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Case Report

CLUSTERED ORIGIN OF LEFT CORONARY ARTERY FROM THE LEFT SINUS OF VALSALVA: UNCHARACTERISTIC DEVELOPMENTAL EVENT IN THE TEMPORALLY REGULATED PROCESS

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ABSTRACT

Background: The coronary artery development is a sequential and progressively regulated process. However, there are number of reports available on the disturbance to this temporal process resulting in variations of the artery. In these instances, the function of the coronary arteries was normal in providing blood supply to the heart. The normal and abnormal coronary artery development has been studied using variety of approaches and the knowledge continues to evolve.

Materials and Methods: The cadaveric specimen was obtained from the "willed body program" for the purpose of student dissection. We report here an anomaly found in a 94-year old Caucasian male died of cerebral artery infarction.

Results and Observations: We observed that the left coronary artery arose from the coronary ostium in a cluster of multiple branches. The right coronary artery arose normally from the right coronary ostium. Further dissection showed the co-dominant nature of the left and right coronary arteries in providing blood supply to the posterior aspect of the heart and the interventricular septum.

Conclusions: Knowledge of coronary artery and its disposition is important in clinical practice especially in coronary artery stent placement, coronary artery bypass surgery and coronary sinus catheterization.

KEY WORDS: Coronary artery, clustered left coronary artery, normal coronary development, anomalous developmental process, clinical significance.

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INTRODUCTION

The anatomic organization and functional distribution of coronary arteries is well described. However, there is paucity of knowledge of normal embryonic development of the coronary arteries and is continuously being experimentally investigated. Likewise, while there are number of variations in coronary arteries have been reported their maldevelopment is not definitely understood and explained.

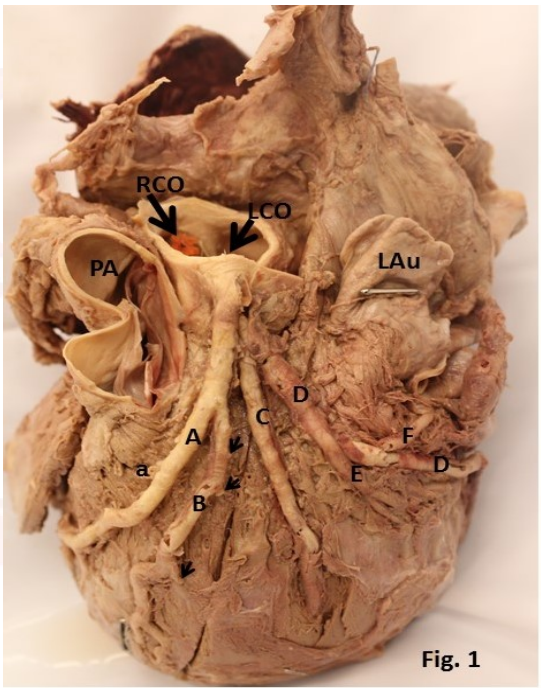
Research since the last 2-3 decades have provided certain theories on the embryonic development of the coronary arterial system. All the cells that contribute to the coronary artery system comes from outside the heart that differentiate into blood vessels only when they are in the heart [1]. It is now established that the coronary arteries are derived from the epicardial tissues, which in turn begins as an extension or outgrowth from the septum transversum and becomes visible near the sinoatrial pole of the heart, and this structure is called ‘proepicardial organ’ [2].

Cells migrate from the pro-epicardial organ and grow over the epicardial surface of the heart, extending as far as the distal outflow tract [3]. Under the influence of Wt1 and Raldh1 genes [4], the epicardial cells become transformed to mesenchyme, penetrating the developing myocardial walls to produce the fibrous matrix of the compact myocardium and the smooth muscular walls of the coronary arteries and veins. It was originally believed that these epicardial coronary arteries obtained their aortic connection by fusion with channels that had budded out from the developing aortic valvar sinuses [5]. Contrarily, the proximal components of the developing epicardial coronary arteries grow into the aortic root [6] subsequent to the completion of aortic root separation from the pulmonary root [7]. Furthermore, microscopic examination of serial sections human embryos (Carnegie stages 13-19) confirmed that the earliest vessels in the heart wall developed subepicardially near the apex at stage 15 and extends at stage 17 the coronary arterial stump communicate with the aortic lumen [8].

Typically, the right and left coronary arteries arises respectively from the right and left sinus of Valsalva. The right coronary artery in 90% of the individual supplies most of the diaphragmatic surface of the ventricular mass. In some cases, the sinus artery arises from a second orifice in the right sinus. The major branches of right coronary artery include marginal, posterior interventricular and perforating arteries. The short left coronary artery which is positioned between the left atrial appendage and the pulmonary trunk branches into left circumflex and left anterior descending arteries. The left coronary artery and its two branches (circumflex coronary and left anterior descending) usually supply major portion of the myocardium, including muscular interventricular septum, papillary muscles, mitral valve, left atrium and in many the AV node. The findings from experimental animal models indicate that the coronary vasculature forms by an elaborate process involving vasculogenesis, angiogenesis, and arteriogenesis [9].

MATERIALS AND METHODS

Fig. 1: RCO: Right coronary ostium; LCO: Left coronary ostium; PA: Pulmonary artery; LAu: Auricle of the Left atrium; A: Left anterior descending artery; B and C: Diagonal arteries; D: Left circumflex coronary artery; E: Left marginal branch; F: Left atrial artery.



Note: For clarity, the great cardiac vein is removed. A soft probe through the single LCO can be passed into each of the branches confirming in deed that all the branches arise from a single ostium. The short arrows indicate septal branches from one of the diagonal arteries (B) and the small cap “a” is the sub pleural branch arising from left anterior descending artery (A).

The cadaveric specimen was obtained from the willed body program for the purpose of student dissection. During medical students’ cadaveric dissection of a 94-year old male Caucasian donor died of cerebral artery infarction we observed that the left coronary artery arose from the coronary ostium in a cluster of four large branches (Fig. 1). The right coronary artery arose normally from the right coronary ostium. Further dissection showed the co-dominant nature of the left and right coronary arteries in providing blood supply to the posterior aspect of the heart and the interventricular septum as observed earlier [10]. The coronary veins were normal and returned the blood through coronary sinus to the right atrium.

The posterior descending artery (PDA) runs in the posterior interventricular groove and supplies the inferior wall and inferior third of the interventricular septum. The artery that supplies the PDA and a posterolateral branch determines the coronary dominance, so there can be three situations: Right-dominance (approximately 70% of the cases) (supply from the RCA), left-dominance (10%) (supply from the LCA), and codominance (20%), the situation in which PDA and posterolateral branches arise from both right and left coronary systems [11].

RESULTS AND DISCUSSION

Development of the coronary arteries: The fact that the epicardial coronary arteries, almost without exception, take their origin from the aortic sinuses adjacent to the pulmonary root suggests that the developmental processes separating the roots (pulmonary and aortic) one from the other is also instrumental in guiding the epicardial coronary arteries to their appropriate aortic origin [12]. It has now also been established that during its development, the ventricular musculature supporting the pulmonary root is impervious to the passage and development of epicardial coronary arteries [12].

Due to the fact that the coronary arteries are formed within the epicardial tissue planes before achieving their connection to the developing aortic valvar sinuses, the location of the sinuses themselves will play a role in determining the definitive morphology of the coronary arterial patterns [12].

The major epicardial coronary arteries attain their aortic connection relatively late in development subsequent to the process of aortico-pulmonary rotation [7, 13]. Coupled with the knowledge that the sub- pulmonary myocardial domains are impervious to the passage of the developing epicardial coronary arteries, appreciation of these facts can bring order to the understanding of the potential random patterns seen in various congenital cardiac malformations, in particular those found in the setting of transposition and common arterial trunk. Number of variations in the origin of coronary arteries have been described in the literature. While some variations have no consequence but others will have profound effect on human. For example, ectopic coronary origin from the pulmonary artery is not compatible with life. Some of the 'sudden death syndrome' in infants is attributed to this anomalous origin of coronary arteries [14]. It seems from the literature most coronary artery variations occur in the left coronary artery [15]. However, the embryological basis of such occurrences is not clearly explained. Recent reports showed that the bifurcation, trifurcation, quadrification and pentafurcations are the branches from a single left coronary artery stem [16]. However, we have for the first time report the "clustered" branching pattern of left coronary from the single ostium of left sinus of Valsalva. Additionally, a soft probe can be passed independently into each of the branches through the single left coronary ostium confirming the clustered origin of multiple branches from a single ostium (Fig. 1).

Recent detailed studies [17, 18] of quail embryo provide a sound explanation to the clustered origin of the left coronary artery from the left sinus of Valsalva. As in the other vertebrates, the epicardium of the quail embryo develops from proepicardial tissue. The proliferating proepicardium consists of "gland-like tubular strands", with heterogeneous cells and structures; has multiple functions and is considered as a transitory organ in the developing heart [2].

Studies of the development of proximal coronary arteries in quail embryonic heart [17, 18], it was observed that multiple capillaries that penetrate the aortic sinus fuse to form a single main coronary trunk. Employing double-immunostaining for QH1 (quail endothelial marker) and smooth muscle-actin a meticulous study [18] described that at 6 to 7 embryonic day (ED), several QH1-positive endothelial strands from the peritruncal ring penetrated the facing sinuses, and in some embryos, several endothelial strands also penetrated the posterior (non-coronary) sinus.

At 7 to 8 ED, the endothelial strands penetrating the facing sinuses seemed to fuse, forming a proximal coronary stem that was demarcated from the aortic wall by the nascent smooth muscle layer of the coronary artery. By 9 ED, two coronary stems were completely formed, and the endothelial strands previously penetrating the non-coronary sinus had disappeared [18]. Furthermore, at all stages examined, there was no QH1-positive endothelial strand penetrating the pulmonary trunk was observed.

We speculate that multiple left coronary artery connected to the left sinus of Valsalva is due to the endothelial strands [18] remained unfused and formed several coronary vessels an atypical developmental event in the temporally regulated process (Fig. 1). Bogers et al. [6] examined human and rat embryos, and noted that "a coronary orifice was never seen in the absence of a proximal coronary artery". Based on their observations, they concluded that the existing theories regarding proximal coronary artery development, which mainly assumed an outgrowth from the aorta were inadequate. Subsequently, using serial sections it was shown that the coronary ostia were formed by ingrowth of a capillary plexus in quail embryos [6, 19].

CONCLUSION

Knowledge of coronary artery and its disposition is important in clinical practice especially in coronary artery stent placement, coronary artery bypass surgery and coronary sinus catheterization [20]. Additionally, when the great cardiac vein is located posterior to left anterior descending artery and in the presence arteriosclerosis the vein may be compressed by the rigid artery, that would impair the venous return. As we observed in the cadaver heart that in addition to left anterior descending and left circumflex coronary arteries there are multiple vessels located within the Brocq and Mouchet's arteriovenous triangle a triangle formed between great cardiac vein, left anterior descending and left circumflex arteries. Much of the variations (bifurcation, trifurcation, quadrification and pentafucation) described in branching of left coronary artery termination comes from a common stem of the artery [15, 16]. But in our study, the left coronary artery arose as multiple branches from one single ostium (Fig. 1).

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Conflict of Interest: The authors declare that they have no conflict of interest.

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REFERENCES

[1]. Reese DE, Mikawa T, Bader DM. Development of the coronary vessel system. Circ Res. 2002; 91: 761–768.

[2]. Viragh S, Challice CE. The origin of the epicardium and the embryonic myocardial circulation in the mouse. Anat Rec. 1981; 201: 157–168.

[3]. Anderson RH, Chiu IS, Spicer DE, Hlavacek AM. Understanding coronary arterial anatomy in the congenitally malformed heart. Cardiology in the Young. 2012; 22: 647–654.

[4]. Perez-Pomares JM, Phelps A, Sedmedmerova M, Carmona R, Gonzalez-Iriarte M, Munoz-Chapuli R, Wessels A. Experimental studies on the spatiotemporal expression of WT1 and RALDH2 in the embryonic avian heart: a model for the regulation of myocardial and valvuloseptal development by epicardially derived cells (EPDCs). Dev Biol. 2002; 247: 307–326.

[5]. Perez-Pomares JM, De La Pompa JL. Signaling during epicardium and coronary vessel development. Circ Res. 2011; 109: 1429-1442.

[6]. Bogers AJ, Gittenberger-de Groot AC, Poelmann RE, Peault BM, Huysmans HA. Development of the origin of the coronary arteries, a matter of ingrowth or outgrowth? Anat Embryol. 1989; 180: 437–441.

[7]. Angelini P. Normal and anomalous coronary arteries: definitions and classification. Am Heart J. 1989; 117: 418–434.

[8]. Silva-Junior GO, Miranda SWS, Mandrim-De-Lacerda CA. Origin and development of the coronary arteries. Int. J. Morphol. 2009; 27: 891-898.

[9]. Erne P. Congenital Anomalies of the Coronary Arteries. European Cardiology. 2009; 5: 12-14.

[10]. Nowak D, Kozlowska H, Zurada A. The relationship between the dimensions of the right coronary artery and the type of coronary vasculature in human fetuses. Folia morphologica. 2011; 70: 13-17.

[11]. Fuster V, Alexander RW, O'rourke RA. *Hurst's The Heart* (10th ed.). McGraw-Hill, 2001; p. 53.

[12]. Theveniau-Heveniau-Ruissy M, Dandonneau M, Mesbah K, Ghez O, Mattei MG, Miquerol L, Kelly RG. The de122q11.2 candidate gene Tbx1 controls

regional outflow tract identity and coronary artery patterning. Circ Res. 2008; 103: 142–148.

[13]. Chiu IS, Anderson RH. Can We Better Understand the Known Variations in Coronary Arterial Anatomy? Ann Thoracic Surg. 2012; 94: 1751-1760.

[14]. Mahowald JM, Blieden LC, Coe JI, Edwards JE. Ectopic origin of a coronary artery from the aorta. Sudden death in 3 of 23 patients. Chest. 1986; 89: 668-72.

[15]. Singh S, Ajayi N, Lazarus L, Satyapal KS. Morphologic Relationship between the Coronary Arteries during Fetal Development. Int J Morphol. 2017; 35: 1197-1202.

[16]. Ogene'O JA, Misiani MK, Olabu BO, Waisiko BM, Murunga A. Variant termination of the left coronary artery: pentafurcation is not uncommon. Eur. J. Anat. 2014; 18: 98-101.

[17].Viragh S, Gittenberger-De Groot AC, Poelmann RE, Kalman F. Early development of quail heart epicardium and associated vascular and glandular structures. Anat Embryol (Berl). 1993; 188: 381-393.

[18].Ando K, Nakajima Y, Yamagishi T, Yamamoto S, Nakamura H. Development of proximal coronary arteries in quail embryonic heart: multiple capillaries penetrating the aortic sinus fuse to form main coronary trunk. Circ. Res. 2004; 94: 346-352.

[19]. Tomanek RJ. Developmental Progression of the Coronary Vasculature in Human Embryos and Fetuses. The Anatomical Record. 2016; 299:25-41.

[20]. Loukas M, Groat C, Khangura R, Owens DG. The normal and abnormal anatomy of the coronary arteries. Clinical Anatomy. 2009; 22:114-128.

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