

Whole Lung Lavage of Nine Children with Pulmonary Alveolar Proteinosis: Experience in a Tertiary Lung Center

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Abstract

Background: Pulmonary alveolar proteinosis (PAP) is a rare disease in children, characterized by intra-alveolar accumulation of large amounts of surfactant proteins, which severely reduce gas exchange. Whole lung lavage (WLL) is the preferred technique for the treatment of severe PAP.

Case Presentation: This report presents nine pediatric cases with advanced PAP who underwent WLL under general anesthesia during a 9 year period. One patient was treated with multiple unilateral WLL without employing cardiopulmonary bypass (CPB) and eight cases were treated by simultaneous lavage of both lungs using partial CPB.

Conclusion: Our experience suggested that partial CPB was useful to support oxygenation during WLL in small children with severe PAP in whom lung separation and selective lavaging of each lung were impracticable.

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Key Words: Pulmonary Alveolar Proteinosis; Children; Cardiopulmonary Bypass; Whole Lung Lavage

Introduction

Pulmonary alveolar proteinosis (PAP) is a rare lung disease in children, with only a limited number of cases reported in the literature. The disease is characterized by alveolar filling with surfactant-associated lipids and proteins, with resultant impaired gas exchange. It has a variable clinical course, from spontaneous improvement to respiratory insufficiency and death due to disease progression or recurrent episodes of pneumonia [1,2]. Removal of the lipoprotein material by whole lung lavage (WLL) is the only effective

treatment for severe cases. It is performed by introducing warm normal saline solution into the lungs and draining a fluid, which removes the lipoprotein material [3]. However, typical WLL by using double lumen endotracheal tube (DLT) to selectively lavage one lung while ventilating the other is most often impracticable in small children. Alternatively, cardiopulmonary bypass (CPB) seems to be helpful to support oxygenation during WLL in small children with PAP when lung lavage cannot be otherwise safely performed [4-6].

We report our experiences with nine pediatric cases of severe PAP treated by WLL under general

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anesthesia either with or without using partial CPB (PCPB) during a 9 year period from 2000 to 2009 in Masih Daneshvari university teaching hospital. PAP was diagnosed in all patients by open-lung biopsy. All subjects presented with life-threatening respiratory insufficiency and progressive patients' disability.

Case Presentation

After placement of standard monitorings, anesthesia was induced with thiopental, midazolam and fentanyl followed by atracurium to facilitate tracheal intubation with a proper size of cuffed single-lumen endotracheal tube and the lungs were mechanically ventilated with 100% oxygen. Then, the radial artery was cannulated for continuous measurement of systemic blood pressure and for obtaining arterial blood gas samples. Anesthetic maintenance consisted of isoflurane with titrated doses of fentanyl and atracurium. The cardiovascular surgical team then inserted the vascular catheters for PCPB without sternotomy in the fully heparinized patient. Activated clotting time was used to monitor coagulation status during CPB. PCPB was commenced while the heart was beating. As the patients' condition was stabilized, ventilation of lungs discontinued and both lungs were lavaged simultaneously in the supine position with 500 ml warm normal saline in each cycle. If severe hypoxemia was encountered, the lavage was interrupted, mechanical ventilation of the lungs

reinstated with 100% oxygen, the instilled fluid was drawn out, and if necessary, the vascular catheters were repositioned. After clearance of returning fluid, WLL was terminated and both lungs were ventilated receiving FIO₂ of 1.0. After reversal of heparin with protamine, PCPB was removed and the patients were transferred directly to the intensive care unit (ICU) and mechanically ventilated. Table 1 shows patients' data.

Case 1

An 11 year-old girl treated with multiple unilateral lavaging of each lung without CPB. At the first lavage, due to unavailability of the proper size of DLT and severity of the disease we lavaged the right lung by our invented method. Following induction of general anesthesia a 4.5 univent tracheal tube was inserted and the cuff of bronchial blocker was positioned at right main bronchus under fiberoptic bronchoscopic guide and positive pressure ventilation was established with FIO₂ 1.0. In order to independently ventilate the left lung during lavage of right lung, an 8 French sized nasogastric tube was inserted along with the univent tube to reach the distal end of the right main bronchus with bronchoscopic visualization. The right lung was lavaged by multiple instillation of warm normal saline via the nasogastric tube while the left lung was ventilated with 100% oxygen. The patient was stable during the 9 hours procedure. Following clearance of aspirated fluid, the univent tube was exchanged for a single lumen tracheal tube. After eight days, the left lung was lavaged uneventfully under one lung ventilation anesthesia using a 26 left DLT.

Table 1: Characteristics of 9 children with pulmonary alveolar proteinosis managed by whole lung lavage

Case	Sex	Age (yr)	Disease duration	WLL on PCPB (n)	WLL without PCPB (n)	Complications during lavage	Follow up duration (yr)	Final outcome
1	F	11	2 yr	0	4		9	remission
2	M	4	2 yr	2	0	severe hypoxia episodes	2	remission
3	M	5	3.5 yr	2	0	severe hypoxia episodes	no	no information
4	M	4	1.5 yr	2	0		5	remission
5	F	4.5	2 yr	1	0	fatal pulmonary bleeding	—	early PO death
6	F	7	1.5 yr	1	0		2	remission
7	M	5	8 mo.	1	0		1	remission
8	F	6	5 mo.	2	2		3	recurrence
9	M	6.5	2 yr	1	0		no	death

F: female, M: male. WLL: whole lung lavage, PCPB: partial cardiopulmonary bypass, mo: months, yr: years, po: post-operative.

Lavage of the right lung and the left lung was again conducted successfully with a similar procedure 2 and 4 months later, respectively. At present (at the age of 20), she has no evidence of PAP recurrence.

Case 2

A 4 year-old boy in whom an already unsuccessful bronchoalveolar lavage by fiberoptic bronchoscopy was complicated by cardiac arrest in another hospital, was admitted to our center. In the operating room, simultaneous lavaging of both lungs was performed after initiation of CPB via right femoral artery (RFA) and vein (RFV) cannulation. Due to repeated dangerous hypoxemia and insufficient venous return, the lavage was discontinued and mechanical ventilation of the lungs reestablished and oxygenation was restored. With advancement of the vascular cannulas to the right atrium and aortic arch for optimal drainage, 10 cycles of lavage of the both lungs were performed within 4 hours. His oxygenation improved and he discharged from the hospital 9 days after procedure. 6 months later, a similar 7 hours procedure was done. After 6 months, the patient was readmitted 2 times for pneumonia and medically treated. In the following 1.5 years the patient has maintained a satisfactory respiratory status.

Case 3

PCPB was established through the RFA and RFV in a 5 year old boy and an acceptable level of oxygenation was preserved during thirteen lavage cycles. Because of recurrence of the disease in 6 months, the second WLL was done using PCPB following cannulation of the right carotid artery (RCA) and the right internal jugular vein (RIJV). Postprocedure oxygenation markedly improved and the patient was discharged one week later. He did not return for further visit any more.

Case 4

A 4 year old boy underwent an uneventful 6 hour-lasting twelve lavage cycles using PCPB through RCA and RIJV. His serious respiratory symptoms recurred 3 months later following a severe flu like syndrome and again he uneventfully underwent the second WLL using the same method. The patient has been symptom-free during 5 years of regular follow up.

Case 5

In a 4.5 year old girl with preoperative prolonged prothrombin time and international normalized ratio (INR) (16.8 seconds and 1.9, respectively), PCPB was established through insertion of RFA and RFV catheters. After seven lavage cycles with a total of 1.8 L of warm normal saline, returning fluid unexpectedly became bloody, the patient desaturated intensely, and hematuria occurred subsequently. So, the lavage was quickly stopped, mechanical ventilation was restored with FiO₂ of 1.0, the lavaged lungs were emptied and the patient maintained on CPB to support oxygenation. However, PaO₂ was 40mmHg, SaO₂ 69%, and PaCO₂ 65 mmHg with a severe metabolic acidosis. After reversal of heparin and separation of the PCPB, the patient was transferred to ICU and controlled mechanical ventilation was maintained while she received vasopressor and inotrope support. Laboratory tests showed a normal platelet count ($148 \times 10^3/\mu\text{L}$) and Hb (12gr/dl). Fresh frozen plasma and packed red blood cells were transfused to treat bleeding. However, bright frothy blood continued through endotracheal tube, PaCO₂ increased to 160 mmHg, PaO₂ decreased to 29 mmHg, metabolic acidosis worsened and the patient died 36 hours after the procedure.

Case 6

After cannulation of RFA and RFV and establishment of PCPB, ten WLL cycles was performed in a 7 year old girl without any serious events and extubated 36 hours later. She remained asymptomatic during a 2 year follow-up.

Case 7

A 5 year old boy received twelve cycles of uneventful WLL following cannulation of femoral artery and vein and initiation of PCPB. The patient was extubated within 24 hours thereafter. One year follow up showed no recurrence of the disease.

Case 8

A 6 year old girl underwent first ten cycles of WLL with using PCPB without complication. Catheters were introduced in the RIJV and in the RCA. 4 months later, the patient suffered another progressive respiratory impairment. We attempted the second WLL with the same method

and the patient remained stable throughout the procedure. She was discharged from the hospital after 5 days, with a marked improvement of her functional class. 2 months later, the third lavage was done on both lungs without PCPB due to recurrence of the disease. Under anesthesia, a 6 mm cuffed single lumen endotracheal tube was placed. Then under fiberoptic bronchoscopic guidance a bronchial blocker was advanced into the targeted main bronchus to achieve lung separation. The patient remained stable throughout the procedure, which allowed bilateral sequential WLL in the same session. She was discharged 11 days later.

At age 9, weight 22 kg, she underwent the fourth WLL due to marked decreased exercise tolerance, severe hypoxemia and cyanosis. This time a 28 DLT was intubated under general anesthesia in order to selectively ventilate and lavage each lung. First the left lung and then the right lung was lavaged independently. The patient tolerated the procedure quite well. She was discharged 2 days later after a marked improvement of her functional class. At present (2 years after last WLL) the patient requires further lung lavage due to recurrence of the illness.

Case 9

A 6.5 year old boy received 12 cycles of WLL on PCPB via femoral artery and vein cannulas. Weaning process was done successfully in the ICU and he discharged from the hospital 3 days later. 8 month follow up was accompanied with a normal life. He died from severe pulmonary infection and hypoxemia 13 months after lavage.

Discussion

PAP is a rare disease in children which can progress to fatal respiratory insufficiency with a reported mortality rate of more than 75%^[7-10]. WLL remains the only effective treatment for severe cases. By WLL, progression of the disease is inhibited in about one third of patients, whereas another one third may require multiple WLL, or the disease may progress to chronic interstitial lung disease or respiratory failure in others^[3].

Techniques for WLL in PAP children should be

determined according to their age, weight and severity of the disease^[6,11]. In adults and older children, WLL can be performed using DLT and one lung ventilation anesthesia. But, this method is technically difficult in small children because the small size of trachea does not allow use of DLT, hence inability to ventilate one lung adequately during lavage of other lung. Alternatively, WLL utilizing CPB was successfully used in this critical age group to support oxygenation during lavage^[4-6]. However, this risky procedure needs expert and cooperative anesthesia and cardiovascular surgery team with a complete familiarity with pulmonary physiology.

Sear et al successfully applied PCPB to support total lung lavage for PAP children in whom the use of DLT was impossible^[12]. Similarly, we performed simultaneous bilateral WLL with the support of peripheral veno-arterial bypass in 8 PAP children because their tracheal size did not permit the use of DLT or bronchial blocker. However, this procedure is technically challenging in children, and potential for serious complications makes the procedure risky in the most severe cases. Absence of ventilation during lavage is the leading cause of desaturation. Furthermore, problem of cannulation techniques may compromise venous return to the CPB circuit, resulting in dangerous hypoxemia, hemodynamic instability or fatal complications. In our experience, inappropriate vascular cannulation techniques resulted in episodes of severe hypoxemia in 2 cases during lavage. In case 5, uncontrolled pulmonary bleeding caused immediate postoperative death. In our opinion, some factors including preoperative disturbance of coagulation function, CPB-related coagulopathy, and heparin anticoagulation contributed to lethal pulmonary bleeding in this patient.

Overall, 7 patients tolerated the procedures relatively well and were successfully separated from bypass. The trachea of all patients was extubated within the day after procedure and they had good post lavage conditions, although one patient died from pulmonary infection 13 months after the procedure. On the other hand, some authors described different methods of unilateral WLL in pediatric patients with PAP by selectively isolating each lung^[13-16]. Likewise, our first older child was successfully treated with a series of unilateral pulmonary lavages without CPB using a

method similar to adult patients^[17]. Also, in the case number 8 two more bilateral sequential WLL without employing PCPB was safely performed in the same session when she grew older.

Alternatively, extracorporeal membrane oxygenation has been effectively used in small children with PAP to avoid hypoxemia during WLL^[18,19]. Recent studies have also implicated GM-CSF but the exact underlying mechanisms are still unclear^[8,20].

Since hypoxemia and infection are the most significant factors influencing the outcome of PAP patients^[4,18], a life-time regular outpatient follow up program for timely diagnosis and treatment of recurrence of the disease and pulmonary infections play a vital and essential role in the patients' outcomes after WLL. However, most of our patients did not cooperate in the planning of regular visits.

Conclusion

Our experience suggested that PCPB was useful to support WLL in small children with advanced PAP when lung lavage cannot be otherwise safely performed.

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