Short communication

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Severe hepatopulmonary syndrome with hypoxemia refractory to liver transplant: Recovery after 67 days of ECMO support

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Abstract

Hepatopulmonary syndrome (HPS) is a complication of end stage liver disease (ESLD) and is manifested by severe hypoxemia, which usually responds to liver transplantation (LT). As compared to patients undergoing LT for other etiologies, patients with HPS present an increased risk of postoperative morbidity and mortality. There is no effective treatment for patients whose hypoxemia does not respond to LT. This subset of patients is at a highly increased risk of death. There are very few reports on the use of extracorporeal membrane oxygenation (ECMO) in this setting with rapid response. However, there is no prior report of ECMO utilization for longer than 4 weeks. We present the case of a 17 year-old male patient who underwent LT for ESLD secondary to chronic portal vein thrombosis and HPS. He received a liver from a deceased donor and presented with severe HPS after LT, requiring ECMO support for 67 days. The patient was discharged home and is breathing in ambient air. He is currently asymptomatic and has a normal liver function.

Keywords

Liver transplantation, hepatopulmonary syndrome, ECMO, artificial kidney, apheresis & detoxification techniques, Artificial lung & respiratory support, Intravascular oxygenators, apheresis & detoxification techniques

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Introduction

Hepatopulmonary syndrome (HPS) is a manifestation of severe end- stage liver disease. HPS is clinically identified by hypoxemia, platypnea, orthodeoxia, elevation of the alveolar-arterial gradient and intrapulmonary vascular dilation (shunt).[1] HPS has a high lethality, and its prevalence in adult patients with cirrhosis is about 15%.[1] In these patients, hypoxemia is related to increased perioperative mortality.

Although HPS was formerly considered a contraindication for liver transplantation (LT),[1–3] LT is currently the most effective therapeutic measure for its reversal.[1–3] Resolution of hypoxemia occurs in more than 70% of those who undergo LT.[1,2]

In rare instances, HPS does not respond promptly to LT, requiring prolonged post-transplant mechanical ventilation, which increases the risk of death. In such cases, additional measures may be taken to manage hypoxemia, including the use of inhaled vasodilators and systemic vasoconstrictors.

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There have been very few successful reports on the use of extracorporeal membrane oxygenation (ECMO),[1–5] lasting up to 4 weeks, since time to recover varies among these patients Herein, we report the case of an HPS patient with refractory hypoxemia who underwent LT and had a satisfactory response after 9 weeks on ECMO.

Case report

A 17-year-old patient with a history of HPS and end-stage liver disease secondary to non-cirrhotic portal vein thrombosis and a Model for End-Stage Liver Disease score of 15 was referred to the authors' institution. He presented with ascites, splenomegaly and prior variceal upper gastrointestinal bleeding. He also had dyspnea, platypnea and orthodeoxia with hypoxemia (arterial oxygen saturation (SaO2) of 72%) for over a year. On physical examination, the patient presented with cyanosis in the extremities and a distended but not tender abdomen. After extensive investigation, idiopathic intrahepatic portal vein thrombosis and thrombosis of the right hepatic vein was evidenced in computed tomographic angiography. Due to portal vein thrombosis and HPS, LT was indicated.

A preoperative agitated saline contrast echocardiogram revealed an ejection fraction of 63%, ventricles and atria without structural alterations, intense pulmonary shunting and absence of pulmonary hypertension. An initial arterial blood gas analysis revealed a PaO2 of 34.9 mmHg and an SaO2 of 59.2%. The exam was repeated at an inspired oxygen fraction (FiO2) of 100%, leading to improved PaO2 (259 mmHg) and SaO2 (99.5%). Spirometry was normal. A chest angiogram revealed intrapulmonary shunting with no other abnormalities.

The patient received an uneventful LT from a deceased donor and was extubated on the first post-transplant day. Surgical re-exploration was indicated on the second post-transplant day due to abdominal bleeding. He was extubated within 24 h of this reoperation, but required non-invasive mechanical ventilation after an episode of desaturation (SaO2 of 73%). He responded favorably to a FiO2 of 50%, maintaining an SaO2 of 89% at rest in room air. Of note, on minimal effort a drop in SaO2 was observed.

By the end of the first post-transplant week, the patient developed worsening dyspnea, requiring intermittent high-flow nasal cannula oxygenation with a FiO2 of 100% to maintain an SaO2 of 90%. An echocardiogram showed an ejection fraction of 60%, no signs of pulmonary hypertension, and a central venous pressure of 3 mmHg. At this point, it was decided to administer nitric oxide through high-flow nasal cannula. A transient improvement in SaO2 was observed, followed by worsening hypoxemia. The patient went back on mechanical ventilation with the following parameters: tidal volume of 8 mL/kg of predicted body weight, PEEP 6 and FiO2 100%, with normal lung compliance and a PaO2/FiO2 ratio of 43. Plain chest X-ray, point-of-care lung ultrasound and a transthoracic echocardiogram excluded potential contributing factors such as overt lung edema, atelectasis, pneumonia and serosal effusions.

Considering persistence or increase of shunt fraction as the likely cause of hypoxemia, other adjunctive therapies (garlic capsules, Trendelenburg position, higher doses of nitric oxide (20 ppm), and methylene blue infusion) were prescribed with no significant improvement. Since refractory hypoxemia (SaO2: 75%) persisted, veno-venous ECMO was initiated on the 17th post-transplant day, using a 25Fr multi-stage venous cannula through the right femoral vein and a 19Fr arterial cannula inserted in the right internal jugular vein, with a blood flow of 65 ml/kg/min and sweep gas of 4.0 L/min of 100% oxygen.

Chest X-ray confirmed drainage cannula tip position at the level of the diaphragm and return cannula tip at the superior vena cava-atrial junction. Anticoagulation was established with non-fractioned heparin, titrated to an ACT level of 160-200s. Pre-membrane SaO2 was below 70% and post-membrane PaO2 was above 350 mmHg at all times, indicating there was no significant recirculation or membrane failure. Respiratory parameters improved and the patient was weaned from mechanical ventilation after 3 days of ECMO support.

Because the patient was still hypoxemic after 1 week on full ECMO support, we decided to perform an invasive investigation through a pulmonary angiogram, which showed a discrete type 2 pattern of disease. Shunt embolization of a few A-V communications did not improve oxygenation, and the patient remained on ECMO support for the following 60 days (totaling 67 days of ECMO support). Two membrane changes were necessary during the ECMO support period.

On the 26th post-transplant day, the patient went into shock and was returned to the operating room for an intra-abdominal hemorrhage. At the time, he was not coagulopathic, but the drainage cannula was chattering intensely over the previous 24 h, in this case probably due excessive diuresis and negative fluid balance. Also, laboratory findings showed elevated liver enzymes and intrahepatic cholestasis. Diffuse bleeding was detected around the liver. The liver graft was swollen and tense, raising the suspicion of repeated liver outflow venous collapse, related to high ECMO flows and loss of the usual aid the native liver would provide in keeping the intra-hepatic vena cave open. With that in mind, the cannula was pulled down several centimeters, resulting in no more line chattering and prompt resolution of graft edema. Nonetheless, oxygenation was not altered by cannula repositioning.

Subsequently, the demand for supplemental oxygen reduced only very slowly. ECMO flows consistently above 5 L/min were required to keep SaO2 above 85%, which seemed to be sufficient, since the patient was awake, without any neurological issues and comprehensively rehabilitating. ECMO was withdrawn when SaO2 was over 85% at room air after a 24 h off-ECMO trial.

The patient was discharged from the hospital 23 days after ECMO decannulation, with no need for supplemental oxygen at home.

The patient was re-hospitalized after 1 month with septic shock secondary to bronchopneumonia, from which he fully recovered. Liver function tests remained normal during this hospitalization and throughout the follow-up period of 22 months.

Discussion

To avoid severe hypoxemia in patients with HPS and maintain oxygen saturation above 85% in the perioperative period, several measures besides O2 supplementation are used, such as nitric oxide, methylene blue, alveolar recruitment maneuvers, inhalation, epoprostenol, and ECMO. Even though ECMO is an invasive procedure with a higher risk of complications, some authors have argued that it can be considered an early rescue strategy for patients with persistent post-transplant intrapulmonary shunting.[2]

There are only five prior reports of ECMO use in patients with HPS refractory to LT, of which the longest period was 28 days.[1–5] Since ECMO was employed for a total of 67 days in the present case, it is the longest period reported in the literature to date.

The Model for End-Stage Liver Disease score may not adequately predict survival in patients with end-stage liver disease and HPS.[2] In HPS, there is a high prevalence of hypoxemia following LT, which contributes to morbidity and mortality and may take weeks or even months to resolve, as was the case with our patient. However, after the critical recovery period, LT has beneficial effects on pulmonary condition in the vast majority of cases.

Common complications of veno-venous ECMO include bleeding, infection, and cannula malpositioning.[1] Mucosal and cannula insertion site bleeding are frequent and are usually managed by adjusting heparin infusion rates.[1,3] In the present case, bleeding was restricted to the abdomen, around a swollen graft, and there were no signs of coagulopathy. As previously stated, high ECMO flows and loss of support of the proximal part of the inferior vena cava after liver transplant, subjecting it to positive abdominal pressures, were key. Monitoring liver function and size by ultrasound in the intensive care unit could help detect this problem at an earlier stage. As occurred in our case, withdrawal of the cannula may be necessary to treat the liver outflow obstruction, if no other cause such as thrombosis is identified. Before and after the hemorrhagic episode discussed above, the course of ECMO was uneventful and high flows were properly maintained, indicating that cannula position was not an issue in itself, but did became so when the patient was overdiuresed.

That, and the fact that this hemorrhagic event did not happen until after 9 days on ECMO, suggest slow recovery of the pulmonary vasculature was the cause of protracted ECMO requirement, and not any ECMO circuit-related issues. We also believe that delivery of highly oxygenated blood to the lungs may have prevented appropriate vasoconstrictive reflexes, therefore extending time to recover. It is possible that the pulmonary vessels remain fully open as a response not only to adequate ventilation, but also to highly oxygenated blood across the vascular bed. Therefore, although ECMO is an invasive procedure with inherent risks, the complication rates are reduced and acceptable when specialized medical and nursing care staff are available.

The present report demonstrates that recovery from hypoxemia can occur with prolonged ECMO therapy. ECMO should be an early consideration for HPS patients who have undergone LT and have persistent hypoxemia and poor response to adjunctive therapies. Also, liver edema should be monitored closely in awake ECMO patients after LT. Finally, there seems to be no time limit for obtaining the benefits of ECMO in HPS refractory to LT.

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