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Cardiac problems in Down syndrome

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Summary Here, we describe the incidence and spectrum of congenital heart defects in children with Down syndrome. Antenatal diagnosis, postnatal presentation, investigation, treatment and treatment outcome are discussed. Endocardial cushion defects (atrioventricular septal defects) are described in detail as they are the most common cardiac lesion in this group of patients.

Practice points:

- 40% of children with Down syndrome have congenital heart disease
- Some babies with significant congenital heart disease will be asymptomatic and have no murmur
- All babies with Down syndrome should have an early screening echocardiogram
- Frusemide 1 mg/kg and spironolactone 1 mg/kg twice daily are given for the treatment of heart failure
- Early involvement of the dietitian is recommended to maximize preoperative weight gain
- Surgery for a large ventricular septal defect or complete atrioventricular septal defect should occur before 6 months of age

Incidence

Down syndrome, or trisomy 21, occurs in 1 in 660 live births.[1] Approximately 40% of these children will have congenital heart disease (CHD). There appears to be no difference whether the chromosome abnormality is due to non-dysjunction (94%), parental translocation (3%) or mosaicism (3%).[2]

The Atlanta Down Syndrome Project[3] showed that of the 227 trisomy 21 children born with CHD, 45% had an atrioventricular septal defect (AVSD; with or without other CHD), 35% had a ventricular septal defect (VSD; with or without other CHD), 8% had an isolated secundum atrial septal defect, 7% had an isolated persistent patent ductus arteriosus, 4% had an isolated tetralogy of Fallot, and 1% had other defects. Similar studies have shown comparable statistics. Left-sided obstructive lesions such as coarctation and valvar aortic stenosis are rare, and transposition of the great arteries has not been reported in Down syndrome.

Antenatal diagnosis

Prenatally, Down syndrome is most often identified in the first trimester when there is advanced maternal age or when maternal serum factors or fetal sonographic findings such as increased nuchal translucency indicate an increased risk. The prenatal detection of a complete AVSD in the setting of usual atrial arrangement (situs solitus) strongly suggests Down syndrome. Conversely, an AVSD in the setting of atrial isomerism does not indicate the syndrome. When a complete AVSD is found antenatally, amniocentesis should always be offered.[4] In

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most surgical series of complete AVSD 70 – 80% will have Down syndrome.

Postnatal diagnosis

As the antenatal diagnosis of Down syndrome improves and more pregnant women opt for termination, we see fewer cases of Down syndrome with undiagnosed CHD. It often seems to be the younger pregnant mothers who slip through the net of antenatal diagnosis and are unexpectedly faced with a child with Down syndrome and CHD. When a child is born with Down syndrome, it is important to have a high level of suspicion that the child may have CHD.

Children with a large AVSD or VSD often do not have a murmur. This is because the ventricular communication is large and the pressure in the left and right ventricles is equal.

In the normal newborn, it takes up to 10 days for the pulmonary vascular resistance (PVR) to fall from the high level seen in the fetus to the level that it will maintain throughout adult life. In the presence of a large VSD or complete AVSD, the fall in PVR may be delayed for 3–6 weeks. Particularly in children with Down syndrome, the delay in the fall of PVR may be greater, and sometimes the PVR does not fall at all. In the setting of a persistently high PVR, pulmonary blood flow is not markedly increased so the child is not breathless at this time despite a large defect. If we therefore depend on clinical examination alone, this important group of patients may be missed. Wren et al.[5] showed that of all the children born with Down syndrome and heart defects in their health region, only 41% had an abnormal cardiovascular finding (almost always a murmur) on neonatal examination. If clinical examination alone were used to screen Down syndrome patients, the majority of patients would thus be missed. Wren found that 34% of Down syndrome babies with CHD remained undiagnosed by 6 weeks of age and 24% by 12 weeks.

So how should newborn babies with Down syndrome be screened? It appears that using clinical symptoms and examination alone is inadequate. Tubman et al.[6] showed that echocardiography performed early in life could detect CHD that might otherwise be missed. Clinical examination, radiography and electrocardiography individually were insensitive albeit highly specific. Sensitivity improved, however, when the three techniques were combined.

An ECG may be helpful in identifying babies with an AVSD. In a child with Down syndrome, a superior mean frontal QRS axis (left or extreme right axis deviation) is virtually diagnostic of an AVSD. A normal ECG does not, however, exclude CHD. It is very helpful for an ECG to be sent with the referral letter to the paediatric cardiologist. Chest X-rays may also be helpful, although again a normal chest X-ray does not exclude CHD.

We consider that all children born with Down syndrome should be referred for early echocardiography. If the child is well and pink with normal cardiovascular examination findings other than a systolic murmur, he or she can be seen electively at an early outpatient appointment. If there are other abnormal findings, such as cyanosis, the child should be seen on a more urgent basis.

Atrioventricular septal defect

Anatomy

The anatomical hallmark of an AVSD is a common atrioventricular junction guarded by a common atrioventricular valve.[7,8] In a partial AVSD (ostium primum ASD), the common valve is divided into two orifices, whereas in a complete AVSD, a common valve guards a common orifice (Fig. 1). In each case, the valve consists of five leaflets: a superior and inferior bridging leaflet, each of which overrides the interventricular septum and has chordal attachments to both ventricles, a left mural leaflet, a right mural and a right anterolateral leaflet. In partial AVSD, a tongue of tissue joins the otherwise free margins of the superior and inferior bridging leaflets, dividing the common valve functionally into two valves, although retaining continuity between the left and right sides of the bridging leaflets.

In a partial AVSD, the bridging leaflets are tethered to the crest of the ventricular septum, leaving only an interatrial communication. In a complete AVSD, the superior and inferior bridging leaflets are free-floating so there will be an interatrial and an interventricular communication. If the superior and inferior bridging leaflets are fused to the atrial septum, there is an interventricular communication that is functionally similar to a large-inlet VSD (Fig. 2). Finally, although rare, if the bridging leaflets are fused to both atrial and ventricular septa, there will be an AVSD with no interatrial or interventricular communication.

In children with Down syndrome, complete AVSDs are more common than partial ones. In the Brompton series, only 10% of children undergoing a repair of partial AVSD had Down syndrome. In

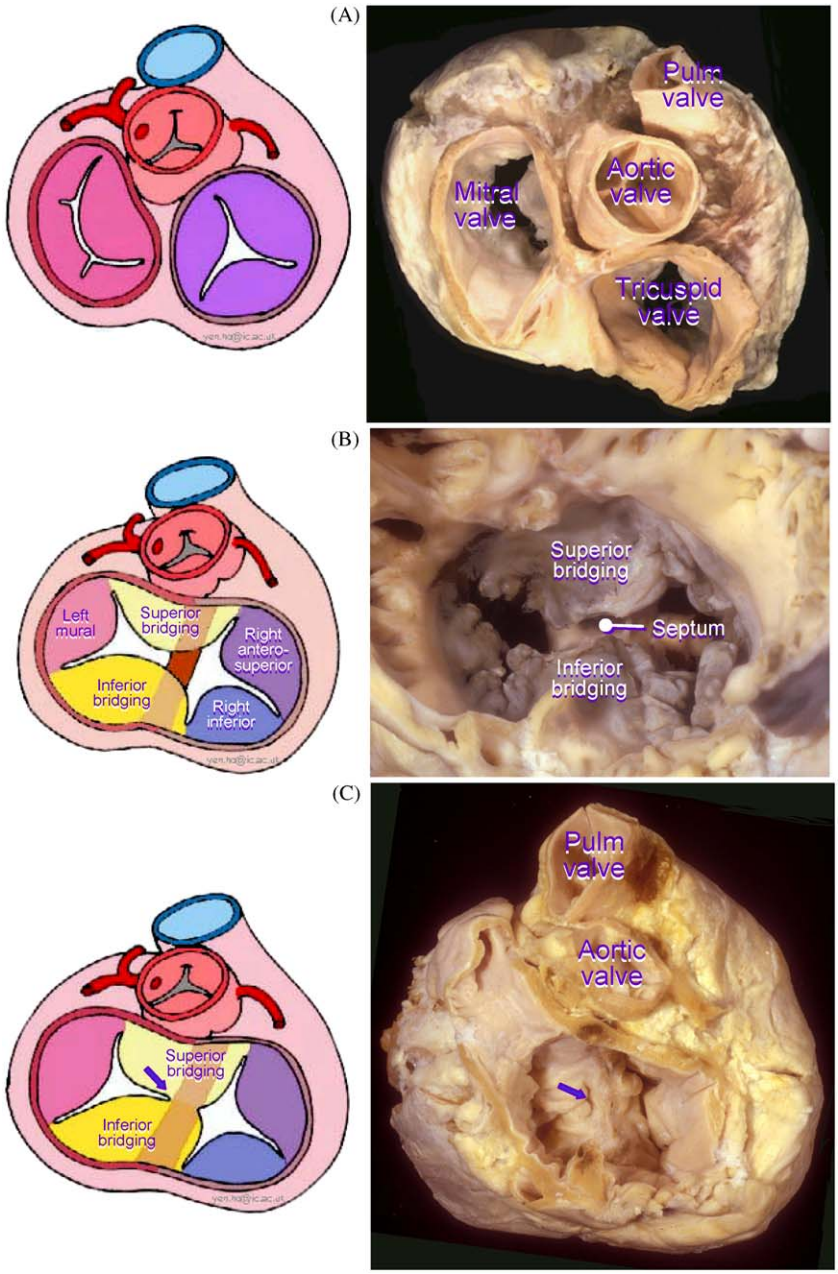

Figure 1 (a) Normal atrioventricular junction. (b) Common atrioventicular junction of a complete atrioventricular septal defect (AVSD). (c) Divided orifice of a common atrioventricular junction of a partial AVSD. (Reproduced by kind permission of Yen Ho.)

comparison, 73% of children undergoing a repair of complete AVSD had Down syndrome.[9]

Presentation

The presentation depends upon the amount of left-to-right shunting at the atrial and or ventricular level. This is dependent upon the size of the atrial and ventricular communications as well as the PVR.

The most common presentation of an isolated complete AVSD in infancy is with symptoms of heart failure. When the PVR falls, there is a large left-to-right shunt with high pulmonary blood flow, and the child becomes breathless, is poor at feeding and shows failure to thrive.

In the scenario of a large VSD and a persistently high PVR, pulmonary blood flow is increased but not torrential. The baby may have no symptoms, and although there will be a loud pulmonary component to the second heart sound, there will not be a murmur. Screening echocardiography is crucial to detect this lesion. If these infants do not have corrective surgery, many will go on to develop

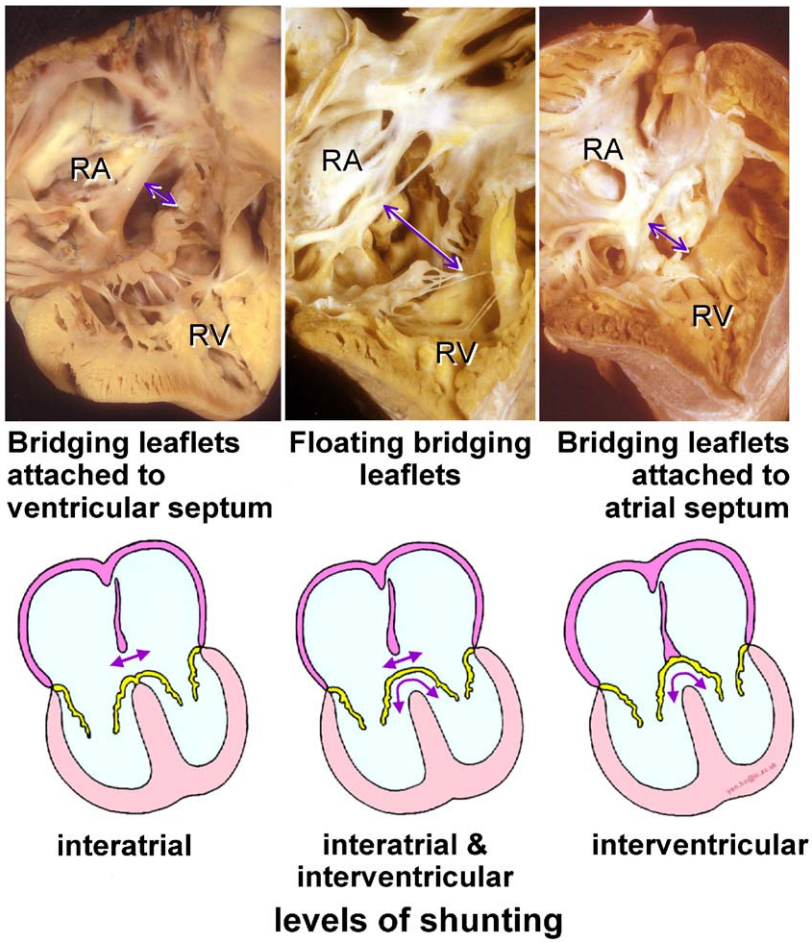

Figure 2 Levels at which shunting can occur in an atrioventricular septal defect (Reproduced by kind permission of Yen Ho.)

pulmonary vascular disease and have reduced life expectancy.

Pulmonary vascular disease is particularly common in patients with Down syndrome and a complete AVSD, even in the first year of life. It has been suggested that upper airway obstruction with subsequent hypoxia and carbon dioxide retention may cause pulmonary vasoconstriction. This, along with a pulmonary vasculature perfused at systemic pressure because of a large AVSD, may promote accelerated pulmonary vascular disease. Because of the risk of irreversible vascular disease in Down syndrome children with complete AVSD, surgery should be undertaken within the first 6 months of life.

Patients with a partial AVSD often escape detection in infancy and present in early childhood with an incidental murmur. Pulmonary vascular disease develops in adult life.

Another factor influencing presentation is the degree of regurgitation through the common atrioventricular valve. Severe regurgitation increases the likelihood of heart failure. Atrioventricular regurgitation is typically more severe in chromosomally normal children than in Down syndrome children.

Other anomalies, such as coexistent tetralogy of Fallot or coarctation, will of course, profoundly alter clinical manifestations.

Investigation

Electrocardiogram

First-degree heart block is common in both partial and complete AVSD. A superior mean frontal QRS axis is usual.

Chest X-ray

When the PVR falls, there will be cardiomegaly and pulmonary plethora. If the PVR remains high, the chest X-ray may be normal. Patients with pulmonary vascular disease will have cardiomegaly and peripheral pruning of the vascular tree with a hypertranslucent appearance, in association with dilatation of the hilar and proximal vessels.

Echocardiography

This is the gold standard[10] of investigation. The anatomy can be fully defined: the presence of a single or partitioned orifice of the common atrioventricular valve; the level, size and direction of shunting across the septum; additional VSDs; the severity of valvar regurgitation; the relative size of the right and left ventricles—is it a balanced or unbalanced AVSD?; the presence of a left superior vena cava, which may make surgery more difficult; and other coexisting anomalies.

Cardiac catheterization and angiography

This is only used if irreversible pulmonary vascular changes are suspected but not definitely present. Detailed measurements of PVR are made, and the response to oxygen and other vasodilators, such as nitric oxide, is determined. If the PVR proves to be high and irreversible, surgery is contraindicated as, following surgery, the child may die of acute right heart failure. In the older patient in whom an elevated PVR does respond to vasodilators, surgery will still carry an increased risk because of acute pulmonary hypertensive crises, which may occur postoperatively and be resistant to therapy.

Management

Breathless babies can initially be treated with diuretics to control heart failure. Nutrition is important, and babies are likely to need high-calorie milk, supplements or even nasogastric feeding in order to gain sufficient weight. Ultimately, however, surgery is required to treat the condition.

The surgical repair of complete AVSD has undergone major advances in the past few years. This has been due to increasing surgical skills and advances in cardiopulmonary bypass technique and postoperative care. In addition, a major factor in improving results has been the earlier age of operation. Infants operated on at under 6 months of age are less likely to experience pulmonary hypertensive crises during the postoperative period. The introduction of inhaled nitric oxide has also helped the management of such crises when they do occur.

As a result of such improvements, the reported hospital mortality rate for the repair of complete AVSD has fallen to as low as 6% in some centres. At the same time, the predicted life expectancy of people with Down syndrome has increased. In view of this, all children with Down syndrome and AVSD are now recommended for early surgical repair.

Current areas of controversy in the surgical management of the child with a complete AVSD include optimal age for repair and the usefulness of pulmonary artery banding, the one-patch versus. two-patch technique, and surgical management of the left atrioventricular valve.[11]

Primary surgical repair in infancy before 6 months of age is the treatment of choice. Pulmonary artery banding still, however, has a role in those with additional VSDs, very small babies and those with ventricular disproportion. In the latter group, when one ventricle is too small for biventricular repair, early pulmonary artery banding is mandatory to lower distal pulmonary artery pressure and vascular resistance. The child will then go down the Fontan/univentricular surgical pathway. Banding is contraindicated in patients with severe atrioventricular regurgitation.

The single-patch technique involves dividing the common valve leaflets and suspending them from a single patch used to close both the atrial and ventricular defects. The two-patch technique involves the use of two separate patches, one to close the interatrial communication and one to close the VSD. It has been suggested that the two-patch technique creates less distortion of the valve tissue, thereby allowing a more accurate reconstruction of the right and left atrioventricular valves.

Achieving a competent non-stenotic left atrioventricular valve at the time of reconstruction is important for outcome. It is controversial whether the left atrioventricular valve should be left as trifoliate or whether the 'cleft' (the zone of apposition between the left ventricular components of the bridging leaflets) should be closed. It has been suggested that leaving the cleft open leads to an increased incidence of residual left atrioventricular valve regurgitation and reoperation.

There is less urgency in the repair of a partial AVSD because the pulmonary vascular disease occurs in adult life. Surgical repair is usually performed at 2–5 years of age before the child starts school. Some surgeons argue, however, that repair should be before this to prevent annular dilatation and degenerative changes in the valve, which might impede surgical outcome.

Long-term issues

The overall long-term prognosis following AVSD repair is good. Left atrioventricular valve regurgitation is common and can be problematic. Up to 10% of patients will require surgery for left

atrioventricular valve repair or replacement. Children with normal chromosomes have a higher risk of requiring reoperation than those with Down syndrome as their valves are more dysplastic.

Other late complications after repair of AVSD include subaortic stenosis, residual VSD, progressive pulmonary vascular disease in patients who underwent relatively late closure of a VSD, late onset of complete heart block, atrial and ventricular arrhythmias, sudden cardiac death and bacterial endocarditis.

All children require bacterial endocarditis prophylaxis post AVSD repair.

Eisenmenger's syndrome

In the setting of a large interventricular communication when surgery has not been performed, progressive pulmonary vascular disease may develop. Sometimes, the PVR does not fall postnatally. Usually, however, as the PVR falls, the left-to-right shunt increases and the child becomes breathless. An improvement in symptoms then reflects either the VSD becoming smaller or a secondary increase in PVR. The symptoms initially regress but as PVR rises to a level greater than systemic vascular resistance, eventual shunt reversal results in cyanosis. Patients become increasingly blue and breathless. They develop progressive right heart failure and are at risk of haemoptysis, endocarditis, cerebral abscess, arrhythmia and sudden death.[12]

Down syndrome children with congenital heart disease now undergo operative repair at a younger age, patients with Eisenmenger's complex tending to be seen in adolescent and adult clinics. The treatment is palliative. The only cure is heart–lung transplantation, which has poor results.

Conclusions

Approximately 40% of children born with Down syndrome will have CHD. Atrioventricular defects and VSDs are the most common lesions. Newborns with these lesions may be asymptomatic and have no murmur. Therefore, all babies born with Down syndrome should have an early echocardiogram to screen for CHD. Babies with Down syndrome and a large ventricular shunt are at risk of developing pulmonary vascular disease early in life. In view of this, they should undergo operative repair or palliation before 6 months of age. After the initial repair, residual left atrioventricular valve regurgitation can be problematic and further surgery may be required.

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