Whole-lung lavage for severe pulmonary alveolar proteinosis assisted by veno-venous extracorporeal membrane oxygenation: a case report

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INTRODUCTION

First reported in 1958, pulmonary alveolar proteinosis (PAP) is an extremely rare disease characterized by accumulation of phospholipoproteinaceous material within the alveoli. The evolution of PAP is variable and treatment modalities are limited. Pharmacological therapeutic targets are being actively developed, but whole-lung lavage (WLL), first described in the 1960s, remains the cornerstone of therapy. The preferential treatment for PAP in our center is sequential WLL, where each lung is separately and sequentially perfused with warmed saline. However, some patients do not tolerate single lung ventilation (SLV), as there is a greater evolution of PAP is variable and treatment modalities are limited. Pharmacological therapeutic targets are being actively developed, but whole-lung lavage (WLL), first described in the 1960s, remains the cornerstone of therapy. The preferential treatment for PAP in our center is sequential WLL, where each lung is separately and sequentially perfused with warmed saline. However, some patients do not tolerate single lung ventilation (SLV), as there is a greater

Key Words: extracorporeal membrane oxygenation; pulmonary alveolar proteinosis; whole-lung lavage

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was performed and a Periodic acid–Schiff positive lipoproteinaceous material was detected. The presence of serum anti-GM-CSF antibodies suggested an autoimmune background; however, the presence of a significant silica exposure should be considered at least as potential trigger for the disease. Since the HRCT scan showed bilateral consolidations (Figure 2), with significant predominance in left lung, a scintigraphy was performed that revealed severe functional asymmetry with a left-to-right perfusion relationship of 19:81% (Figure 3). Because of the progressive worsening of exertional dyspnea, severe hypoxemia, and asymmetric ventilation-perfusion not allowing SLV, ECMO-assisted WLL was proposed to the patient.

After noninvasive monitoring with electrocardiograph, noninvasive blood pressure measurement, and pulse oximetry, the patient underwent total intravenous anesthesia with propofol and fentanyl; muscular relaxation was achieved using rocuronium. Selective intubation was performed with a 39F left double-lumen endobronchial tube introduced into the left mainstem bronchus controlled by bronchofibroscopy. Radial arterial and jugular venous catheters were placed and enabled continuous hemodynamic monitoring. A bolus of heparin (2000 I.U.) was administered prior to cannulation for the VV-ECMO. The infusion (50-cm-long 21-Fr; Medtronic, Minneapolis, USA) and drainage (55-cm-long 25-Fr; Maquet-Cardiopulmonary-AG, Hirrlingen, Germany) cannulae were placed percutaneously by Seldinger technique in the right and left femoral veins, respectively. VV-ECMO was initiated using a miniatuized, compact ECMO circuit with continuous pressures and venous saturation monitoring (HLS Set Advanced 7.0; Maquet-Cardiopulmonary-AG), with an initial blood flow of 3.44 L per minute and a sweep gas (100% oxygen) flow of 2.0 L per minute (Figure 3).

Pulmonary lavage was performed with instillation and drainage of 1000 mL of warmed saline (37°C) in each lung at a time, through gravity with the patient being positioned in the reverse Trendelenburg and Trendelenburg positions, respectively. This procedure was repeated 6 times in the left lung and 14 times in the right lung. The fluid collected was initially white and cloudy, and it progressively became clearer. The FiO₂ values on ECMO were determined according to the patient PaO₂ and varied between 0.6 and 0.8 for the duration of the procedure. The left lung was rinsed with 2400 mL of warm saline with 510 mL being absorbed over 40 minutes, and the right lung was rinsed with 15,700 mL of warm saline with 600 mL being absorbed over 90 minutes. During the 180 minutes of the procedure, several incidents of hypotension were registered, mostly related to vigorous pulmonary saline inflow. They were spontaneously reversed and did not require any intervention. Temperature and electrolyte levels were uneventfully monitored throughout the procedure. Diuresis was stimulated using furosemide (10 mg).
After completion of the bilateral lung lavage, the patient was reintubated with an endotracheal tube size 8.5 and the remaining fluid was removed from the lungs bronchoscopically. The sedated and mechanically ventilated patient remained hemodynamically stable and was admitted to the intensive care unit (ICU) with continued support of the VV-ECMO. Given the clinical stability and absence of complications, the patient was weaned off ECMO 2 hours after WLL. Lower-limb Doppler sonography was performed and deep venous thrombosis of the cannulated vessels excluded. The patient was extubated four hours after ICU admission and was discharged to the ward 24 hours later. He improved clinically and functionally with resolution of the respiratory failure ($pO_2$ 71 mmHg, $FiO_2$ 21%) and was discharged after two days with no further complications.

**DISCUSSION**

The evolution of PAP is variable and treatment modalities are limited. WLL remains the gold-standard therapy as it provides long-lasting benefits in most patients [12]. WLL is usually well tolerated, as shown in previous studies [7, 10, 12], partially because auto-immune PAP is the most common form and patients normally do not have significant structural damage of lung parenchyma. In our center, the reference site for all patients that present with PAP in northern Portugal, the preferential treatment for PAP is sequential WLL with SLV. A total of 18 WLL have been performed with no major complications [7]. In this clinical case, however, PAP was associated with silicosis and bilateral consolidations, more extensive in the left lung, which was demonstrated by severe ventilation/perfusion impairment in lung scintigraphy. The patient wasn’t able to tolerate SLV, because there is a greater risk of severe hypoxemia with this method. In these extremely rare cases of high-risk patients, ECMO-assisted WLL becomes a valid alternative [10, 13], as it allows the WLL to be performed without lung ventilation. We chose the VV-ECMO modality because of its lower rate of complications when compared with venoarterial ECMO [14]. Moreover, VV-ECMO could improve pulmonary arterial oxygenation, reducing pulmonary hypertension [15].

We agree with other reports about the importance of lavage being performed in both lungs in the same session as it improves the outcome [10], and we also believe it is safer to perform lavage of one lung at a time, as it minimizes the risk of hemodynamic instability. The saline infusion used for lavage was warmed up to 37°C, to mitigate the risk of cardiac arrhythmias, as shown in previous reports [16].

Despite its higher costs and associated risks, bilateral WLL with the support of VV-ECMO proved to be an effective and safe treatment in patients with PAP with severe hypoxemia that precludes the WLL method with SLV. Since these cases are extremely rare, published data are scarce and the ideal protocol has not yet been established. Future prospective studies are warranted.

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