□ CASE REPORT □

Portopulmonary Hypertension Associated with Congenital Absence of the Portal Vein Treated with Bosentan

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Abstract

Portopulmonary hypertension (PPHTN) is pulmonary arterial hypertension (PAH) associated with portal hypertension. It is a common condition among liver transplantation candidates; however, its association with congenital absence of the portal vein (CAPV) has not yet been established. CAPV is a very rare developmental anomaly, which is usually accompanied by abnormal mesenteric drainage that bypasses the liver. Here, we report a rare case of severe PPHTN secondary to CAPV.

Key words: congenital absence of the portal vein, portopulmonary hypertension, pulmonary hypertension, bosentan therapy

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Case Report

A 12-year-old boy with pulmonary arterial hypertension (PAH) detected by electrocardiogram and echocardiogram was admitted to our hospital. His vascular abnormalities were first detected six years earlier during a physical examination required upon entering elementary school, but his parents had not sought medical attention. During the previous six years, he did not experience symptoms, nor show any signs other than slight dyspnea during physical education class [New York Heart Association (NYHA) class II].

A physical examination revealed no cardiovascular, hepatic, or gastrointestinal abnormalities. The patient's blood pressure was 120/70 mmHg, heart rate was 78 bpm, and no murmur was detected by auscultation. The patient was 159 cm high, and weighed 88.0 kg. A chest radiogram revealed conspicuous hilar pulmonary artery dilatation and the cardiothoracic ratio (CTR) was 47.9%. An electrocardiogram showed right ventricular hypertrophy and a regular sinus rhythm.

An echocardiogram revealed normal left ventricular wall motion without asynergy, and ventricular septum flattening during systole (Fig. 1). The right ventricle was enlarged and

mild tricuspid regurgitation was present. Peak velocity of tricuspid regurgitation was 4.0 m/s, tricuspid regurgitation pressure gradient (TRPG) was 64 mmHg, and right ventricular pressure was estimated at 74 mmHg. Inferior vena cava was not dilated and respiratory variations were normal, but a dilated main pulmonary artery was observed. Pulmonary regurgitation was moderate and end diastolic pressure gradient was estimated at 14 mmHg. Right heart catheterization showed severe PAH with systolic pulmonary arterial pressure of 80 mmHg, cardiac index of 3.53 L/min/m², pulmonary vascular resistance of 500 dyne/s/cm⁵, and mean right atrial pressure of 11 mmHg (Table 1). Severe PAH was confirmed by these findings.

Results of blood screening on admission suggested a liver function abnormality, and included alkaline phosphatase 1,466 IU/L, γ -glutamyl transpeptidase 713 IU/L, aspartate aminotransferase 76 IU/L, alanine aminotransferase 51 IU/L, serum ammonia 107 μ g/dL. Tests for hepatitis B or C viral infection were negative. Liver ultrasonography, magnetic resonance imaging, and abdominal computed tomography revealed the absence of the portal vein and the presence of a portosystemic shunt, which poured directly into the inferior vena cava (Fig. 2). Based on these findings, we diagnosed congenital absence of the portal vein (CAPV).

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Figure 1. Serial ultrasound imaging of the heart. A) and B) Parasternal short-axis view showing the flattened ventricular septum (arrow) during systole. C) Color Doppler examination showing mild tricuspid regurgitation. Tricuspid regurgitation pressure gradient was 64 mmHg. D) Apical four-chamber view showing enlarged right atrium and right ventricle. LA: left atrium, LV: left ventricle, RA: right atrium, RV; right ventricle, TRPG: tricuspid regurgitation pressure gradient

Table 1. Right Heart Catheterization Findings

	systole/diastole	mean
Pulmonary capillary wedge pressure (mmHg)		12
Pulmonary artery (mmHg)	80/32	54
Right ventricle (mmHg)	86/6	14
Right atrium (mmHg)	14/12	11
Aorta (mmHg)	128/76	92

The following tests were conducted to rule out other diseases or conditions that can cause PAH. Results of a transesophageal echocardiogram revealed neither partial anomalous pulmonary venous return nor atrial septal defect. Contrast-enhanced ultrasonography showed no right-to-left shunt. Three-dimensional computed tomography of the chest revealed no abnormal vessels in the azygos vein or other veins in the area. The cardiac catheterization also confirmed the absence of an intrapulmonary right-to-left shunt or left-to-right shunt; however, some peripheral pulmonary artery branches were narrowed. Arterial blood gas measurements in room air included PO_2 87.8 Torr and PCO_2 37.7 Torr. The test of pulmonary function revealed obstructive lung disturbance (VC 115.5%, $FEV_{1.0}$ 61.9%), which was assumed to be due to the patient's asthma, but was not considered severe enough to cause cor pulmonale. Sleep apnea syndrome was ruled out by polysomnography (apnea-hypopnea index 1.2/h). Autoimmune diseases were excluded because elevations of dsDNA, ssDNA and RNP antibody levels were not

detected. Ventilation-perfusion scintigraphy revealed no ventilation-perfusion mismatch, ruling out the possibility of hepatopulmonary syndrome and chronic thromboembolism. From these findings, we diagnosed a case of PPHTN secondary to CAPV.

Bosentan hydrate treatment was initiated; 62.5 mg taken twice daily for 4 weeks, and 125 mg taken twice daily beginning the fifth week (1). After twelve months of bosentan therapy, the patient's TR has remained mild, and his PAH did not show much improvement. His TRPG remained at 59 mmHg and he has remained asymptomatic. Regular follow up is to be continued.

Discussion

The association of PPHTN with CAPV has previously been described only once in the literature (2). PPHTN is a severe but common complication of liver cirrhosis (3), and its pathogenesis is only poorly understood. According to the currently accepted theory, the portosystemic shunt resulting from portal hypertension leads to an increase in pulmonary blood flow and shear stress. The subsequent endothelial injury initiates a cascade of events that produces the characteristic vascular pathologic changes. Genetic susceptibility, environmental insult, and imbalance of several humoral mediators may also be factors in PPHTN pathogenesis (4, 5). Al-

Figure 2. Enhanced abdominal computed tomography (below) and its 3D restructured image (above) showing absence of the portal vein and abnormal drainage of splenic vein and inferior mesenteric vein (superior mesenteric vein is not shown clearly). Extrahepatic shunt pours directly into the inferior vena cava (arrow). Ao: aorta, IVC: inferior vena cava

though widely-approved treatment has yet to be established, treatment may include the following: anticoagulation therapy, epoprostenol, endothelin-receptor antagonist, or liver transplantation. The endothelin-receptor antagonist bosentan has been reported to improve symptoms, as measured by both the NYHA score and walking distance (6-10). Survival has been variously reported as six months median survival

time to 50% mortality at the end of five years. Prognosis is poor in cases graded as severe by the World Health Organization (WHO) classification (11, 12).

To the best of our knowledge, 65 CAPV cases have been reported in the literature. According to our statistics, the age at diagnosis has ranged from 28 fetal weeks to 64 years old. Of these cases, 69.2% of patients were diagnosed before the age of 15 and 69.2% were women. CAPV often accompanies cardiovascular anomalies such as dextrocardia, ventricular or atrial septal defects, and ductus arteriosus; skeletal anomalies such as hemivertebrae, fifth finger anomalies, and Goldenhar syndrome; biliary atresia, and hepatic tumors. Congenital heart diseases were detected in 33.8% of patients with CAPV—of these cases, 36.3% had atrial septal defects, 22.7% had ventricular septal defects, and 22.7% had patent ductus arteriosus.

PAH associated with CAPV is uncommon, observed in only 3 of the 65 cases (4.6%). Two PAH cases were mild and did not require further investigation other than a chest x-ray, which showed pulmonary artery dilatation (13, 14). In the third case, a pencil-sized pulmonary embolus adherent to the pulmonary artery endothelium was revealed on autopsy, proving that it was not a case of PPHTN, but PAH caused by embolism (15).

The natural history and long-term prognosis of CAPV is unclear; only one published report has described the long-term follow up of a patient (16). However, the range of the age at diagnosis suggests that CAPV is not a life-threatening condition and that comorbidities determine its clinical course. In the present case, the severe PAH was considered to require therapeutic intervention.

Other examinations of this patient revealed focal nodular hyperplasia of the liver, slight mental retardation, obesity, an undescended testis, and a hemivertebra. We performed a search, but could not find a genetic syndrome that includes all of this patient's disorders.

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