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CLINICAL REPORT

Combination of extracorporeal membrane oxygenation and high-frequency oscillatory ventilation saved a child with severe ARDS after pulmonary resection

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Abstract We report a case in which a 2-year-old girl who underwent a right middle and lower lung lobectomy for congenital cystic adenomatoid malformation suffered massive bleeding and developed acute respiratory distress syndrome (ARDS) during the operation. She was ventilated with a high level of F_IO_2 (0.75–1.0), PEEP (10–20 cmH_2O), and PIP (33–55 cmH_2O) to maintain SPO_2 (>90%). Following transfer to the ICU, continuous hemodialysis was introduced to reduce excessive blood volume. However, pulmonary oxygenation did not improve, and marked subcutaneous emphysema occurred on postoperative day 3 (POD 3). We introduced veno-venous (V-V) extracorporeal membrane oxygenation (ECMO) to rest the lung, and V-V ECMO was changed to right and left atrial ECMO because of unsatisfactory oxygen support on POD 23. A CT scan showed almost the entire lung had collapsed, even though we had administered diuretics, steroids, nitric oxide, sivelestat, and surfactant for ARDS. We applied high-frequency oscillatory ventilation (HFOV) with a mean airway pressure of 20 cmH_2O, frequency of 9.2 Hz, and amplitude of 38 cmH_2O on POD 45. The collapsed lung was then gradually recruited, and pulmonary oxygenation improved (P/F ratio = 434). ECMO was successfully weaned on POD 88. The patient required a tracheostomy, but she was able to function without a ventilator on POD 142. Although HFOV has failed to show a mortality benefit in ARDS patients, the unique lung recruitment by HFOV can be a useful therapeutic option for severe ARDS patients in combination with sufficient lung rest produced by ECMO.

Keywords Extracorporeal membrane oxygenation · High-frequency oscillatory ventilation · ARDS · Postpneumonectomy pulmonary edema

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Introduction

Lung injury following pulmonary resection with no identifiable cause, especially after pneumonectomy, has been termed postpneumonectomy pulmonary edema, and has alarmed both anesthesiologists and thoracic surgeons because of its high mortality rate, from 20% to as much as 100% [1, 2]. We report a case of severe acute respiratory distress syndrome (ARDS) following right middle and lower lobectomies in a 2-year-old patient suffering from congenital cystic adenomatoid malformation (CCAM). The patient was treated with extracorporeal membrane oxygenation (ECMO) for 86 days and high-frequency oscillatory ventilation (HFOV) for 50 days. She was subsequently discharged 253 days following the operation.

Case report

The patient was a 2-year-old girl weighing 10 kg scheduled for a lower lobectomy of the right lung for CCAM (Fig. 1a).

During the procedure, she had massive bleeding (>3,500 g) from the pulmonary vessels because of an unexpected adhesion between the middle and lower lobes. Eventually both middle and lower lobes were resected, but rapid and massive transfusion of red blood cells (RBC, 13 units), fresh-frozen plasma (FFP, 10 units), platelet concentrate (PC, 10 units), and 5% albumin (2,750 ml) was needed to maintain blood pressure. In addition, as there was severe pulmonary bleeding from the right lung and pulmonary edema with massive foamy sputa during the operation, her lung compliance gradually decreased. Although we considered introduction of ECMO during the procedure, vascular access could not be obtained in the left lateral position. Therefore, we applied a high fraction of inspired oxygen concentration (F_IO_2), 1.0, high positive end-expiratory pressure (PEEP), 20 cmH_2O, and high positive inspiratory pressure (PIP), 55 cmH_2O, to maintain hemoglobin saturation (SpO_2) above 90%. Following transfer to the intensive care unit (ICU), her blood pressure and heart rate were 130/85 mmHg and 160 bpm, respectively, with continuous intravenous infusion of epinephrine (0.3 μg/kg/min). There was a marked coarse crackle on auscultation, with massive foamy sputa, and marked air leakage was detected from the right lung. Transthoracic echocardiography showed a dilated right ventricle and relatively small but well-contracted left ventricle with flat interventricular septum, suggesting pulmonary hypertension. Her blood gas analysis showed pH 7.169, PaO_2 221 mmHg, $PaCO_2$ 46.8 mmHg, and base excess, –12.0 mEq/l. We applied continuous hemodialysis (CHD) to reduce excessive blood volume. However, as pulmonary oxygenation did not improve, we could not decrease F_IO_2, PIP, and PEEP to less than 0.8, 33, and 10 cmH_2O, respectively, by postoperative day (POD) 3. Subsequently, marked subcutaneous and

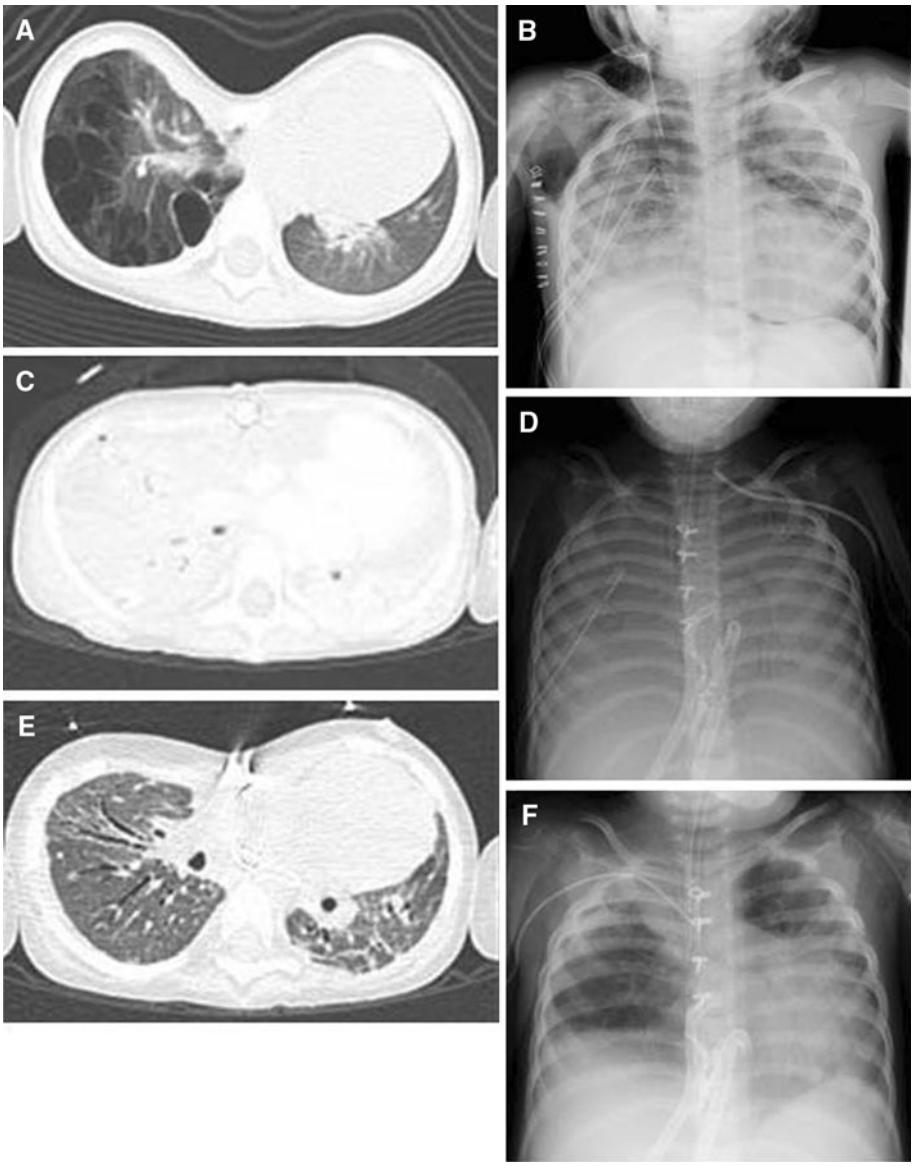

Fig. 1 Changes in computed tomography (CT) scan and chest X-ray images of lung conditions. **a** CT image before operation shows multiple cystic lesions in right lung and a funnel chest. **b** Chest X-ray shows subcutaneous and mediastinal emphysema. **c** CT image just after establishment of right atrial and left atrial extracorporeal membrane oxygenation (ECMO) on postoperative day (POD) 25: the entire lung was consolidated. **d** Chest X-ray before high-frequency oscillatory ventilation (HFOV) commencement on POD 45. **e** CT image before ECMO weaning on POD 83; although ground-glass opacity and traction bronchiectasis were still seen, lung inflation was obtained. **f** Chest X-ray before ECMO weaning on POD 86

mediastinal emphysema occurred on POD 3 (Fig. 1b). We therefore decided to introduce veno-venous (V-V) ECMO using percutaneous cardiopulmonary support (Capiox EBS; Terumo, Kanagawa, Japan) for oxygen support and lung rest with a double-lumen catheter (15 Fr.) cannulated in the right jugular vein. Even with the ECMO support with blood flow of 1.2–1.8 l/min/m^2, we could not reduce F_IO_2 to less than 1.0 to maintain PaO_2 above 60 mmHg. V-V ECMO was changed to right and left atrial (RA–LA) ECMO by right atrial blood withdrawal and left atrial blood supply to take advantage of maintained left ventricular function. The right and left atrial catheters (12 Fr. and 18 Fr., respectively) were sited by cardiac surgeons under general anesthesia on POD 23. It was found on a chest computed tomography (CT) scan taken on POD 25 that almost the entire lung was collapsed (Fig. 1c).

In addition to mechanical support, we tried several treatments for ARDS, including positional changes for dependent lung recruitment and drugs such as diuretics, methylprednisolone (2–0.5 mg/kg for 26 days), nitric oxide as a rescue therapy for pulmonary oxygenation (3–10 ppm for 13 days just after the operation), sivelestat sodium hydrate (0.2 mg/kg/h for 12 days), and lung surfactant (120 mg/kg), although those therapies have not been proved to improve the prognosis of patients with ARDS. None of these agents was sufficiently effective to wean the ECMO, and administration of steroid was ceased on POD 31 when severe phlegmon by methicillin-resistant *Staphylococcus aureus* was found in the right neck and inguinal regions where the cannulae for V-V ECMO were located. There had been no improvement in the collapsed lung on chest X-ray for 39 days since ECMO was introduced (Fig. 1d), and the tidal volume (TV) of the patient was almost 0 ml measured on pressure control ventilation with 18 cmH_2O PIP and 8 cmH_2O PEEP on POD 41 (Fig. 2). Therefore, we tried HFOV (3100B HFOV; VIASYS Healthcare) with mean airway pressure of 20 cmH_2O, frequency of 9.2 Hz, and amplitude of 38 cmH_2O just for 8 h on POD 42, and found a subtle increase in TV to 6 ml with the same ventilator conditions (Fig. 2). We decided on the continuous use of HFOV, and the collapsed lung was gradually recruited on CT scan and chest X-ray (Fig. 1e, f). Measured TV also increased up to 30 ml on POD 85 (Fig. 2). Improvement of pulmonary oxygenation was confirmed with a PaO_2/F_IO_2 ratio of 434 measured during a short cessation of RA–LA ECMO. ECMO was successfully weaned on POD 88. However, a serious cerebral and subdural hemorrhage with left hemiplegia occurred on POD 76, and emergency neurosurgical operations for removal of the hematoma and external decompression were performed, although we maintained ECMO with anticoagulants of nafamostat mesilate (15–20 mg/h) or heparin (200–600 units/h), depending on the possibility of bleeding complications, to maintain activated clotting time between 150 and 200 s. As shown on Fig. 2, we applied HFOV for 50 days, and 6 days following weaning from ECMO the ventilation mode was changed from HFOV to airway pressure release ventilation (APRV/Bivent) with two levels of continuous positive airway pressure (CPAP) (PEEP-high and -low = 20–10 and 0 cmH_2O, time-high and

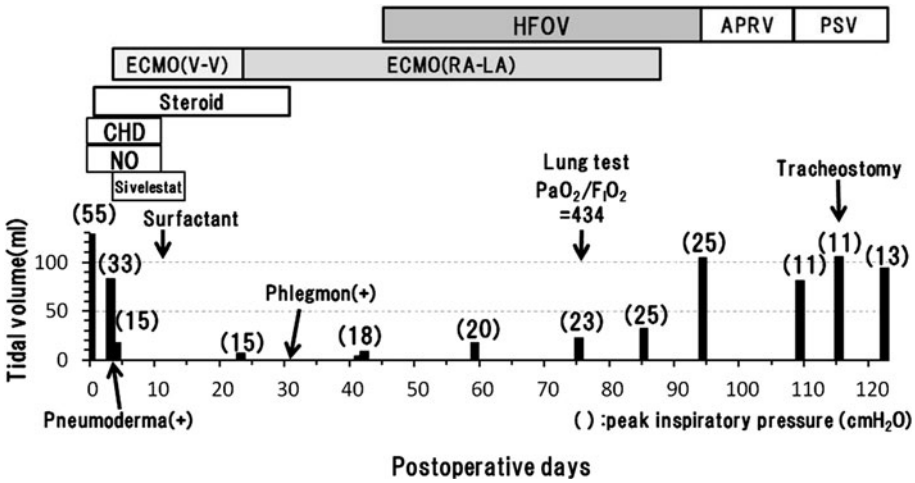

Fig. 2 Clinical course with intermittent data of tidal volume. After admission to the ICU, continuous hemodialysis (*CHD*) and inhalational nitric oxide (*NO*) were applied for the patient, but marked pneumoderma occurred on postoperative day (POD) 3. Therefore, veno-venous (V-V) ECMO was introduced, and later changed from V-V to right atrial and left atrial (RA–LA) ECMO consequent to insufficient oxygen support. *Black vertical bars* indicate tidal volumes of the patient measured with pressure control or support ventilation. Each *number* in *brackets* above each bar indicates peak inspiratory pressure (cmH_2O) when measured. Tidal volumes (TV) markedly decreased after pneumoderma, partly because of limited airway pressure, but just before HFOV it became almost 0 cmH_2O on POD 41 because of a collapsed lung. After the application of HFOV, TV gradually increased, and the patient was successfully weaned from ECMO on POD 88. *APRV* airway pressure release ventilation; *PSV* pressure support ventilation

-low = 3.7 and 0.4 s, PSV-high and -low = 5 and 0 cmH_2O, respectively) because bullas were newly pointed out on a CT scan and it was desirable to continue the open lung strategy. APRV was changed to pressure support ventilation (5–8 cmH_2O pressure support with 3–7 cmH_2O PEEP) on POD 109.

The patient moved from the ICU to a general ward on POD 122 following a tracheotomy on POD 115. Mechanical ventilation ceased on POD 142. She gradually recovered from neurological complications such as hemiplegia and was discharged from the hospital on POD 253 without oxygen therapy.

Discussion

Lung injury following pulmonary resection with no identifiable cause, especially after pneumonectomy, has been termed postpneumonectomy pulmonary edema or permeability pulmonary edema, and has alarmed both anesthesiologists and thoracic surgeons because of its high mortality rate, from 20% to as much as 100% [1, 2]. The incidence is variably reported as 2.5–9% after pneumonectomy and 1–7% after lobectomy, with no cases following segmentectomy, wedge resection, or open lung biopsy [3]. This postoperative lung injury shares similar clinical, radiologic, and histopathological characteristics with acute lung injury/acute respiratory distress syndrome (ALI/ARDS) as defined by the American–European Consensus Committee [4], and the guidelines on ALI/ARDS have been adopted to describe it [5]. However, the etiology of this lung injury is not well understood. It is considered to be a result of multiple causative and aggravating factors, such as elevated pulmonary vascular pressure after extended lung resection, pulmonary endothelial damage, high intraoperative ventilator pressure, especially during one-lung ventilation, ischemia/perfusion injury, overhydration, lymphatic disruption, acute inflammatory, reaction and surgical trauma [1, 3, 6].

In the present patient, several possible factors led to the development of ARDS during pulmonary resection. This patient had a congenital funnel chest with a relatively hypoplastic left lung (Fig. 1a), and eventually she had a right middle and lower lobectomy. Therefore, the remaining lung volume might have been unexpectedly small, and the increased pulmonary perfusion flow might contribute to endothelial damage. In addition, the remaining lung, especially the right upper lobe, was exposed to direct and indirect stresses by the surgery itself, massive transfusion including blood products that could result in overhydration after obtaining hemostasis, and high inspired oxygen and high airway pressure resulting in ventilator-induced lung injury (VILI). Transfusion-related acute lung injury was also considered as a possible reason for ARDS, although we did not confirm this with serological examination.

ECMO has been used as a rescue therapy for more than two decades in children with ALI/ARDS with reported survival rates greater than 50% [7]. Peek and colleagues demonstrated a significant improvement in survival without severe disability at 6 months in patients transferred to a specialist center for consideration for ECMO treatment compared with continued conventional ventilation (CV) in a randomized controlled trial [8]. They suggested that the preferable factor of ECMO was lung rest from high pressure and F_IO_2 ventilation, minimizing the iatrogenic contribution to lung injury. We introduced ECMO to this patient following subcutaneous and mediastinal emphysema. Considering the problems of VILI, we should have introduced ECMO earlier in her clinical course, but we expected improvement of pulmonary edema with reduction of blood volume by CHD, positional changes for dependent lung recruitment, nitric oxide, steroid use, and so on. However, her pulmonary oxygenation continuously deteriorated, finally resulting in barotrauma. We changed the blood circulation mode for ECMO from V-V to RA–LA because of the limited oxygenation support by V-V ECMO and maintained LV function. ECMO with left atrial blood supply has been reported as a beneficial method in combination with a left ventricular assisting device for end-stage dilated cardiomyopathy complicated with severe pulmonary edema [9], but no case has been reported in patients with ARDS, so far as we know.

Even with long lung rest with ECMO support, there was no improvement in the collapsed lung for 39 days. We introduced HFOV as a theoretically better ventilation, compared with CV. Then, we found a subtle but significant increase in TV from 0 to 6 ml just after an 8-h trial of HFOV, and following HFOV application led to lung recruitment sufficient to wean the patient from ECMO without barotrauma. The potential advantages of HFOV over CV include the delivery of smaller tidal volume (1–3 ml/kg), limiting alveolar overdistension; the application of higher mean airway pressure (mPaw) than that in CV, promoting more alveolar recruitment; and the maintenance of a constant mPaw during inspiration and expiration, thus preventing end-expiratory alveolar collapse [10]. Although HFOV has failed to show a mortality benefit in ARDS patients so far [11–13], several reports suggested the usefulness of HFOV in the management of fragile or damaged lungs in animals [14–16] and humans [17, 18].

We continued to use HFOV with high MAP even after the head complication because the patient had an emergency operation of external decompression of the skull to control intracranial pressure (ICP) and ECMO itself was useful to control $PaCO_2$ and PaO_2, which affected ICP.

Bennett and colleagues also demonstrated that HFOV was safely applied for ARDS patients with concomitant intracranial hypertension secondary to acute brain injury [19].

We believe that the present patient could not have survived without the unique recruitment ability of HFOV, which was applied in combination with ECMO.

Conclusion

Although HFOV has failed to show a mortality benefit in ARDS patients, the unique lung recruitment by HFOV can be a useful therapeutic option for severe ARDS patients in combination with sufficient lung rest produced by ECMO.

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