A Re-transplant case for hepatopulmonary syndrome without liver cirrhosis or portosystemic shunt after living-donor liver transplantation

Introduction

Hepatopulmonary syndrome (HPS) usually occurs with cirrhosis or chronic liver disease (CLD) or portosystemic shunting (PSS). The prevalence of HPS reportedly ranges between 5% and 30% in adults with cirrhosis and between 9% and 29% in children with CLD[1,2]. Liver transplantation (LT) is the only definitive and effective treatment for HPS[3-13]. However, it is rare for HPS to occur in patients after LT. We experienced a case of HPS after LT without significant liver disease or PSS. We were able to successfully treat this patient with prompt second living donor liver transplantation (re-LDLT). We describe this case with some literature review.

Case presentation

The patient was an 8-year-old girl who underwent LDLT at the age of 11 months for fulminant hepatitis. The donor was her mother. The graft was in the lateral segment. Mild acute rejection occurred twice, at 5 months and 42 months after LDLT. It was refractory, and was treated with pulse steroid therapy and immunosuppressive drugs. Liver biopsy had been performed regularly, which showed that liver fibrosis remained at stage F2 (METAVIR score) at 1 year before re-LDLT. Eight years after her initial LDLT, cyanosis and digital clubbing developed. The shunt ratio on ^{99m}Tc-macroaggregated albumin lung perfusion scintigraphy (^{99m}Tc-MAA lung scan) was

32%. She had not experienced biliary abnormalities like as biliary stricture, cholangitis. There was no cardiopulmonary disease, so we diagnosed her illness as HPS. Head, chest, and abdominal enhanced computed tomography and abdominal ultrasonography showed no significant shunt. However, percutaneous transhepatic portography showed earlier enhancement of the hepatic vein and inferior vena cava than usual. Per-rectal portal scintigraphy was also performed, which showed a shunt index of 25.7% (normal: <10%). We speculated that there were micro shunts between the portal vein and the hepatic vein in the graft liver. One year after the diagnosis of HPS, the shunt ratio on the ^{99m}Tc-MAA lung scan worsened to 42% (Fig. 1A). Re-LDLT was performed promptly, with the uncle as the donor and the graft in the left lobe +S1. Although severe hypoxemia due to persistent HPS occurred after re-LDLT, the selective pulmonary vasodilator inhaled nitric oxide at 1–5 ppm improved oxygenation gradually. Ventilatory support was withdrawn on postoperative day (POD) 32. Oxygen therapy was discontinued on POD 50. Afterwards, the clinical course was stable and she was discharged.

Histopathological examination of her explant liver (Fig. 2) revealed portal expansion and ductular proliferation in some interlobular connective tissues. Although these findings showed no neoplastic changes and were not in conflict with the findings in shunt vessels that were predicted from preoperative percutaneous transhepatic portography, it was difficult to clarify primary disease. Fibrosis stage was F2 (METAVIR score), which was the same result as for liver biopsies

performed regularly before repeat LDLT. The shunt ratio on ^{99m}Tc-MAA lung scan performed 5 months after re-LDLT normalized to 6% (Fig. 1B). For 30 months after re-LDLT, hypoxemia has not appeared.

Discussion

There are some case reports and case series in which HPS occurred before LT and severe hypoxemia continued for a while after LT[3]. However, our patient had an unusual presentation in that HPS was not recognized before LT. HPS might have developed de novo without cirrhosis or PSS following her initial LT. To the best of our knowledge, there are five reports of post-transplant HPS in pediatric patients in the latest 30 years[12–16] (Table 1).

De Goyat et al and Namgoong et al each reported their case in which portal vein thrombosis or portal vein stenosis, which may cause portal hypertension, was recognized[13,14]. In addition, esophageal varix, a finding in PSS, were recognized in both patients and moderate acute rejection was developed in the case of Namgoong. A common finding between our case and their cases was rejection as described by Namgoong et al[13]. Alhosh et al. reported a pediatric case of HPS secondary to nodular regenerative hyperplasia (NRH), as a case with atypical cause of HPS [12]. NRH is a relatively rare condition characterized by widespread transformation of the hepatic parenchyma into benign small regenerative nodules that can lead to the development of non-cirrhotic portal hypertension. The patient had NRH, a liver disease, which was different from our

patient. Avendano et al and Rajwal et al reported cases of post-transplant HPS without any known pathogenesses. The patients did not have chronic rejection or billiary stricutre that might develop HPS[15,16]. In our case, no obvious cause for HPS was found, but mild and refractory acute rejection occurred twice prior to the development of HPS. Some findings that could indicate stress on the liver were common to these three patients, including our patient. In the case reported by Rajwal et al[16] histological examination of the second liver explant showed portal expansion and ductular proliferation, which were also found in our patient (Fig. 2). They speculated that HPS, which was the indication of LT, could be secondary to cholangitis with biliary stricture. Although the primary cause of HPS was different in our case, the graft liver in both patients might have been stressed long enough to develop HPS. It was unclear how HPS developed, but we speculated based on the histopathological findings that portal expansion or ductular proliferation could be the cause of HPS.

In all six pediatric patients, including our patient, HPS developed with unknown pathogenesis after LT without any known pathogenesis of HPS like cirrhosis or PSS. Fortunately, all were treated successfully with re- LDLT. In all patients, their graft had been stressed by various factors. It is possible that long-term stress on the graft was the cause of HPS. This unusual presentation of HPS is intriguing. HPS should be considered in a hypoxemic patient with hepatic or biliary abnormalities who does not have cardiopulmonary disease. To avoid difficulties in diagnosis or treatment, further research is needed to clarify the mechanism of HPS.

Conclusion

We experienced a case of HPS without significant liver disease or PSS after LT. The patient was successfully treated with re-LDLT.

References

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