Case Report

22q11 Deletion Syndrome with Vascular Anomalies

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Abstract

DiGeorge syndrome, also termed 22q11.2 deletion syndrome, represents a spectrum of disorders that include thymic aplasia/hypoplasia, parathyroid aplasia/hypoplasia, conotruncal vascular anomalies, and velocardiofacial (Shprintzen) syndrome. This case report describes a novel constellation of cardiovascular anomalies in a 31-year-old patient with 22q11.2 deletion confirmed by fluorescence *in situ* hybridization at the age of 24. CT angiogram of the thorax revealed a right aortic arch with mirror image branching and unilateral absence of the left pulmonary artery with collateral flow through left intercostal arteries and hypertrophied left bronchial artery. This particular cluster of vascular findings has not been previously described in the imaging literature in a patient with known 22q11.2 deletion.

Keywords: *22q11 deletion syndrome, DiGeorge syndrome, proximal interruption of the left pulmonary artery, right aortic arch with mirror image branching*

Introduction

DiGeorge syndrome (DGS) represents a spectrum of disorders that was first described in 1965 consisting of congenital absence of the thymus and hypoparathyroidism, with consequent immunologic deficiency and hypocalcemia.[1] The association of this syndrome with a chromosomal deletion of a portion of the long arm of chromosome 22 was subsequently identified. Multiple conotruncal cardiac malformations have been associated with DGS. In this case report we present a novel constellation of vascular anomalies not previously described in a patient with known 22q11.2 deletion.

Case Report

A 31-year-old man with 22q11.2 deletion syndrome confirmed by fluorescence *in situ* hybridization at the age of 24 underwent computed tomography (CT) angiogram of the thorax to evaluate known right aortic arch (RAA) with additional suspected vascular anomalies. CT of the chest demonstrated RAA with mirror imaging branching, absence of the left pulmonary artery with collateral left lung flow from the left internal mammary artery through intercostal arteries, and hypertrophied left bronchial artery. The thymus was absent [Figures 1a-d and 2].

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Discussion

DiGeorge syndrome (DGS), now recognized as one of the most common genetic disorders, was first described in 1965 by Dr. Angelo DiGeorge and consisted of congenital absence of the thymus and hypoparathyroidism, with consequent immunologic deficiency and hypocalcemia.[1] Since both the thymus and parathyroid glands derive from common primordial embryologic structures, the third and fourth pharyngeal arches simultaneous deficiencies of these glands is not surprising. The clinical syndrome was widened to include conotruncal cardiac abnormalities and dysmorphic facies.[2] Most of the cases with DGS, over 90%, possess a monosomic deletion of chromosome 22q11.2 (a portion of the long arm of chromosome 22).[3] The spectrum of disorders is also known as CATCH 22 syndrome (cardiac defects, abnormal facies, thymic hypoplasia, cleft palate, and hypocalcemia resulting from 22q11.2 deletions). DGS is an autosomal dominant chromosomal disorder with a frequency of approximately 1 in 4000 live births.[4] Ninety percent of cases are due to a spontaneous mutation in patients, while 10% of

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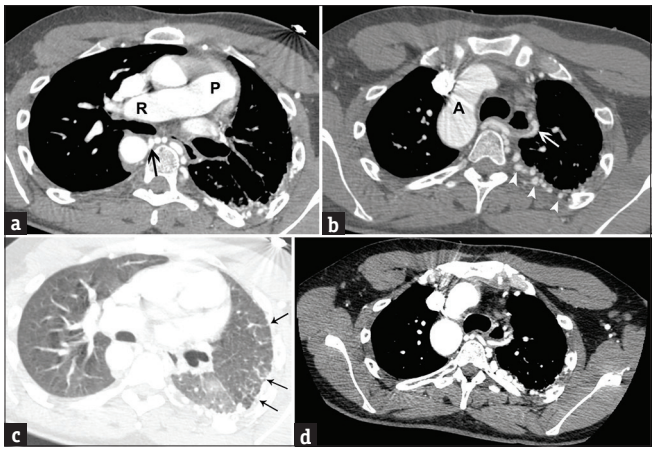

Figure 1: A 31-year-old man with 22q11.2 deletion syndrome who presented for evaluation of vascular anomalies. (a) Contrast-enhanced computed tomography of the thorax axial image demonstrates the main pulmonary trunk (P) giving rise to the right pulmonary artery (R) with the absence of the left pulmonary artery and hypertrophied collateral left bronchial artery (black arrow). (b) Computed tomography axial image demonstrates a right-sided aortic arch (A) and hypertrophied collateral left intercostal arteries (white arrow heads) and bronchial artery (white arrow) supplying the left lung. (c) Computed tomography axial image in lung window shows reticular opacities penetrating the peripheral left lung parenchyma representing intercostal artery collaterals (arrows). The left lung is slightly smaller compared to the right. (d) Computed tomography axial image shows no discernible thymic tissue in the anterior mediastinum.

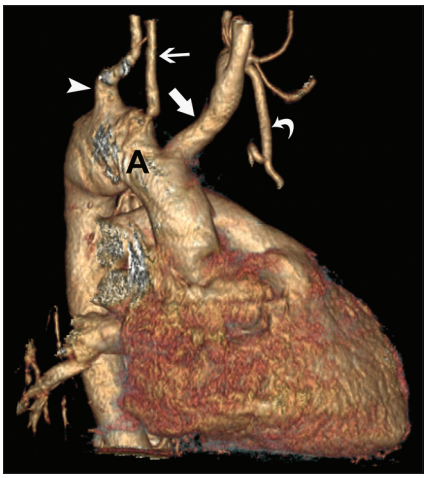

Figure 2: Volume-rendered computed tomography angiographic image from the right anterior oblique perspective from the same patient shows the right-sided aortic arch (A) with mirror image branching: left brachiocephalic trunk (thick arrow), right common carotid artery (thin arrow), and right subclavian artery (arrow head). Note hypertrophied left internal mammary artery.

cases are inherited from a parent. There is phenotypic variation in the abnormalities identified in patients with 22q. 11.2 deletions, and conversely, patients with specific phenotypic presentations have varying frequencies of the chromosomal deletions; a minority of patients with the deletion present with the classic DiGeorge triad of conotruncal cardiac abnormalities, hypoplastic thymus, and hypocalcemia.[5]

Age at presentation varies according to the specific anomalies found in the patient. Neonates diagnosed with DGS and 22q11.2 deletions often manifest clinically significant conotruncal defects that include subaortic stenosis with malalignment of the infundibular septum, truncus arteriosus, and tetralogy of Fallot.[6] In the absence of severe conotruncal defects, patients may present in infancy and early childhood with unusual or intractable infections due to thymic underdevelopment (hypoplasia or aplasia) and deficient T-cell function.

Thymic hypoplasia or aplasia is easier to detect in the neonate or infant since the normal size of the thymus is proportionately larger in the pediatric population. It is proportionately largest at birth, but it continues to grow during childhood, reaching a maximum absolute weight between 12 and 19 years. The thymus subsequently involutes and is gradually replaced by fat. On CT, the gland is a bilobed triangular soft-tissue structure, most commonly anterior to the ascending. The normal thymus can still be identified in nearly 100% of patients under the age of 30.[7] In this patient with DGS, no thymic tissue is evident in the anterior mediastinum. Secondary to faulty thymic development, DGS immunodeficiency may be partial or complete, characterized by decreased or absent circulating T-cells with decreased cell-mediated immunity, with an associated increase in susceptibility to infections, classically fungal and viral agents.[8]

22q. 11.2 deletions have also been described in up to 25% of patients with aortic arch abnormalities without intracardiac defects.[6] Arch anomalies, resulting from abnormal embryologic development, include RAA, cervical aortic arch, aberrant or isolated subclavian artery, and interrupted aortic arch. Cardiac neural crest cells that originate from the dorsal neural tube migrate ventrally into pharyngeal pouches three, four, and then six. These cells then proliferate and integrate into the parenchyma that develops into the aortic arches and great vessels during the 3rd gestational week.[9] Two ventral aortae and two dorsal aortae fuse to form the aortic sac and midline descending aorta, respectively.[6] Six primitive pharyngeal arches appear and three of them regress. The third arch forms the common carotid and cervical internal carotid artery; the fourth arch forms the adult aortic arch. The sixth arch contributes to the ductus arteriosus and central pulmonary arteries. Thus, abnormalities of the aortic arch and thymus can be associated, since the fourth pharyngeal arch is involved with development of both structures.

The patient herein described demonstrated RAA with mirror imaging branching, the second most common

variant of RAA after RAA with aberrant right subclavian artery. This anomaly results from regression of a distal portion of the dorsal aorta, which promotes the left fourth aortic arch to become the proximal subclavian artery rather than the aortic arch. There is also regression of the left sixth arch with persistence of the right, which forms a ductus between the right arch and the right pulmonary artery.[10] The right arch passes between the superior vena cava and the right side of the trachea and esophagus. This aortic anomaly is strongly associated with congenital cardiac disease including tetralogy of Fallot, truncus arteriosus, tricuspid atresia, and transposition of the great arteries with pulmonary valve stenosis in 98% of cases,[6] though these cardiac anomalies were not present in this patient.

Pulmonary artery malpositions also occur in patients with 22q11.2, including crossing of the arteries proximally as they proceed to their respective lungs.[11] Unilateral absence of the left pulmonary artery has also been described to be associated with truncus arteriosus in patients with the 22q11.2 microdeletion.[12] Proximal interruption of the pulmonary artery is now the preferred term since the pulmonary arterial network within the lung parenchyma is intact.[13] The involved lung receives oxygenated blood through systemic collateral arteries including bronchial, internal mammary, innominate, and subclavian vessels. Our patient received collateral flow via the left intercostal and bronchial arteries.

Conclusion

This patient, with known DGS and documented 22q. 11.2 deletion, manifests a constellation of unusual anatomic findings: RAA with mirror imaging branching and left proximal interruption of the pulmonary artery with collateral arterial flow to the left lung from the left intercostal and bronchial arteries. DGS results from defective development of the third and fourth pharyngeal arches which adversely affects the development of the thymus and parathyroid glands, aorta, and great vessels. Although each individual anatomic variant is not surprising in this patient with known chromosomal deletion, it is important to recognize this cluster of unusual imaging findings and raise the possible diagnosis of DGS in the event the genetic abnormality is not yet recognized since this chromosomal abnormality is passed on to progeny in an autosomal dominant fashion.

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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