# Pentalogy of Cantrell with a double-outlet right ventricle: Prenatal Diagnosis, Delivery and Immediate Postnatal Surgical Repair

# Pentalogia de Cantrell com um ventrículo direito de saída dupla: Diagnóstico Pré-Natal, Parto e Reparação Cirúrgica Pós-Natal Imediata

DOI:10.34117/bjdv7n10-138

Recebimento dos originais: 13/09/2021
Aceitação para publicação: 13/10/2021

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**RESUMO**
A Pentalogia de Cantrell é uma doença congênita rara, havendo apenas cerca de 250 casos relatados. A síndrome consiste em uma variedade toracoabdominal de ectopia cordis, associada a cinco defeitos principais em: linha mediana anterior supraumbilical de parede abdominal, porção anterior do diafragma, parte inferior do esterno, pericárdio parietal e malformações cardiovasculares. A sua letalidade é alta, conforme gravidade e extensão das alterações, de forma que a assistência pré-natal se faz fundamental ao diagnóstico precoce e à investigação das anomalias, a fim de proporcionar um melhor prognóstico. Nesse sentido, objetiva-se relatar o caso de um neonato com variante completa da síndrome. O diagnóstico foi realizado no período intrauterino por meio de avaliação ultrassonográfica, identificando-se defeito de fechamento de paredes torácica e abdominal (onfalocele), ectopia cordis e anomalia estrutural cardíaca. Na ecocardiografia fetal, foram evidenciados: dupla via de saída de ventrículo direito, estenose pulmonar, aorta cavalgando septo interventricular e persistência de veia cava superior esquerda. Houve interrupção da gestação por parto cesariano, com idade gestacional de 36 semanas e 3 dias. O recém-nascido foi submetido a cuidados intensivos e correção cirúrgica, mas faleceu horas depois.

**Palavras-chave:** Pentalogia de Cantrell, Ectopia Cordis, Ultrassonografia Pré-Natal, Relatos de Casos.

**ABSTRACT**
The Pentalogy of Cantrell is a rare congenital disorder, with only 250 reported cases. It consists of a thoracoabdominal variety of ectopia cordis associated with abnormalities that affect the ventral abdominal wall; the diaphragm; the sternum; the pericardium; and the cardiovascular system. Its lethality rate gets higher the more severe and widespread the affection, which emphasizes the importance of prenatal care for early diagnosis. Hereof, we aim to report the case of a newborn with a complete variant of the syndrome.

Diagnosis was performed in the intrauterine period by ultrasound assessment, which detected defects in the closure of the thoracoabdominal wall, ectopia cordis and cardiac structural abnormalities. Fetal echocardiography revealed a double-outlet right ventricle, pulmonary stenosis, overriding aorta and a persistent left superior vena cava. At 36 weeks and three days, the pregnancy was terminated by cesarean delivery. The newborn underwent intensive care and surgical correction, but died hours later.

**Keywords:** Pentalogy of Cantrell, Ectopia Cordis, Ultrassonography, Prenatal, Case Reports.

## 1 INTRODUCTION

The Pentalogy of Cantrell is a rare congenital disease which was first described by Cantrell et al. in 1958 and classified by Toyama in 1972 [1,2]. Its incidence is estimated at 1:65.000 live births and it is more common amongst males, with a ratio of 1,35:1 [3,4]. Up until today, there are only about 250 cases depicted in the literature and 72% of them took place in Europe and The United States [4,5].

The etiology of Cantrell's Pentalogy is still unknown. The most accepted hypothesis suggests it results from disorders of the development and migration of the mesoderm, between the 14$^{th}$ and 18$^{th}$ days of embryonic life [1]. The syndrome consists of a thoracoabdominal variety of ectopia cordis associated with five main abnormalities which affect the supraumbilical midline of the ventral abdominal wall (omphalocele); the anterior portion of the diaphragm; the lower section of the sternum; the parietal pericardium; and the cardiovascular system [1]. Therefore, the affliction presents with an elevated lethality rate, which gets higher the more severe and widespread the extent of the anomalies [6].

Given the complexity of the Pentalogy, early diagnosis and multidisciplinary approach in prenatal and postnatal care are vital for adequate follow-up of the pregnancy and appropriate therapeutic intervention of the newborn. In this paper, a complete case of the syndrome in a patient undergoing intensive neonatal care and surgical intervention will be described. The present study was approved by the Research Ethics Committee of the Medical Sciences Center of the Federal University of Paraíba, under the number CAAE 40491220.4.0000.8069, and the informed consent form was signed by the newborn's legal guardian for publication of the report.

## 2 CASE REPORT

An 18-year-old primigravida woman, A.S.S., originally from João Pessoa – Paraíba (PB), was sent to the High Risk Prenatal Care Unit at Lauro Wanderley University Hospital (HULW), with gestational age of 20 weeks and 4 days according to a first trimester ultrasound, due to obstetric ultrasonography evidence of omphalocele and ectopia cordis, under the diagnostic hypothesis of Cantrell's Pentalogy.

The patient underwent follow-up at HULW and had her personal and family history investigated. However, neither maternal-based pathologies nor family history of congenital malformation were identified.

A morphological obstetric ultrasound performed during the twenty-second week of pregnancy showed a single cephalic male fetus, with a defect in the closure of the thoracic and abdominal walls (an omphalocele with liver tissue in its herniated content), ectopia cordis, subaortic ventricular septal defect, an overriding aorta and overlapping left toes.

The fetal echocardiogram showed a regular bradycardic sinus rhythm, pulmonary stenosis, visceroatrial situs solitus, a chest wall defect and ectopia cordis, with completely extrathoracic heart. Furthermore, persistent left superior vena cava draining into the coronary sinus, aortic overriding affecting over 50% of the interventricular septum, atrioventricular concordance and double-outlet right ventricle were identified. Moreover, the ductus arteriosus was not found.

The patient was referred to the Obstetric Emergency Unit of HULW at 34 weeks due to fetal hemodynamic centralization as demonstrated by an ultrasound. Corticosteroid therapy was performed for fetal lung maturation, and it was decided the pregnancy would be terminated by cesarean delivery, which happened at 36 weeks and 3 days of gestational age. Upon birth, clinical examination of the newborn showed Apgar scores of 6/6/7, weight of 2.365 grams and 46 centimeters of height. Additionally, ectopia cordis, an omphalocele of approximately 7 centimeters containing intestinal loops restrained by a thin membrane and other malformations such as low setting of the external ear, saddle nose and clubfeet were found (**Figure 1**). The male newborn was placed under the neonatology team's care, but his health condition deteriorated and a surgical approach was considered the best fit.

Aged 26 hours of life and under invasive mechanical ventilation, sedoanalgesia, vasoactive drug (dobutamine), antibiotic therapy (oxacillin and amikacin) and intravenous hydration, the neonate followed to Dom José Maria Pires Metropolitan

Hospital (HMDJMP) in order to be submitted to surgical intervention. He was well adapted, hydrated, ruddy in complexion and presented impaired cardiac auscultation, symmetric breath sounds without adventitious murmurs, satisfactory diuresis, adequate peripheral perfusion and strong pulses and showed no signs of meconium elimination upon clinical assessment.

On his second day of life, the newborn underwent surgical repair of the complete ectopia cordis. An incision was performed in the upper third of the remaining sternum, followed by extensive dissection of the cardiac structures and bilateral pleural space, as well as detachment of the skin and subcutaneous cellular tissue up to the posterior axillary lines (**Figures 2 and 3**). Bilateral costotomy and pleural drainage, along with closure of the thoracoabdominal wall with bovine pericardium over the omphalocele were also executed. During the postoperative period, the neonate incurred with cardiorespiratory arrest (CPA) in pulseless electrical activity (PEA), which was reversed with reanimation maneuvers. However, the patient progressed in a severe manner, with need for vasoactive drugs and worsening of hemodynamic parameters. The newborn proceeded with respiratory acidosis, cardiogenic shock, hypoxia and finally passed away hours after the surgery.

Figure 1 – Initial clinical examination of the newborn.

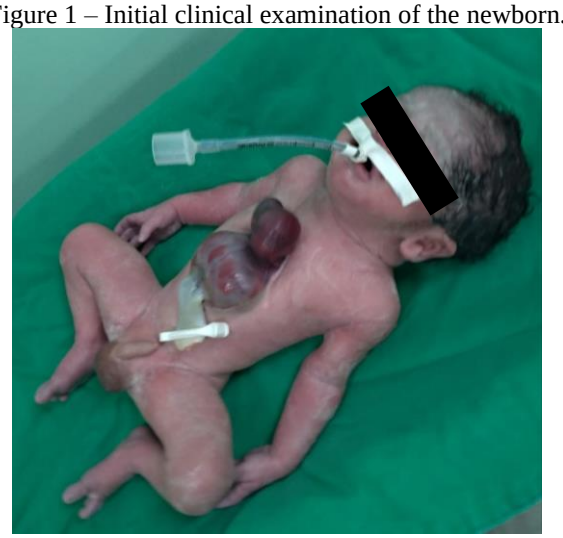


Figure 2 – Ectopia cordis in a newborn.

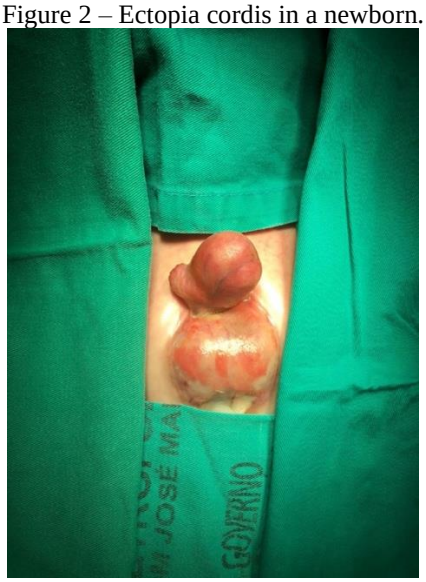
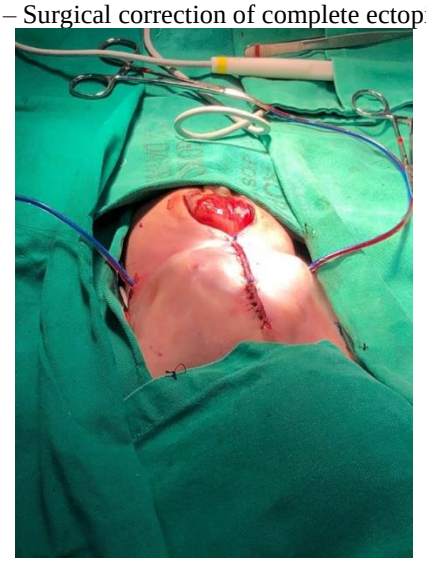


Figure 3 – Surgical correction of complete ectopia cordis.



## 3 DISCUSSION

The Pentalogy of Cantrell is a rare and complex congenital disorder and may present itself in complete or incomplete forms. Thus, the diagnostic hypothesis must be raised upon the coexistence of ectopia cordis and abdominal wall defect (omphalocele) [2].

In 1972, Toyama suggested the following classification of the syndrome according to the clinical manifestations exhibited: class I, a precise diagnosis, containing all five defects classically described; class II, a probable diagnosis, with four defects present, including intracardiac and abdominal wall abnormalities; and class III, an incomplete expression, with a diverse combination of the defects, including a sternal abnormality [2]. In the present case, ectopia cordis, closure defects of the thoracic and abdominal walls and intracardiac malformations were the features observed, which places it in Toyama's class I.

Overall, the clinical manifestations of the Pentalogy of Cantrell consist of cardiovascular anomalies and other congenital disorders. In 1998, Vazquez-Jimenez et al. performed a literature review with 153 cases of the syndrome. Out of these, 127 patients had cardiac malformations, including ventricular septal defect (72%), atrial septal defect (34,6%), left ventricular diverticulum (32,3%), pulmonary atresia or stenosis (31,5%), Tetralogy of Fallot (17,3%), dextrocardia (15%), transposition of the great arteries (6,3%), persistent left superior vena cava (5,5%), anomalous pulmonary venous drainage (5,5%), persistent ductus arteriosus (5,5%), tricuspid atresia (5,5%), persistent truncus arteriosus (3,9%), atrioventricular septal defect (3,2%), right ventricular diverticulum (3,1%), left ventricular aneurysm (1,6%) and double-outlet right ventricle (1,2%). Other congenital anomalies were additionally observed, affecting the sternum in 91 (59,5%) patients; the abdominal wall in 114 (74,5%) individuals; the diaphragm in 87 (56,9%) cases; and the pericardium in 64 (41,8%) patients. Amongst the closure irregularities of the abdominal wall, the omphalocele was most often described, affecting 72 (63,2%) out of the 114 cases [4].

Furthermore, other studies have shown an association between the Pentalogy of Cantrell and other infirmities, such as spina bifida [7], craniorachischisis [8], exencephaly [9], cleft lip and palate, hypertelorism, micrognathia [10], pulmonary hypoplasia, scoliosis and defects in the extremities, like sirenomelia, hypoplasia, clinodactyly and ectrodactyly [11-13].

The cardiovascular anomalies identified in this case include subaortic ventricular septal defect, overriding aorta, atrioventricular concordance, pulmonary stenosis, double-outlet right ventricle and persistent left superior vena cava draining into the coronary sinus. As for other congenital defects, low setting of the external ear, saddle nose, clubfeet and overlapping left toes were found.

Therefore, early diagnosis and verification of the extension of the malformations are relevant steps when it comes to fetal prognosis, allowing for better planning of possible intrauterine and neonatal interventions. Diagnosis is already possible during a first trimester scan, by visualizing ectopia cordis and omphalocele on the 2D obstetric ultrasound. However, diagnostic confirmation has been reported during different gestational periods, according to the extent of the defects, since milder manifestations are often harder to detect [14-16].

When facing such diagnostic hypothesis, more complex tests may be in order, such as 3D ultrasounds, fetal echocardiography and fetal nuclear magnetic resonance, as

a means to provide more accurate information regarding the extent and severity of the defects and allow for the best therapeutic planning. Plus, fetal karyotype is recommended given the association between the Pentalogy and aneuploidies, such as trisomy 18 [16].

By the end of the 20th century, the estimated survival rate of the Pentalogy of Cantrell was 37,3%, but scientific advances in neonatal intensive care and pediatric surgery have increased it up to 61% [4, 17]. Nonetheless, the syndrome remains a surgical challenge, given the variety and severity of the associated malformations [6].

In general, coverage of the cardiac structures, repositioning of the heart in the mediastinum, reparation of intracadiac defects and reconstruction of the thoracic wall are the main steps of the surgical intervention [18]. In the current study, the newborn underwent surgical reparation of the ectopia cordis on his second day of life, with cardiac repositioning and closure of the thoracoabdominal wall, including the suture of the omphalocele with bovine pericardium.

The prognosis of the Pentalogy of Cantrell is reserved, since most newborns are unable to make it through their first days of life. Patients still present considerable mortality and morbidity, even after initial stabilization and surgical correction, especially when there is significant ectopia cordis, due to complications such as impaired cardiac function, chronic lung disease and developmental delay [6]. In the reported case, the patient went through surgical intervention but progressed severely, presenting PCR in PEA and then proceeding to cardiogenic shock regardless of the reversion of the PCR with neonatal reanimation maneuvers, resulting in his death mere hours after the procedure.

## 4 CONCLUSION

The Pentalogy of Cantrell is a rare and complex disorder. It demands proper identification and management of the associated anomalies according to their phenotype and extent. Thus, fetal prognosis depends on the adequate provision of prenatal care, feasibly allowing for early diagnosis and investigation of the abnormalities by use of ultrasound assessment and other techniques. Not only that, but successful handling of the affliction largely rests on the capable performance of the multidisciplinary team, in order to lead the most suitable therapeutic planning.

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