CASE REPORT

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Unique cardiac anomaly due to lateralization of a straight trunco-conal septum

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SUMMARY

Congenital heart disease is present in 4-50/1000 live births worldwide, causing about 10% of infant mortality. Congenital heart disease arises when there is a defect in the process of development of the heart through looping, remodeling, realignment and septation of the primitive endothelial tube. Here we describe a case of congenital heart disease where there was formation of straight trunco-conal septum with lateralization. It has caused transposition of great vessels, atretic non communicating stenosed pulmonary trunk, and blind outflow tract of left ventricle. There was renal anomaly too in the form of horseshoe kidney. The entire developmental anomaly could be traced back to the period between the 6th and the 9th week of intrauterine life. The neonate died within half an hour of birth.

Key words: Congenital cardiac anomaly – Intrauterine life – Prenatal investigation – Autopsy – Cardiac dissection – Cardiac development

INTRODUCTION

Worldwide, the incidence of congenital heart disease (CHD) varies from 4 to 50/1000 live births (Hoffman, 1995). Almost a third of these children have severe anomalies, associated with other organ systems as a part of known and unknown chromosomal anomalies (Hoffman and Christianson, 1978). The same is also true in India (Khalil et al., 1994; Saxena, 2005). It is reported that almost 10% of the infant mortality rate in India could be attributed to CHD either directly or indirectly (Saxena, 2005). In addition, a significant number of cases of congenital heart disease (0.8 to 4.2/1000) are present within the age group of 0-15 years. Many of them are unaware of their disease but battling with frequent respiratory infections and inability to perform to the maximum ability according to their age (Saxena, 2005). Most frequent lesions among them were ventricular septal defect, atrial septal defect, patent ductus arteriosus, Fallot's tetralogy, aortic stenosis and pulmonary stenosis (Chadha et al., 2001). It is necessary to understand the embryonic development of the heart and the great vessels, and the factors regulating it to understand the various developmental anomalies that affect their normal anatomical structure and their manifestations.

Heart develops from two primary endothelial tubes that fuse in the midline to form a single median heart tube. This tube undergoes looping, remodeling, realignment and septation to finally form a four chambered heart (Abdulla et al., 2004). The cardiac progenitor cells are found in the anterior part of the primitive streak. Endoderm-derived signals like BMP2, FGF8, Crescent, and Shh/Ihh act as inducers of cardiac mesoderm formation by causing expression of numerous cardiogenic transcription factors like Nkx2.5, GATA, myocardin, and Tbx20. Mesoderm-derived inhibitory signals are Chordin, Noggin, Wnt1, 3 & 8 and Serrate (Brand, 2003). These inducer and inhibitory signals interplay and eventually produce a functional heart. Derangement of temporal and spatial distribution of these factors can cause mis-folding of the

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heart-tube and faulty septation, the latter being the commonest mechanism of congenital heart anomaly. It has been observed that in avians and mammals a gradient in the expression of Tbx-5 helps in the separation of the right and left ventricles (Poelmann et al., 2014). The vascular system develops ahead of developing heart and forms three closed circulation loops in parallel – the systemic, pulmonary and placental circulation. The arterial end is attached as the ventral aortae to the heart tubes and the venous end, as the sinus venosus. The paired ventral aortae are linked to the cranial part of the dorsal aortae through a series of arteries that traverse the pharyngeal arches found on the sides of the head of the embryo. The further re-modeling of these arch arteries and their annexations to the systemic arteries give rise to the formation of the carotid and subclavian systems as well as the arch of the aorta and the ductus arteriosus connecting the left pulmonary artery to the arch of aorta (Schoenwolf et al., 2015). Thus, the vascular system goes through the process of regressions, remodeling and anastomoses to produce a system of arteries and veins, which are necessary for maintaining a placenta-dependent circulation of the fetus and then its conversion into a lung-dependent circulation of newborn. This complex mechanism of development opens up avenues for developing anomalies that are often due to genetic errors or environmental teratogens, but in most of the cases the causes are multifactorial (Bruneau, 2008).

Here, we are reporting a type of cardiovascular developmental anomaly in a full-term male fetus that to the best of our knowledge has not been reported in literature.

THE CASE

A full term, male baby was delivered to a 21 year, primigravida woman, who had an uneventful gestational period. Routine prenatal screening had suggested a normal fetus. She had no history of diabetes, hypertension or ante-natal infections. Delivery of the baby was done at home by a trained birth attendant. The child cried after birth but within half an hour he became unresponsive and was taken to a nearby hospital, where he was declared dead on arrival.

At autopsy, weight of neonate was 2730 grams, his crown-heel length was 49 cm, and the circumference of the head, chest and abdomen were 32 cm, 30 cm and 28 cm, respectively. There was no external deformity in the neonate.

Within the chest cavity, the right lung showed mild distension and weighed 46 grams; while the left lung had a liver-like consistency and weighed 26 grams. About 20 ml of a straw-colored fluid was present in the pleural cavity. The thymus was normal and was occupying the anterior part of the superior mediastinum. The pericardium was normal (Fig. 1). Within, the superior mediastinum arch of the aorta was running from left to right and gave rise to the left subclavian, left common carotid and then right brachiocephalic artery from proximal to distal in that order. The right ventricle was normal externally and ascending aorta was originating from it. The left ventricle was bulbous in appearance and pulmonary trunk was originating from it. On dissection of the heart, the foramen ovale was patent, the tricuspid valve was normal and the right ventricle was normal with the aorta originating from it. The left atrium and the bicuspid valve were normal. The left ventricular wall was hypertrophied with obliteration of cavity. The pulmonary trunk was attached to the outflow tract of left ventricle with a septum closing the communication of the pulmonary trunk with the ventricular cavity (Figs. 2, 3). The circumference of the pulmonary trunk was 7 mm and that of the aorta was 24 mm. The pulmonary trunk was running from left to right, parallel to the aorta and gave three innominate branches. Ductus arteriosus could not be identified and no ventricular septal defect was present. The heart weighed 20 grams.

In the abdominal cavity, the liver and spleen were normal. The stomach and coils of the small and large intestine were positioned normally. Caecum and appendix were present in the right pelvic fossa. The kidneys were fused at their lower poles across the midline in the form of a horse-shoe kidney (Fig. 4). It was present in the pelvic cavity and ureters anterior to it (isthmus of the horseshoe kidney). The rectum, anal canal and its external open-

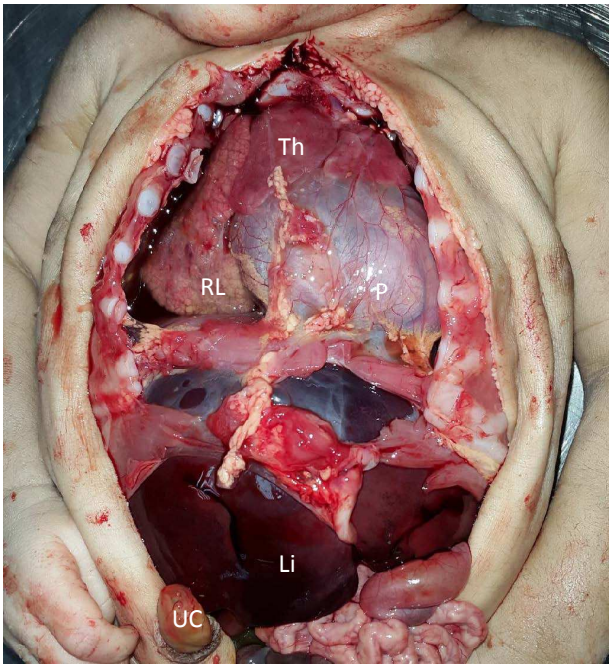

Fig. 1.- Vision of the opened thorax and abdomen of a full term male fetus showing a normal disposition of the Pericardium (P), Right lung (RL), Thymus (Th), Liver (Li) and the Umbilical cord (UC).

ing were normal.

DISCUSSION

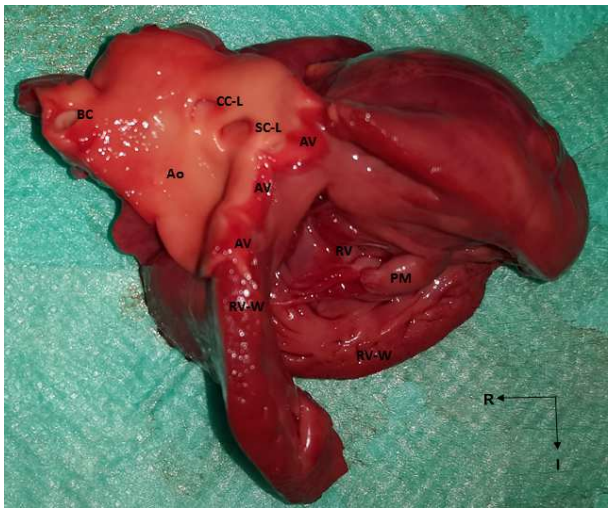

Fig 2. Image showing the anomalous heart with the opened cavity of the right ventricle (RV) showing its wall (RV-W) and a papillary muscle (PM). Its outlet leading to the aorta (Ao) that has been laid open is guarded by a valve with three semilunar leaflets (AV). The lumen of the aorta also reveals the ostia of its three branches left subclavian (SC-L), left common carotid (CC-L) and brachiocephalic (BC) arteries. The directional arrows are pointing to the right (R) and inferior (I).

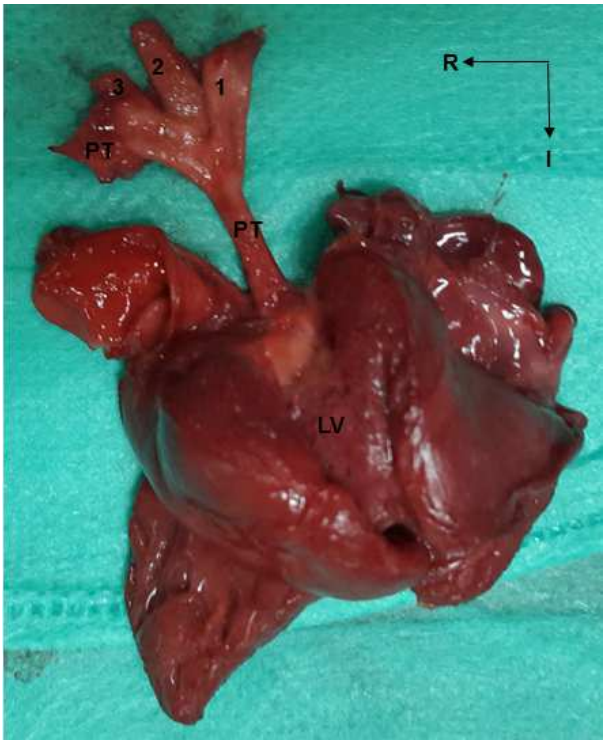

Fig. 3.- Photograph of the anomalous heart showing the open left ventricle (LV) and an attached but blind pulmonary trunk (PT) from which three unnamed branches are seen arising (1, 2 and 3). The directional arrows are pointing to the right (R) and inferior (I) directions.

Here, we report a developmental cardiovascular anomaly in a male neonate who had transposition of great arteries and a blind-outlet hypertrophied left ventricle.

Cardiac developmental anomalies are the most common cause of immediate postnatal deaths and the majority of them are not detected during prenatal screening, detection rate being about 35-40% (Kurinczuk et al., 2010). Most common cardiac anomalies leading to early death are a hypoplastic left heart, complete transposition of the great arteries, double-inlet left ventricles and total anomalous pulmonary venous connection (Hoffman, 1995).

In a necropsy study on fetal and perinatal deaths, Tennstedt et al. (1999) found that about 8% of cases cardiac defects were diagnosed at necropsy only. The commonest cardiac deformities that they encountered were ventricular septal defects, atrioventricular septal defects, hypoplastic left heart, double outlet right ventricle, coarctation of the aorta, transposition of the great arteries, aortic valve stenosis, tetralogy of Fallot, truncus arteriosus communis, pulmonary valve stenosis/ atresia, tricuspid atresia, single ventricle and atrial septal defect. In two-third of cases, the cardiac defect was also associated with extra-cardiac anomalies involving the central nervous system, the genitourinary system and the gastrointestinal system. Abu-Harb et al. (1994) also found that some cardiac diseases such as pulmonary stenosis and transposition of great arteries cause death in hours, while in cases such as endocardial fibroelastosis, truncus arteriosus, tricuspid and pulmonary atresia, and tetralogy of Fallot, death ensues within a day, if left undetected and untreated.

In the present case, the neonate had hypertrophied left ventricle with blind outlet and transposition of the great arteries, wherein the ascending aorta arose from the right ventricle and the ste-

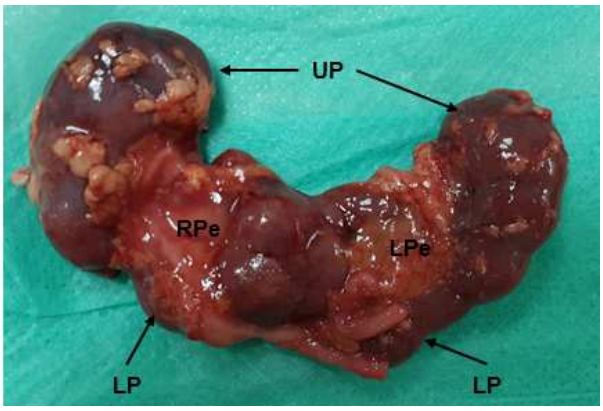

Fig. 4.- Anomalous kidneys found in the case. The lower poles (LP) of the kidneys are fused, while the upper poles (UP) are separated. The right and left pelves (LPe and Rpe) are seen anterior to the fused lower poles.

nosed pulmonary trunk was attached to the left ventricle without any communication with the ventricular cavity. This neonate did not have a ductus arteriosus or a ventricular septal defect. He did have an atrial septal defect in the form of a patent foramen ovale. He died within half an hour of birth.

Anomalous fetal heart developmental process may explain findings of this case. The aorta had originated from the right ventricle, which may be caused by a disturbance in the contribution of second heart field and/or cardiac neural crest to the outflow tract (Schoenwolf et al., 2015) and the formation of a straight trunco-conal septum in the outflow tract instead of a spiral septum; hence, the arch of the aorta becomes right sided. The straight trunco-conal septum also explains the pulmonary trunk running in parallel with the aorta. The septum was lateralized towards the pulmonary trunk causing atresia and stenosis of the pulmonary trunk. Blind outflow tract of the left ventricle in the presence of a normal bicuspid opening of the inflow tract has led to the hypertrophy of the myocardium of left ventricle. The pulmonary trunk had three innominate branches, which may be due to anomalies in modification process during the formation of the aortic arch, the pulmonary trunk and their branches from the outflow tract and pharyngeal arches. Most of these developmental changes occur between the 4^{th} and 8^{th} weeks of development, which is a crucial period of organogenesis (Schoenwolf et al., 2015).

The kidney had horse-shoe anomaly, which may be because of fusion of two metanephros during the process of relocation which occurs during 6^{th} to 9^{th} weeks of development (Poelman et al., 2014).

While the renal anomaly was compatible with life (Sharma and Bapna, 1986), the cardiovascular anomaly was not, since there was no vascular connection to the pulmonary system for oxygenation of the blood. Therefore, when the placental circulation was cut off, the neonate could barely take a few breaths and died (Barron et al., 2009; Piran, 2002).

Some pre-natal fetal screening methods are in need of development to detect these life-incompatible developmental defects so that the fetus can be terminated with planned abortion and the mother need not to carry it to term. Prenatal detection can also help in early management of life -compatible cardiac defects, leading to less morbidity and mortality (Bonnet et al., 1999).

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