Severe Pulmonary Hypertension Associated with a Small Ventricular Septal Defect

GEORGE S. BISSET III, M.D., AND STEPHEN S. HIRSCHFELD, M.D.

SUMMARY A case of progressive pulmonary hypertension in a child with a small ventricular septal defect is presented. Natural history studies have indicated that children with small ventricular septal defects can be followed conservatively. This case represents a contradiction to that rule and suggests that further study must be directed toward defining the etiology of pulmonary hypertension in patients with congenital heart disease.

SMALL to medium-sized ventricular septal defects (VSDs) are usually associated with minimal risk of development of pulmonary vascular disease, particularly in early years. Most authorities have advocated nonsurgical, conservative management of children with pulmonary arterial systolic pressures less than 40% of systemic pressure, and pulmonary-to-systemic flow ratios (Qp:Qs) less than 2:1. However, in this report, we describe a child with progressive pulmonary vascular disease in association with a small VSD that underwent spontaneous closure.

Case Report

JF was born after an uncomplicated pregnancy and delivery in rural Louisiana. His mother was an 18-year-old, gravida 1, para 1, abortus 0, healthy white female. At 3 days of age, the child was discharged from the hospital with a normal physical examination. At 4 weeks of age, he was seen by a pediatrician, who noted a cardiac murmur. He was referred to Charity Hospital of New Orleans, where tachypnea with a respiratory rate of 65 beats/min was noted. The pulse rate on admission was 170 beats/min; systolic blood pressure 80 mm Hg; and height and weight at the tenth percentile. The examination revealed a mildly distressed, acyanotic infant with a hyperactive precordium. The S1 was normal and S2 was split with a loud P2. A grade III/IV holosystolic murmur was noted at the lower left sternal border. A mid-diastolic rumble was heard at the apex. The lungs were clear, and the liver edge was palpable 3 cm below the right costal margin. The child had mild peripheral edema and all pulses were easily palpable. A chest roentgenogram revealed moderate cardiomegaly and increased pulmonary vascularity. The ECG revealed biventricular hypertrophy and left atrial enlargement. The hematocrit was 40%. Therapy for congestive heart failure was initiated with digoxin and furosemide.

The infant responded well and underwent cardiac catheterization at 2 months of age. The study revealed right ventricular and pulmonary artery pressures of 60/5 and 60/20 mm Hg (mean 31 mm Hg), respectively. The left ventricular pressure was 85/5 mm Hg. The Qp:Qs ratio was 3.7:1. Angiographically, the patient had a large, subaortic VSD.
Because of steady improvement, treatment with digoxin and furosemide was discontinued after 6 months. The patient remained in the tenth percentile of height and weight, but continued to thrive. At that time, the mid-diastolic rumble had disappeared and the P₂ had decreased somewhat in intensity.

At 16 months of age, a repeat cardiac catheterization was performed. The child was premedicated with meperidine and phenergan and both right- and left-heart studies were performed. The right atrial mean pressure was 3 mm Hg. The right ventricular and main pulmonary artery pressure were 42/4 and 38/16 mm Hg (mean 20 mm Hg), respectively. The aortic pressure recorded simultaneously with the main pulmonary artery pressure was 110/65 mm Hg (mean 75 mm Hg) (fig. 1). The mean left pulmonary capillary wedge pressure was 6 mm Hg. The left ventricular pressure was 110/4 mm Hg. The oximetric Qp/Qs ratio was 1.5:1. Angiographically, the patient had a small, subaortic VSD (fig. 2). The maximum pulmonary vascular resistance, calculated with an assumed oxygen consumption of 170 ml/min/m², was 2.1 U/m². The pulmonary systemic resistance ratio (Rp/Rs) was 0.12.

The patient was examined 2 years later. The cardiac murmur remained holosystolic, but was grade II/VI. The P₂ was slightly increased at that visit.

At 3 years, 10 months of age, the patient was reexaminined in clinic. At that time the right ventricle was larger to palpation, the pulmonic closure sound was tambouric, and the cardiac murmur had disappeared. The chest roentgenogram revealed cardiomegaly with a main pulmonary artery which was markedly dilated. The ECG revealed increasing right ventricular hypertrophy. An M-mode echocardiogram demonstrated a dilated (1.9 cm), thickened (0.4 cm) right ventricle. The left ventricle and left atrium were of normal size. The right ventricular systolic time intervals revealed a right preejection period (RPEP) of 100 msec and a right ventricular ejection time (RVET) time of 240 msec. The RPEP/RVET ratio was 0.42.

A cardiac catheterization was performed the next month. Small doses of ketamine were administered for sedation. The mean right atrial pressure was 5 mm Hg. The main pulmonary artery and right ventricular pressures measured on pullback were 95/78 mm Hg (mean 84 mm Hg) and 95/8 mm Hg, respectively. Simultaneous aortic and main pulmonary artery pressures performed several minutes later were 124/70 mm Hg (mean 92 mm Hg) and 90/70 mm Hg (mean 79 mm Hg), respectively (fig. 3). The right and left pulmonary artery pressures were 90/70 and 88/68 mm Hg, respectively. The calculated pulmonary vascular resistance was 15.7 U/m². The Rp/Rs was 0.92. No oximetric shunt was demonstrated. The absence of an intracardiac shunt was also confirmed angiographically, with two-dimensional and Doppler echocardiography. On 100% oxygen, the main pulmonary artery pressure fell to 72/50 mm Hg (mean 59 mm Hg).

At no time did this patient reside or visit in any location other than rural Louisiana, thus excluding any exposure to high altitude.

**Figure 1.** Simultaneous aortic and main pulmonary artery pressure curves (AO and MPA), recorded on a 100-mm Hg scale. The electrocardiographic tracing is illustrated in two leads at the top of the figure. These catheterization data were obtained at 16 months of age.

**Figure 2.** Left ventriculogram in a cephalad-angled left anterior oblique projection, demonstrating a small subaortic ventricular septal defect (arrow). At this time, the patient was 16 months of age, and had a pulmonary-to-systemic flow ratio of 1.5:1.
After 16 months, sure, low resistance VSD in congestive heart failure. A distinct contradiction to the rule, creating a unique artery pressure with small VSDs peak systolic pulmonary have been well delineated. The natural history studies of uncomplicated VSDs time with an infant age with Rp/Rs greater than 0.49 at final catheterization. For an Rp/Rs ratio of less than 0.2, we found an Rp/Rs greater than 0.49 at final catheterization. For children with small VSDs (less than 2.0:1 Qp:Qs and peak systolic pulmonary artery pressures less than 50 mm Hg), they found no evidence that low pulmonary artery pressure tends to rise in later life. Our patient is a distinct contradiction to the rule, creating a unique problem.

In summarizing this patient's history, one is faced initially with an infant with a high-flow, high-pressure, low-resistance VSD in congestive heart failure. After 16 months, the defect has diminished substantially in size, appearing as a low-flow, low-pressure, low-resistance VSD. Over the next 2½ years, the child underwent spontaneous closure of the VSD with the coincident appearance of severe pulmonary hypertension (table 1).

Bloomfield, Hoffman and Rudolph, Collins et al., and others have reported on large numbers of infants and children followed with VSDs. The consensus is that several conditions affect the development of pulmonary vascular disease in patients with congenital heart disease: the size of the defect, the reactivity of the pulmonary vascular bed, left atrial pressure, and rate of involution of fetal pulmonary arterial architecture.

In our patient, the second cardiac catheterization indicated that the defect was small and left atrial pressure was low. He demonstrated a hyporeactive pulmonary vascular bed, as evidenced by his very early history of congestive heart failure. The third cardiac catheterization indicated that the patient still had a small component of pulmonary vasoconstriction, as evidenced by his fall in resistance with oxygen.

The etiology for this child's pulmonary hypertension is not clear. It could not be classified simply as primary pulmonary hypertension because of the concurrent cardiac problem. It may be reasonable to suspect two different diseases in this particular child.

The paradoxical relationship between a spontaneously closing VSD and progressive pulmonary hypertension, to our knowledge, has not been reported previously. However, the conclusions are unclear. The development of pulmonary vascular disease in patients with d-transposition of the great arteries (with VSD or intact ventricular septum) has been well recognized. These children represent a different entity, however, because of chronic systemic hypoxemia, excessive bronchial collateral flow to the lungs, and polycythemia. The child reported by Berman et al. developed progressive pulmonary vascular disease after very early correction of d-transposition of the great arteries, at a time when the above-mentioned factors would not be expected to play a significant role. They suggested that pulmonary arterial thromboses were responsible for the development of his pulmonary vascular disease. In our patient this is a possible etiologic explanation.

Saalouke et al. described two patients with partial anomalous pulmonary venous drainage with intact atrial septum who developed pulmonary vascular disease. They speculated that a reflex increase in pulmonary arterial tone, secondary to right atrial distension or pulmonary venous distention, could result in pulmonary vascular disease over time. In our patient, this

![Figure 3](image_url) 

**Figure 3.** (left) Simultaneous aortic and main pulmonary artery pressure curves (AO and MPA), recorded on a 200-mm Hg scale. The aortic pressure is 124/70 mm Hg and the main pulmonary artery pressure is 90/70 mm Hg. (right) Main pulmonary artery pressure recorded on a 100-mm Hg scale. These recordings were obtained at 3 years, 11 months.

Table 1. Hemodynamic Data

<table>
<thead>
<tr>
<th>Age</th>
<th>Pulmonary artery pressure</th>
<th>Systemic artery pressure</th>
<th>Qp:Qs</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 months</td>
<td>60/20/(32)</td>
<td>85/?</td>
<td>3.8:1</td>
</tr>
<tr>
<td>16 months</td>
<td>38/16/(20)</td>
<td>110/66/(75)</td>
<td>1.5:1</td>
</tr>
<tr>
<td>4 years</td>
<td>90-95/70-78/(82)</td>
<td>124/70/(92)</td>
<td>1:1</td>
</tr>
</tbody>
</table>

Abbreviation: Qp:Qs = pulmonary-to-systemic flow ratio.
explanation does not seem plausible because there was no evidence of pulmonary venous obstruction or right atrial hypertension on the second catheterization. Perhaps our patient and patients with congenital heart disease who develop Eisenmenger's syndrome have another associated congenital deficiency (either biochemical or microanatomical) in the pulmonary vascular bed, leading to later development of pulmonary vascular disease. Perhaps if patients with primary pulmonary hypertension had been seen much earlier in life, a diagnosis of congenital heart disease would have been recognized. Certainly, other explanations could be possible.

The clinical implication of this report underscores the importance of following infants with VSDs, perhaps even after closure has occurred. The natural history may not be as clearly defined as previously thought.

References
Severe pulmonary hypertension associated with a small ventricular septal defect.
G S Bisset, 3rd and S S Hirschfeld

Circulation. 1983;67:470-473
doi: 10.1161/01.CIR.67.2.470

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1983 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on
the World Wide Web at:
http://circ.ahajournals.org/content/67/2/470

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally
published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the
Editorial Office. Once the online version of the published article for which permission is being requested is
located, click Request Permissions in the middle column of the Web page under Services. Further
information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/