Extracorporeal membrane oxygenation with nafamostat mesilate as an anticoagulant for massive pulmonary hemorrhage after living-donor lobar lung transplantation

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Living-donor lung lobar transplantation has become an acceptable treatment for selected patients with end-stage pulmonary disease. A few cases of extracorporeal membrane oxygenation (ECMO) for acute severe respiratory failure after lung transplantation have been reported.¹⁻³ We present our experience with ECMO for acute respiratory failure resulting from pulmonary hemorrhage after living-donor lobar lung transplantation.

Clinical Summary

On June 23, 2001, a 27-year-old woman with end-stage primary pulmonary hypertension underwent bilateral living-donor lobar transplantation with her father's right lower lobe and her brother's left lower lobe under cardiopulmonary bypass. Postoperative immunosuppression was a triple-drug therapy consisting of cyclosporine (INN ciclosporin), azathioprine, and prednisone. Two episodes of acute rejection required high-dose methylprednisolone intravenously. On postoperative day 15, severe hypoxia with a massive hemoptysis developed. The arterial oxygen saturation (Sao₂) was 62% with 100% oxygen. Chest radiography revealed pulmonary hemorrhages in the right graft (Figure 1). Bronchoscopic examination demonstrated normal bronchial healing. She was placed on differential mechanical ventilation with a fraction of inspired oxygen of 1.0. Positive end-expiratory pressure of the right lung was 15 cm H₂O, and that of the left lung was 5 cm H₂O. At the same time, acute renal failure had developed. She was therefore treated with ECMO and continuous hemodiafiltration.

Peripheral cannulation was achieved through the left femoral vein with a 17F venous cannula and through the left femoral artery with a Dacron polyester fabric graft with a 19F arterial cannula. The ECMO circuit included a centrifugal pump (CAPIOX EBS; Terumo Corporation, Tokyo, Japan) and a polypropylene hollow

fiber membrane oxygenator (CAPIOX SX; Terumo Corporation). All the components of the circuit were treated with heparin coating. We decided to give extra nafamostat mesilate through continuous infusion of 1.0 to 1.7 mg/(kg · h), keeping the activated clotting time between 180 and 200 seconds. Immediately after initiation of ECMO, the Sao₂ increased from 62% to 89%, and we gradually reduced the ECMO flow from 2.5 to 1.0 L/min and the fraction of inspired oxygen from 1.0 to 0.6, keeping the Sao₂ between 95% and 100%. After 43 hours and 23 minutes of ECMO, the cannulas were removed without any complication, and the patient was successfully weaned from ECMO. On postoperative day 36, the patient was weaned from continuous hemodiafiltration, and she was extubated the next day. On postoperative day 106, the patient was discharged from the hospital without any respiratory support.

Discussion

Primary graft failure is a significant complication after lung transplantation. ECMO can be used as a temporary support to allow the graft function to improve. Fortunately, ECMO after lung transplantation was only needed in 2.7% of the cases, as reported by Meyers and colleagues.¹ Zenati and associates³ reported that 3.6% of patients required ECMO after lung transplantation. ECMO can be lifesaving, although mortality remains high. Zenati and associates³ reported a mortality of 25%. Meyers and colleagues¹ reported a mortality of 42% for 12 patients in whom ECMO had been used for the same condition.

A pulmonary hemorrhage is a rare but serious complication after lung transplantation and is associated with serious morbidity. Pulmonary hemorrhage in lung transplant recipients may be caused by ischemic and infectious necrosis or by local hemodynamic factors. Local hemodynamic factors may be especially related to increased blood flow in the transplanted lung in a living-donor lung lobar transplantation, because the living-donor lung graft size is smaller than the bilateral transplant lung graft size. Therefore the living-donor lung graft vascular bed is smaller than the bilateral transplant lung graft vascular bed. In this case, graft function improved during ECMO.

ECMO is administered to patients with respiratory and circulatory failure in a state of shock accompanied by risk of bleeding. Thus the use of heparin is restrained. We used nafamostat mesilate as an anticoagulant during ECMO, because the patient had acute respiratory failure caused by pulmonary hemorrhage, accompanied by high risk of bleeding. Nafamostat mesilate is a synthetic protease inhibitor that has been found to inhibit various kinds of enzyme activities for coagulation. There are a few reports of

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Figure 1. Chest radiograph showing pulmonary hemorrhage in right graft.

ECMO with nafamostat mesilate as an anticoagulant.^{4,5} Nagaya and coworkers⁴ reported that bleeding was well controlled by nafamostat mesilate administration in 8 of 12 patients who had

some hemorrhagic complications before or during ECMO. Daimon and associates⁵ reported ECMO in a patient with acute respiratory failure caused by pulmonary hemorrhage in a Goodpasture-like syndrome.

ECMO was successfully used to treat a patient with acute respiratory failure from pulmonary hemorrhage after living-donor lobar lung transplantation with nafamostat mesilate as an anticoagulant. Nafamostat mesilate may be the first choice as an anticoagulant during ECMO for patients with a high risk of bleeding.

References

1. Meyers BF, Sundt TM, Henry S, Trulock EP, Guthrie T, Cooper JD, et al. Selective use of extracorporeal membrane oxygenation is warranted after lung transplantation. *J Thorac Cardiovasc Surg.* 2000; 120:20-6.
2. Glassman LR, Keenan RJ, Fabrizio MC, Sonett JR, Bierman MI, Pham SM, et al. Extracorporeal membrane oxygenation as an adjunct treatment for primary graft failure in adult lung transplant recipients. *J Thorac Cardiovasc Surg.* 1995;110:723-6.
3. Zenati M, Pham SM, Keenan RJ, Griffith BP. Extracorporeal membrane oxygenation for lung transplant recipients with primary severe donor dysfunction. *Transpl Int.* 1996;9:227-30.
4. Nagaya M, Futamura M, Kato J, Niimi N, Fukuta S. Application of a new anticoagulant (Nafamostat Mesilate) to control hemorrhagic complications during extracorporeal membrane oxygenation—a preliminary report. *J Pediatr Surg.* 1997;32:531-5.
5. Daimon S, Umeda T, Michishita I, Wakasugi H, Genda A, Koni I. Goodpasture's-like syndrome and effect of extracorporeal membrane oxygenator support. *Intern Med.* 1994;33:569-73.