Hepatopulmonary syndrome: Case report of the evidence of intrapulmonary shunt on ^{99m}Tc-MAA scintigraphy and contrast transthoracic echocardiography

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Abstract
The hepatopulmonary syndrome (HPS) is characterized by arterial oxygenation defect induced by intrapulmonary vascular dilatations in the setting of liver disease. We report a 57-year-old woman with a history of liver cirrhosis presented with progressive cyanosis, exertional dyspnea and a dry cough. Oxyhemoglobin saturation was 88.5% on room air. Contrast transthoracic echocardiography (cTTE) and technetium-99m-macroaggregated albumin (^{99m}Tc-MAA) scintigraphy showed an intrapulmonary shunting and confirmed HPS.

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Introduction

Hepatopulmonary syndrome (HPS) is characterized by arterial hypoxemia caused by intrapulmonary vascular dilatations associated with liver disease [1]. The prevalence of HPS occurs in patients (5%-32%) with liver cirrhosis and portal hypertension. It increases mortality risk [2, 3]. Typical signs and symptoms of HPS include cyanosis, digital clubbing, orthodeoxia and exertional dyspnea [1, 4]. It is crucial to confirm intrapulmonary vascular dilatation in the diagnosis of HPS. Contrast transthoracic echocardiography (cTTE) with agitated saline is a high sensitive, non-invasive practical method to detect intrapulmonary vascular dilatation [4, 5]. Technetium-99m-macroaggregated albumin (^{99m}Tc-MAA) scintigraphy is also an useful tool to determine the shunt fraction based on quantitatively analyzing both brain uptake and whole-body uptake, particularly in the patients with concomitant obstructive pulmonary disease [5]. Liver transplantation is the only currently available and successful treatment in most patients with HPS due to the lack of effective therapy plan [6]. However, mortality after liver transplantation is significantly increased in the patients with severe HPS [7]. Therefore, early diagnosis, appropriate evaluation of HPS is crucial and may help improve the prognosis. We reported that a 57-year-old woman with a history of liver cirrhosis presented with hypoxemia and was definitely diagnosed as HPS.

Case report

A 57-year-old woman presented with progressive cyanosis, exertional dyspnea and a dry cough for 2 years and visited our hospital in June 2022. Her past medical history included splenectomy in 2008 due to chronic hepatitis B viral liver cirrhosis, and hypertension for ten years. As for laboratory tests, hemoglobin was 19g/dL, liver and kidney function were normal. Arterial blood gas samples with patient breathing room air in sitting position at rest were abnormal: PaO_2 was 46.8mmHg (normal range, 80-110), $PaCO_2$ was 38.9mmHg (normal rang, 35-45), oxyhemoglobin saturation was 88.5% (normal range, 91-99). Dyspnea symptom can be improved subjectively when the patient laid down. Chest computed tomography (CT) and pulmonary angiography (Figure 1A) were normal. Evidence

of liver cirrhosis was noted on abdominal CT (Figure 1B). Transthoracic echocardiography did not demonstrate an intracardiac abnormality. Contrast transthoracic echocardiography with intravenous agitated saline revealed that the microbubbles can be found in the left heart for six cycles after the right cardiac chamber's opacification (Figure 2A, B). Technetium-99m-MAA scintigraphy was performed to further evaluation the intrapulmonary shunting. The perfusion lung scan revealed a normal perfusion pattern without perfusion defects. Increased radiotracer accumulation in the extrapulmonary organs in brain, thyroid and kidneys were observed (Figure 2C). An estimated shunt fraction was 12%, suggesting a potential intrapulmonary shunting. Diagnosis of HPS was finally confirmed based on liver disease, a defect in oxygenation and intrapulmonary vascular dilatation.

The patient received therapy with oxygen inhalation, and symptoms alleviated to some extent. After one-year follow-up, the patient declined for liver transplantation and had persistent exertional dyspnea.

Discussion

Hepatopulmonary syndrome was probably identified in 1977, which was preceded by compelling descriptions based on autopsy and clinical findings [8, 9]. Hepatopulmonary syndrome is usually found in the patients with liver cirrhosis and portal hypertension. It also occurs in both acute or chronic hepatitis and hepatic venous obstruction without portal hypertension [10]. The characteristic of HPS is gross microvascular dilatation occurring within the pulmonary precapillary and capillary ves-

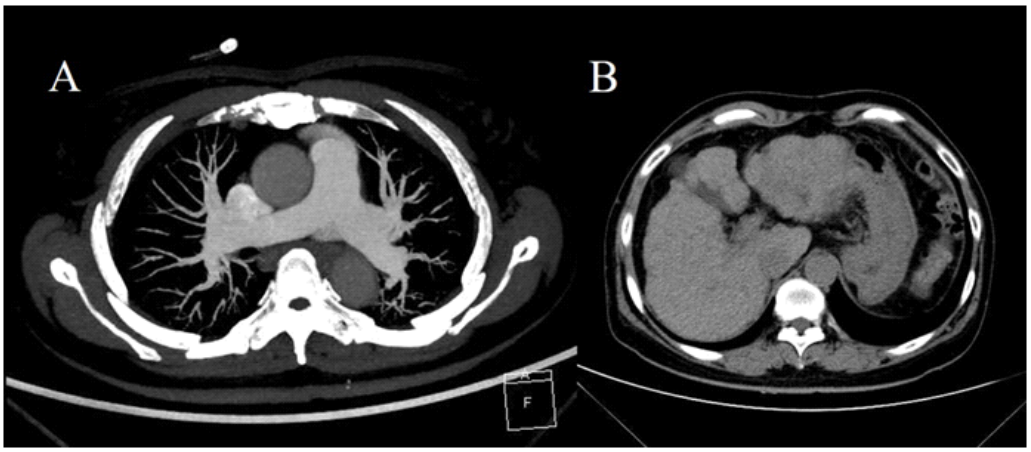

Figure 1. Computed tomography pulmonary angiography (A) demonstrated no pulmonary emboli. Abdomen CT showed the evidence of liver cirrhosis.

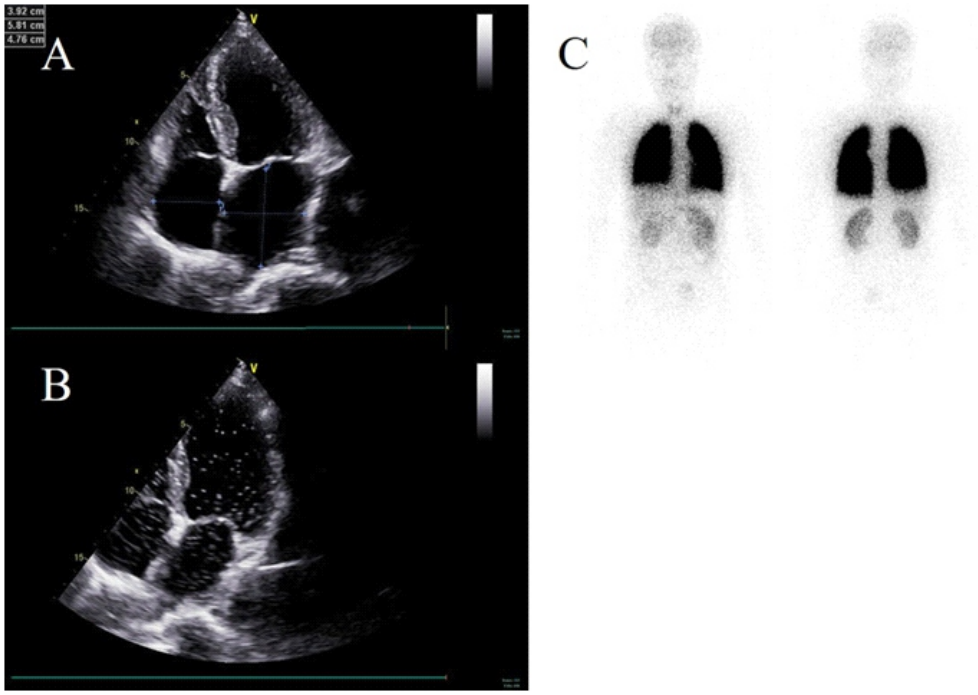

Figure 2. Contrast transthoracic echocardiography at four-chamber apical window (A) revealed that microbubbles were detected in the left cardiac chamber (B) for six cycles after intravenous agitated saline injection. Technetium-99m-MAA scintigraphy showed intense radiotracer uptake in the lungs and the extrapulmonary organs in brain, thyroid and kidneys.

sels. In addition, a few pleural and pulmonary arteriovenous communications and portopulmonary venous anastomoses may be contribute to the intrapulmonary shunting [9]. The causes of microvascular dilatation are various. Among them, nitric oxide plays an important factor for the development of pulmonary vascular dilatation. The levels of nitric oxide in exhaled air are increased in the patient with HPS, and decreased to normal range after liver transplantation [11]. Nitric oxide is a potential vasodilator, and its overproduction can lead to gross intrapulmonary vasodilation, and impaired pulmonary microvascular endothelial. Microvascular dilatation, impaired microvascular endothelial, increased blood flow and low diffusing capacity may result in anatomic and functional shunt physiology, ultimately leading to orthodeoxia [4].

Contrast echocardiography with intravenous agitated saline is the most common clinical screening test for intrapulmonary vasodilatation because it is a simple, low cost, safe and non-invasive technique. The microbubbles with a diameter ≤90μm can be captured in the normal pulmonary capillary bed [1]. There is distinguish HPS from hypoxemia and other etiology when microbubbles were detected in the left heart after ≥3-6 cardiac cycles following microbubbles appearance in the right heart [5]. Some literatures reported that cTTE in a standing position can increase the sensitivity due to the expansion of the pulmonary basal blood vessels for the gravity [12, 13]. Technetium-99m-MAA is a large albumin particle with a diameter >20μm, which persists in the normal pulmonary capillaries. Radiotracer accumulation in extrapulmonary organs, include kidneys, brain, spleen, indicate the diagnose of HPS. It has been reported that sensitivity of ^{99m}Tc-MAA scintigraphy is 66.7% in severe patients [14], and higher than that of cTTE in detecting intrapulmonary shunt in child with HPS [15].

Liver transplantation is definitely treatment for HPS. The 5-year survival rate in the patients with HPS is 76% after liver transplantation [16]. Long-term oxygen therapy remains the most frequently approach for patients with severe hypoxemia to alleviate symptoms.

In conclusion, HPS should be taken into consideration when the patient with liver cirrhosis suffered from hypoxemia. Combiningc TTE with ^{99m}Tc-MAA scintigraphy has the potential to improve diagnosis performance for HPS and management of patient treatment.

The authors declare that they have no conflicts of interest.

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