CASE REPORT

Undiagnosed DiGeorge syndrome presenting in middle age with an aortic root aneurysm and chronic dissection

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SUMMARY

DiGeorge syndrome is the second commonest cause of congenital heart disease after trisomy 21. This case illustrates an undiagnosed case of DiGeorge syndrome for a patient who had a ventricular septal defect repair in childhood. He survived well into his adult years, and was only diagnosed post mortem after an unsuccessful repair of an aortic root aneurysm. The case serves as an example supporting genetic screening of children with congenital heart disease, and lifelong cardiology follow-up for patients with a confirmed genotype.

BACKGROUND

DiGeorge syndrome, also known as velocardiofacial syndrome, is characterised by a 22q11 chromosomal microdeletion. Its incidence in live births has been estimated at 1 in 4000,¹ and it is the commonest interstitial deletion. The phenotype of this deletion is highly variable, and is dependent on the embryological pattern of migration of the neural crest cells from the third and fourth pharyngeal pouches. We describe the case of a patient with previously undiagnosed DiGeorge syndrome presenting in middle age with an aortic root aneurysm and chronic dissection, as well as vascular malformations to the right subclavian, coeliac and left iliac arteries.

CASE PRESENTATION

A 59-year-old man presented to his general practitioner with a productive cough. He had a routine chest radiograph taken (figure 1), which showed cardiomegaly and unfolding of the aorta. He was otherwise well and asymptomatic. His medical history included a previous ventricular septal defect repair when he was 9 years of age, as well as an appendectomy and tonsillectomy as a child. He suffered from recurrent sinus and ear infections, and had required bilateral myringoplasties.

He took bisoprolol 5 mg daily for hypertension. There was no family history of note. He was unemployed and lived with his parents. He had no children. He was active, attending his local gym regularly, and held a glider pilot license. He did not smoke. He drank 4 units of alcohol a week.

On examination, he had dysmorphic facial features, with low set ears and midface flattening. He weighed 102 kg, and had a height of 169 cm and body mass index of 35.7 kg/m². His pulse rate was 80 bpm, in sinus rhythm, with a blood pressure of 150/60 mm Hg. His peripheral oxygen saturations

were 96% on air. He had a healed midline sternotomy scar. He had a severe diastolic murmur over his aortic region.

An echocardiogram showed a severely dilated aortic root, 7.7 cm in diameter, at a distance of 2 cm from his annulus. The ascending aorta maximum diameter was 9.3 cm. The aortic arch was 3.1 cm across, with a normal descending aorta width. The aortic valve was tricuspid, and there was severe aortic regurgitation. His left ventricle was dilated, with an ejection fraction of 54%.

He was admitted to our tertiary referral centre via his local hospital, for further investigation.

INVESTIGATIONS

The patient had normal renal function with baseline creatinine of 76 mg/dL and normal clotting function. His platelets were $137 \times 10^9/L$ and haemoglobin was 13.3 g/dL. His corrected calcium was within normal limits.

A cardiac MRI demonstrated the aneurysm arising at the aortic annulus and extending up the ascending aorta, compressing the right pulmonary artery, superior vena cava and left atrium. The right atrium was closely opposed to the superior sternum. Two dissection flaps were evident: one in the anteromedial wall of the proximal aorta just above the left and right coronary cusps; the other was limited to the anterolateral wall of the mid ascending aorta. There was no coarctation.

Figure 1 Chest radiograph: increased cardiothoracic ratio; unfolding of the aorta evident on the right of the mediastinum (illustrated with white asterisk).

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Figure 2 CT aortogram—three-dimensional reconstruction of the aortic arch. The aortic root and ascending aorta are grossly aneurysmal, measuring 96 mm in diameter. The aberrant right subclavian is illustrated with a white asterisk.

A CT aortogram similarly showed the patient's aortic aneurysm (figure 2). It also demonstrated aberrant vasculature. His right subclavian artery arose from the distal arch, taking a retro-oesophageal course into the right arm. His coeliac axis was significantly narrowed and his superior mesenteric artery was sharply angulated, but his abdominal viscera were perfused normally. He had a very large number of lumbar collaterals. His left external and internal iliac arteries gave rise to numerous significant collaterals. These collaterals, together with lumbar collaterals, reconstituted the left external iliac, which was significantly narrowed at its origin.

TREATMENT

The patient proceeded to have an aortic valve, root and ascending aorta replacement. He had a re sternotomy combined with a left thoracotomy. The aortic valve was replaced with a Freestyle 29 mm bioprosthetic valve and aortic root, and the ascending aorta with a 34 mm diameter 20 cm length Gelseal graft. The left and right coronary ostia, which had been dissected out in a button fashion, were reimplanted into the root prosthesis in their anatomical position. The patient was on cardiopulmonary bypass for 108 min, with a cross-clamp time of 79 min. Following removal of the aortic cross-clamp, there was bleeding from the tissue surrounding the aorta. This was repaired. Then, post cardiopulmonary bypass, there was massive diffuse bleeding, refractory to local and systemic pro-coagulant therapies. It was not possible to close the patient's chest.

Despite sustained efforts with transfusions, inotropic support, continuous venovenous haemofiltration and chest re-exploration, the patient died from refractory bleeding and multiorgan failure on the third postoperative day.

OUTCOME AND FOLLOW-UP

Cytogenetic testing had been performed prior to this patient's surgery, in search of a possible explanation for his dysmorphic features and abnormal vasculature. His karyotype was 46 XY. Fluorescent in situ hybridisation showed a deletion of region q11.2 on one chromosome 22, consistent with DiGeorge syndrome. Post mortem analysis was unremarkable except for aortic tissue that was taken intraoperatively. This showed a chronic, healed U-shaped dissection, with dense fibrosis of the media, and atheroma of the intima.

DISCUSSION

DiGeorge syndrome represents the second most common genetic cause of congenital heart disease after trisomy 21, and this heart disease is the main cause of mortality.¹ Cardiac defects are present in approximately 75% of patients with DiGeorge syndrome,¹ in particular conotruncal malformations. Sinus of Valsalva² and pulmonary artery aneurysms have been described.³ One paediatric study⁴ looking at 93 children under the age of 13 years found evidence of aortic root dilation on 10 screening echocardiograms. The authors stated that further echocardiographic screening may be warranted to assess these patients in adolescence and adulthood. Given the pathological post mortem findings in this case, the dilation of the aortic root may be secondary to evolution of the chronic dissection, rather than DiGeorge syndrome per se.

The phenotype of a 22q11 deletion can be highly variable. The patient was 59 years old. Median life expectancy of those surviving childhood was 41.5 years in one prospective study.⁵ For those adult patients with no congenital heart disease, life expectancy was still only 47.3 years.

This patient also had unusual vascular arterial malformations, which are not commonly seen in the DiGeorge syndrome phenotype. His aberrant right subclavian artery arising from the distal aortic arch has been described elsewhere.⁶ The vascular stenoses of the coeliac axis and external iliac artery were most likely congenital in nature, but given the patient's age, they may have been atheromatous.

The wider phenotype of this patient is consistent with the genetic diagnosis of DiGeorge syndrome. Congenital heart defects, recurrent infections and abnormal facies are all well recognised features. Midface and palate abnormalities are common, as are low set ears. Other features can include hypertelorism and narrowed palpebral fissures. The absence of family history is not surprising. The majority of cases are de novo mutations.⁶

Learning points

- ▶ The phenotypic presentation of DiGeorge syndrome is highly variable.
- ▶ Genetic testing for patients with congenital heart disease should be considered where the underlying cause has not been identified.
- ▶ Lifelong cardiology follow-up should be considered for patients with a confirmed genotype of DiGeorge syndrome.

Competing interests None declared.

Patient consent Obtained.

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