PORTOPULMONARY HYPERTENSION IN PEDIATRIC PATIENTS

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Objectives To investigate the clinical presentation, manifestations, and response to therapy of portopulmonary hypertension (PPHTN) in pediatric patients.

Study design This study was a retrospective chart review describing the evaluation and course of 7 patients with PPHTN.

Results Causes of portal hypertension (HTN) included biliary atresia (3 cases), cavernous transformation of the portal vein (2 cases), and primary sclerosing cholangitis and cryptogenic cirrhosis (1 case each). The median interval from the diagnosis of portal HTN to PPHTN was 12.1 years. Four patients presented with a new heart murmur, 4 presented with syncope, and 3 presented with dyspnea. Although electrocardiograms (ECGs) and chest x-rays were normal in 3 and 2 patients, respectively, echocardiograms diagnosed pulmonary HTN in all 7 patients. Five patients had cardiac catheterizations; the average mean pulmonary artery pressure was 65 ± 20 mm Hg. Response to therapy was variable, and 4 patients died. Postmortem lung tissue examination revealed plexiform lesions and pulmonary arteriopathy.

Conclusions Because symptoms are subtle and may be overlooked, pediatric patients with portal HTN who develop a new heart murmur, dyspnea, syncope, or who are being evaluated for liver transplantation require evaluation for PPHTN. ECG and chest x-ray are insensitive screens for PPHTN. An echocardiogram and cardiology evaluation is essential for the diagnosis. *(J Pediatr 2005;147:20-6)*

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Portopulmonary hypertension (PPHTN) is one of the pulmonary vascular disorders complicating chronic liver disease.[1] In 1998 the World Health Organization (WHO) classified PPHTN as pulmonary arterial hypertension (HTN) associated with liver disease or portal HTN.[2] PPHTN is defined by elevated mean pulmonary arterial pressure (PAP) (> 25 mm Hg at rest), increased pulmonary vascular resistance (PVR) (>3 Wood units · m^2), and normal pulmonary capillary wedge pressure (<15 mm Hg) in the presence of portal HTN.[3] Both hepatic and extrahepatic causes of portal HTN may lead to PPHTN. The prevalence of PPHTN in adult patients with cirrhosis is 0.25% to 0.73% based on autopsy series[1,4] and 3.5% to 8.5% in liver transplant candidates.[1,5] The diagnosis of PPHTN is usually made 4 to 7 years after the diagnosis of portal HTN in adults.[1,6]

There are only limited numbers of case reports of children with PPHTN. Pediatric patients with biliary atresia, portal vein thrombosis, focal nodular hyperplasia, and congenital hepatic fibrosis have been reported with pulmonary arterial HTN.[7-15] To more fully characterize the clinical presentation, cardiopulmonary abnormalities, and clinical course, we report our experience with 7 children who developed PPHTN.

METHODS

A retrospective review of patient records in the Pediatric Liver Center, Children's Hospital identified 7 pediatric patients with PPHTN diagnosed between 1995 and 2004 (Table I). All of these children had been previously enrolled in an institutional review board–approved protocol for prospective longitudinal evaluation of childhood pulmonary

CTPV	Cavernous transformation of the portal vein	PPHTN	Portopulmonary hypertension
ECG	Electrocardiogram	PVR	Pulmonary vascular resistance
HTN	Hypertension	WHO	World Health Organization
PAP	Pulmonary arterial pressure		

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Table 1. Clinical information on patients with PPHTN

Patient	Age	Age at portal HTN	Age at PPHTN	Liver disease	Associated diseases	Liver biopsy findings
1	27 yrs	3.5 yrs	18.2 yrs	CTPV	None	ND
2	13.8 yrs*	10.11 yrs	13.8 yrs	BA	None	Portal fibrosis
3	20.4 yrs*	2 yrs	20.4 yrs	CC	CP, scoliosis, prematurity	Portal fibrosis
4	13 yrs*	10 mths	11.9 yrs	CTPV	Juvenile polyposis	Steatohepatitis
5	11 yrs	8.11 yrs	3 mths	PSC	ASD	Portal fibrosis
6	18 yrs	8 mths	17.3 yrs	BA	None	ND
7	7 mths*	4 mths	7 mths	BA	Complex CHD	Portal fibrosis

BA, biliary atresia; *CC*, cryptogenic cirrhosis; *PSC*, primary sclerosing cholangitis; *CHD*, congential heart disease; *CP*, cerebral palsy; *ASD*, atrial septal defect; *ND*, not done; *CTPV*, cavernous transformation of the portal vein.
*Age at death.

HTN, for which written informed consent was obtained from the parents or guardians. Data obtained from the medical record included age at diagnosis of portal HTN and PPHTN, cause of portal HTN, symptoms and/or signs precipitating the evaluation for pulmonary HTN, and additional review of chest x-ray, electrocardiogram (ECG), Doppler echocardiogram, right heart catheterization results, lung and liver histology (if available), response to treatment, and overall outcome for each patient. Review of patient records was approved by the institutional review board and was exempted from written consent.

Case Summaries

Patient 1, a Caucasian female, presented with splenomegaly and esophageal hemorrhage at age 3.5 years. Portal venogram demonstrated cavernous transformation of the portal vein. The patient underwent partial splenic embolization at age 7 years due to esophageal variceal bleeding refractory to sclerotherapy. At age 16 she developed syncope, which over the next 2 years progressed to shortness of breath, dyspnea on exertion, and orthopnea. Cardiac evaluation included an abnormal chest x-ray (Figure 1), ECG, echocardiogram, and a ventilation-perfusion scan that was negative for a pulmonary embolus (PE) (Table II). Severe pulmonary HTN was documented by cardiac catheterization (Table III). Because the patient initially refused continuous intravenous epoprostenol therapy, nifedipine was initiated. Due to clinical deterioration, epoprostenol treatment was started at age 22 years, and home-inhaled nitric oxide was added at age 24 years.[16] At age 26, she developed thyroiditis and was started on tapazol. Progressive pulmonary arterial HTN right-sided heart failure, and syncope were associated with a right ventricular systolic pressure of 156 mm Hg on echocardiography. A graded balloon atrial septostomy was performed without recurrence of syncope. The patient has been found to be an unacceptable candidate for a heart-lung-liver transplant at multiple centers. She is now 27 years old and remains homebound with a WHO functional classification of IV.

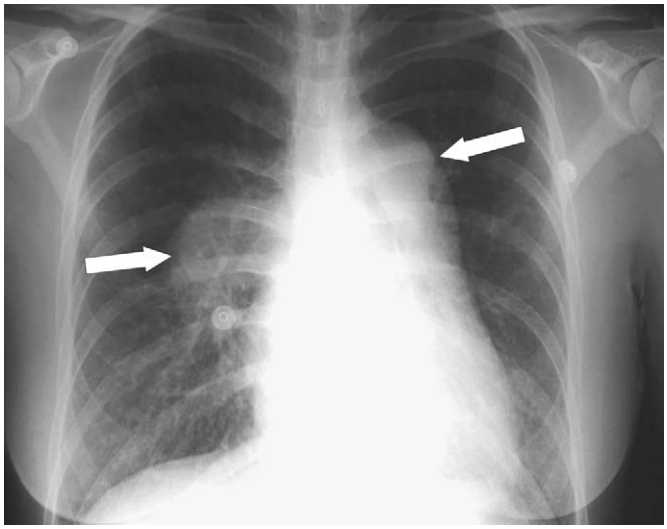

Figure 1. Chest x-ray of patient 1, with arrows indicating dilated pulmonary arteries.

Patient 2 underwent a Kasai portoenterostomy for biliary atresia at age 59 days. At age 10 years, after an exercise-induced syncopal episode, she was found to be anemic with splenomegaly. An upper intestinal endoscopy revealed esophageal varices, which were treated with endoscopic sclerotherapy. Despite attempted variceal ablation and prophylactic propranolol, she continued to have episodic variceal bleeding. At age 13 years she was admitted to the intensive care unit with hematemesis, treated with an octreotide infusion, and found to have portal hypertensive gastropathy without actively bleeding esophageal varices. A soft systolic ejection murmur was noted. Cardiac evaluation included an abnormal chest x-ray and echocardiogram and a normal ECG (Table II). She acutely became hypotensive and suffered a fatal cardiorespiratory arrest. Postmortem examination demonstrated pulmonary arteriopathy with plexiform lesions.

Patient 3, a Caucasian female with cerebral palsy secondary to prematurity, developed jaundice and rectal