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Case Report

Hepatopulmonary Syndrome Improved by Living-related Liver Transplantation : A Case Report

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ABSTRACT

Progressive dyspnea developed in a 61-year-old man with cryptogenic liver cirrhosis, and hepatopulmonary syndrome was diagnosed. Physical examination revealed jaundice (total bilirubin, 4.5 mg/dl), spider nevi, and clubbed fingers. Arterial blood gas analysis showed an arterial oxygen pressure of 57.5 mm Hg and an alveolar-arterial oxygen difference of 42 mm Hg. A ^{99m}Tc-macroaggregated albumin pulmonary perfusion scan demonstrated uptake in the brain and kidneys suggestive of an intrapulmonary shunt. The right-to-left shunt ratio was calculated to be 30.6%. The patient underwent living-related liver transplantation using an extended right lobe graft donated by his younger brother. Both the arterial oxygen pressure (102 mm Hg) and the right-to-left shunt ratio (7.4%) had normalized by 8 months after liver transplantation, and the patient has since been weaned off home oxygen therapy. (Jikeikai Med J 2010 ; 57 : 39-41)

Key words : hepatopulmonary syndrome, liver transplantation, liver cirrhosis

INTRODUCTION

Hepatopulmonary syndrome (HPS) was first reported by Kennedy and Knudson in 1977[1] and is defined as the triad of liver disease, arterial deoxygenation, and intrapulmonary vascular dilatation (IPVD). The prevalence of HPS in patients with chronic liver disease ranges from 15% to 32%[2]. Spontaneous resolution of HPS is rare, and the only effective surgical treatment is liver transplantation. We report herein a case of HPS which showed marked improvement after living-related liver transplantation (LRLT).

CASE REPORT

A 61-year-old man with a 5-year history of liver dysfunction had received a diagnosis of cryptogenic liver cirrhosis at the age of 58 years. Serum markers for viral hepatitis, anti-nuclear antibody, and anti-mitochondrial antibody were negative, and the patient had no history of alcohol abuse. He was treated with ursodeoxycholic acid until the age of 60 years, when he complained of progressive dyspnea, for which home oxygen therapy was started. When he was referred to our hospital for further evaluation, HPS was diagnosed and LRLT was scheduled.

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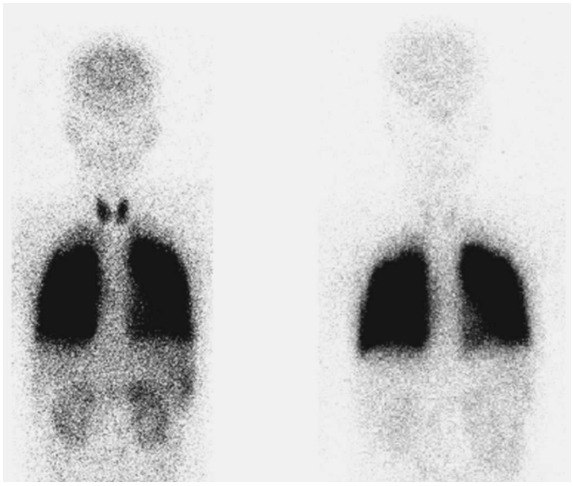

Fig. 1. ^{99m}Tc-MAA lung scanning showing uptake in the brain and the kidneys. The R-L shunt ratio improved from 30.6% preoperatively (Fig. 1a) to 7.4% 8 months after LRLT (Fig. 1b).

Table 1. Sequential changes in arterial blood-gas tensions and R-L shunt

		Pre-op.	Post-op. day				
			14	24	89	178	245
pH		7.503	7.438	7.463	7.46	7.42	7.45
pCO_2	(mmHg)	33.2	27.9	29.3	26.7	35	30
pO_2	(mmHg)	57.5	61.8	62.1	51.8	85	102
pO_2(A-a)	(mmHg)	42	57.6	55.2	66.7	21	10.2
R-L shunt	(%)	30.6	33.2	24.7	19.2	15.5	7.4

At the time of admission, the patient had jaundice (total bilirubin, 4.5 mg/dl), spider nevi, clubbed finger, and esophageal varices, but ascites and hepatic encephalopathy were absent. The Child-Pugh score was 5, the Model for End-Stage Liver Disease (MELD) score was 14, and the United Network for Organ Sharing-modified MELD score was 24. Arterial blood gas analysis obtained the following results: pH, 7.503; arterial carbon dioxide pressure ($PaCO_2$), 33.2 mm Hg; arterial oxygen pressure (PaO_2), 57.5 mm Hg; arterial oxygen saturation (SaO_2), 89.1%; and alveolar-arterial oxygen difference ($A\text{-}aDO_2$), 42 mm Hg. Respiratory function testing obtained the following results: the ratio of forced expiratory volume in 1 second to forced vital capacity, 83.1%; and the percent vital capacity, 93.3%. Pulmonary perfusion imaging using ^{99m}Tc-macroaggregated albumin (MAA) (Fig. 1a) exhibited uptake in the brain and kidneys in addition to uptake in the lungs, suggesting an intrapulmonary shunt. The right-to-left (R-L) shunt ratio was calculated as 30.6% by comparing ^{99m}Tc-MAA accumulation in both lungs with whole-body radioactivity. The results of chest radiography were unremarkable, and contrast-enhanced echocardiography suggested delayed opacification in the left atrium and ventricle.

The patient underwent LRLT in November 2007 with an extended right lobe graft with the caudate lobe donated by his younger brother. The graft weight was 662 g and the graft volume/recipient standard liver volume ratio was 56.6%. The right hepatic vein was reconstructed with a third-party homograft. The operation was uncomplicated and lasted 15 hours 34 minutes; the estimated blood loss was 4,600 mL. The immunosuppressant agents administered were tacrolimus and methylprednisolone. Pathological examination of the resected liver specimen showed liver cirrhosis with veno-occlusive lesions.

Postoperative recovery was favorable and without any major complications, and the patient was discharged on postoperative day 32 with normal liver function. The arterial blood gas saturation was measured sequentially after LRLT (Table 1) and showed gradual improvement in arterial oxygenation and a decrease in $A\text{-}aDO_2$. A significant improvement of the R-L shunt was also shown with pulmonary perfusion scanning (Fig. 1b). All these variables were normalized by 8 months after LRLT, and the patient has not needed home oxygen therapy since that time.

DISCUSSION

HPS is a pulmonary complication of chronic liver diseases. Although HPS commonly occurs in patients with liver cirrhosis, some patients with non-cirrhotic portal hypertension and fulminant hepatic failure may be affected. Exertional dyspnea is the most common symptom, and the presence of spider nevi, cyanosis, digital clubbing, and severe hypoxemia suggests HPS. Diagnostic criteria for HPS are as follows: PaO_2 less than 80 mm Hg or $A\text{-}aDO_2$ more than 15 mm Hg while the patient is breathing room

air[3], positive findings on contrast enhanced echocardiography or abnormal uptake in the brain (>6%) on radioactive lung perfusion scanning, and portal hypertension with or without cirrhosis.

The exact mechanism causing HPS is unclear, but IPVD is thought to be a pathologic hallmark[4]. IPVD can be caused by increased circulating levels of vasodilators, including nitric oxide, prostaglandins, progesterone, and estradiol, and by decreased circulating levels of vasoconstrictors, including endothelin-1 and serotonin. In the present case, we measured such vasodilators and vasoconstrictors in the serum to evaluate the etiology of HPS, but the levels of most were within their normal ranges preoperatively, and no significant changes were observed after LRLT. In an experimental model, intestinal endotoxin has been found to be one vasodilator that could cause HPS due to the failure of the damaged liver to clear it[5]. The cause of HPS in the present case remains unclear, but multiple factors are thought to be related to the development of HPS.

The prognosis is poor if HPS is treated medically; the 5-year survival rate of patients with HPS treated medically is 23%, but the survival rate after liver transplantation increases to 76%, which is similar to that after liver transplantation in patients without HPS[6]. Therefore, liver transplantation is the treatment of choice for patients with HPS. Because the long-term survival rate for patients with HPS and a PaO_2 of 60 mm Hg or less was reported to be worse even after liver transplantation[6], patients with HPS should undergo liver transplantation before PaO_2 deteriorates further. In fact, the United Network for Organ Sharing gives extra MELD score points for HPS[7]. In the present case, the PaO_2 was 57.5 mm Hg preoperatively, and the patient was judged to be a good candidate for LRLT. The postoperative oxygenation gradually improved and had normalized by 8 months after LRLT, which is in agreement with previous studies describing the improvement in PaO_2 occurring over months to years, depending on the severity of hypoxemia[6]. The mechanism for the improvement in oxygenation after liver transplantation in patients with HPS has been reported to be the reversibility of diffuse dilatation of the pulmonary precapillary vessels[8]. In the present case, such a mechanism seems reasonable.

Conclusion

The present case of HPS complicating cryptogenic cirrhosis was treated successfully with liver transplantation, and marked improvements in oxygenation and R-L shunt were obtained. Because hypoxemia is frequently progressive and because a low PaO_2 predicts poor survival in patients with HPS associated with advanced liver cirrhosis, early liver transplantation should be considered for patients with a PaO_2 of 60 mm Hg or less.

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