Rapid evolution from "normal" left ventricular outflow tract to fatal subaortic stenosis in infancy

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SUMMARY Serial clinical, echocardiographic, haemodynamic, and angiocardigraphic data support the conclusion that over four months severe discrete subaortic stenosis evolved from a previously angiocardigraphically normal left ventricular outflow tract in an infant who had a successful repair of thoracic aortic coarctation. This case supports those who suggest that a myocardial factor may play an important role in the change in form and function of some congenitally malformed hearts.

There has been some speculation that the relatively discrete forms of subaortic stenosis (fibrous, fibromuscular, or tunnel) in the patient with normal ventriculoarterial connections and intact ventricular septum are acquired and not congenital.¹ Support for this view is based in part on the clinical, morphological, and angiocardigraphic observation that the discrete form of subaortic stenosis is rarely recognised in the neonate, and that clinically severe subaortic obstruction is uncommon in the first year of life.²⁻⁸ Furthermore, it has been stated that the type of collagen responsible for the fibrous membrane is not found in the newborn heart.¹

We report the serial clinical, echocardiographic, haemodynamic, angiocardigraphic, and surgical observations in an infant who unequivocally developed severe subaortic stenosis in the first year of life.

Case report

A male infant presented to The Hospital for Sick Children, Toronto, at 7 weeks of age with tachycardia and a heart murmur. At birth he weighed 2892 g and was the product of a full-term uncomplicated gestation, labour, and delivery. For a week before admission, he had been noted to be fretful and sweaty.

He was a well-developed, acyanotic infant of normal appearance weighing 4.1 kg. The pulse was 140, respiratory rate 40, and blood pressure, 140 mmHg systolic in the right arm and 70 mmHg

in the legs. The femoral pulses were very weak, while the brachial pulses were strong. Cardiac examination showed a quiet praecordium, normal first and second heart sounds, and a grade 2/6 blowing systolic ejection murmur at the left upper sternal border. The liver was palpable 2.0 cm below the right costal margin.

The chest radiograph showed mild cardiac enlargement, and normal pulmonary markings. The 12 lead electrocardiogram showed sinus tachycardia at 160/min, a frontal QRS axis of +120 degrees, and evidence of a right ventricular conduction delay. The two-dimensional echocardiogram showed a severe thoracic coarctation of the aorta and a normal left ventricular outflow tract.

The infant did not respond to antihypertensive and antifailure treatment. Cardiac catheterisation was performed nine days after admission as a prelude to surgical intervention. The haemodynamic data are given in the Table. A full right heart study was performed, but the left atrium could not be entered. Via a right axillary artery cutdown, the ascending aorta and left ventricle were catheterised. After haemodynamic data were obtained, angiocardigrams were performed in the left ventricle (Fig. 1), ascending aorta, and main pulmonary artery.

The catheter data showed a normal arterial oxygen saturation, with left-to-right shunting at atrial level, and raised right ventricular and pulmonary artery pressures. No gradient was recorded on withdrawal with an NIH side-hole catheter

Table Haemodynamic data

	Study no. 1		Study no. 2	
	Oxygen saturation (%)	Pressure (mmHg)	Oxygen saturation (%)	Pressure (mmHg)
Superior vena cava	70	—	44	—
Inferior vena cava	60	—	47	—
Right atrium, mid	80	m=2	70	m=6
Right ventricle	89	54/5	85	77/2
Pulmonary artery	88	42/12 (24)	83	62/15 (35)
Pulmonary capillary wedge	—	m=7	—	m=10
Left ventricle	98	155/7*	91	252/10
Ascending aorta	98	155/73 (93)*	92	88/52 (64)
Descending aorta (at diaphragm)	NE	—	—	88/52

Study no. 1 at 2 months of age.

Study no. 2 at 6½ months of age.

*Post-angio withdrawal.

NE, not entered; m, mean.

from the inflow and apex of the left ventricle to the ascending aorta.

The biplane aortogram showed severe thoracic coarctation of the aorta, and mild hypoplasia of the aortic isthmus. The aortic valve was thought to be bicuspid. In the long axis view the biplane left ventriculogram showed (Fig. 1a) an intact ventricular septum, a normal left ventricular outflow tract, a hypercontractile left ventricle, mild hyper-

trophy of the left ventricular free wall, and no mitral regurgitation. The pulmonary arteriogram showed pulmonary arteries of normal calibre, normal pulmonary venous drainage, and left-to-right shunting at atrial level. The following day the coarctation was uneventfully repaired, using a left subclavian flap aortoplasty. The infant was discharged 10 days later with a soft systolic murmur, no evidence of heart failure, and good femoral pulses. His drug therapy included digoxin and hydralazine.

He remained reasonably well (though with a poor weight gain) until 6 months of age, when he became sweaty, breathless, and tachypnoeic. He was readmitted in heart failure. His weight was 4.9 kg, heart rate 150, and respiratory rate 80. The systolic blood pressure in the right arm was 86 mmHg and in the right leg 80 mmHg.

Cardiac examination disclosed a prominent left ventricular impulse, and a systolic thrill at the lower left sternal border. The pulmonary closure sound was mildly increased in intensity. A loud grade 4/6 systolic ejection murmur was noted along the left sternal border and a gallop rhythm was conspicuous. The femoral pulses were normal. The liver edge was 4.0 cm below the right costal margin.

The chest radiograph showed moderate cardiomegaly and pulmonary venous congestion. The electrocardiogram showed sinus tachycardia, a

Fig. 1 Left ventricular cineangiocardigram at 2 months of age, filmed in the elongated axial projection (a) and right anterior oblique of this projection (b). Though the coarctation is not well seen in this injection, the left ventricular outflow tract is widely open (black arrows) and angiocardigraphically normal in appearance. The left ventricular free wall is hypertrophied. The ascending aorta (AO) is of normal calibre. No pressure gradient was recorded on withdrawal between the left ventricle and ascending aorta.

Fig. 2 Two dimensional echocardiogram at 6 months of age. Long axis view (diastole). The subaortic area is severely narrowed and the left ventricular free wall and ventricular septum are severely hypertrophied. RV, right ventricle; Ao, aorta; LA, left atrium; LVW, left ventricular free wall; S, interventricular septum.

frontal QRS axis of -60 degrees, biatrial enlargement, a right ventricular conduction delay, and an R/S progression across the praecordium suggesting left posterior hemiblock. A repeat two-dimensional echocardiogram now demonstrated very severe subaortic obstruction (Fig. 2) interpreted as characteristic of fibromuscular subaortic stenosis.

A second catheter study two days after admission (Table) showed no gradient between the left pulmonary capillary wedge pressure and the left ventricular end-diastolic pressure and raised right ventricular and pulmonary artery pressures. No pressure gradient was recorded across the previously repaired coarctation. The left ventricular

Fig. 3 Left ventricular cineangiocardigram at 6½ months of age after repair of aortic coarctation. There was no pressure gradient across the repair but a peak systolic gradient of 164 mmHg across the left ventricular outflow tract. These systolic and diastolic frames show very severe subaortic stenosis (black arrow), some distance beneath the aortic valve. The left ventricle is hypercontractile and the free wall is severely hypertrophied.

pressure (recorded in the apex and inflow of the left ventricle with a fluid-filled side-hole NIH catheter), however, was 252/10 mmHg and the pressure in the ascending aorta was 88/52 (mean 64) mmHg.

Biplane left ventricular cineangiography disclosed pronounced hypertrophy of the left ventricular free wall, with severe subaortic stenosis (Fig. 3), the angiocardigraphic appearance being consistent with either the fibromuscular or the tunnel form. Eight days later, resection of a subaortic fibromuscular obstruction was performed. Severe hypertrophy of the ventricular septum was observed with endocardial sclerosis. The entire left ventricular outflow tract seemed narrowed. The subaortic area between the left and right coronary commissures was incised and tissue was resected and sent for histological examination. A sinus venosus atrial septal defect was also closed. The patient died several hours after operation. Consent for necropsy was refused.

Histopathological examination of the endomyocardial fragments showed severe endocardial sclerosis, hypertrophied myocardial cells, and some interstitial fibrosis.

Discussion

We have presented persuasive evidence that subaortic stenosis evolved rapidly in an infant previously shown to have an angiographically normal left ventricular outflow tract, and that this phenomenon followed successful repair of a severe aortic coarctation. That severe subaortic obstruction was acquired in just four months is beyond dispute, but were the left ventricular outflow tract and the underlying myocardial matrix truly "normal"?^{9 10}

Unfortunately we do not have the morphological histopathological data to answer this fundamental question. Beçu and Somerville and their colleagues in a series of informative papers, however, have shown that focal areas of dysplastic myocardium can occur in patients with isolated pulmonary valve stenosis and other congenital cardiovascular anomalies,^{1 9-13} and, Somerville quoting Beçu,¹ states that areas of dysplastic myocardium identical to that found in hypertrophic cardiomyopathy are present low in the ventricular septum in infants dying from other diseases in whom mild fixed subaortic stenosis has been found. She postulates that this abnormal septal myocardium contracts abnormally, develops secondary changes resulting in turbulence, and thus stimulates the formation of a discrete form of subaortic stenosis.¹

While it is intriguing to consider that the change in form and function of the left ventricular outflow tract in our infant could be causally related to the

strategic disposition of focal areas of dysplastic myocardium, other anatomical factors must be considered. Rosenquist and his colleagues have reported increased mitral aortic separation in 22 patients with discrete subaortic stenosis and note that the aortic annulus in these patients may be smaller than normal.¹⁴ It would be fascinating to determine the histopathological character of the myocardium responsible for such mitral-aortic separation. Finally, though this report concerns just one patient, our findings tend to support the conclusion of Somerville that abnormalities of the left ventricular outflow tract are not "simple" or "discrete", but rather reflect a more diffuse process with manifestations in myocardium, semilunar valve, and aorta.^{1 9 10 13}

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