Case Reports and Reviews

Case Report

The Pathogenesis of Aorto- Atrial Connection

Manal Mohamed Helmy Nabo

Consultant Paediatric Cardiology, Al Riyadh, Ministry of Health, AlMadina Al Mounawara, Ministry of Health, Saudi Arabia.

Abstract

The presence of an abnormal connection between the descending aorta and the right atrium is an accidentally discovered finding during echocardiography. The patient may be asymptomatic or suffering from unexplained heart failure. This anomaly raises many questions about its cause. In pediatrics, this abnormal finding should be excluded in patients who present with unusual congenital features.

Any patient showing signs of DiGeorge syndrome (22q11 deletion syndrome) should undergo a detailed echocardiographic study, looking specifically for this anomaly, as these patients have a higher incidence of aortic arch anomalies.

The pulmonary arch arteries (PAAs) are important in the development of the aorta and its major cervical branches. Any abnormal connection seen in relation to the aorta is most likely due to an abnormal genetic pathway responsible for the development of an aorto–atrial connection.

There are two forms of this anomaly: an aorto–atrial tunnel and an aorto–atrial fistula.

An aorto–atrial tunnel results from overregulation of mesenchymal cells, leading to true neovascular formation connecting the aorta and the atrium.

An aorto–atrial fistula results from resorption of normal developing structures, associated with downregulation of mesenchymal cell function.

The cause of both anomalies arises from changes affecting progenitor cells of the second heart field (SHF). These progenitors are responsible for regulating the development of endothelial cells (ECs) that line the PAAs..

Correspondence

Manal Mohamed Helmy Nabo

Consultant Paediatric Cardiology, Al Riyadh, Ministry of Health, AlMadina Al Mounawara, Ministry of Health, Saudi Arabia.

- Received Date: 11 Nov 2025
- Accepted Date: 21 Nov 2025
- Publication Date: 24 Nov 2025

Keywords

Aortic arch, Aorto atrial connection, Fistula, DiGeorge syndrome

Copyright

© 2025 Authors. This is an open- access article distributed under the terms of the Creative Commons Attribution 4.0 International license.

The Regulation of Pulmonary Arch Arteries (PAAs) Formation

The three symmetrical pairs of the pharyngeal arch arteries (PAAs) are responsible for the formation of the aortic arch and its main branches. The endothelial cells that line these arches are derived from the second heart field (SHF) [1]. Defects in the formation or remodeling of the PAAs can lead to several cardiac or vasculo-cardiac abnormalities.

Endothelial cells require the expression of VEGFR2 (vascular endothelial growth factor receptor-2). In the absence of VEGFR2, a compensatory mechanism takes place and is regulated by Tbx1, resulting in angiogenesis and the formation of new vascular connections among the pharyngeal arch arteries. One of the abnormal vascular connections that may occur is the aorto-atrial connection.

In cases of decreased numbers of SHF-derived vascular progenitors, as seen with loss of VEGFR2, a compensatory angiogenic response arises from nearby veins. Venous-derived cells migrate into the pharyngeal arches, proliferate, incorporate into the PAAs, acquire arterial identity, and contribute to the morphogenesis of a new vascular network ending in abnormal vascular connections [2–6]. Tbx1 is the major disease gene in 22q11 deletion syndrome.

Therefore, there are two key genetic factors associated with the formation of an aorto-atrial connection: Tbx1 and VEGFR2, which regulate the development and number of SHF-derived endothelial cells (ECs). The endothelium of the PAAs originates from the mesodermal core of the arches, whereas their vascular smooth muscle is predominantly derived from the cardiac neural crest (CNC) [7–9].

When the number of SHF-derived ECs is reduced, PAA development can be rescued by compensatory endothelium. This compensatory mechanism can be influenced by other genetic insults, such as mutations in Fgf10 and Fgf8. The expression of Fgf10 and Fgf8 in the pharyngeal mesoderm may contribute to human congenital heart and vascular defects.

Clinically, any patient with congenital anomalies should be examined for this abnormal vascular connection, as it may be missed early in life and later present with symptoms of heart failure. The most commonly reported anomaly of this type is a connection between the descending aorta and the right atrium. Over time, such patients may develop heart failure and a deteriorating general condition.

Transcatheter device closure of this abnormal connection is widely used, with good documented success rates. The result is restoration of normal vascular circulation without excess hemodynamic burden on the heart.

Citation: Nabo MM. The Pathogenesis of Aorto- Atrial Connection. Case Rep Rev. 2025;5(5):80.

References

1. Graham A. Development of the pharyngeal arches. Am J Med Genet A.2003; 119:251–256. doi: 10.1002/ajmg.a.10980
2. Wang X, Chen D, Chen K, Jubran A, Ramirez A, Astrof S. Endothelium in the pharyngeal arches 3, 4 and 6 is derived from the second heart field. Dev Biol. 2017; 421:108–117. doi: 10.1016/j.ydbio.2016.12.010
3. Warkala M, Chen D, Ramirez A, et al. Cell-extracellular matrix interactions play multiple essential roles in aortic arch development. Circ Res. 2021;128: e27–e44. doi:10.1161/CIRCRESAHA.120.318200 Nagelberg D, Wang J, Su R, et al. Origin, specification, and plasticity of the great Vessels of the heart. Current Biology. 2015; 128:2099–2110. doi: 10.1016/j.cub.2015.06.076
4. Paffett-Lugassy N, Singh R, Nevis KR, et al. Heart field origin of great vessel precursors relies on nkx2.5-mediated vasculogenesis. Nature Cell Biology. 2013;128: 1362–1369. doi: 10.1038/ncb2862
5. Li P, Pashmforoush M, Sucov HM. Mesodermal retinoic acid signaling regulates endothelial cell coalescence in caudal pharyngeal arch artery vasculogenesis. Dev Biol. 2012; 361:116–124. doi: 10.1016/j.ydbio.2011.10.018
6. Jiang X, Rowitch DH, Soriano P, McMahon AP, Sucov HM. Fate of the mammalian cardiac neural crest. Development. 2000;127: 1607–1616
7. Brown CB, Wenning JM, Lu MM, Epstein DJ, Meyers EN, Epstein JA. Cre- mediated excision of Fgf8 in the Tbx1 expression domain reveals a critical role for Fgf8 in cardiovascular development in the mouse. Dev Biol. 2004;267:190–202
8. Engleka KA, Gitler AD, Zhang M, Zhou DD, High FA, Epstein JA. Insertion of Cre into the Pax3 locus creates a new allele of Splotch and identifies unexpected Pax3 derivatives. Dev Biol. 2005; 280:396–406