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Isolated Innominate Artery in 22q11 Microdeletion

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Abstract. A patient with an isolated left innominate artery (with a right-sided cervical aortic arch) is described. This is the first report of such an anomaly associated with chromosome 22q11 microdeletion. The abnormality represents an interruption in the primitive aortic arch that is atypical for this chromosome deletion.

Key words: DiGeorge syndrome — 22q11 deletion — Aortic arch anomaly — Isolated innominate artery — Cervical aortic arch

Isolated innominate artery is an extremely rare abnormality with only a small number of case reports in the literature. There is no recognized pattern of association with any cardiovascular abnormality or syndrome. The anomaly has occurred combined with ventricular septal defect, atrioventricular septal defect, pulmonary stenosis, double-outlet right ventricle, coarctation of the aorta, aortic atresia, Down's syndrome, Goldenhar syndrome, and CHARGE association [1, 4, 8, 9]. We report a case of isolated left innominate artery with a right-sided cervical aortic arch in a boy with acyanotic tetralogy of Fallot and 22q11 microdeletion.

Case Report

A 35-week-gestation premature male infant was found to have transient neonatal hypocalcemia. Cytogenetic testing revealed 22q11.2 microdeletion in the baby and his mother (Oncor D22575 probe). He was mildly dysmorphic with a short neck, a thin upper lip, slightly low-set ears, overfolded upper helices, and mild rhizomelic limb shortening. Although the CD4 and CD8 T cell subsets were slightly reduced there was no clinically significant immunological deficit. Chest x-ray revealed a thymic shadow. He was, therefore, diagnosed as partial DiGeorge syndrome and referred for cardiology review.

Examination revealed a single second heart sound and a long systolic murmur. Echocardiography demonstrated tetralogy of Fallot with a mildly restrictive right ventricular outflow tract and valvular pulmonary stenosis (gradient 45 mmHg). There was a single large perimembranous ventricular septal defect with left to right shunting. Over the first few months of life he failed to thrive and presented on numerous occasions with wheezy episodes, lung collapse, and lower respiratory tract infections. Barium swallow demonstrated moderate gastroesophageal reflux but no indentation of the barium filled esophagus.

Cardiac catheterization confirmed the intracardiac anatomy and demonstrated large pulmonary arteries with an elevated pulmonary artery pressure (50% systemic levels) and a Q_p/Q_s of 2.7:1. There was a right sided cervical aortic arch. The first branch off the arch was the right common carotid artery and the second and last branch was the right subclavian artery (Fig. 1A). There were multiple enlarged posterior thoracic wall collaterals from the descending aorta.

An isolated left-sided innominate artery was opacified by flow from one large tortuous descending aorta collateral (Fig. 1B) and by retrograde flow from the left-sided vertebral and carotid arteries via the circle of Willis (Fig. 1C). The isolated innominate communicated with the pulmonary trunk via a large patent arterial duct. The intracardiac defect was corrected at 13 months of age and the duct was ligated. Recovery was complicated by ventricular tachycardia and respiratory problems. Ultimately, he died of viral pneumonia several months later. Postmortem examination demonstrated a right-sided aortic arch ascending into the neck and confirmed the anatomy of the head and neck vessels observed at cardiac catheterization. There was no microscopic evidence of pulmonary vascular disease.

Discussion

The cardiac defects classically described in DiGeorge syndrome are interrupted aortic arch type B and truncus arteriosus. However, the association between chromosome 22q11 microdeletion and tetralogy of Fallot is now well recognized. An association between 22q11 deletion and aortic arch abnormalities such as right aortic arch, cervical aortic arch, aberrant left subclavian artery, and isolated left subclavian artery has also been observed, particularly in the context of tetralogy of Fallot [5]. Although 22q11 deletion has previously been described in tetralogy of Fallot with a right-sided cervical aortic arch [6], we believe that this is the first case in which the additional finding of an isolated left innominate artery has been reported. Isolated left innominate artery may be clinically significant because there is a potential for subclavian steal, with reversed

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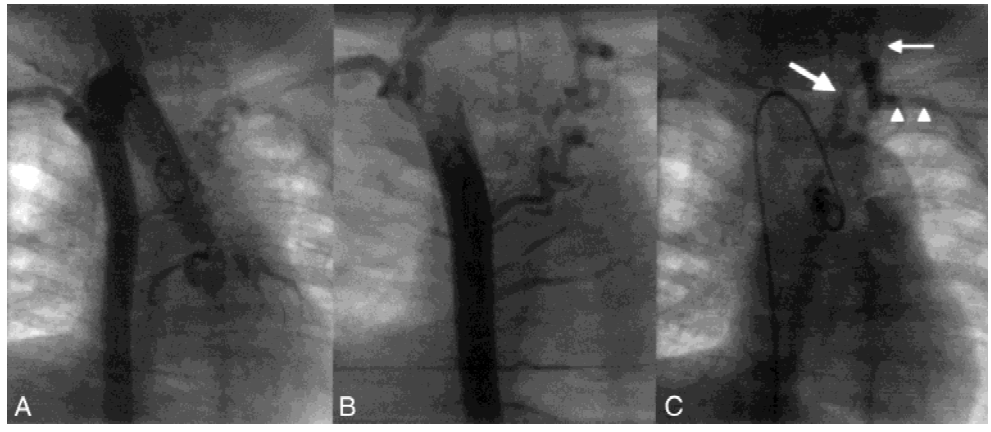

Fig. 1. (A) The early phase of the aortogram demonstrates a right-sided cervical aortic arch. The first branch is the right carotid, which bifurcates early to form the internal and external carotid arteries. **(B)** Later frames demonstrate prominent posterior thoracic wall collateral arteries from the descending aorta, with one particularly prominent tortuous collateral feeding the isolated left innominate artery. **(C)** The isolated innominate artery is seen in the final frames of the aortogram. The subclavian artery (*arrowheads*) fills by retrograde flow from the left carotid and vertebral arteries (*thin arrow*). The innominate communicates with the pulmonary artery via a large patent arterial duct (*thick arrow*).

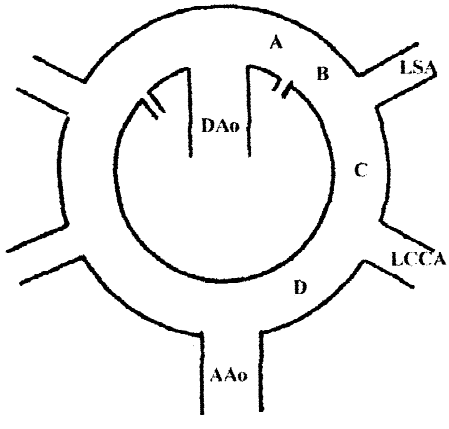

Fig. 2. Hypothetical double aortic arch of Edwards [2]. The left arch can be interrupted in four zones, designated A to D by Garti and Aygen [3], to generate a right aortic arch. *LSA*, left subclavian artery; *LCCA*, left common carotid artery; *DAo*, descending aorta; *AAo*, ascending aorta.

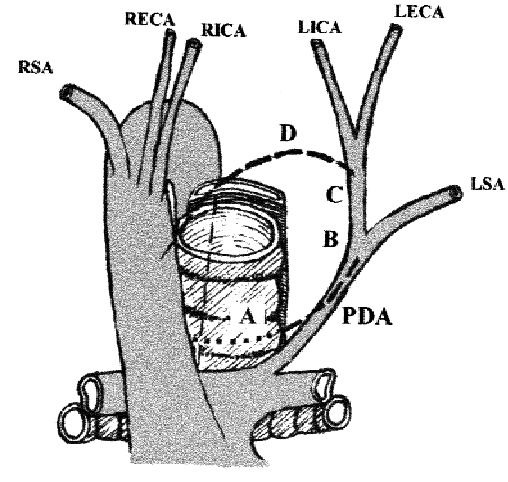

Fig. 3. Diagram of a right cervical aortic arch with isolated left innominate artery *RSA*, right subclavian artery; *RECA*, right external carotid artery; *RICA*, right internal carotid artery; *LICA*, left internal carotid artery; *LECA*, left external carotid artery; *LSA*, left subclavian artery; *PDA*, patent arterial duct. The position of the hypothetical left aortic arch is superimposed on the diagram and its sections, labeled A to D, correspond with the sections illustrated in Fig. 2. Section D has regressed and is indicated by a dashed line, section C persists as a short vessel connecting the left subclavian to the left carotid artery, section B persists as a short vessel connecting the left subclavian to the PDA, and section A has regressed and is indicated by a dashed line that starts from the cranial end of the PDA and passes posterior to the trachea and esophagus to join the descending aorta.

flow in the left carotid and vertebral arteries causing syncope.

Edwards [2] originally proposed a hypothetical double aortic arch to facilitate understanding of the development of aortic arch abnormalities. A right aortic arch is assumed to result from regression of a section of the primitive left arch. Interruption of the left arch may occur in four different zones [3] (Fig. 2). Interruption at points A and D results in an isolated left innominate artery (Fig. 3). Where there is a right aortic arch with an isolated left innominate artery there may be a vascular ring only if the atretic segment at zone A persists as a fibrous cord posteriorly and the ring is completed to the left by a patent arterial duct. Although the respiratory symptoms in this case might be explained by a vascular ring, the absence of a posterior indentation on the barium esophagram makes such a diagnosis unlikely.

According to the aortic arch model, interrupted aortic arch type B and aberrant left subclavian artery both involve a break in the primitive left arch at point C. Mirror-image right aortic arch involves a break at point A and isolated left subclavian artery involves a break at points A and C. Because these are the arch abnormalities associated with 22q11 deletion, it is suggested that breaks at points A and C are part of the 22q11 deletion phenotype. The finding of isolated left innominate artery is therefore novel in that it involves interruptions at points A and D.

Approximately 90% of individuals with DiGeorge syndrome and velocardiofacial syndrome have a microdeletion of chromosome 22q11.2. Recent research suggests that haploinsufficiency of the human *UFD1* gene, found within the 22q11.2 region, is responsible for the 22q11 phenotype [10]. There is strong evidence that a gene within the 22q11.2 region regulates cranial neural crest cells, which in turn regulate the development of the primitive aortic arches and migrate to influence outflow tract septation. It is superficially attractive to view this case of isolated left innominate artery as an additional example of defective aortic arch formation secondary to deficiency in the neural crest caused by 22q11 deletion. However, it is suggested that interruptions at point D in the embryonic arch are unlikely to be caused by the normal range of deletions within the 22q11 region because an isolated innominate artery is not seen frequently as part of the 22q11 phenotype. Indeed, all the reported cases of isolated innominate artery lack features of 22q11 deletion, such as characteristic facies or defects of outflow tract septation. Furthermore, none of the reported cases of aberrant innominate artery (resulting from a single break at point D) have features of the 22q11 phenotype, with the exception of one case of tetralogy of Fallot without documented dysmorphic features [7]. This supports the proposition that there is no causative link between deletions in the DiGeorge critical region on chromosome 22 and breaks in the primitive left arch at point D.

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References

1. Delgado C, Barturen F (1998) Coarctation of the aorta with right aortic arch and isolation of the left innominate artery: a surgical challenge in a patient without collateral posterior brain circulation. *J Thorac Cardiovasc Surg 116*:657–659
2. Edwards JE (1948) Anomalies of the derivatives of the aortic arch system. *Med Clin North Am 32*:925–949
3. Garti IJ, Aygen MM (1979) Right aortic arch with aberrant left innominate artery. *Pediatr Radiol 8*:48–50
4. Kaku S, Pinto F, Lima M (1996) Isolation of the left brachiocephalic artery associated with right aortic arch and left sided arterial duct. *Cardiol Young 6*:239–241
5. Momma K, Kondo C, Ando M, Matsuoka R, Takao A (1995) Tetralogy of Fallot associated with chromosome 22q11 deletion. *Am J Cardiol 76*:618–621
6. Momma K, Kondo C, Matsuoka R (1996) Tetralogy of Fallot with pulmonary atresia associated with chromosome 22q11 deletion. *Am J Cardiol 27*:198–202
7. Nakajima Y, Satomi G, Kawamura T, et al (1993) Right aortic arch with aberrant retroesophageal innominate artery: a report of 2 cases and review of the literature. *Int J Cardiol 38*:247–251
8. Nath PH, Castanega-Zuniga W, Zollikofer C, et al (1981) Isolation of a subclavian artery. *Am J Roentgenol 137*:683–688
9. Papagiannis J, Kanter RJ, Heide RSV, et al (1996) Isolated innominate artery in asplenia syndrome with aortic atresia: newly recognised cardiovascular complex. *Am Heart J 131*:1042–1044
10. Yamagishi H, Garg V, Matsuoka R, Thomas T, Srivastava D (1999) A molecular pathway revealing a genetic basis for human cardiac and craniofacial defects. *Science 283*:1158–1161