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CASE REPORT

EXPLORING THE COMPLEXITY OF CONGENITALLY CORRECTED TRANSPOSITION OF THE GREAT ARTERIES: ULTRASOUND DIAGNOSIS AND CLINICAL IMPLICATIONS - AN INTEGRATIVE APPROACH AND CASE REPORT

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ABSTRACT

INTRODUCTION: Congenitally corrected transposition of the great arteries (CCTGA) is a rare congenital heart disease that presents challenges in prenatal ultrasound diagnosis. Early and accurate identification of this condition is crucial for treatment planning and proper patient monitoring.
OBJECTIVE: This study aims to analyze the challenges of ultrasound diagnosis of CCTGA, highlighting the importance of confirming the occurrence of double atrioventricular and ventriculoarterial discordance for an accurate diagnosis. Additionally, it presents an illustrative case report to exemplify the prenatal echocardiographic diagnosis of this condition.
METHODS: An integrative literature review was conducted, with an emphasis on the prenatal ultrasound/echocardiographic diagnosis of CCTGA. Seven articles were selected from a search in the PUBMED and Virtual Health Library databases, using the keywords "corrected transposition of the great arteries" and "prenatal fetal diagnosis." The case report presented in this study was analyzed alongside the selected studies to contribute to the understanding of the challenges in diagnosing this condition.
CASE REPORT: The presented case describes a prenatal echocardiographic diagnosis of CCTGA without other associated cardiac abnormalities. It highlights the importance of careful evaluation of routine echocardiographic views to facilitate the accurate diagnosis of this condition.
DISCUSSION: The discussion addresses the importance of identifying specific ultrasound markers, such as double atrioventricular and ventriculoarterial discordance, to confirm the diagnosis of CCTGA. Additionally, it discusses the challenges and strategies for early and accurate diagnosis of this condition, especially when found in isolation without other associated cardiac abnormalities.
CONCLUSION: The integrative review and case report presented in this study reinforce the importance of careful and systematic prenatal echocardiographic evaluation for the diagnosis of CCTGA. Confirming the occurrence of double atrioventricular and ventriculoarterial discordance is essential for an accurate diagnosis of this condition. Early and correct identification of CCTGA allows for appropriate treatment planning and monitoring of patients affected by this rare congenital heart disease.

KEYWORDS: CONGENITALLY CORRECTED TRANSPOSITION OF THE GREAT ARTERIES, PRENATAL ULTRASOUND, DIAGNOSIS, ECHOCARDIOGRAPHY, CONGENITAL HEART DEFECTS.

INTRODUCTION

Congenitally corrected transposition of the great arteries (CCTGA) is an uncommon heart defect characterized by the atria connecting to anatomically discordant ventricles, and the ventricles connecting to discordant and transposed great arteries. Parallel vessels are evident in CCTGA, but since this sign is also present in transposition of the great arteries (TGA), a cardiac anomaly that requires major cardiac surgery in the postnatal period, it is important to differentiate between these entities prenatally. It is a rare congenital heart anomaly, representing less than 1% of live births with congenital heart disease. Most cases of CCTGA have associated anomalies, but isolated forms are rarely detected prenatally, with the isolated variant accounting for 9-16% of all cases[1].

Embryologically speaking, a mirror image looping (to the left) of the primitive heart tube during embryonic development places the anatomical left ventricle on the right side. The great arteries also present a discordant connection, maintaining the laterality. In this way, the pulmonary and systemic venous returns are properly directed to the aorta and pulmonary arteries, respectively, causing these

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two connection anomalies to neutralize each other, minimizing hemodynamic repercussions[2]. This double discordance results in a physiologically corrected circulation, but the left ventricle supports the pulmonary circulation and the right ventricle supports the systemic circulation[2,3].

CCTGA is not inherently associated with intrauterine congestive heart failure. In the absence of congestive heart failure, there is no indication to alter standard obstetric management. However, delivery should be performed in a tertiary referral center where a pediatric cardiologist is present at the time of birth[2].

The importance of this review lies in identifying ultrasound markers that could detect fetuses with CCTGA, whether isolated or associated with other cardiac malformations. This, in turn, aids ultrasonographers performing routine obstetric or fetal echocardiographic examinations in identifying fetuses with this congenital heart disease.

METHODOLOGY

This is an integrative literature review aimed at synthesizing the main findings associated with CCTGA, a rare congenital heart disease, as described in case reports and multicenter studies published in major medical journals worldwide. To illustrate the difficulty of diagnosis, we describe a case report of a fetus diagnosed prenatally with isolated CCTGA without other associated cardiac or extracardiac abnormalities.

For this study, in order to satisfy the strategy of clinical practice based on scientific evidence, we established the following PICO/PIO question: "Is there a single ultrasound marker that can define the diagnosis of congenitally corrected transposition of the great arteries? If not, what would be the best ultrasound criterion for the definitive diagnosis?"

The PUBMED and VHL (Virtual Health Library) databases were searched using the following descriptors: "corrected transposition of the great arteries" AND "prenatal fetal diagnosis".

Using the descriptors for searching scientific studies, without using filters for temporal restriction and other filters, 40 studies were returned by the search in PUBMED and 58 studies were returned in the VHL, between the years 1975 and 2024. The selection criteria for the studies included those whose themes fit the objectives of this integrative review and that could answer the guiding question.

Among the 40 studies returned by PUBMED, seven studies were selected because they met the study's interest in the diagnosis of Corrected Transposition of the Great Arteries (CCTGA) in fetal life. From the 58 studies in BVS, seven studies were chosen for meeting the criteria of interest, all of which were discarded due to duplication found with those selected by PUBMED. Additionally, a review of a specialized textbook on fetal cardiology was conducted. Thus, this integrative review was based on seven (7) studies identified in the literature and one (1) textbook (Figure 1).

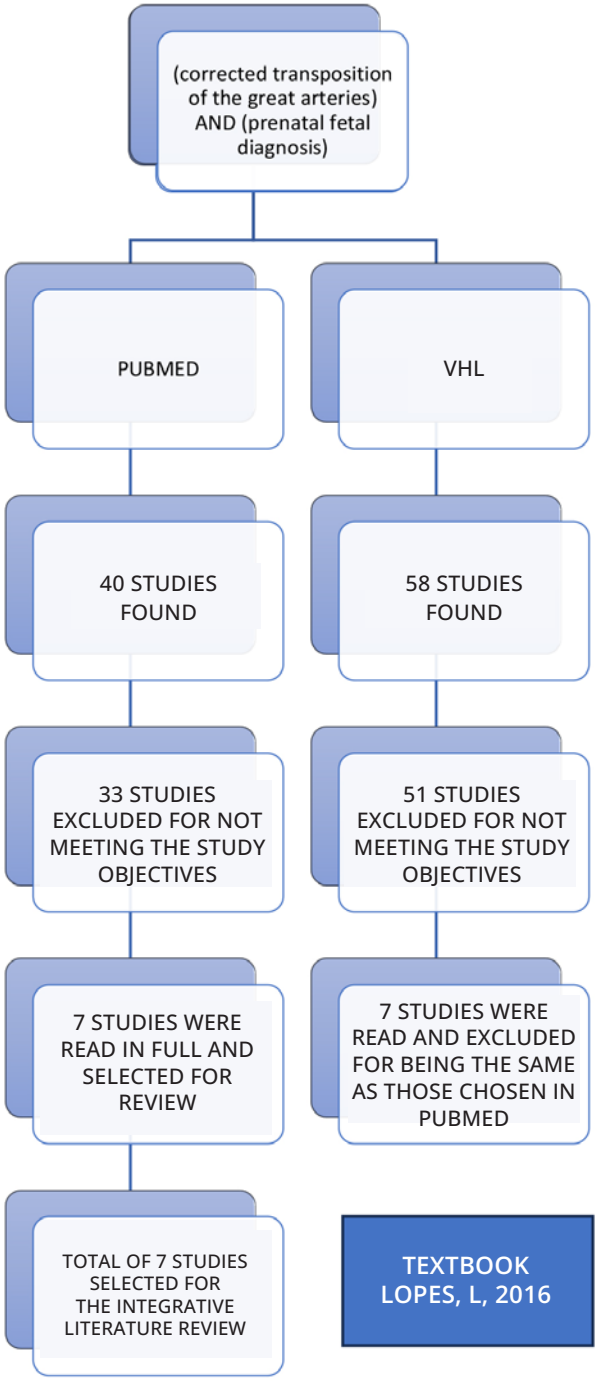


Figure 1: Flowchart of the study selection process.

Table 1 categorizes the selected studies for use in the integrative literature review, along with the designs of each study.

STUDY	DATABASE	JOURNAL	DESIGN
E1- Congenitally corrected transposition of the great arteries: clues for prenatal diagnosis. McEwing, et al., (2004)[1]	PUBMED	Ultrasound Obstet Gynecol. 2004 ;23(1):68-72.	Case Report
E2- Atrioventricular and ventriculoarterial discordance (congenitally corrected transposition of the great arteries): echocardiographic features, associations, and outcome in 34 fetuses. Sharland, et al., (2005)[3]	PUBMED	Heart. 2005 ;91(11):1453-8.	Retrospective cohort study
E3- Diagnosis, characterization and outcome of congenitally corrected transposition of the great arteries in the fetus: a multicenter series of 30 cases. Paladini, et al., (2006)[4]	PUBMED	Ultrasound Obstet Gynecol. 2006 ;27(3):281-5.	Retrospective cohort study
E4- Postnatal outcome following prenatal diagnosis of discordant atrioventricular and ventriculoarterial connections. Day et al., (2019)[5]	PUBMED	Pediatr Cardiol. 2019;40(7):1509-1515.	Retrospective cohort study
E5- Prenatal diagnosis and outcome of congenital corrected transposition of the great arteries - a multicenter report of 69 cases. Vorisek et al., (2021)[6]	PUBMED	Ultraschall Med. 2021;42(3):291-296.	Retrospective cohort study
E6- Prenatal diagnosis, associated findings and postnatal outcome in fetuses with congenitally corrected transposition of the great arteries. Krummholz, et al., (2021)[7]	PUBMED	Arch Gynecol Obstet. 2021 ;303(6):1469-1481.	Retrospective cohort study
E7- Congenitally corrected transposition of the great arteries: fetal diagnosis, associations, and postnatal outcome: a fetal heart society research collaborative study. Cohen, et al., (2023)[8]	PUBMED	J Am Heart Assoc. 2023;12(11):e029706.	Retrospective cohort study

Table 1 - Categorization of Studies

RESULTS

The final sample of this review consisted of seven publications, selected based on the predetermined inclusion criteria. The selected works were published between 2004 and 2024, covering the last 20 years.

The studies in this integrative review are summarized in ascending chronological order in Table 2, listing the results found and the relationship of responses to the questions of interest.

Study	Objective	Response to the questions of interest
E1	To describe the prenatal ultrasound characteristics and neonatal evolution of three cases of essentially isolated corrected transposition	Only the detection of both double discordance of the atrioventricular and ventriculoarterial connections is capable of confirming the diagnosis of CCTGA by ultrasound.
E2	To identify fetal echocardiographic characteristics, associations, and results of atrioventricular and ventriculoarterial discordance in a cohort of 34 fetuses.	Only the detection of the concomitant occurrence of double atrioventricular and ventriculoarterial discordance is capable of confirming the diagnosis of CCTGA by ultrasound.
E3	To describe the anatomy, associated anomalies, and evolution in a cohort of 30 cases of CCTGA detected prenatally.	Only the detection of both atrioventricular and ventriculoarterial double discordance is capable of confirming the diagnosis of CCTGA by ultrasound.

E4	To describe the spectrum of atrioventricular and ventriculoarterial discordant connections diagnosed during fetal life, as well as the medium-term outcome (beyond 5 years of age and up to early adulthood) in a cohort of 98 fetuses with prenatal diagnosis.	Only the detection of the simultaneous occurrence of double discordance of atrioventricular and ventriculoarterial connections is capable of confirming the diagnosis of CCTGA through ultrasound.
E5-	To investigate the natural history, associated anomalies, and outcomes of a cohort of 69 patients with a prenatal diagnosis of CCTGA.	Only the detection of the concomitant occurrence of double discordance atrioventricular and ventriculoarterial is capable of confirming the diagnosis of CCTGA, by ultrasound.
E6	To analyze the anatomical characteristics and associated malformations in a cohort of 37 cases of CCTGA detected prenatally and to evaluate the prenatal course, neonatal outcome, and medium-term follow-up.	Only the detection of double discordance between the atrioventricular and ventriculoarterial connections is capable of confirming the diagnosis of CCTGA through ultrasound.
E7	To investigate the natural history, associated anomalies, and outcomes of a cohort of 205 fetuses diagnosed with CCTGA.	Only the detection of both double discordance in atrioventricular and ventriculoarterial connections is capable of confirming the diagnosis of CCTGA through ultrasonography.

Table 2 - Illustrates the objectives and answers to questions of interest.

All selected studies were conclusive and unanimous in affirming that only the confirmation of double discordance, atrioventricular and ventriculoarterial, is capable of confirming the prenatal ultrasonographic diagnosis of CCTGA.

DISCUSSION

The congenitally corrected transposition of the great arteries (CCTGA) is a rare congenital heart defect characterized by the atria connecting to the ventricles in an anatomically discordant manner, and the ventricles connecting to the great arteries in a discordant and transposed manner. Parallel vessels are evident in CCTGA, but as this sign is also present in complete transposition of the great arteries (TGA), a cardiac anomaly that requires major cardiac surgery in the postnatal period, it is important to differentiate the entities prenatally. It is an uncommon congenital heart anomaly, accounting for less than 1% of live births with congenital heart disease. Most cases of CCTGA have associated anomalies, but isolated forms are rarely detected prenatally, with the isolated variant accounting for 9-16% of all cases[1] .

The venoatrial connections are normal, and the discordance in both atrioventricular and ventriculoarterial connections allows hemodynamic compensation (Figure 2). Careful examination of the ventricles allows distinguishing between the morphological right and left ventricles and detecting the atrioventricular discordance[1].

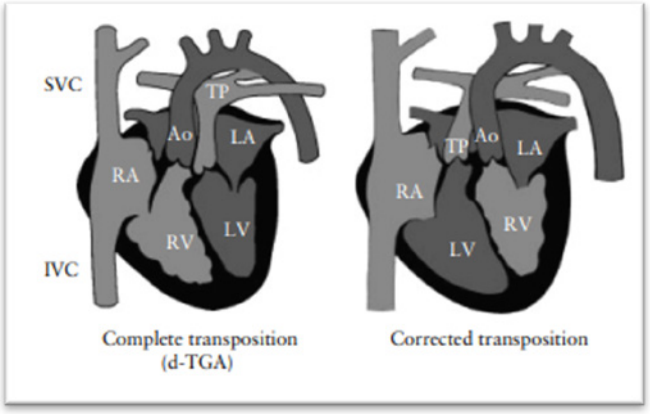


Figure 2: RA, right atrium; LA, left atrium; RV, right ventricle; LV, left ventricle; Ao, aorta; TP, pulmonary trunk; IVC, inferior vena cava; SVC, superior vena cava1.

Reiterating, in CCTGA, the right atrium drains into a morphological left ventricle on the right side through the mitral valve, and the left atrium drains into a morphological right ventricle on the left side through the tricuspid valve (atrioventricular discordance). The morphological left ventricle is connected to the pulmonary artery, while the aorta arises from the morphological right ventricle (ventriculoarterial discordance). The great vessels have a parallel course without crossing, with the aorta usually located anteriorly and to the left of the pulmonary trunk (Figure 3). This results in a physiologically corrected blood flow, with the morphological right ventricle controlling the systemic circulation in postnatal life[7].

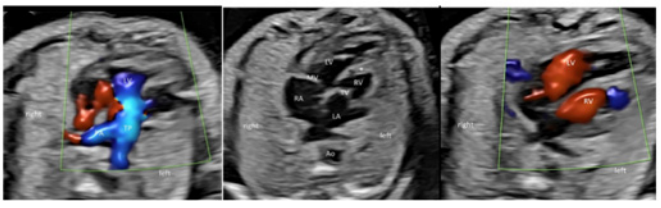


Figure 3: Ao - aorta, LA - left atrium, RA - right atrium, TV - tricuspid valve, MV - mitral valve, RV - right ventricle with left morphology, LV - left ventricle with right morphology[7].

Sharland et al.[3] published the first retrospective cohort of 34 fetuses with prenatal diagnosis of CCTGA, from patients treated at a tertiary cardiology center, aiming to confirm the position of the ventricle with the moderator band, the parallelism or abnormality in the orientation of the great arteries, associated cardiac abnormalities, outcomes, and postnatal confirmation of findings, confirming the high prevalence of associated heart diseases and the rare occurrence of the isolated form.

Paladini et al.[4] conducted a retrospective multicenter study of 30 cases of CCTGA with prenatal diagnosis confirmed by autopsy or postpartum echocardiography. In this study, with a mean gestational age at diagnosis of 25.5 weeks, the authors suggest a low correlation between CCTGA and chromosomal and extracardiac anomalies, confirming the high prevalence of associated cardiac abnormalities. The associated anomalies found are in accordance with values derived from pediatric literature. They are, in decreasing order of frequency: ventricular septal defects, pulmonary stenosis/atresia, anomalies of the left tricuspid valve (including dysplasia, Ebstein-like insertion, "straddling", tricuspid atresia), rhythm disorders, and dextrocardia, and are consistent with those mentioned in subsequent retrospective multicenter studies, as shown in Table 3.

Anomalias Associadas (%)	Sharland (2005)	Paladini (2006)	Day (2019)		Vorisek (2020)	Krummholz (2021)		Cohen (2023)	Literatura pediátrica	TOTAL
			Pré-Natal	Pós-Natal		Pré-Natal	Pós-Natal			
Defeito septal ventricular	62,0	70,0	65.3	67.4	75.9	73	73,5	68.3	70-84	**69,4**
Obstrução pulmonar	35.2	40,0	28.6 (21.4+civ)	32.6 (23.3+civ)	35.2	35.1	55.9	38.4	30-50	**20,6**
Anormalidades da valva tricúspide	26.4	33.3	ND	ND	33.3	18,9	23.5	19.6	14-56	**25,8**
Bloqueio atrioventricular completo	ND	13.3	ND	ND	18.5	5.4	11.8	11.3	12-33	**12,1**
TCCGA isolada	14.7	13.4	15.3	20.9	13,0	13.5		21.5	9-16	**16,1**
Anomalias do arco aortico	11.7 CoAo	10.0	14.3 CoAo	9.3 CoAo	9.3	13.5	29.4	10.7	13,0	**13,5**

Table 3 illustrates the most prevalent associated anomalies with CCTGA found in the selected studies.

Associated anomalies

After reading the studies thoroughly and comparing them, it was possible to evaluate the occurrence of associated anomalies – table 3.

The most frequent cardiac anomaly in all studies was ventricular septal defect (VSD), with occurrence ranging from 69.4% in the selected studies. In the study by Vorisek et al.[6], most VSDs were large, diagnosed in the B-mode, and involved the membranous septum, with no specific percentage found. In the largest representative cohort of CCTGA to date, Cohen et al. [8] estimated the percentage of perimembranous VSD at 52.9%, inlet VSD at 23.2%, muscular VSD at 11.6%, double outlet VSD at 5.8%, and malalignment VSD at 1.5%[8].

Pulmonary obstruction presented with varying degrees, from mild stenosis to severe degrees of atresia, with an incidence of 20.6%.

Tricuspid valve abnormalities were found in 25.8%, with the most frequent being Ebstein's anomaly, tricuspid regurgitation, and straddling of the tricuspid valve.

Aortic arch anomalies and complete atrioventricular block were found in 13.5% and 12.1%, respectively.

Other abnormalities, no less important, were recognized by the studies, such as right ventricular hypoplasia, persistent left superior vena cava, heterotaxy, and pericardial effusion. When evaluating the presence of isolated CCTGA, the total incidence was 13.5%.

The prenatal ultrasound diagnosis of CCTGA is possible with good accuracy, especially in specialized centers. It is recommended to focus on differentiating the left and right ventricles on echocardiography, for example, by identifying the morphological right ventricle in the four-chamber view by its posterior and left position, a prominent moderator band, a more irregular endocardial surface, more apical attachment of the atrioventricular (tricuspid) valve, and distal and central attachment of the papillary muscles. In contrast, the morphological left ventricle is characterized by a smooth surface, a more elongated shape, a less apical insertion of the mitral valve, and papillary muscles that attach to the lateral wall of the ventricle. This identification is important, particularly when a parallel course of the great arteries is found, to distinguish CCTGA from complete transposition of the great arteries (TGA), a cardiac anomaly that requires different management shortly after birth[7].

Unless there are associated malformations, CCTGA may not be easily identified during routine ultrasound investigation and can be confusing for ultrssonographers and those inexperienced in fetal heart examination. The fetal spectrum is therefore biased towards these cases. However, prenatal detection during obstetric screening is clearly possible, as most fetuses (91%) in this series were referred due to a suspected problem during routine obstetric screening[8].

The cardiac assessment aimed at diagnosis through the evaluation of routine ultrasound or echocardiographic sections facilitates the diagnosis. In a publication for the International Society of Ultrasound in Obstetrics and Gynecology (ISUOG), Carvalho et al.[9] recommend a guide for good ultrasound practices for the detection of congenital heart diseases in low-risk groups - ISUOG Practice Guidelines (updated): fetal cardiac screening, 2023[9]. The authors acknowledge that the assessment of the fetal heart goes beyond the four-chamber view and the three vessels and trachea (some lesions, such as transposition of the great arteries, coarctation of the aorta, may not be evident only in the four-chamber plane). Complementing the four-chamber view with views of the outflow tract and great vessels in the cardiac screening exam has played an important role in improving the detection of congenital heart diseases. The guideline proposes a

checklist to be followed by ultrssonographers for good practices to improve the assessment of the fetal heart. It proposes a systematization of the exam, with axial scanning, starting at the fetal abdomen and tilting the transducer cephalically, as demonstrated in figures 4 and 5[9].

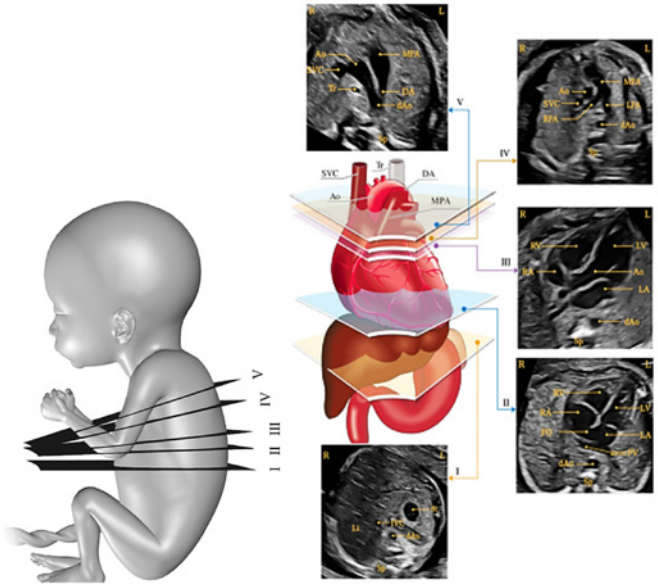


Figure 4 and 5. Illustrates the left five transverse planes in a fetal model and the left ultrasonographic images of these planes. I - transverse plane of the abdomen – situs solitus (St) fetal stomach, (dAo) descending aorta, (IVC) inferior vena cava, (Sp) spine, (Li) liver; II - transverse plane of the heart - four-chamber view - (RV, LV) right and left ventricles, (RA, LA) atria, (FO) foramen ovale, (PV) pulmonary veins; III - long axis of the left ventricle with aortic output - (Ao) ascending aorta; IV - short axis of the pulmonary trunk leaving the right ventricle - (MPA) main pulmonary artery, (RPA) right and (LPA) left pulmonary arteries; V - transverse section of the three vessels and trachea9 - (SVC) superior vena cava, (DA) ductus arteriosus, (Tr) trachea. L, left, R, right.

CASE REPORT

35-year-old primigravida, without known comorbidities, except for gestational hypothyroidism. On 02/03/2023, she underwent a fetal morphological ultrasound examination at a reference service, with an estimated gestational age of 23 weeks and 6 days, where it was observed: 'parallel arteries emerging from the ventricles, with the aorta connected to the right ventricle and the pulmonary artery connected to the left ventricle,' without other detectable abnormalities by the method and concluded as: transposition of the great arteries (Figure 6).

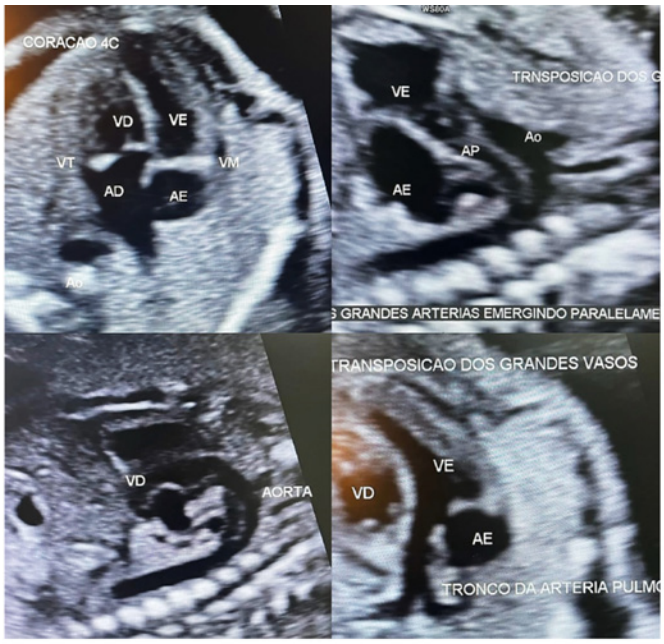


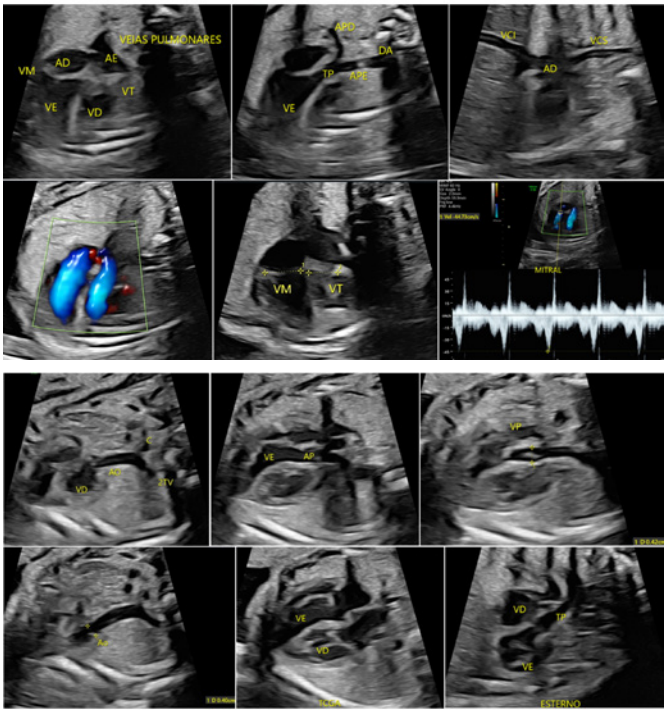
Figure 6: Four-chamber view followed by parallel great vessels. Lower images represent the great vessels, aorta from the right ventricle, and pulmonary trunk from the left ventricle. Courtesy of Dr. Alexandre Henrique Sidney de Andrade.

She was referred to our service for a color Doppler echocardiogram on 02/28/2023, at 27 weeks and 3 days of gestational age, confirming the findings. The following report was issued (figures 7-23):

- Fetus in cephalic presentation, with the back to the left;
- Heart rate 142 bpm, sinus rhythm;
- Abdominal situs solitus; Heart in levoposition and levocardia, presenting four chambers;
- Presents venoatrial concordance;
- Presents atrioventricular and ventriculoarterial discordance - corrected transposition of the great arteries (CTGA), left ventricle of right morphology and right ventricle of left morphology. Aorta emerges from the right morphology ventricle and the pulmonary artery emerges posteriorly from the left morphology ventricle;
- Intact interventricular septum, without any detectable communication by the method;
- Normal septal thickness for gestational age;
- Cardiac chambers with normal dimensions;
- Pulmonary arteries and aorta flow with antegrade flow directions.
- Evaluation of the tricuspid, mitral, and ductus venosus valves without evidence of retrograde flow;
- Foramen ovale with anatomical characteristics, presenting right-to-left flow, with a usual appearance lamina;
- Mitral valve measuring 9.7mm (Z score=1.29), with peak systolic velocity of 44.7cm/s; Aortic valve measuring 4.0mm (Z score=-0.61), with peak systolic velocity of 70.5cm/s;

• Tricuspid valve measuring 7.9mm (Z score=-0.63), with peak systolic velocity of 48.5cm/s; Pulmonary valve measuring 4.2mm (Z score=-1.90), with peak systolic velocity of 64.6cm/s;

DIAGNOSTIC IMPRESSION:
• Corrected Transposition of the Great Arteries (CTGA).
All photographic documentation of this fetal echocardiography at 27 weeks and 03 days is presented below (Figures 7-23), illustrating the findings, the connections, the normality and functionality of the heart valves, as well as documenting the absence of other associated cardiac abnormalities and confirming the case as isolated CCTGA.



Figures 7-23 - Illustrate ultrasound images of the fetal echocardiogram. RV right ventricle; Ao aorta; 2TV two vessels trachea; LV left ventricle; PA pulmonary artery; PV pulmonary valve; PT pulmonary trunk; RA right atrium; LA left atrium; MV mitral valve; TV tricuspid valve; RPA right pulmonary artery; LPA left pulmonary artery; DA ductus arteriosus; IVC inferior vena cava; SVC superior vena cava.

After the study, the pregnant woman was referred by her attending obstetrician to a tertiary referral center for scheduling the birth with a cardiologist present at the time of delivery.

On 05/03/2023, at 36 weeks of gestation, at the request of the tertiary referral center team, a new color Doppler echocardiogram was performed in a specialized service, confirming the findings of the previous study, concluding the diagnostic hypothesis as corrected transposition of the great arteries.

The birth was via cesarean section at 39 weeks and 1 day, on 05/24/2023, with 14 hours of ruptured membranes and clear amniotic fluid. The male newborn was born well with an APGAR score of 9/9, without alterations on the initial physical examination. The newborn was referred to the neonatal intensive care unit for further investigation of the heart condition.

On 05/26/2023, still in the neonatal intensive care unit, a two-dimensional echocardiogram was performed, confirming the findings of the prenatal examinations. Additionally, there was a minimal patent ductus arteriosus shunt, mild tricuspid regurgitation, and mild narrowing at the level of the aortic isthmus, without causing significant gradients.

The newborn progressed without complications, was discharged from the hospital on 05/29/2023 and returned to the pediatric cardiologist on 06/272023. The family was advised to schedule a two-dimensional color Doppler echocardiogram when the child reaches one year of age.

CONCLUSION

The present integrative review showed that congenitally corrected transposition of the great arteries (CCTGA) is a rare congenital heart defect, more commonly associated with other congenital heart diseases and less prevalent when found in isolation without other abnormalities, as in the presented case. Directed cardiac evaluation for diagnosis, through routine echocardiographic cuts, facilitates diagnosis.

Responding to the guiding question (PICO), all selected studies were conclusive and unanimous in affirming that only the confirmation of the occurrence of double discordance, atrioventricular and ventriculoarterial, is capable of confirming the prenatal ultrasonographic diagnosis of CCTGA.

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