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Case Report

Clustered origin of the left coronary artery from the left sinus of Valsalva: Uncharacteristic developmental event in the temporally regulated process

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ABSTRACT

Coronary artery development is a sequential and progressively regulated process. However, there are a 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 a variety of approaches and the knowledge continues to evolve. The cadaveric specimen was obtained from the "willed body program" for the purpose of student dissection. During the cadaveric dissection of a 94-year old male Caucasian we observed that the left coronary artery arose from the coronary ostium in a cluster of multiple branches. A detailed study of the origin of the left coronary artery showed that there is one ostium from which multiple branches arose. The right coronary artery arose normally from the right coronary ostium. The coronary veins were normal and returned the blood through the coronary sinus to the right atrium. The anomalous finding is discussed in the light of what is already known about the normal coronary artery development and rationalize a possible explanation. We conclude that the abnormal development of the coronary artery is rarely detrimental and provides adequate blood circulation to the heart. However, knowledge of such malformation is important in clinical practice.

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 come 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 arise 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 the 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 portions 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

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 who 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 the 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 LCX), and codominance (20%), the situation in which PDA and posterolateral branches arise from both right and left coronary systems [11].

RESULTS AND DISCUSSIONS

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)

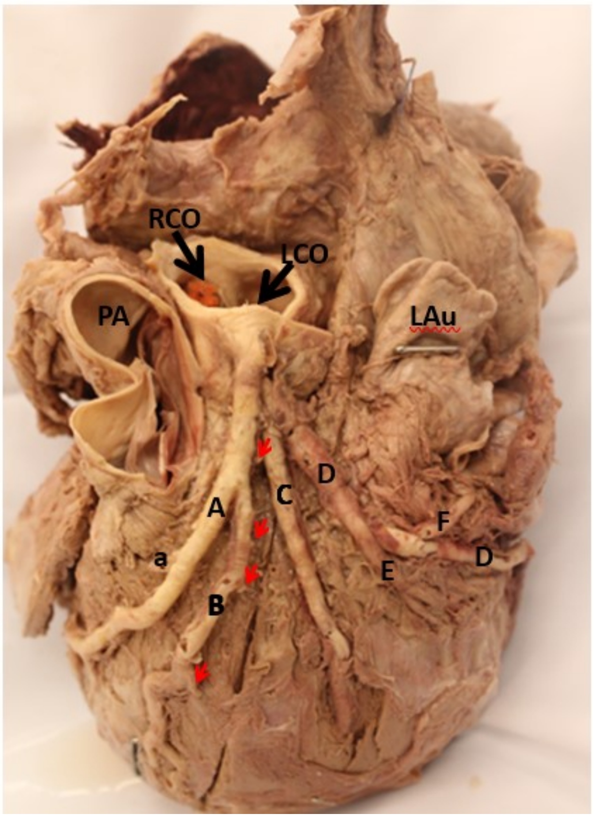

Fig. 1: RCO: Right coronary ostium; LCO: Left coronary ostium; PA: Pulmonary artery; LAu: Auricle of the Left atrium; A: Left anterior descending artery; B and C: Diagonal arteries; D: Left circumflex coronary artery; E: Left marginal branch; F: Left atrial artery.

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).

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 aorticopulmonary 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 humans. 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 and references therein]. 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, in this study we have for the first time reported the "clustered" branching pattern of the left coronary from the single ostium of the 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 Virágh et al., 1993 [17]; Ando et al., 2004 [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]. In a detailed study of the development of proximal coronary arteries in quail embryonic heart, Virágh et al (1993) [17] and Ando et al (2004) [18] 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 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 observed.

We speculate that multiple left coronary artery connected to the left sinus of Valsalva (Fig. 1) is due to the endothelial strands [18] remained unfused and formed several coronary vessels an atypical developmental event in the temporally regulated process.

Bogers et al. (1988) [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, Bogers et al. (1988) [6] concluded that the existing theories regarding proximal coronary artery development, which mainly assumed an outgrowth from the aorta were inadequate. Subsequently using serial sections, [6], Tomanek, 2016 [19] were able to show that the coronary ostia were formed by ingrowth of a capillary plexus in quail embryos.

CONCLUSION

Knowledge of coronary artery and its disposition is important in clinical practice [20] especially in coronary artery stent placement, coronary artery bypass surgery and coronary sinus catheterization. Additionally, when the great cardiac vein is located posterior to left anterior descending artery and in the presence of 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 arterio-venous 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 [16.17]. But in our present study, the left coronary artery arose as multiple branches from one single ostium (Fig. 1).

ABBREVIATIONS

AV node: Atrioventricular node**; PDA:** Posterior descending artery**; RCA-**Right Coronary Artery**; LCX-** Left Coronary Circumflex**; QH1-**Quail endothelial marker**; ED-**Embryonic Day**.**

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Conflicts of Interests: None

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