Persistent pulmonary hypertension late after neonatal aortic valvotomy: a consequence of an expanded surgical cohort

M Burch, L Kaufman, N Archer, I Sullivan

Background: Survival of neonates with critical aortic stenosis has improved over the past decade. Models based on morphological characteristics have been designed to help determine whether early survival is more likely after biventricular repair (surgical or balloon aortic valvotomy) or after a single ventricle staged palliative surgical strategy. However, late follow up data are lacking.

Objective: To report follow up data on survivors of neonatal aortic valvotomy who had persistent pulmonary hypertension caused by restriction to left ventricular filling.

Results: Of four medium term survivors of neonatal valvotomy for critical aortic stenosis who had persistent pulmonary hypertension, one died aged 4 years and the other three have severe limitation of effort tolerance.

Conclusions: This previously unreported late complication of “successful” biventricular repair for neonatal critical aortic stenosis is an important consideration in determining the initial management.
was undertaken. At follow up there was persisting pulmonary hypertension and development of mild left ventricular inflow obstruction. At age 4 years, syncope preceded by abdominal pain occurred on three occasions. Cardiac catheterisation showed slightly subnormal pulmonary artery pressure and an end diastolic gradient of 6 mm Hg between indirect left atrial and left ventricular pressures. Reoperation was carried out. Both mitral valve papillary muscles were hypertrophied, with short chordae. The papillary muscles were mobilised by dividing adherent fibrotic trabeculations. At the end of the procedure, left atrial mean pressure was 11 mm Hg and left ventricular end diastolic pressure was 21 mm Hg. Left ventricular biopsy showed notable fibroelastosis with thickening of the endocardium (fig 1). There was symptomatic improvement, with no further syncope, but poor growth and limited effort tolerance has persisted. Cardiac catheterisation was done most recently at the age of five years (table 1).

Case 4

Aortic stenosis was diagnosed at 20 weeks’ gestation. The left ventricular cavity was of normal size, but there were bright myocardial echoes, most notably around the left ventricular free wall and the septal surface of the left ventricle (fig 2), and impaired systolic function. There was retrograde flow in the aortic arch, indicating right ventricle dependent flow through the arterial duct. Against expectation, at 31 weeks’ gestation there was improvement in left ventricular function with restoration of anterograde flow in the aortic arch. Normal delivery occurred at 39 weeks’ gestation, with a birth weight of 2.4 kg. Surgical valvotomy was undertaken on the second day of life, using cardiopulmonary bypass. He made an uneventful recovery. However, at follow up there was poor growth, limited effort capacity, episodes suggesting presyncope, and features of pulmonary hypertension. Cardiac catheterisation was done at 6 years of age (table 1). Echocardiography showed that the right ventricle was enlarged and the tricuspid regurgitation velocity confirmed increased right ventricular systolic pressure. The left ventricular cavity was of normal size with good systolic function, but had persistence of bright myocardial echoes. Peak systolic flow velocity in the ascending aorta was 2.7 m/s and there was moderate aortic regurgitation. It was felt that further aortic valve surgery was not indicated. Treatment with β-blockade and angiotensin converting enzyme inhibition was begun, but there had been no improvement in the haemodynamic measurements when cardiac catheterisation was repeated seven months later.

DISCUSSION

The most comprehensive data available on early survival of neonates born with critical aortic valve stenosis are those reported from the Congenital Heart Surgeons Society study: an initial “biventricular repair”, essentially balloon or open aortic valvotomy, was done in 116 patients, and an initial Norwood operation in 179. Mathematical models for survival were calculated for each pathway and then used to predict the optimal pathway for each patient, based on functional and morphological features. Not surprisingly, the neonates entered on the biventricular repair pathway had greater aortic valve, aortic root, and mitral valve indexed diameters than the Norwood cohort. Surprising, perhaps, was a predicted five year survival benefit favouring the Norwood pathway in 50% of those who had biventricular repair. Conversely, biventricular repair was predicted as more favourable in 20% of those neonates who underwent the Norwood procedure. The main risk factors for death after aortic valvotomy were young age, a small aortic valve, a short left ventricle, and a high grade of

Table 1 Cardiac catheterisation details

<table>
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<tr>
<th>Patient number</th>
<th>Year of birth</th>
<th>Age at first surgery (days)</th>
<th>Catheter data</th>
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<th>Age (years)</th>
<th>Outcome</th>
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LVEDP, left ventricular end diastolic pressure (mm Hg); NYHA, New York Heart Association; PA, mean pulmonary artery pressure (mm Hg); PCW, mean pulmonary capillary wedge pressure (mm Hg).
endocardial fibroelastosis’. The last of these was graded subjectively by echocardiography, but this grading correlated only weakly with necropsy grading of endocardial fibroelastosis in the hearts that were available for comparison. This suggests that it should not be assumed that bright endocardial echoes necessarily reflect the same process, even if this appearance provides useful prognostic information.

Late follow up data after neonatal interventions for critical aortic stenosis are lacking. Our previous experience was that hospital survivors of aortic valvotomy had reasonable medium term survival (93% at 10 years, 84% at 15 years) with a good functional result, though often with the need for further left ventricular outflow tract surgery.1 We had not recognised late pulmonary hypertension in survivors of neonatal intervention for critical aortic stenosis at the time of that report. Similar medium term (more than five years) follow up data were reported for neonates operated in the same era.4,5

Left ventricular outflow tract obstruction in fetal life is known to cause endocardial fibroelastosis,6,7 with increased production of collagen and elastic fibres. There may also be other myocardial changes such as fibrosis, necrosis, or calcification, perhaps explaining some of the discrepancy between bright left ventricular endocardial echoes and the histological diagnosis of endocardial fibroelastosis. Almost certainly, an increasing number of neonates with these myocardial changes in the context of critical aortic valve stenosis have been surviving neonatal interventions over the past decade.

The likely explanation for the severe pulmonary hypertension persisting up to 12 years after neonatal aortic valve surgery in the patients in this report is restriction to left ventricular filling. Bright left ventricular endocardial echoes were seen prenatally in the two patients who underwent prenatal echocardiography. Endocardial fibroelastosis was confirmed by left ventricular myocardial biopsy in a third patient. Pulmonary hypertension is a well known consequence of restrictive cardiomyopathy8 and isolated endocardial fibroelastosis.7 Interestingly, isolated endocardial fibroelastosis is now rarely seen, possibly because of a link between this condition and the mumps virus, which is now uncommon since the introduction of the MMR vaccine.10

The recent data referred to above have provided information about the interventional strategy (aortic valvotomy versus Norwood procedure) that is most likely to result in survival up to five years after neonatal intervention for critical aortic valve stenosis.1,4 However, it was acknowledged that these data could not yet examine long term complications.3 Late problems occur with a functionally single ventricle surgical strategy, even in patients with a good medium term outcome. In those who undergo biventricular repair, the likely need for further intervention because of recurrent left ventricular outflow obstruction or aortic regurgitation is well known. Restriction to left ventricular filling secondary to altered heart muscle physiology may be an additional important determinant of the long term outcome. Further information about this previously unreported late complication of “biventricular repair” may help to inform the decision about whether to use neonatal aortic valvotomy or the Norwood operation, and may also lead to consideration of additional or alternative surgical approaches such as left ventricular endocardial resection and autograft replacement of the aortic root, or transplantation, in selected patients.

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