring the airway pressure changes, air leakage and placing supporting pillows under the thighs, head and axilla.

Case reports

Case 1. A female patient, 31 years of age, was admitted to the hospital with exertional dyspnea experienced for two years. She had a three pack-year history of smoking. Her dyspnea had progressively increased, and hemoptysis and cough had developed one month earlier. She had never been exposed to occupational dust, and her past medical history was unremarkable. On physical examination, her pulse was 122/min and respiratory rate, 28/min. Bilateral crackles were audible at both lung bases. On laboratory analyses, the white cell count was 9100/mm³, the erythrocyte sedimentation rate (ESR) 8 mm/h and lactate dehydrogenase was 523 mg/dl (normal range (N), 240-480). Cholesterol and triglyceride levels were 219 mg/dl (N, <200 mg/dl) and 164 mg/dl (N, <150 mg/dl), respectively. Blood gas analysis showed moderate hypoxemia (PaO₂, 49.2 mmHg). Pulmonary function tests revealed a restrictive pattern with a reduced DLCO (55%) value. A chest X-ray detected bilateral opacities at the mid-lower zones (Fig. 1). A thoracic high resolution computerized tomography (HRCT) revealed bilateral diffuse ground glass opacities and interlobular septal thickening. Bronchoalveolar lavage (BAL) fluid revealed a milky turbid appearance. A transbronchial
lung biopsy (TBLB) was taken, and histopathologic examination revealed PAS (+) lipoproteinaceous material deposition (Fig. 2). Accordingly, a diagnosis of PAP was made. WLL was planned; however, due to the poor clinical condition of the patient with hypoxemia and her relatively high-risk profile, she was not considered as a suitable candidate for general anesthesia. Therefore, MSL under local anesthesia was performed. A total of 2000 ml saline was instilled, and approximately 1600 ml was aspirated from the right lung. MSL lasted approximately 1 hour without any complication. Following MSL, the PaO₂ level increased to 60.3 mmHg on breathing ambient air and remained stable until the WLL procedure scheduled a few days later. The patient was re-evaluated and consequently scheduled for general anesthesia.

In total, 13 liters of warmed saline solution were instilled, and 12 liters were obtained (Figs. 3 and 4). Immediately after the procedure, the double-lumen tube was replaced with a single-lumen tube by an anesthesiologist. The patient was transferred to the ICU, and mechanical ventilation was continued for 12 hours. There was no complication except mild hypokalemia and metabolic acidosis.

After one month, WLL of the right lung was performed using the same technique mentioned above. During WLL, severe hypoxia (SpO₂ <70%) and an increase in airway pressure (40 cmH₂O) developed 2 hours after the initiation of the single-lung ventilation due to malpositioning of the double-lumen tube. The patient was immediately extubated and reintubated with the double-lumen tube, and correct positioning of the tube was confirmed by fluoroscopy and fiberoptic bronchoscopy. The rest of the procedure was uneventful. In this second procedure, a total of 12 liters of saline was instilled, and 11 liters was drained without any complications. After these combined lavage procedures, marked clinical, physiological and radiological improvements (Fig. 5) were observed. PaO₂ and diffusion capacity increased to 85 mmHg and 75%, respectively (Fig. 6).

Case 2. A female, 44 years of age, was admitted to the hospital with exertional dyspnea for a one-year period. She had a five pack-year history of smoking and had worked in a cloth factory for five years. There was no significant exposure to organic or inorganic material. On physical examination, her pulse and respiratory rate were 76/min and 26/min, respectively. Bilateral crackles were audible at both lung bases. On laboratory analyses, the white cell count and ESR were normal. The blood gas analysis showed hypoxemia (PaO₂, 56 mmHg), and pulmonary function tests revealed a restrictive pattern with a decreased value of DLCO (58%). Chest radiograph revealed bilateral infiltrations at the mid-lower zones (Fig. 7) and thoracic HRCT showed bilateral diffuse ground glass opacities and interlobular septal thickening showing a crazy paving pattern. Bronchoalveolar lavage fluid revealed a milky turbid appearance. The diagnosis of PAP was established by open lung biopsy.

A combined lavage procedure was planned as in case 1. MSL was performed using a total of 2600 ml warmed saline for the right lung and 2300 ml for the left lung until blood gases became high enough (above 60 mmHg) for general anesthesia. Two WLL procedures were performed separated by an interval of 1 month. The first WLL was carried out using

Figure 5. Radiological resolution after therapy in case 1.

Figure 6. Oxygen pressure readings of cases 1 and 2 indicating the success of the combined lavage procedures.

Figure 7. Chest X-ray on admission revealing bilateral infiltration at the middle and lower zones (case 2).

Figure 8. Drained fluids of one lung obtained by WLL in case 2.
Pulmonary alveolar proteinosis is a rare disorder characterized by the accumulation of lipoproteinaceous material within the alveolar compartment (1). PAP is classified as congenital, secondary and idiopathic. The pathophysiology of PAP is characterized by several mechanisms; surfactant protein B mutations and granulocyte monocye colony-stimulating factor receptor defects, inability of the macrophage to catabolize surfactant, and the presence of certain systemic disorders and exposure to various materials. Idiopathic PAP is rare, with a prevalence of 0.37/100,000 individuals, yet it constitutes 90% of all cases (5,6). Surgical lung biopsy is the gold standard for the diagnosis of PAP, but in an appropriate clinical setting, a diagnosis can be confirmed by BAL and/or TBB (7). In this report, the diagnosis of PAP was made by TBLB in case 1 and surgical lung biopsy in case 2. According to the aforementioned descriptions, these two cases were determined to be idiopathic PAP lacking a secondary reason.

Discussion

Whole-lung lavage is now considered to be the most effective treatment for PAP (4,15-16). There are no standard indications for WLL, although the following criteria have been proposed: daily life activity-impairing dyspnea, \( \text{PaO}_2 \leq 60 \text{ mmHg} \) and shunt fraction >10-12% (6). The major adverse effect of WLL is hypoxemia that can be improved with a high inspired oxygen concentration. Hemodynamic changes can also occur with single-lung ventilation which may necessitate invasive monitoring during the procedure. The major risks of WLL concern the correct placement of the double-lumen endotracheal tube. In the case of wrong replacement, spilling of fluid from the lavaged lung to the ventilated lung can occur. Other complications include pleural collections, hydropneumothorax, barotrauma and hypothermia. Due to these potential complications and since the patients are usually hypoxemic and in poor clinical condition, WLL is frequently impossible to be performed. In such cases, multiple segmental or lobar lavage by FB has been reported as a possible alternative to WLL. In several case reports, it has been reported that MSL is a simple and safe procedure which has led to an improvement in PAP (3,17). However, the fluid yielded by this method is small, and the volume of lavage fluid is limited. Hence, it is useful for patients with less advanced disease (3). In contrast, our cases had advanced disease and poor clinical condition with hypoxemia, thus they were not good candidates for therapy with MSL alone. MSL was carried out initially in order to prepare the patients for WLL. Although there have been many publications, there is no published report of the use of MSL and WLL together in the same case.

Cheng et al reported three cases treated with MSL under local anesthesia (3). They instilled warm saline solution via a syringe in 50-ml aliquots at the orifice of the lobar bronchus and all segments which was removed by suction. They stopped the procedure when the returning fluid became clear or the patient could no longer tolerate the discomfort. They repeated the procedure two to five times, and in each procedure, one lobe was lavaged. The volume of instilled fluid for one lobe was changed from 1700 to 2050 ml. In contrast, since our main aim was to prepare patients for WLL, we instilled the same volume of solution, and we discontinued the procedure earlier as the aspirated fluid became bright. After MSL or ‘prewash’, in both cases, we observed clinical and physiological improvements with an increase in \( \text{PaO}_2 \) level. Thus, WLL was subsequently performed.

There are several important concerns when performing WLL. The first step should include appropriate degassing of the lung to be lavaged. Preoxygenization prior to degassing is very important to ensure replacement of alveolar nitrogen with oxygen, as residual bubbles can diminish the access of lavage fluid to the alveolar space and consequently the efficacy of WLL. In the presented cases, adequate degassing was noted. Second, performing chest percussion can enhance the removal of the accumulated material (18). Hammon et al reported that during WLL, manual chest percussion is superior to mechanical percussion (19). Indeed, in case 1, the initial fluid returns were typically milky, but after the fifth cycle, the fluid became clearer (Figs. 3 and 4). Then, manual chest percussion was performed, and we observed that the manual percussion enhanced the removal of proteinaceous material making the receiving fluids turbid again. Therefore, we strongly recommend manual chest percussion throughout the procedure. We halted the procedure when the returning fluid became clear. After WLL, in both patients, marked clinical and physiological improvements were noted without any serious complications (Fig. 6).

Anesthesia for WLL is a challenging procedure for several reasons. As discussed above, these patients are commonly associated with severe hypoxia increasing the anesthesia-associated risks. The risk of pneumothorax is also increased. Moreover, single-lung ventilation is required for anesthesia.
for WLL. Single-lung ventilation increases the risk of shunting, hypoxia and carbon dioxide retention. Pre-existing respiratory failure exacerbates the detrimental effects of single-lung ventilation. In addition, alveolar lavage leads to more ventilation-perfusion mismatch. An extensive evaluation is required during the recruiting phase to evaluate whether the patient is able to undergo WLL under general anesthesia. Possible complications should be discussed with the patients and relatives. The anesthesiology team should be familiar with lung separation and single-lung ventilation techniques, possible complications and pathological changes during long-lasting anesthesia procedures (20). In the present cases, patients were strictly examined and evaluated for their ability to undergo general anesthesia. Moreover, after the initiation of general anesthesia, proper monitoring was started and close hemodynamic and respiratory data were obtained. Positioning of the double-lumen tube was confirmed several times during the procedure. These measures were the determining factors for the successful outcome of the patients during the immediate postoperative period. Without any doubt, the successful outcome of WLL requires close collaboration of the thoracic physicians and the anesthesiology team.

In this report, we described our experience using combined lavage techniques for the management of PAP. MSL, or ‘preshash’, is recommended for hypoxemic patients prior to WLL to improve oxygenation. These two techniques (MSL and WLL) can be used consecutively in patients with PAP who are initially unable to undergo general anesthesia. Several precautions should be taken in the surgical room for the safety and the success of the procedure such as close monitoring and repositioning of the patient, maintenance and inspection of the correct tube position, and manual chest wall percussion.

References