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A fascinating case of complex congenital heart disease

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ABSTRACT

Complex congenital heart disease (CHD) constitutes a significant non-infectious contributor to childhood morbidity and mortality, particularly prevalent in developing countries with an estimated incidence of nearly 1/100 births. The spectrum of CHD spans from isolated atrial septal defects that necessitate no immediate intervention to intricate structural cardiovascular abnormalities demanding multiple interventions early in the neonatal period. Patients afflicted with complex CHD often manifest symptoms such as respiratory distress, cyanosis of the skin, feeding difficulties, and failure to thrive, becoming evident within the initial 48 h post-birth. In this context, we present an intriguing case of a male child with complex CHD. This case study is accompanied by a concise exploration of the embryology of the heart, shedding light on the intricate developmental processes that may underlie such congenital anomalies.

Key words: Pediatric cardiology; Congenital heart defects; Cyanosis; Respiratory distress

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INTRODUCTION

Congenital heart disease (CHD) represents a substantial non-infectious burden on childhood health worldwide, particularly in developing nations. Among these defects, complex congenital heart defects stand out as a significant health concern, contributing to elevated rates of morbidity and mortality in affected children. Ranging from isolated atrial septal defects with no immediate intervention required to intricate structural cardiovascular abnormalities necessitating multiple early interventions in the neonatal period, the spectrum of CHD presents a diverse clinical landscape.[1-3]

Children born with complex CHD often exhibit a range of symptoms, including respiratory distress, cyanosis of the skin, feeding difficulties, and failure to thrive, becoming apparent within the initial 48-h post-birth. The urgency and complexity of intervention vary widely within this patient population, underscoring the need for a comprehensive understanding of the underlying mechanisms and contributing factors to guide effective management.[4,5]

In this context, we present a case of a male child with complex CHD. Through a detailed examination of this case, we aim to provide valuable insights into the clinical manifestations, and diagnostic challenges associated with complex congenital heart defects. In addition, we delve into a concise exploration of the embryology of the heart, unraveling the developmental processes that may contribute to the genesis of such congenital anomalies. This study endeavors to contribute to the broader knowledge base in the field and enhance the clinical management of patients with complex CHD.

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CASE REPORT

A 3-year-old male child presented with complaints of dyspnea, cyanosis of the skin and mucous membranes, and pedal edema. An in-depth review of the patient's medical history revealed a recurring pattern of dyspnea and lower respiratory tract infections (LRTI) since birth. The child was born through normal vaginal delivery as a term baby, weighing 3.5 kg, immediately crying post-birth. Notably, the patient exhibited increased work of breathing, tachypnea 6 h after birth, feeding difficulties, and failure to thrive. Clinical examination at birth showed central cyanosis with a peripheral oxygen saturation (SpO_2) of 78% on 4 L of oxygen, a respiratory rate of 72/min, and auscultation findings suggestive of a holosystolic murmur at the left sternal border. Chest X-ray revealed cardiomegaly with pulmonary hyperemia. Given these clinical manifestations, suspicion of congenital cyanotic heart disease was raised. Prostaglandin E1 infusion was administered, resulting in improved oxygen saturation. Subsequent 2D echocardiography confirmed transposition of the great arteries, total anomalous pulmonary venous connections with atrial and ventricular septal defects, as well as pulmonary stenosis. Despite the urgent recommendation for immediate cardiac surgery, financial constraints prevented the intervention. The patient experienced multiple hospital admissions due to recurrent LRTI and respiratory distress.

The patient presented to our institute at 3 years of age, with complaints of swollen legs, labored breathing, and cyanosis with finger clubbing. Motor development delay and short stature were evident. Vital signs revealed a blood pressure of 100/60 mmHg, pulse rate of 130 bpm, respiratory rate of 35/min, and oxygen saturation of 80% at room air. Auscultation identified fine bibasal crepitations and a holosystolic murmur at the left sternal border.

A computed tomography (CT) pulmonary angiogram was performed on February 13, 2014, and revealed atrioventricular (AV) concordance with ventriculoarterial discordance. The aorta was seen to arise from the right ventricle and the pulmonary artery was seen from the left ventricle indicating D-type transposition of great vessels (Figure 1a and b). The pulmonary veins from both lungs were seen to drain into a common channel before draining into the right atrium – A total anomalous pulmonary venous connection (Figure 1c). Double superior vena cava was noted with the right superior vena cava draining into the right atrium and the left superior vena cava into the left atrium (Figure 2). Atrial septal defect and a large ventricular septal defect (~13 mm) were also noted (Figure 3). The right coronary artery was seen to arise from the left coronary cusp (Figure 4). The focal segmental narrowing was noted at the infundibulum of the main pulmonary artery indicating pulmonary artery stenosis. A septum was noted, segregating the right atrium into two chambers, referred to as cor triatriatum dextrum (Figure 5).

The patient underwent Glenn's surgery, a palliative procedure establishing connections between the right superior vena cava and right pulmonary artery, as well as between the left superior vena cava and left pulmonary artery. The post-operative period was uneventful. After 7 years, the patient presented with breathlessness, yet cyanosis was absent. A follow-up CT pulmonary angiogram revealed a double superior vena cava, with the right superior vena cava draining into the right pulmonary artery and the left superior vena cava into the left pulmonary artery, indicative of post-Glenn's surgery changes (Figure 6). The other anatomical findings remained consistent with those observed in the initial CT pulmonary angiogram.

DISCUSSION

The heart, as the primary functional organ, undergoes intricate developmental processes during embryogenesis.[6] By the 4th week, a primitive heart initiates blood pumping, and by the 7th week, most of the gross development is accomplished. Its complex development involves simultaneous events and originates from the splanchnic mesoderm (cardiogenic area) cranial to the developing mouth, ventral to the developing pericardial sac, and dorsal

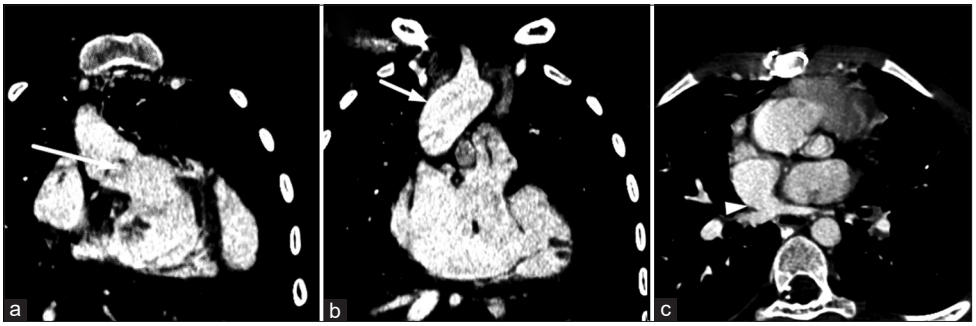

Figure 1: Origin of ascending aorta and total anamalous pulmonary venous connection. (a and b) coronal sections of computed tomography (CT) pulmonary angiogram images showing ascending aorta (arrow) arising from right ventricle, (c) axial sections of CT pulmonary angiogram image showing pulmonary veins from both lungs draining into a common channel (arrowhead) before draining into the right atrium

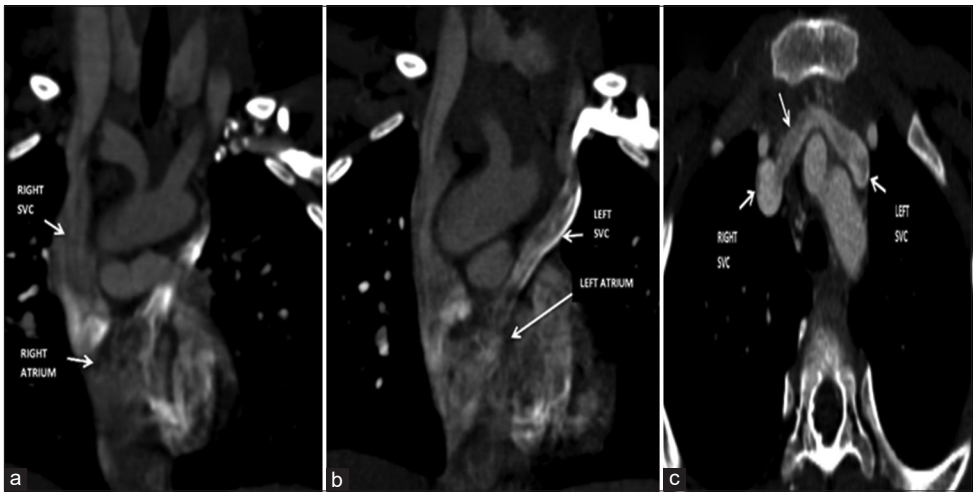

Figure 2: Double superior vena cava. (a) coronal computed tomography (CT) pulmonary angiogram images showing the right superior vena cava draining into the right atrium; (b) coronal CT pulmonary angiogram images showing the left superior vena cava draining into the left atrium; (c) axial CT pulmonary angiogram images showing the connection between the right and left superior vena cava

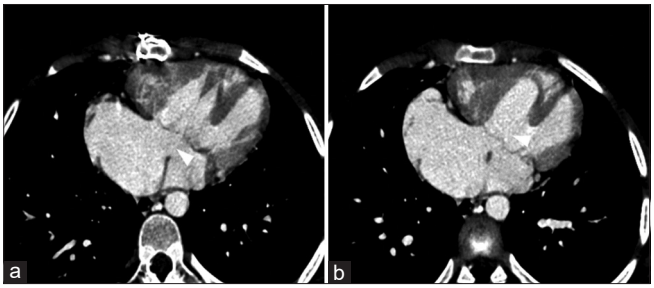

Figure 3: Atrial and ventricular septal defects. (a) axial section of computed tomography (CT) pulmonary angiogram image showing the atrial septal defect (arrowhead); (b) axial section of CT pulmonary angiogram image showing the ventricular septal defect (arrowhead)

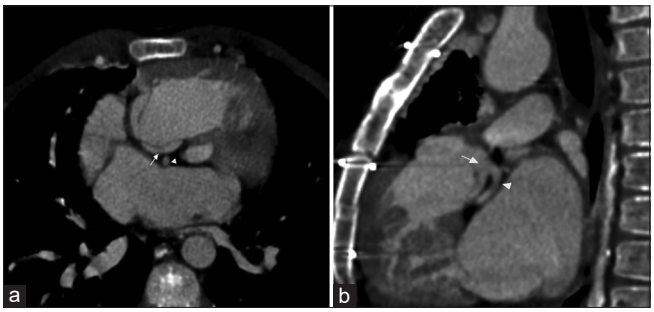

Figure 4: Right coronary artery. (a) axial and (b) sagittal computed tomography pulmonary angiogram images showing the right coronary artery (arrowhead) arising from the left coronary cusp (arrow)

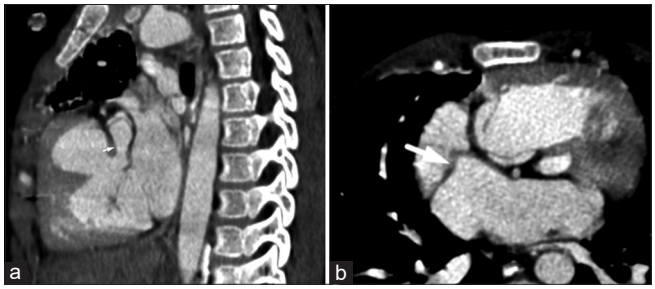

Figure 5: Pulmonary artery stenosis and cor-triatum dextrum. (a) sagittal computed tomography (CT) pulmonary angiogram image showing focal short-segment luminal narrowing at the origin/infundibulum of the main pulmonary artery. (b) axial CT pulmonary angiogram image showing a septum (arrow) separating the right atrium into two chambers

to the developing nervous system. The heart primordium becomes evident around the 18th day, and as the head fold completes, developing heart tubes lie ventrally in the embryo, dorsal to the developing pericardial sac. Subsequent lateral folding leads to the fusion of the two heart tubes, forming a single endocardial heart tube that begins to beat around the 22nd–23rd day.[7-10] This fusion occurs in a craniocaudal direction, with the initially suspended heart tube within the pericardial cavity. The dorsal mesogastrium initially suspends the heart tube, but this structure subsequently degenerates to accommodate further growth.[9-12]

The heart tube exhibits faster growth than the pericardial sac, resulting in five alternating dilatations separated by four constrictions: Truncus arteriosus, bulbus cordis, primitive ventricle, primitive atrium, and sinus venosus. The venous end of the endocardial heart tube is the sinus venosus, while the arterial end is the truncus arteriosus. Looping of the heart tube begins around the 23rd day of development, with the bulbus cordis moving ventrally, caudally, and to the right, while the primitive ventricle moves dorsally, cranially, and to the left. This looping leads to the fusion and internal communication of different parts of the heart, including the formation of an AV canal and the primary interventricular foramen. The left and right primitive ventricles are formed, respectively, by trabeculation in the bulbus cordis and the primitive ventricle.[12-14]

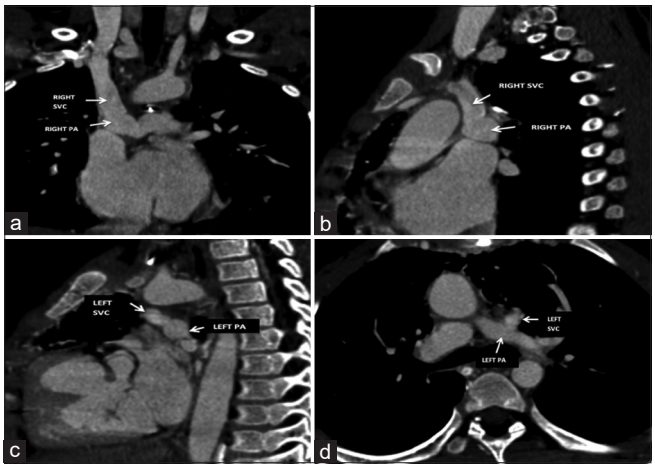

Figure 6: Double superior vena cava. (a) coronal and (b) sagittal computed tomography (CT) pulmonary angiogram images showing right superior vena cava draining into right pulmonary artery, (c) sagittal and (d) axial CT pulmonary angiogram images showing left superior vena cava draining into the left pulmonary artery

During the 4th week, the sinus venosus develops two lateral expansions called horns (right and left) and a body. Each horn receives three veins: The common cardinal vein (from the fetal body), vitelline vein (from the yolk sac), and umbilical vein (from the placenta). The right horn forms the smooth posterior wall of the right atrium (sinus venarum), receiving the superior and inferior vena cava. The left horn and body atrophy form the coronary sinus, and the left common cardinal vein forms the oblique vein of the left atrium. The trabeculated anterior part of the right atrium is derived from the primordial common atrium, with the crista terminalis internally and the sulcus terminalis externally demarcating the two parts. As the left atrium grows, these veins are incorporated into it, forming the smooth part of the left atrium.[14-16]

In the 4th week, a sickle-shaped septum grows from the roof of the common atrium toward the developing cushions, dividing the primitive atrium into right and left atria. The septum primum creates an ostium primum allowing inter-atrial communication. The upper part of the septum primum gradually resorbs, forming an opening called ostium secundum. Another septum, the septum secundum, descends on the right side of the septum primum, forming an incomplete partition between the two atria and resulting in the formation of a valvular foramen, the foramen ovale, persisting until birth. Failure of fusion of the septum primum with the endocardial cushions leads to atrial septal defect.[14,15]

Four AV endocardial cushions, two laterals, an anterior, and a posterior, encircle the AV canal. During week 5, the anterior and posterior cushions project into the canal, dividing it into left and right AV orifices. After their fusion, mesenchymal tissue proliferates about the AV orifice, forming the AV valves. Disruption in this process leads to the development of AV septal defect. In the 4th week, the muscular interventricular septum forms, a thick crescentic fold growing toward the fused endocardial cushions.[13-15] A tissue extension from the right side of the endocardial cushion binds with the muscular interventricular septum to form the membranous portion of the interventricular septum. Disruption in this process leads to the development of ventricular septal defect.

The semilunar valves separately form as outpouchings of the truncal endocardial cushions. During week 5, endocardial cushions also appear in the truncus arteriosus, forming the truncal septum, which spirals away from the heart, dividing the truncus into the pulmonary and aortic channels. Non-spiral development of this septum leads to the transposition of great arteries.[14,15]

The dorsal mesenchyme protrusion, originating from the caudal end of the dorsal mesocardium that suspends the heart tube, begins to proliferate. As the septum primum grows downward, this proliferating mesenchyme forms the dorsal mesenchyme protrusion, which, together with the septum primum, moves toward the AV canal. The pulmonary vein develops in the dorsal mesenchyme protrusion and, through its growth and movement, is placed in the left atrium.[15,16] The main pulmonary vein, opening into the left atrium, gives two branches into each lung. Deviation of the dorsal mesenchyme protrusion to the right results in the pulmonary vein being placed in the right atrium instead of the left, leading to total anomalous pulmonary venous return.[17-19]

During the 4th week of embryonic life, a symmetrical pattern of venous channels is observed. Three pairs of cardinal veins exist, with the anterior cardinal veins draining the cephalic half and the posterior cardinal veins draining the caudal half of the embryo. Common cardinal veins enter the respective horns of the sinus venosus. Between the 5th and 7th weeks, an oblique anastomotic channel develops between the right and left anterior cardinal veins, diverting venous blood from the left to the right side. This leads to the superior vena cava developing from two sources: The extra pericardial part from the right anterior cardinal vein caudal to the transverse anastomosis and the intrapericardial part from the right common cardinal vein. The left superior vena cava results from the persistence of the left anterior and left common cardinal veins.[20,21]

CONCLUSION

A detailed understanding of embryonic heart development is essential for uncovering the origins of CHD. Our

exploration highlighted key developmental processes, including the formation of crucial structures such as the AV canal, septa, and valves. Disruptions in these events can lead to various CHDs, such as atrial and ventricular septal defects, and transposition of great arteries.

Insights gained from this study provide a foundation for clinicians and researchers, offering valuable perspectives for diagnostic and therapeutic advancements in managing congenital heart defects. Continued research in this field is crucial for refining our understanding and improving clinical outcomes for individuals affected by these conditions.

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SD- Reviewed images and wrote the manuscript; **JJ**- Involved in the initial diagnosis, wrote and critically reviewed the manuscript; **RR-** Involved in the initial diagnosis, wrote and critically reviewed the manuscript

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