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Brief Report

Down syndrome and transposition of the great arteries

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Abstract There is an old adage in paediatric cardiology that, despite the high prevalence and wide spectrum of CHD, transposition of the great arteries does not occur in trisomy 21. We present a case of transposition of the great arteries, ventricular septal defect, and pulmonary stenosis in a patient with trisomy 21.

Keywords: Transposition great arteries; Down syndrome; genetics

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We report a case of transposition of the great arteries with ventricular septal defect and pulmonary stenosis in a patient with trisomy 21. Literature review indicates that 40–50% of all patients born with trisomy 21 will have a CHD.[1–3] The most common primary defect described is the atrioventricular septal defect (37–44%) followed by ventricular septal defect and secundum atrial septal defect (8–15%). The most common cyanotic CHD is tetralogy of Fallot (4–6%).[1–3] Worldwide population studies between 1985 and 2015 that cumulatively analysed over 18,000 patients with CHD failed to find a case of transposition of the great arteries in trisomy 21.[1–7]

Patel et al[8] published results from the Society of Thoracic Surgeons Congenital Heart Surgery database from 2010 to 2013 detailing the prevalence of non-cardiac and genetic abnormalities in infants undergoing cardiac surgery. Of 318 neonates with Down syndrome, there was one reported case of transposition of the great arteries;[8] however, no further details are available regarding this case.

Case report

We report the case of a female infant born at 36+1 weeks of gestation following spontaneous onset of labour. She had an antenatal diagnosis of duodenal atresia and trisomy 21. Routine fetal anomaly scan reported a normal heart. Following delivery, a murmur was heard, her oxygen saturations were 85% on 30% oxygen, and she was admitted to the neonatal ICU. Chest X-ray showed oligaemic lung fields and cardiomegaly. An echocardiogram on day 1 of life demonstrated transposition of the great arteries, a single, large subpulmonary ventricular septal defect, and a dysplastic pulmonary valve with subpulmonary stenosis. Bidirectional flow across a stretched patent foramen ovale was present. The ductus arteriosus was closed.

As oxygen saturations were acceptable, prostaglandin treatment was not commenced. On day 3 of life, the duodenal atresia was repaired. After the neonatal period, oxygen saturations became more difficult to maintain, and the patient underwent a balloon atrial septostomy followed by a balloon pulmonary valvuloplasty (left ventricular outflow tract $V_{max} = 4.1$ m/s) at 6 and 7 weeks of life, respectively. Owing to obstructive sleep apnoea, a bronchoscopy and CT angiogram were performed, which suggested inonimate artery compression of the trachea but no vascular ring. She underwent a surgical aortopexy. The combination of these procedures significantly improved her oxygen saturations, and diuretic treatment was necessary to control mild pulmonary oedema. Her course was further complicated by necrotising enterocolitis, which was treated conservatively. She was discharged home on day 78 of life.

The patient is now 15 months old with oxygen saturations ranging between 85 and 92% in room air.

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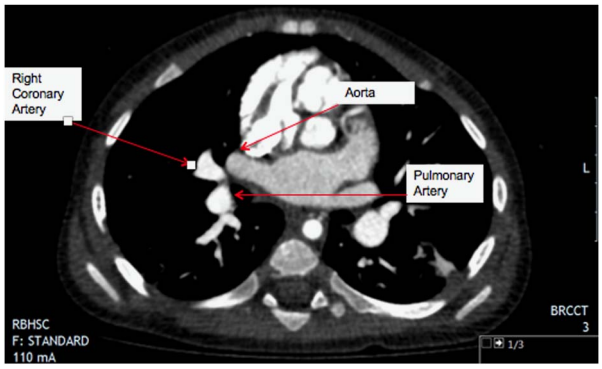

Figure 1.
CT angiogram demonstrating anterior:posterior relationship of great arteries.

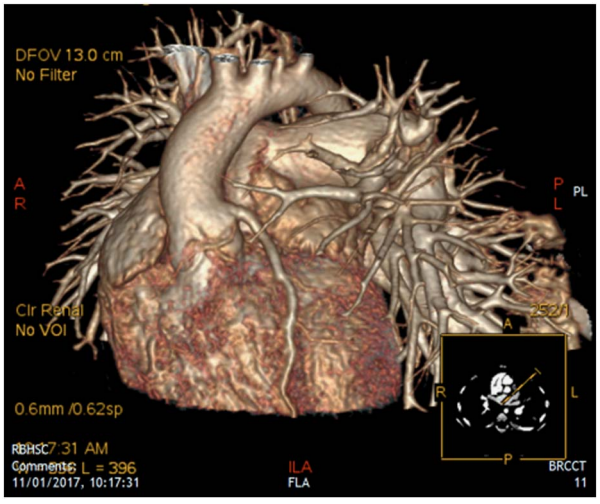

Figure 2.
3-D reconstruction from CT angiogram demonstrating anterior aorta with left anterior descending artery.

She is currently awaiting surgical correction in the form of the Nikaidoh procedure.

CT angiogram images are presented in Figures 1 and 2.

Discussion

In 1989, the Baltimore–Washington Infant Study noted the absence of transposition of the great arteries in Down syndrome, and suggested that there may be a genetic influence on the embryological mechanisms that result in transposition.[1] Other review articles have since claimed that transposition of the great arteries is "virtually absent" in Down syndrome.[2,3] Large studies such as these have resulted in the general belief that Down syndrome and transposition of the great arteries are not seen together. This case illustrates that, although this association is rare, the possibility of transposition of the great arteries in a child with Down syndrome may occur.

Genetics studies from the United States of America have reported human molecular and cardiac data that narrow the Down syndrome CHD gene region.[9] The Down syndrome cell adhesion molecule gene region is thought to be important as it is expressed in the heart during cardiac development, spans more than 840 kb of the candidate region, and encodes a cell-adhesion molecule. These studies propose Down syndrome cell adhesion molecule as a candidate gene region for Down syndrome CHD.[9] A large study by Costain et al[10] showed that genome-wide copy-number variations contribute to genetic risk for transposition of the great arteries. Smaller, rare, copy-number variations helped narrow critical regions for conotruncal defects at chromosomes 10q26 and 13q13.

These genetic studies may indicate that a "protective genetic influence" for transposition of the great arteries in Down syndrome is less likely. Potentially as the two genetic mechanisms that result in the development of these conditions are completely unrelated, the probability of acquiring both conditions is low.

Most maxims in medicine are made to be contradicted, and it seems that transposition of the great arteries can occur in Down syndrome.

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None.

Conflicts of Interest

None.

Ethical Standards

Written informed consent was obtained from the parent of the patient detailed in the case report.

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