Successful repair of an atrial septal defect associated with right to left shunting

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SUMMARY An atrial septal defect was successfully repaired in a young woman despite the presence of pulmonary hypertension and right to left shunting. Before repair both isoprenaline infusion and 100% inspired oxygen produced significant falls in pulmonary artery pressure and pulmonary vascular resistance. A lung biopsy specimen at operation indicated a considerable decrease in the concentration of parenchymal pulmonary arteries and an absence of intimal fibrosis or medial hypertrophy.

Pulmonary artery banding performed in infancy, as part of the management of a ventricular septal defect, may have contributed to the underdevelopment of the pulmonary vascular tree. The reduced number of pulmonary arteries is a possible explanation for the pulmonary hypertension.

It is uncommon for an isolated atrial septal defect to be associated with right to left shunting unless severe pulmonary hypertension is present. Operation is usually not recommended in such patients. We report a young patient with an atrial septal defect associated with pulmonary hypertension and right to left shunting who underwent successful repair. We believe that underdevelopment of the pulmonary tree, which was shown by lung biopsy, was associated with a pre-existing ventricular septal defect and pulmonary artery banding.

Case report

As an infant the patient presented with heart failure and a murmur was detected. She was acyanotic and at catheterisation at the age of nine months the atrial septum was crossed and a left to right shunt at the ventricular level was shown. Pulmonary artery pressure was not measured. Right and left ventricular systolic pressures were 51 mm Hg and 80 mm Hg respectively. Medical management was recommended and catheterisation (at age two) confirmed a left to right shunt at the ventricular level and pulmonary hypertension (table 1). Infusion of tolazoline hydrochloride resulted in a small fall in pulmonary resis-

tance and an increase in the pulmonary systemic flow ratio. Pulmonary artery banding was performed.

When she was three and a half years old repeat catheterisation indicated a bi-directional shunt at the ventricular level. There was a 20-36 mm Hg peak systolic gradient across the region of the band and the distal pulmonary artery pressure was raised (64/30 mm Hg). The ventricular septal defect was closed and the band removed; apart from several early postoperative episodes of cyanosis the subsequent course was uneventful.

At the age of 19, when she was 20 weeks pregnant, the patient presented with haemoptysis, and an initial diagnosis of pulmonary embolism was excluded by pulmonary angiography. A limited study of the right heart showed pulmonary artery pressure of 55/22 (mean 35 mm Hg). Bi-directional shunting at the atrial level with a small net right to left shunt was detected. Table 1 does not include the results of this study. The arterial oxygen saturation was 88% on room air. Subsequent bronchoscopy showed prominent submucosal vessels in the bronchi and it was thought that rupture of these vessels had caused the haemoptysis. Physical findings included an active right ventricle on palpation, wide fixed splitting of the second heart sound, and a soft ejection systolic murmur along the upper left sternal border. There was no evidence of clubbing. The electrocardiogram showed sinus rhythm, right axis deviation, and right ventricular hypertrophy. Chest x ray showed a normal sized heart and normal vascular pattern. A cross

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Fig 1 Sequence of cross sectional images recorded from the apical four chamber acoustic window and corresponding line drawings of a saline injection showing a bi-directional shunt at atrial level. Top panel: this systolic frame shows deviation of the interatrial septum toward the left atrium and microbubbles (*) filling the right atrium and also the left atrium (***). Middle panel: this shows a diastolic frame with microbubbles in the orifice of the mitral valve (***) and entering the left ventricle. A small area of washout is seen in the right atrium (**). Bottom panel: this is the next frame in the cycle and the negative area in the right atrium is larger (**). LA, left atrium; LV, left ventricle; PV, pulmonary vein; RA, right atrium; RV, right ventricle.

Table 1 Results of cardiac catheterisation

	Age									
Age	9.5 month		2 yr	3.5 yr		19.5 yr		20 yr†		
Intervention	—	—	T	—	—	I	100% O ₂	—	I	
Right atrium (mean mm Hg)	—	—	—	—	4	2	3	4	3	
Right ventricle (mean mm Hg)	51/0	82/0	—	100/ 0	60/ 3	—	—	55/ 4	—	3
Main pulmonary artery										
systolic/diastolic	—	84/32	85/30	64/30	55/30	45/32	42/24	55/25	70/30	
(mean mm Hg)	—	42	47	43	43	38	30	38	45	
Left atrium (mean mm Hg)	8	8	—	—	5	3	3	6	3	
Left ventricle (mm Hg)	80/ 0	100/ 6	—	—	130/ 5	—	—	—	—	
Aorta										
Systolic/diastolic	—	100/50	100/60	115/52	130/70	105/55	125/70	122/68	145/55	
Mean pressure (mm Hg)	—	63	66	72	82	82	90	82	78	
Pulmonary resistance (units/m ²)	—	5.6	3.9	9.5	13.8	7.5	8.1	9.5	6.4	
Systemic resistance (units/m ²)	—	19	21	21	21	14	28	20	11	
Cardiac index (l/min/m ²)	3.1*	3.3*	3.2*	3.5*	3.9	6.0	3.2	4.0	7.0	
Pulmonary flow/systemic flow	1.7/1	2.3/1	3.8/1	1.3/1+	0.8/1+	0.84/1+	1.2/1+	1	1	
Left to right shunt (l/min/m ²)	2.2	4.2	8.8	1.6	0.27	0.54	0.8	0	0	
Right to left shunt (l/min/m ²)	0	0	0	0.6	1.07	1.51	0.3	0	0	

*Assuming an oxygen consumption of 120 ml/min/m². †Six months after closure of the atrial septal defect. I, isoprenaline; T, tolazoline hydrochloride; +, bi-directional shunt.

sectional echocardiographic study with saline injection showed bi-directional shunting at the atrial level (fig 1). Because of hypoxia the patient was prescribed supplemental nasal oxygen which eliminated the arterial desaturation. The patient tolerated vaginal delivery at 34 weeks' gestation. The premature infant was well at discharge.

After delivery, repeat catheterisation (table 1) showed moderate pulmonary hypertension, and

isoprenaline infusion reduced the pulmonary vascular resistance from 13.8 units/m² to 7.5 units/m². The arterial oxygen saturation on room air was 83%. There was a bi-directional shunt at the atrial level with a net right to left shunt. The pulmonary systemic flow ratio increased from 0.8 to 0.84 with isoprenaline infusion. When the patient breathed 100% oxygen pulmonary artery pressure fell and the net shunt was left to right. Contrast injection in the

Fig 2 A section of the lung biopsy specimen showing the paucity of parenchymal arteries. Only one artery is seen centrally.

inferior vena cava showed flow across the interatrial septum and left to right shunting on recirculation. Left ventricular cineangiography indicated an intact ventricular septum. A 1×2 cm atrial septal defect was surgically closed.

A lung biopsy (fig 2) performed at operation showed that the density of the small arteries was reduced; the ratio of pulmonary arteries to alveoli was 1:18 (normal for this age, 1:6). The ratio was assessed by examining a number of fields although only one artery is shown in the figure. Intra-acinar arteries appeared to be dilated but without evidence of muscular hypertrophy. Pre-acinar arteries showed minimal muscular hypertrophy without intimal lesions. The alveolar walls were delicate without fibrosis and the radial alveolar count of 10 was within the normal range.

Catheterisation (table 1) performed six months after operation indicated no evidence of shunting and the pulmonary vascular resistance fell from 13.8 units/m² before operation to 9.5 units/m² after operation. The results of exercise testing performed six months and 18 months after operation showed improvement in exercise capacity (table 2). Post-operatively there was no significant desaturation with exercise.

Discussion

The initial presentation during pregnancy with signs of pulmonary hypertension and arterial desaturation suggested progressive pulmonary hypertension. Proximal pulmonary artery thrombosis has been reported as a cause of this¹ and was excluded by the normal pulmonary angiogram.

Table 2 Results of treadmill exercise testing

	Preoperative	Postoperative 6 months	Postoperative 18 months
Exercise duration (min) (Bruce protocol)	6.2	7.2	8.1
Heart rate (beats/min):			
Rest	100	82	64
Maximal	163	163	172
Systolic blood pressure (mm Hg):			
Rest	118	110	102
Maximal	142	160	152
Diastolic blood pressure (mm Hg):			
Rest	64	60	68
Maximal	54	60	76
Peak oxygen consumption (ml/kg/min)	12.5	19.1	18.4
Oxygen saturation (%):			
Rest	93	97	—
Maximal	79	94	—

After closure of a ventricular septal defect most infants show resolution of pulmonary hypertension; however, a few became worse. Before the pulmonary artery banding the pulmonary vascular resistance was raised and there was further increase after the band was placed. The postoperative pulmonary resistance at the age of 20 was very similar to that at the age of three and a half.

The pulmonary vascular resistance (13.8 units/m²) and arterial desaturation are adverse prognostic factors for operation.² The reduction in resistance with isoprenaline and when 100% oxygen was breathed suggested considerable pulmonary vascular reactivity. The value of 7.5 units/m² was similar to that at which others recommend closure of a ventricular septal defect associated with pulmonary hypertension.³ However, a lower resistance value can be associated with histological evidence of severe pulmonary vascular disease.⁴

The development of the alveolar region starts prenatally. The number of alveoli increases until about eight years of age and the growth of intra-acinar arteries follows that of the alveoli.⁵⁻⁷ The period of most rapid growth is before the age of three.^{7,8} The density of small arteries increases more than alveolar density such that the ratio of arteries to alveoli at birth is 1:20, but by adulthood it is 1:6.⁹ Muscularisation of these distal arteries lags, and the adult pattern of muscularisation as related to size does not develop until late childhood or early adulthood.^{5,7,9,10}

Reduction in arterial density (graded by the Reid-Rabinovitch system) is a late finding in pulmonary hypertension caused by congenital heart disease. It is usually associated with muscular hypertrophy of the pre-acinar and intra-acinar arteries and correlates with a moderate to severe increase in pulmonary vascular resistance.^{9,11}

Growth of the pulmonary vascular bed may have been affected before banding and a decrease in the number of intra-acinar pulmonary arteries has been reported in infants with large ventricular septal defects.¹² Between the time of banding and repair of the ventricular septal defect (when the patient was three and a half) pulmonary vascular resistance increased from 5.6 units/m² to 9.5 units/m², pulmonary blood flow decreased, and mean pulmonary artery pressure remained the same. It may be that pulmonary artery banding in this patient at the age of two may have contributed to the hypoplasia of the pulmonary vascular bed by reducing pulmonary blood flow during the period of pulmonary arterial growth. Although the pressure drop across the band was modest it reduced pulmonary flow considerably and caused a net right to left shunt. In animal models banding of the pulmonary artery decreased the

density of the parenchymal arteries.¹³ A similar decrease in density of the parenchymal arteries has been found in neonates with pulmonary atresia.¹⁴ Occlusion of the alveolar wall arteries was detected in several patients with pulmonary hypertension associated with congenital heart disease, and it was suggested that this helped explain the reduction in intra-acinar arterial numbers.¹⁵ A reduction in distending pressure was suggested as a possible mechanism for this. In the patient we studied the banding reduced systolic pulmonary artery pressure from 85 to 64 mm Hg while pulmonary vascular resistance increased. There are not sufficient abnormalities in the pre-acinar arteries to explain the persistent pulmonary hypertension, and the intra-acinar arteries seem to be morphologically normal without an abnormal degree of muscularisation. This suggests that the persistent pulmonary hypertension is secondary to hypoplasia of the pulmonary vascular bed.

Most patients with an atrial septal defect associated with severe pulmonary hypertension will not benefit from closure. However, a few like this patient, who show a reduction in pulmonary hypertension with pharmacological agents may be candidates for closure. A preoperative lung biopsy may be helpful in deciding on management. Recognition of the histological pattern of reduced parenchymal arteries on lung biopsy may help to explain pulmonary hypertension. The lack of intimal fibrosis or medial hypertrophy in the pulmonary arteries is unusual given the degree of pulmonary hypertension.

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