Case Report

Complete Resolution of Hepatopulmonary Syndrome after Liver Transplantation

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ABSTRACT

Hypoxemia is found in 10-40% of cirrhotic patients. Hepatopulmonary syndrome (HPS) is a unique condition presenting in patients with liver diseases and/or portal hypertension. A 51-year-old man who was a known case of alcohol and chronic hepatitis C-related decompensate cirrhosis was referred to our hospital for cadaveric liver transplantation. The patient developed severe persistent hypoxemia with increased alveolar-arterial oxygen tension gradient [$P(A\text{-}a)DO_2$] during the postoperative period. Pulmonary embolism was excluded by pulmonary artery catheterization. Contrast echocardiography demonstrated an extracardiac (or intrapulmonary) shunt and the diagnosis of HPS was made. He required intubation, mechanical ventilation and a prolonged stay in the intensive care unit. $P(A\text{-}a)DO_2$ gradually decreased and arterial blood gas returned to normal within 6 months following liver transplantation. Although the presence of HPS in cirrhotic patients is associated with high mortality, liver transplantation is the only established treatment for HPS. Screening for HPS in liver transplant candidates is recommended for the improvement of pre- and post-transplantation survival.

Key words : Hepatopulmonary syndrome, hypoxemia, cirrhosis, liver transplantation

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INTRODUCTION

Hypoxemia occurs in 10-40% of cirrhotic patients.[1] Pulmonary symptoms and pulmonary abnormalities are common in cirrhotic patients and up to 70% of cirrhotic patients waiting for liver transplantation complain of dyspnea.[2] Abnormalities of arterial blood gas (ABG) and pulmonary function test (PFT) are found in 45% and 50% of patients with chronic liver disease, respectively.[3] Intrinsic cardiopulmonary disorders not specifically related to liver disease, as well as unique conditions associated with the existence of chronic liver disease and/or portal hypertension, can be the causes of pulmonary dysfunction in cirrhotic patients.[2] Hepatopulmonary syndrome (HPS) is defined by a widened age-corrected alveolar-arterial oxygen tension gradient [$P(A\text{-}a)O_2$] on room air with or without

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hypoxemia.[2,4,5] The presence of HPS results from intrapulmonary vasodilatation in the presence of hepatic dysfunction or portal hypertension.[2,4,5] Herein, we report a complete resolution of HPS in a Thai cirrhotic patient after he underwent liver transplantation.

CASE REPORT

A 51-year-old man who was a known case of alcoholic cirrhosis was referred to our hospital for cadaveric liver transplantation. His past medical history is notable for frequent hospital admissions due to sepsis, upper gastrointestinal bleeding and hepatic encephalopathy. He had a history of smoking for 20 years but quit 10 years ago. Physical examination revealed lethargy, fatigue, moderate jaundice, clubbing of fingers and moderate ascites. Investigations showed 42 IU/l aspartate aminotransferase, 29 IU/l alanine aminotransferase, 7.3 mg/dl total protein, 2.4 mg/dl albumin, 3.8 mg/dl total bilirubin, 1.4 mg/dl direct bilirubin, prothrombin time of 14.7 sec, international normalized ratio of 1.27, positive antibody to hepatitis C virus (anti-HCV) and a HCV viral load (Amplicor HCV Monitor Test, Roche Diagnostic, NJ) of 996,000 IU/ml. Chest radiography and electrocardiography showed normal findings. Echocardiography was normal with an ejection fraction of 74%. Gastroscopy revealed small and moderate size varices. The diagnosis of alcohol and chronic hepatitis C-related child class C cirrhosis was made.

Five months after being listed for transplantation, the patient underwent cadaveric orthotopic liver transplantation (OLT) with Roux-en-Y choledochojejunostomy. The mean intraoperative pulmonary arterial pressure was 15 mmHg. After the operation, he was transferred to the intensive care unit (ICU), and his respiration was supported by a mechanical ventilator. Severe hypoxia was noticed perioperatively and it persisted throughout the postoperative period. During the first 7 days after OLT, chest radiography revealed pulmonary congestion and right pleural effusion, which was treated by diuretics. Ten days post-OLT, although chest radiography showed no pulmonary congestion, the patient still had severe hypoxia leading to high FiO_2 (greater than 0.6) requirement. The ABG revealed a $P(A\text{-}a)O_2$ of 430 mmHg at the FiO_2 of 0.8 (Table 1), suggesting the presence of a shunt. The initial differential diagnoses of hypoxemia were pulmonary embolism, anatomical shunt (e.g. intracardiac shunt), and HPS. The pulmonary arterial pressure of 19/11 mmHg and pulmonary capillary wedge pressure of 6 mmHg from the right heart catheterization excluded pulmonary embolism and intracardiac shunt as the cause of severe hypoxemia. Contrast echocardiography by injecting agitated saline intravenously confirmed an extracardiac (or intrapulmonary) shunt by documenting air bubbles in the left heart chamber after 5 beats. Severe persistent hypoxemia resulted in prolonged intubation and mechanical ventilation (for 30 days) despite attempted weaning of mechanical ventilation. Several complications such as hospital-acquired pneumonia, sepsis, acute renal failure and herpes simplex virus infection occurred during the 55 days of ICU stay. Following ICU, the patient received intensive rehabilitative care. He was hospitalized for 79 days. Room air ABG prior to discharge showed a PaO_2 of 65.6 mmHg, O_2 saturation of 96.8% and a $P(A\text{-}a)O_2$ of 46 mmHg, which was markedly reduced from that of immediate post-OLT (Table 1). Double therapy of tacrolimus and prednisolone was the mainstay of immunosuppressive regimen in this case.

Six months after OLT, the patient felt markedly improved and was able to continue his daily active life. Room-air ABG showed a PaO_2 of 100 mmHg and $P(A\text{-}a)O_2$ of 13 mmHg. (Table 1) PFT revealed normal spirometry without evidence of airway obstruc-

Table 1. Arterial blood gas of this patient

Post-liver transplantation	Day 1	Day 3	Day 7	Month 1	Month $2\frac{1}{2}$	Month 6
FiO_2	0.8	0.8	0.75	0.50	Room air	Room air
pH	7.5	7.5	7.5	7.6	7.5	7.44
$PaCO_2$	41	51	50	22.7	30.7	29.5
PaO2	89.1	64.7	69.6	69	65.6	100
HCO_3	33.4	39.3	40	21.2	24.7	20.3
$P(A\text{-}a)O_2$	430	442	403	259	46	13

tion. At 2 years post-OLT, he felt well with stable liver and respiratory function.

DISCUSSION

HPS occurs when pulmonary microvascular dilatation impairs arterial oxygenation in the setting of liver disease and/or portal hypertension.[4-6] HPS is found in 15-20% of cirrhotic patients waiting for liver transplantation.[4-6] HPS was diagnosed in our patient following liver transplantation due to the persistence of severe hypoxemia. The diagnosis of HPS could have been made before transplantation if the complaint of dyspnea and the presence of clubbing of fingers had been noticed, and an ABG had been done while waiting for liver transplantation. Using a pulse oximeter to measure O_2 saturation level as a non-invasive screening test for detecting mild hypoxemia (or PaO_2 less than 70 mmHg) provided a sensitivity of 96% and a specificity of 76%.[2,4,5] The need for ABG testing in cirrhotic patients will be limited if a pulse oximeter is adopted as a screening measure.[2,4,5] If HPS is suspected, microbubble contrast echocardiography is the preferred screening test for intrapulmonary vasodilatation.[4-7] HPS may coexist with other cardiopulmonary disorders.[5] A macroaggregated albumin (MAA) scan may be useful in determining whether HPS contributes to hypoxemia in HPS patients concomitant with obstructive pulmonary disease.[4-7] The MAA scan was not performed in this case. However, PFT was used to exclude obstructive and intrinsic pulmonary disease at 6 months after OLT. The pathological hallmark of HPS is microvascular dilatation within the pulmonary arterial circulation, which is resulted from excessive vascular production of vasodilators, particularly nitric oxide.[4,5,8] Abnormal gas exchange of HPS is characterized by anatomical shunting, a diffusion-perfusion defect and ventilation-perfusion mismatching.[7,8]

Mortality is higher in cirrhotic patients with HPS than those without HPS even after adjusting for chronic liver disease severity.[9] Liver transplantation is the only established effective treatment for HPS based on the complete resolution or significant improvement in gas exchange in more than 85% of patients.[4-6] The gas exchange of our patient became normalized by 6 months after transplantation. The length of time for hypoxemia to normalize after transplantation, however, varies and may be more than 1 year.[4-6] Increased post-liver transplantation mortality, primarily arising from serious complications such as pulmonary hypertension, cerebral embolic hemorrhage, and immediate postoperative deoxygenation requiring prolonged mechanical ventilation,[4-6,11-13] is more common in patients who have HPS than those who do not have HPS.[4-6,10] Screening for HPS, especially with a pulse oximeter, is a cost-effective strategy that can improve the survival of transplant candidates.[14] This report highlights the awareness of the presence of HPS among cirrhotic patients awaiting liver transplantation.

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