Successful Extracorporeal Membrane Oxygenation Support for Acute Pulmonary Thromboembolism during Adult Liver Transplantation

Ju Yong Lim, M.D., Pil Je Kang, M.D., and Doo Hwan Kim, M.D.

Dear Editor:

Most coagulation factors are synthesized in the liver. Hence, the levels of most coagulation factors are decreased in cases of chronic liver disease. Chronic liver disease was previously considered as an acquired bleeding disorder, and basic laboratory tests of anticoagulation, including prothrombin time and activated partial-thromboplastin time (aPTT), were used to assess the risk of bleeding.[1] However, a new hypothesis states that the coagulation system is rebalanced in chronic liver disease, with a decrease in the levels of natural anticoagulant factors, such as protein C and anti-thrombin, and a decrease in the levels of most of the coagulation factors under physiologic conditions.[1] Moreover, patients with chronic liver disease are considered to be procoagulant in many reports.[2,3] This could be explained by the increased levels of factor VIII mediated by the von Willebrand factor.[4,5] Consequently, patients with chronic liver disease are more likely to be at increased risk of venous or arterial thrombosis.[6-8] Here, we report a case of acute pulmonary thromboembolism that developed during adult liver transplantation (LT), which was managed successfully with venoarterial (VA) extracorporeal membrane oxygenation (ECMO) support.

A 61-year-old woman with a 1-year history of hepatitis B liver cirrhosis (LC) was scheduled to undergo elective adult-to-adult living donor LT. In addition to LC, she was also diagnosed with diabetes mellitus. Preoperative transthoracic echocardiography indicated normal biventricular and valvular function, with a left ventricular ejection fraction (LVEF) of 71%. Abdominal and pelvic computed tomography showed a large amount of ascites and esophageal varix with a cirrhotic liver. The laboratory findings were not remarkable, except for the low platelet count (65,000/ dL), and slightly elevated aspartate transaminase levels (57 IU/L) and total bilirubin levels (2.5 mg/dL).

A skin incision was made with the patient under general anesthesia with stable...
initial vital signs. According to the LT anesthesia protocol, 6 packs of red blood cells and fresh frozen plasma were infused by using the Fluid Management System (FMS, Belmont, MA, USA) as volume replacement to maintain the systolic blood pressure at approximately 120 mmHg. Arterial blood gas analysis and end-tidal CO2 showed unremarkable findings, until a sudden decrease in blood pressure occurred after 3.5 h during the preanhepatic phase. Despite the administration of 1 mg of epinephrine, the hypotension persisted. Hence, a transesophageal echocardiography (TEE) probe was placed and the heart function was evaluated. On TEE, severe right ventricular failure and a D-shaped left ventricle were observed. Based on the suspicion of massive pulmonary thromboembolism, 10,000 units of heparin was injected. Nevertheless, cardiac arrest occurred and cardiac compression was initiated. After 15 min of cardiac compression, spontaneous circulation was restored. However, recurrent ventricular fibrillation subsequently occurred. The ECMO team at our institute was consulted for extracorporeal cardiopulmonary resuscitation. During the cannulation of the peripheral femoral artery and vein, an additional 10,000 units of heparin was administrated for pharmacological thrombolysis. After 20 min of cardiac compression, ECMO was successfully established and spontaneous circulation was restored. Nevertheless, despite maximal ECMO support, severe biventricular dysfunction was observed on TEE. Moreover, ongoing bleeding was noted in the operative field, ECMO flow was unstable at 30-70%, and the mean blood pressure was approximately 50 mmHg. Hence, a massive transfusion was performed via anesthesiology. After surgery for 16 h, the patient was transferred to the intensive care unit (ICU) under ECMO support. The patient was also prescribed norepinephrine (0.3 mcg/kg/min), epinephrine (0.3 mcg/kg/min), and vasopressin (0.05 u/min). Due to the intractable bleeding tendency, the abdominal wound was left open and packed with gauze; moreover, as anticoagulation could not be initiated because of ECMO, massive transfusion was continued in the ICU. Transthoracic echocardiography was performed on postoperative day (POD) 1 under ECMO support, and showed severe biventricular dysfunction with LVEF of 8%. On POD 2, the operative site bleeding subsided and the vital signs became stable to under 80% on ECMO support. Epinephrine administration was tapered out, and norepinephrine and vasopressin doses were tapered to 0.1 mcg/kg/min and 0.01 u/min, respectively. Bedside transthoracic echocardiography showed improved biventricular contractility. ECMO weaning was attempted under inotropic support (norepinephrine [0.1 mcg/kg/min], dobutamine [3 mcg/kg/min], vasopressin [0.01 u/min]). Successful ECMO removal was performed after approximately 10 h of the weaning trial, without any systemic anticoagulation. On POD 3, abdominal wound closure was performed in the operation room. On POD 4, echocardiographic follow-up showed fully recovered, normal cardiac function. The patient was discharged on POD 64 without any complications and has been doing well at an out-patient-clinic.

Contrary to the previous belief that patients with chronic liver disease are at risk of bleeding, a procoagulant imbalance is believed to exist in chronic liver disease.[3] The possible clinical implications of this procoagulant imbalance include portal or peripheral vein thrombosis and arterial thrombosis.[6-10] Moreover, intraoperative thromboembolic events, such as pulmonary thromboembolism (PTE) as a result of bleeding due to coagulopathy, have become a major concern during LT for end-stage liver disease.[11,12] In fact, the incidence of intraoperative PTE during adult LT ranges from 1.2% to 6.25%.[13,14] In particular, Sakai et al.[15] reported 20 cases of intraoperative PTE during adult LT (4%) among 495 LTs. PTE occurred during the non-hepatic phase, particularly 30 min after graft reperfusion, in most cases. Moreover, that study indicated that the PTE group had poorer outcomes than the non-PTE group in terms of patient survival and graft survival. These patients were treated with heparin infusion or thrombolytic agents, and none of the patients were receiving ECMO support. In our present case, 10,000 units bolus of heparin was administrated immediately after PTE was suspected on

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TEE. However, the restoration of spontaneous circulation was not maintained. Furthermore, PTE occurred during the preanhepatic phase. Hence, the patient was at a risk of dying even before receiving the neo liver, and needed to be sustained over the remaining 10-12 h of the transplantation procedure. Therefore, VA ECMO support was established as a rescue therapy, and the LT could be successfully completed. Similarly, Tejani et al.[16] has reported a case wherein VA ECMO was used as a rescue therapy for cardiac arrest during adult LT.

One of the major concerns during VA ECMO support is the administration of appropriate anticoagulation. The guidelines recommend anticoagulation with heparin during ECMO, with a target aPTT of 1.5 to 2.5 times the baseline value.[17] However, it is challenging to follow this guideline in cases of multiple trauma or post-surgical bleeding. In our present case, intractable bleeding occurred intraoperatively. Moreover, massive transfusion, rather than anticoagulation, was performed to maintain the ECMO flow and adequate mean blood pressure. Therefore, systemic anticoagulation was not initiated throughout the ECMO support period. Instead, ECMO weaning was attempted to avoid unnecessary anticoagulation or thromboembolic complications as soon as the vital signs stabilized and heart function improved. Other cases also reported successful non-heparinized ECMO support in multiple trauma patients for up to 5 days.[18,19] Hence, it is notable that clinical conditions such as active bleeding, which does not appear suitable for systemic anticoagulation, may not be a contraindication for ECMO support if the underlying causes can be resolved and the patient can be weaned from ECMO within a few days.

In conclusion, patients with chronic liver disease do not experience auto-anticoagulation, contrary to the previous belief. Instead, they are at risk of venous or arterial thromboembolism. Hence, clinicians should be aware of the possibility of acute PTE during adult LT. Therefore, non-heparinized ECMO support can be used a rescue therapy in cases of PTE during LT without any additional bleeding risk.

References

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