DiGeorge syndrome and anomalous right aortic arch with arch-on-arch and figure-of-eight configurations: Aortic sac maldevelopment and left brachiocephalic artery abnormal remodeling

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ABSTRACT

We report a 6-month-old female infant with deletion of chromosome 22q11.2 (DiGeorge/VFS TUPLE 1), normal atrial arrangement with concordant atrioventricular connection, pulmonary atresia, large subaortic ventricular septal defect, diminutive native pulmonary arteries, a characteristic weird-shape right aortic arch with arch-on-arch appearance and figure of 8 configuration. We presented the cardiac computed tomographic angiographic and cardiac angiographic features. Using Autodesk 3ds Max 2018 software, we explained and illustrated the speculative embryologic etiology of this bizarre aortic archanomaly with the extensive abnormal remodeling of the left brachiocephalic artery, based on a "five-embryonic aortic arches" concept. As to the best of the authors' knowledge, this is the first report of a genetically confirmed case of DiGeorge syndrome and an exceedingly rare type of right aortic arch anomaly with embryologic explanation according to the "five-embryonic-aortic-arches" concept. It seems that the constellation of pulmonary atresia, bizarreshaped right aortic arch due to abnormal development of the aortic sac, and abnormal remodeling of the left brachiocephalic artery may be strongly suggestive of DiGeorge syndrome.

Keywords: Right aortic arch- microdeletion 22 q 11.2 - fifth aortic arch- pulmonary atresia-embryology

We report a 6-month-old female infant who was referred to the outpatient clinic for the evaluation of cyanosis. On inspection, she had clubbing, low-set ears, hypertelorism, broad nasal bridge, and slightly bulbous nasal tip. On cardiac auscultation, there was a single second heart sound with machinery murmur on the back. Chest X-ray revealed up-turned cardiac apex, concave main pulmonary artery segment, decreased pulmonary vascular markings, and a shadow on the upper right sternal border. On echocardiography, she had normal atrial arrangement with concordant atrioventricular connections, normally related great arteries with pulmonary atresia, large subaortic ventricular septal defect, diminutive native pulmonary arteries, and a bizarre-shaped right aortic arch. A large-caliber abnormal artery arose from the left side of the ascending aorta, slightly above the aortic valve, as the first branch of the aortic arch. Cardiac computed tomographic angiography and catheter angiography of the heart showed that both the left common carotid artery and the left subclavian artery arose from this vessel. This artery ended up in the pulmonary vascular bed through a serpentine and figure-of-8–shaped course [Figures 1-3 and Videos 1-5]. In addition, the pulmonary vascular bed was supplied by two other sources: a bronchopulmonary collateral artery

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on the left side and the diminutive native pulmonary arteries [Video 4]. The right common carotid artery arose directly as the second branch, after this abnormal artery, from the right aortic arch. The left common carotid artery originated as the first branch from this abnormal artery. The right subclavian artery originated as the last branch of the right aortic arch, and the left subclavian artery arose as the last branch of this abnormal artery.

Interphase fluorescence *in situ* hybridization (FISH) analysis of intact cells, using DiGeorge/VCF TUPLE 1 and 22q13.3 Deletion Syndrome Probe Combination, showed deletion of chromosome 22q11.2 (DiGeorge/VFS TUPLE 1).

According to the excellent review of Gupta *et al.*, this abnormal artery could not be a persistent fifth aortic arch (PFAA), because the first requirement for being called as a PFAA, that is the artery should arise proximal to the brachiocephalic artery, is not fulfilled. Actually, both the left common carotid artery and the left subclavian artery arose from this abnormal vessel, which denotes that this vessel is the result of extensive abnormal remodeling of the left brachiocephalic artery but not a persistent left fifth aortic arch.[1-3]

Furthermore, recently, Graham *et al.*[4] showed that there are only five aortic arches in the human embryo at Carnegie stage 15. They stated that based on the presence of definitive molecular markers of pharyngeal pouches, there are four pharyngeal pouches and five aortic arches in human embryo and each pouch lies between two aortic arches.[4] Based on this "5-embryonic aortic-arch concept," the embryologic basis of this unusual aortic arch anomaly can be well explained [Figure 4].

Normally, the aortic sac divides into two horns: one on the right that develops brachiocephalic artery and

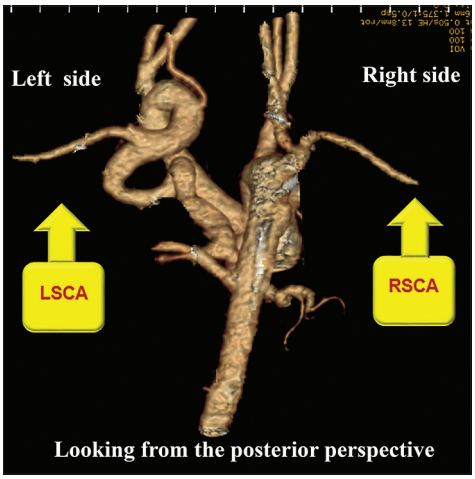

Figure 1: This cardiac computed tomography angiographic image showing the origin of right and left subclavian arteries from the posterior perspective. As is seen, the left subclavian artery arises as the last branch from this abnormal artery

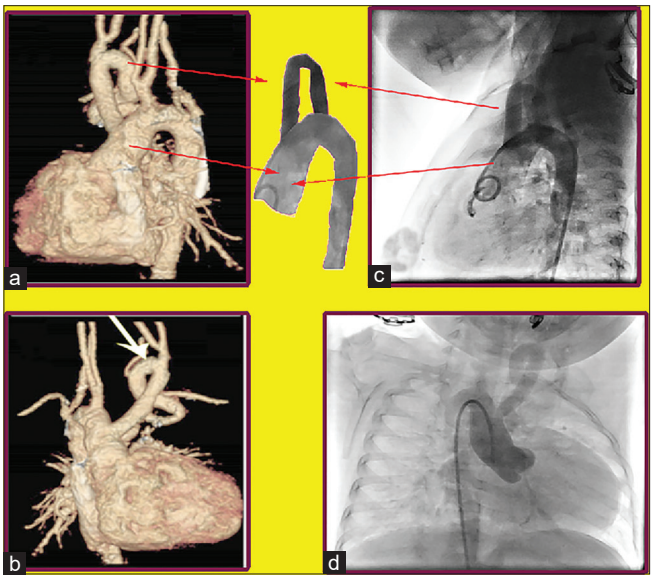

Figure 2: The upper panel (a and c) showing the arch-on-arch appearance produced by the aortic arch (at the bottom) and the arch produced by the bent of the abnormal artery (at the top) in the lateral projection on cardiac computed tomography angiography and catheter angiography. The lower panel (b and d) indicates the figure-of-eight configuration produced by the tortuous course of the abnormal artery on computed tomography angiography and the corresponding image on catheter angiogram in the anteroposterior view

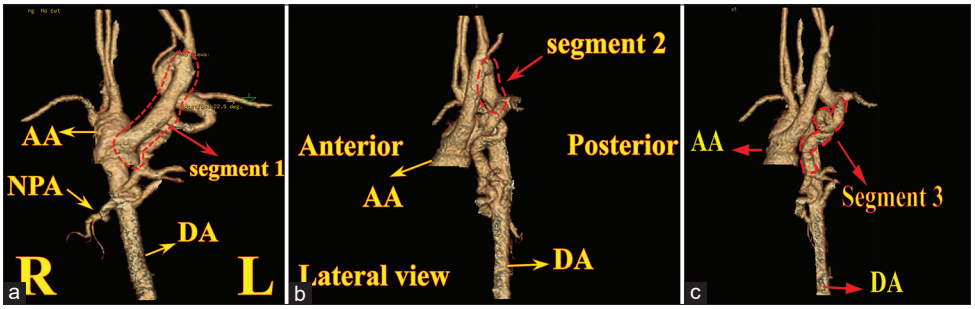

Figure 3: (a-c) The different parts (segments) of this abnormal artery. The speculative embryologic explanations for this anomalous aortic arch are the persistence of the left ventral aorta, the left carotid duct, and the dorsal aorta between the fourth and sixth aortic arch. The right horn makes the proximal segment of the right aortic arch, and the left horn, which is of unusually large caliber and of abnormally long length, associated with extensive abnormal remodeling of the left brachiocephalic artery, creates an appearance of dual ascending aortas (AA: ascending aorta, DA: descending aorta, NPA: native pulmonary arteries)

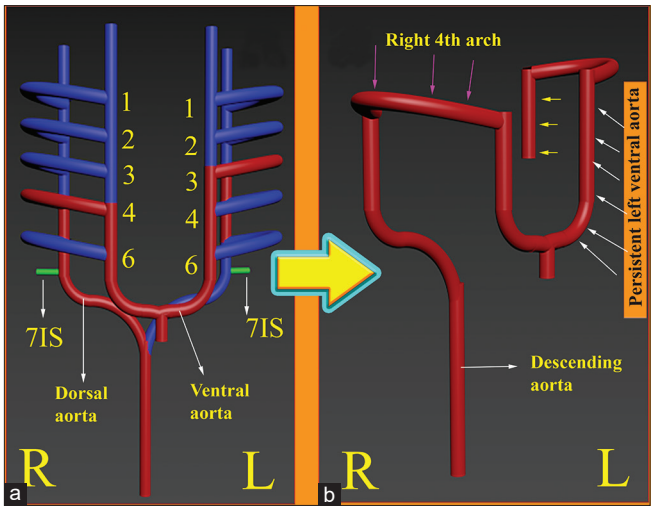

Figure 4: (a) Possible embryologic basis of this abnormal aortic arch based on a "5-embryonic aortic arch concept" that has been recently reported by Graham *et al*. The two green structures represent the right and left seventh cervical intersegmental arteries (7IS) which form subclavian arteries. To form this complex aortic arch anomaly, all segments shown in red should have persisted and those demonstrated in dark blue should have disappeared. (b) The final aortic arch is shown. The multiple white arrows indicate the persistence of left ventral aorta. The three yellow arrows depict the persistence of the carotid duct and the three purple arrows on the right show the persistence of the right fourth aortic arch

the other on the left that makes the proximal segment of the aortic arch. In this case, the right horn makes the proximal segment of the right aortic arch and the left horn is of unusually large caliber and also is of abnormally long length. This, in addition to the extensive abnormal remodeling of the left brachiocephalic artery, creates an appearance of the dual ascending aortas due to persistence of the left ventral aorta between the origin of the sixth and the origin of the third aortic arch and also. Nevertheless, we should bear in mind that the above explanations are speculations on the embryologic basis of this complex aortic arch anomaly and further evidence is essential to confirm these hypotheses.

Reported similar cases with analyzed that FISH test is exceedingly rare.[5] However, a relatively similar report by Lee *et al*. and our case suggest that the co-existence of this unusual type of right aortic arch may be characteristic, if not diagnostic, of 22q11.2 deletion syndrome.[5] Notwithstanding, more cases are necessary to definitely confirm this suggestion.

In conclusion, this case implicates two important learning points. First, abnormalities of the aortic sac development and remodeling of the brachiocephalic artery can contribute to the development of weird-shaped aortic arch anomalies. Second, the constellation of pulmonary atresia, right aortic arch, and abnormal development of aortic sac associated with abnormal remodeling of the left brachiocephalic artery seem to be strongly suggestive of DiGeorge syndrome. Hence, if genetic testing is not available in such patients, following the precautions regarding perioperative management of patients with DiGeorge syndrome are strongly warranted.[6]

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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