Cantrell Syndrome—A Rare Complex Congenital Anomaly: A Case Report and Literature Review

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Cantrell syndrome (CS) or pentalogy of Cantrell is defined as a rare condition involving a midline anterior abdominal wall defect, a distal sternal cleft, a defect of the anterior diaphragm, and a defect of the apical pericardium with pericardio-peritoneal communication, as well as intracardiac anomalies. We report the case of a male newborn with type 2 CS diagnosed during intrauterine life based on ultrasonographic evaluation. Clinical examination at birth revealed an abdominal wall defect with extrathoracic displacement of the heart and a diastasis of the sagittal suture. Postnatal echocardiography revealed tricuspid atresia, partial extrathoracic and extra-abdominal displacement of the heart and liver, a large ventricular septal defect, severe subpulmonary stenosis, hypoplasia of the pulmonary artery, and a large hourglass-shaped left ventricle secondary to narrowing of the heart at the level of its extrathoracic displacement. Computed tomography showed additional abnormalities including increased left ventricular volume with extrathoracic apical aneurysmal dilatation below the xiphoid process at the level of anterior abdominal wall, a hypoplastic right ventricle, partial transparietal herniation of the left hepatic lobe adjacent to a left ventricular diverticulum, and an adrenal hematoma. The newborn received intensive medical management during his first week of life; however, surgical management had to be postponed owing to his unstable condition. Eventually, it was performed on the 14th day of life, but unfortunately, the newborn died shortly after the procedure.

Keywords: Cantrell syndrome, ectopia cordis, prenatal diagnosis, fetal screening, ultrasound examination

INTRODUCTION

Cantrell syndrome (CS) or pentalogy of Cantrell was first described in 1958. It involves multiple congenital anomalies such as a midline anterior abdominal wall defect, a distal sternal cleft, a defect in the anterior diaphragm, and a defect of the apical pericardium with pericardio-peritoneal communication, as well as intracardiac anomalies (1). The prevalence of this syndrome varies between 1:65,000 and 1:200,000 cases (2), although all patients do not present with all the
and 30 gestational weeks at a regional hospital; however, at 35 gestational weeks, ultrasonography revealed an abnormal fetal thoracic wall.

Prenatal ultrasonography revealed a fetal thoracoabdominal wall defect with partial displacement of the left ventricle and the liver associated with rotation and elongation of the heart and a high index of clinical suspicion for intracardiac malformations such as tricuspid atresia, a ventricular septal defect, and pulmonary artery hypoplasia (Figures 1–3).

**Clinical Findings**

Based on the aforementioned findings, she was admitted to the Obstetrics and Gynecology Clinic in Târgu Mure at 39 gestational weeks, where she underwent a cesarean section. The male newborn weighed 3,100 g with an APGAR score of 7. Clinically, he demonstrated a superior abdominal wall defect, a partial extrathoracic displacement of the heart, and a partially herniated liver (these structures being covered by a very thin skin layer), and also a diastasis of the sagittal suture (Figure 4). The newborn was intubated, and we applied a saline-soaked gauze pad on the thoracoabdominal and cranial defects to maintain humidity.

**Diagnostic Assessment**

Postnatal echocardiography confirmed the prenatal diagnosis and also showed a partial extrathoracic and extra-abdominal displacement of the heart and liver, a large ventricular septal defect, great arteries originating from the left ventricle with the aorta situated anteriorly, a posterior deviation of the outlet septum causing severe subpulmonary stenosis, hypoplasia of the pulmonary artery, and a large hourglass-shaped left ventricle secondary to narrowing of the heart at the level of its extrathoracic displacement.

We also performed thoracoabdominal CT-angiography, which showed complex cardiac malformations consisting of large ventricular and atrial septal defects, an increased left ventricular volume, with apical extrathoracic aneurysmal dilatation below the xiphoid process at the level of the abdominal midline, hypoplasia of the right ventricle, and a reduced caliber of the pulmonary trunk artery. Abdominal CT revealed partial transpiairetal herniation of the left hepatic lobe adjacent to a left ventricular diverticulum, and an increase in the size of the right adrenal gland with hyperdense contents suggesting an adrenal hemorrhoma. Cranial CT revealed a diastasis of the sagittal suture causing subcutaneous herniation of the venous sagittal sinus.

**Therapeutic Intervention**

Following admission to the Neonatal Intensive Care Unit, the newborn was administered ampicillin and amikacin, fluconazole, prostaglandin E, and phenobarbital (because he presented with multiple seizures), and also received daily dressing changes. During the first week of life, he showed multiple episodes of bradycardia and low oxygen saturation despite undergoing orotracheal intubation; therefore, surgical intervention was postponed until he was hemodynamically stable. He underwent surgical intervention at 14 days of age, consisting in the

**CASE REPORT**

**Presenting Concerns**

A 31-year-old woman, gravida 2 para 1, presented for a prenatal ultrasonographic examination at 36 gestational weeks owing to a suspicion of a fetal thoracic wall defect. Her personal history revealed a spontaneous abortion and no consanguinity. She underwent routine ultrasonographic examinations at 13, 22,
FIGURE 1 | Fetal ultrasonographic image shows an extrathoracic left ventricle (RV, right ventricle; LV, left ventricle; MV, mitral valve; TV, tricuspid valve).

FIGURE 2 | Fetal ultrasonographic image shows an extrathoracic left ventricle, a ventricular septal defect and pulmonary artery hypoplasia (L, liver; VSD, ventricular septal defect; PA, pulmonary artery).
replacement of the heart inside the thorax via a systemic-pulmonary shunt procedure, with vascular prosthesis, the ligation of both persistent arterial canal and pulmonary artery trunk, and repair of the diaphragm defect. The abdominal wall defect was also sutured, but the thorax remained open. The surgical procedure was performed in extracorporeal circulation, and lasted 4 h and 15 min.

Follow-Up and Outcome
Postoperatively, the newborn developed multiple episodes of tachyarrhythmia and low cardiac output suggesting an inability of the heart to adjust to the intrathoracic pressure. Unfortunately, the newborn died 5 h postoperatively secondary to progressive hemodynamic deterioration, metabolic acidosis, and hypoxia.

DISCUSSION
CS is an extremely rare condition. Prognosis depends upon the severity of the various complex components/anomalies that define this syndrome. The etiology of both EC and CS remains unknown, and most cases occur sporadically (12). The heart originally develops in the cephalic part of the embryo and reaches its final location by the 16th–17th day of embryogenesis, whereas complete developmental fusion leading to formation of the thoracic and abdominal cavities occurs by the 9th week of embryonic life (1, 13). Incomplete fusion can cause a wide range of disorders, varying from isolated EC to complete ventral evisceration (14). Different theories have been proposed to explain the etiology of this condition such as the amniotic rupture theory that describes EC with amniotic bands, although isolated EC may occur secondary to other etiological contributors such as exposure to intrauterine drugs (15). In our case, the mother denied any drug intake during pregnancy. Notably, a few cases of EC are reported to be associated with chromosomal abnormalities (16). In our case, there was no history of consanguinity, and genetic testing was negative.

Prenatal imaging studies are essential not only for prenatal counseling but also for adequate postnatal therapeutic planning. CS and EC can be easily diagnosed prenatally using two-dimensional (2D) or even three-dimensional (3D) ultrasonography combined with Doppler to ensure high accuracy. In a study performed on 12 patients with CS, the authors reported that 2D ultrasonography could establish the diagnosis in 11 patients, although 3D assessment provided additional information in all patients. Furthermore, they highlighted that the additional information can improve surgical management in these cases (17). Similarly, Desselle et al. suggested that the correlation between 2D and 3D examination is useful in surgical management in such newborns (2). The earliest prenatal diagnosis of CS is reported to have been established between 9 and 11 gestational weeks (18, 19). Unfortunately, in our case, the thoracic wall defect was suspected only at 35 gestational weeks. Therefore, we emphasize that accurate and timely prenatal diagnosis depends upon the sonographer’s expertise in fetal ultrasonography. Pirasteh et al. also described a patient in whom intrauterine ultrasonography performed...
at 19 gestational weeks did not reveal any abnormalities, and the diagnosis of CS was established only after birth (20). Nevertheless, it is important to mention that although accurate prenatal diagnosis of this rare condition is essential for effective postnatal management, the timing of the prenatal diagnosis does not affect the outcome. In addition to ultrasonography, magnetic resonance imaging (MRI) is a useful diagnostic tool for prenatal diagnosis; however, it is useful only in selected cases. CT can be used when MRI is not available. We also performed CT, which confirmed the echocardiographic findings and provided additional information regarding intracardiac defects and revealed an apical aneurysmal dilatation of the extrathoracic heart. Abdominal CT additionally revealed a hematoma of the right adrenal gland.

EC can present with both, intracardiac and other associated anomalies. Intracardiac anomalies associated with EC, in the order of decreasing prevalence are ventricular septal defect, atrial septal defect, tetralogy of Fallot, a left ventricular diverticulum, and pulmonary hypoplasia (21). Our patient also presented with ventricular and atrial septal defects, pulmonary hypoplasia, and a left ventricular diverticulum, and additionally showed tricuspid atresia—an intracardiac defect that has not been reported previously in patients with EC described in the literature. In addition to the aforementioned intracardiac defects, other anomalies have been reported to be associated with EC such as trisomy 18, cleft lip and palate, neural tube defects, hydrocephaly, genitourinary malformations, pulmonary hypoplasia, abdominal wall defects varying from diastasis to omphalocele, as well as bowel and liver evisceration (22). Our patient also showed omphalocele and an ectopic liver, which concurs with studies reported in the literature; however, he additionally showed a diastasis of the sagittal suture causing herniation of the venous sagittal sinus. Türkçapar et al. described a case of a fetus with lumbosacral lordosis, a large omphalocele, a herniated liver, and EC (23).

The prognosis of CS and EC depends upon both, the complexity of the anomalies and the location of the ectopic heart. Based on the Toyama classification (8), we diagnosed our patient with a class II CS because the newborn presented with a midline supraumbilical abdominal wall defect and intracardiac anomalies without a pericardial or diaphragmatic defect. In contrast, a recent review of cases diagnosed with CS between 1998 and 2007 observed that class I CS was the most common type, accounting for > 50% of the cases (24).

The surgical management of EC primarily involves 4 steps: soft tissue coverage of the heart, replacement of the heart into the thoracic cavity, repair of the intracardiac defects, and reconstruction of the chest wall (21). Therefore, optimal management of these patients requires coordination between a multidisciplinary team involving a neonatologist, a radiologist, a pediatric surgeon, a cardiologist, a pediatric cardiac surgeon, a plastic surgeon, and experienced nurses (25). Nevertheless, the general prognosis depends upon the promptitude of surgical intervention, which in our case was postponed owing to the patient's unstable status. Perhaps this fact led to the unfavorable prognosis in our patient, who underwent surgery only on the 14th day of life. Therefore, the patient died shortly after the procedure secondary to an inability of the heart to adjust to the intrathoracic conditions.

CONCLUSIONS

Accurate prenatal diagnosis is essential for effective postnatal management of CS. In our case, the intrauterine ultrasonographic findings observed during the 3rd trimester were suggestive of CS. The complex cardiac malformations concomitant with other malformations worsened our patient's condition and prevented prompt surgical management during the early days of life.

TABLE OF CONTENTS SUMMARY

Cantrell syndrome is characterized by a midline anterior abdominal wall defect, defects in the diaphragm and in the apical pericardium, which communicates with the peritoneum, as well as intracardiac defects.

AUTHOR CONTRIBUTIONS

CM, COM, and LM conceptualized and designed the study, drafted the initial manuscript, and reviewed and revised the manuscript. LG and MC designed the data collection
instruments, collected data, carried out the initial analyses, reviewed and revised the manuscript. HS and HG, AC were involved in the surgical management, designed the data collection instruments, coordinated and supervised data collection, and critically reviewed the manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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