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Role of fetal echocardiograms in determining the delivery location of fetuses with cardiac anomalies

Abstract

Neonates born with duct-dependent lesions often require the care of high risk obstetrics and feto-maternal teams in tertiary surgical facilities. However, three fetuses in which prenatal fetal echocardiography demonstrated the presence of both TOF and RAA and the absence of DA were delivered and clinically managed at local facilities. This was made possible because they remained healthy for the initial three to four weeks following birth, suggesting that the co-occurrence of the aforementioned conditions might naturally select patients and protect them from expected complications. Using fetal echocardiography to determine the risk index of the fetuses is of interest as it can prevent the emergency transport of neonates, especially for neonates with cardiac anomalies. Therefore, utilizing fetal echocardiography as a method to determine risk index would allow hospital staff and families to minimize risks and maximize the effective use of resources available at their disposal.

Keywords: right-sided aorta, RAA; TOF; ductus arteriosus, fetal ultrasound, fetal echocardiography

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Abbreviations: TOF, tetralogy of fallot; VSD, ventricular septal defect; LV, left ventricle; RV, right ventricle; PV, pulmonary valve; RAA, right-sided aortic arch; DA, ductus arteriosus; PA, pulmonary artery; MAPCAs, major aortopulmonary collateral arteries; NSAIDs, nonsteroidal anti-inflammatory drugs

Introduction

Congenital heart diseases are the most common birth defects occurring in about 1 in 125 births.[1] They are brought on due to unusual changes in the anatomy of the heart that occur during embryological development and persist after birth. Approximately 3.5% of all infants born with a congenital heart disease suffer from Tetralogy of Fallot (TOF) [1]. TOF was first described by Neils Stensen in 1671 and is a common malformation of the heart, which is equally prevalent in both genders, across races and ethnicities.[2] Infants born with TOF are usually cyanotic and require surgical correction to improve their prognosis.[3] The term TOF refers to a tetrad of cardiac defects that occur simultaneously. These include[4]:

a. Ventricular septal defect (VSD): This defect leads to communication between the left ventricle (LV) and right ventricle (RV).

b. RV outflow tract obstruction: Most commonly due to an anterior displacement of the infundibular septum as well as stenosed Pulmonary Valve (PV).

c. RV hypertrophy: This occurs as a consequence of RV outflow tract obstruction and increased pressures in the RV.

d. Overriding aorta: A defect where the aorta is positioned right above the VSD and emerges from both the ventricles.

The aorta is divided into three parts: the ascending aorta, the arch of the aorta, and the descending aorta. Normally, the arch of the aorta descends to the left of the trachea (left aortic arch). However, in some cases, it descends to the right side of the trachea. In fact, approximately 25% of TOF cases are associated with the simultaneous occurrence of a right-sided aortic arch (RAA).[5] Such variations have been well documented in the literature and account for 0.1% of the population with cardiac complications. When they are isolated, they are clinically benign and not necessarily symptomatic.[6–8]

The cardiovascular system undergoes significant adaptations from fetal to adult life. The developing fetus gets oxygenated blood from the placenta in comparison to adults receiving it from their lungs. The fetal heart has special structures to redirect blood ejected from the RV so that it can bypass the nonfunctional fetal lungs. The ductus arteriosus (DA) is one such special structure; it helps in directing blood from the pulmonary artery (PA) to the descending aorta. Soon after birth, there are drastic changes in pulmonary and intracardiac pressures. If the DA remains patent postnatally, blood is shunted from the aorta to the PA. This abnormality has been noted in 5 to 10% of all congenital heart defect cases, excluding premature infants.[9] In order to prevent blood from being shunted to the PA, the DA undergoes a physiological closure. This structure is then referred to as the ligamentum arteriosum.[9]

The DA is universally present in normal fetal life. However, in patients with further aortic anomalies, the DA is often absent or diminutive. For example, an absent DA has been noted to occur in 50-75% of patients with a congenital heart disease called truncus arteriosus.[10] In patients with truncus arteriosus, since the common arterial trunk originates from both the left and right ventricles, and pulmonary arteries arise directly from the common trunk, a DA is not required to support fetal circulation. Apart from truncus arteriosus, an absent DA can also occur in patients with TOF and pulmonary atresia. A compensatory mechanism that the fetus may use in these cases to maintain sufficient pulmonary perfusion is major aortopulmonary collateral arteries (MAPCAs). MAPCAs are derived from the splanchnic vascular plexus and can persist in such conditions. They allow for systemic blood to flow to different areas of the lungs, thereby compensating for the absence of DA.[11,12]

This commentary follows three fetuses with both TOF and RAA in whom the DA was absent. During an obstetric ultrasound of mothers conducted between 20 and 28weeks of gestation, it was noticed that the three fetuses had TOF. Additionally, an unobstructed RAA and antegrade flow across PV were noted in the ultrasound. A fetal echocardiogram confirmed the diagnosis of TOF and absence

of a DA. The rest of the fetal anatomy was normal. Two of the three patients delivered a live term baby by emergency cesarean section while the third patient delivered a live term baby by vacuum assisted delivery. Upon birth, the neonates did not require prostaglandin administration or immediate surgical correction. Physicians were able to ensure proper care of these cases at local healthcare facilities and did not require to transfer them to tertiary facilities for treatment. This is beneficial as transport of neonates often entails risks, costs, and parental stress. The rarity of the simultaneous occurrence of the aforementioned cardiac anomalies and the challenges they pose in clinically managing such patients makes our report of special interest to imaging specialists and pediatric cardiologists.

Discussion

The DA is a crucial structure during fetal life. It is one of many shunts within the developing fetal cardiovascular system that redirects blood from the immature pulmonary system to the placenta. Normally, approximately 60% of the fetal RV output is shunted from the PA to the aorta via the DA. Only about 10% of the fetal RV output reaches the developing, high-resistance, pulmonary system.[13] Consequently, the absence of DA prenatally can cause significant changes in volume and pressure loads of the RV, which may eventually cause fetal demise. The literature has reported cases of fetuses with absent DA.[14–16] We propose three possibilities for this finding:

a. The DA was never formed in fetal life.

b. The DA was formed in early fetal life, but underwent agenesis or premature closure.

c. The DA is present but cannot be imaged due to anatomical variations.

During embryological development, aortic arches arise from the aortic sac. The aortic arches are embedded in the pharyngeal arches, which are located behind the pharynx. As the fetus develops, the pharyngeal arches undergo drastic rearrangement and agenesis to form the mature cardiovascular system. However, normally, the 6th arch does not undergo agenesis and remains as a patent DA. It has been postulated that the failure of development of the 6th pharyngeal arch or involution of an immature DA may be responsible for the absence of a DA in these fetuses.[17,18]

In some fetuses, the DA is formed initially but undergoes agenesis or premature closure later on during gestation. Such cases have been particularly noted in instances of maternal exposure to nonsteroidal anti-inflammatory drugs (NSAIDs).[19,20] NSAIDs (e.g. aspirin) work by inhibiting the enzyme cyclooxygenase which plays a crucial role in the biosynthesis of prostaglandins. Prostaglandins are involved in maintaining the patency of the DA.[21] However, there is no documentation of maternal exposure to NSAIDs in the three cases we have described in our report.

As previously stated, in some cases DA is present but cannot be imaged due to anatomical variations. For instance, a study conducted by Seth et al revealed that although RAA is a relatively rare condition, its incidence is apparently significantly higher in cases than controls (64% versus 14% respectively, $p<0.001$).[22] This study defined its cases as TOF patients with absent DA and controls as TOF patients with a patent DA. Sometimes, in cases of RAA, the DA can be present between the right PA and the RAA. However, it is more common for it to be found between the left PA and the subclavian or the brachiocephalic artery instead of the aortic isthmus. This region is superimposed by the transverse arch of the aorta, which makes the echocardiographic visualization and Doppler examination of the DA difficult.[23]

Interestingly in cases of RV outflow tract obstruction like pulmonary stenosis or TOF, fetuses may not have a DA and still function without any significant hemodynamic changes. Seth et al reported a 9% prevalence of absent DA in 115 fetuses diagnosed with TOF.[22] It is hypothesized that the agenesis of the DA would have had to occur relatively early during the embryological development of such fetuses. This would allow other normal fetal shunts such as the ductus venosus, patent foramen ovale, along with the VSD to grow and accommodate the hemodynamic changes in the absence of a DA. If the agenesis of the DA were to occur later during gestation, these structures may not be able to accommodate for the hemodynamic changes.

Determining the exact timing and etiology of absence or closure of the DA in patients with TOF using echocardiographic can be challenging. However, it is crucial to know this piece of information as it can greatly impact treatment plans and prognosis. In severe narrowing of pulmonary stenosis of TOF cases, a patent duct is required as a compensatory mechanism to maintain adequate circulation and prevent severe oxygen desaturation. This phenomenon is referred to as duct dependence. Use of prostaglandin to maintain ductal patency in these babies becomes crucial for their survival. Babies who do not have a DA to start with pose a significant challenge in their early management and the only option for them is an elective surgical intervention for stabilization. In fact, all three cases described in this report required definitive surgery between 4weeks and 4months of age. This is of special interest as the timing for definitive surgery for these cases was earlier than the usual elective time of 4-6months for repair of TOF in most institutions. However, considering that our three cases remained healthy without surgery for the initial 3 to 4weeks following birth, we wonder whether they are naturally selected, which allowed them to survive their neonatal period without the expected complications.

Neonates with duct dependent lesions often require management by high risk obstetrics and feto-maternal teams in tertiary surgical facilities. However, since our cases were healthy for the initial 3 to 4weeks following birth, they were clinically managed at local facilities. Based on our cases, the detection of the simultaneous occurrence of a RAA, TOF and absent DA via fetal echocardiography would imply that the patient is naturally selected and protected from the expected complications. If so, the patient would most likely not require emergency neonatal transport to tertiary facilities. Using fetal echocardiography to help predict the risk index of the fetuses with cardiac anomalies is of interest as it can help prevent emergency transport of neonates. Transporting neonates to different facilities entails risks that include hypoglycemia, temperature instability, and hypo or hypercapnia.[24] In fact, neonates with cardiac abnormalities are particularly susceptible to hypothermia.[24] Furthermore, since our cases were treated locally, we were able to maximize our resources and decrease the stress associated with travel and separation from family and home.

Lastly, it is important to note that in TOF patients with anatomical variations such as a RAA, the DA might be present but just difficult to image. For instance, physicians suspected the presence of a tortuous PDA arising from the base of the innominate artery in one of our patients. However, that could not be seen on numerous fetal echocardiographic investigations. Pediatricians, cardiologists and imaging specialists must be trained to not misinterpret such cases as not having a DA, as this might change their treatment plan. Patients without a DA would not benefit from prostaglandin administration, whereas patients with a DA would require prostaglandin administration. Thus, it would be vital to consider the various possibilities described in our report

when dealing with such patients. Parents must be also counseled with regards to the best choice of institution for safe delivery and postnatal care.

Conclusion

We report three cases of TOF in whom the DA was absent. Coincidentally, all cases were noted to have RAAs. The infrequency of the simultaneous occurrence of these conditions and their unexpected postanal course make the clinical management of such neonates of special interest to pediatricians, cardiologists and imaging specialists. Consequently, health care teams should be trained to appropriately counsel families and provide best possible care.

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Conflicts of interest

Author declares there are no conflicts of interest.

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