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Thoracoabdominal Wall Defect with Complete Ectopia Cordis and Gastroschisis: A Case Report and Review of the Literature

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ABSTRACT

Ventral wall defects are extremely rare anomalies that are likely caused by the failure of the ventral wall to close during week 4 of development. We report a case of severe thoracoabdominal wall defect including complete thoracic ectopia cordis and gastroschisis. This combination represents a novel constellation of findings in a single patient. This unique case further demonstrates an anatomically normal heart with age-appropriate development and an intact diaphragm. We review the literature of other reports and discussions of entities that share overlapping features with this case.

Key words: ectopia cordis, gastroschisis, ventral body wall defect, Cantrell's syndrome

INTRODUCTION

Ventral body wall defects, including ectopia cordis, gastroschisis, and bladder exstrophy, result from the failure of the ventral wall to close during week 4 of development. We report a case of a thoracoabdominal ventral body wall defect with associated extrusion of the heart and abdominal organs, including liver, stomach, intestines, and spleen. This combination is so rare that its prevalence practically precludes quantification. Furthermore, to our knowledge, such a case has never been reported in the absence of craniofacial malformations or significant intracardiac defects. This case also presents an interesting semantic dilemma regarding appropriate classification, as multiple descriptors have been used to characterize elements of this constellation of anomalies. Suggested possibilities include gastroschisis, ectopia cordis, Cantrell's syndrome, and limb-body wall complex (LBWC), which are briefly discussed below.

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CASE REPORT

The decedent is a phenotypic male fetus at 24-weeks estimated gestational age born to a 22-year-old G2P0010 mother. At 17 weeks in gestation (determined by last menstrual period), maternal blood screening tests revealed strongly abnormal α-fetoprotein levels (>15 MoMs). Transabdominal ultrasound revealed a large abdominal wall defect with multiorgan herniation, including the heart, intestines, and liver. Given the poor prognosis, the decision to terminate the pregnancy was made.

At autopsy, the body was that of a male fetus with weight, length, and morphology corresponding to an average gestational age of 24 weeks. The external examination was significant for a thoracoabdominal ventral wall defect measuring 5.25 cm, located to the right of the umbilicus (Fig. 1). Above the diaphragm, the sternum was nonfused and the heart was exposed, with no pericardial sac (Fig. 2). The external anatomy of the heart was normal. The foramen ovale was patent, there was a probe-patent membranous ventricular septal defect (1–2 mm), and the ductus arteriosus was patent, as appropriate for 24 weeks' gestation. The lungs were of normal morphology and location, within the pleural cavities—the parietal and visceral pleural layers were intact. Below the diaphragm, the liver, spleen, stomach, and intestines were exposed and without an overlying peritoneal sac. The gross morphology of these organs was normal. The kidneys and bladder were present in the usual locations, also with normal morphology. Microscopic examination of all organs showed unremarkable, age-appropriate histology. The placental autopsy was significant only for velamentous cord insertion and moderate acute inflammation of fetal membranes. Cytogenetic studies could not be performed as a result of lack of cell propagation in culture, most likely secondary to a prolonged postmortem interval.

Gastroschisis

Gastroschisis, also called abdominoschisis, laparoschisis, and paraomphalocele, is a congenital ventral wall defect

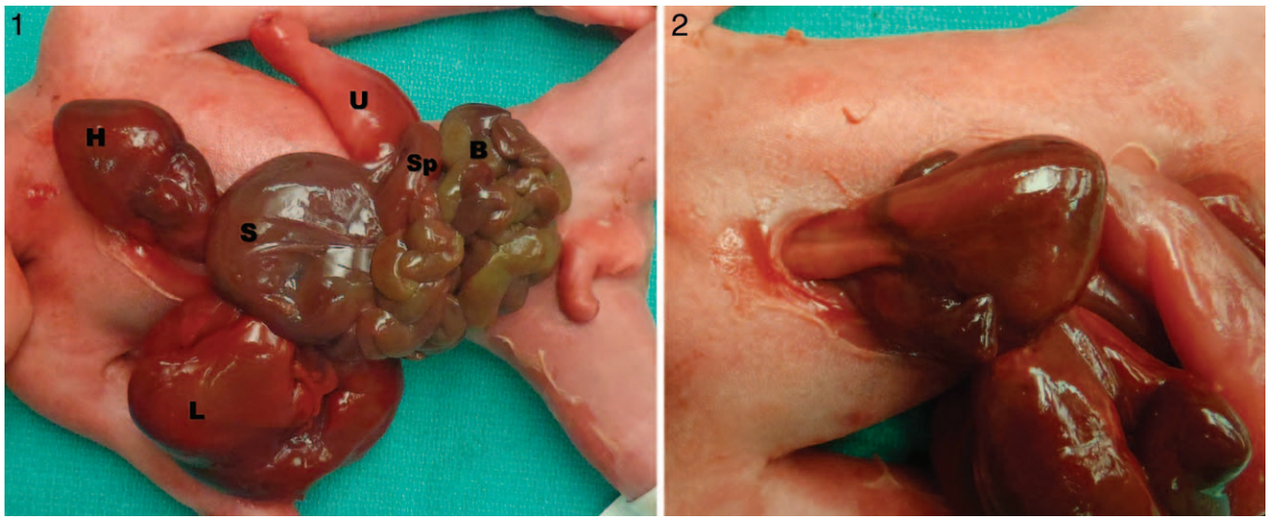

Figure 1. A 5.3-cm ventral body wall defect with extrusion of the heart (H), liver (L), stomach (S), bowel (B), and spleen (Sp). The defect is to the right of the umbilicus (U). Note the absence of overlying pericardial and peritoneal sacs.
Figure 2. The heart is completely outside the thorax through a cleft sternum; the pericardial sac is absent. The position of the great arteries and morphology of the atrial appendages are normal. Internal examination of the heart reveals normal, age-appropriate cardiac anatomy.

in which contents of the peritoneal cavity protrude through a lateral opening in the abdomen. The term is derived from the Greek ''gaster,'' meaning ''belly,'' and ''schisis,'' meaning ''fissure.'' Unlike an omphalocele, in which the peritoneal sac covers the viscera, abdominal organs in gastroschisis are not covered by a parietal membrane. The defect is characteristically located to the right of the umbilicus. The estimated prevalence of gastroschisis is 3.73 per 10 000 births [1] in the United States, and its incidence is increasing. The etiology of this anomaly is unknown; only 1.2% of gastroschisis cases occur with chromosomal abnormalities and 0.2% with single gene mutations [2]. Additionally, reports of clustered occurrences of gastroschisis suggest that teratogenic effects may be involved. Given the rarity of these associations, the cause of gastroschisis is likely a multifactorial combination of genetic and environmental factors. In addition, a strong association with young maternal age is consistently reported in the literature [3]. The prognosis for cases of isolated gastroschisis is excellent except when severe bowel injury is present [4].

Ectopia cordis

Ectopia cordis, occurring at a rate of approximately 8 per 1 million live births, is a rare congenital defect in which the heart is completely or partially displaced outside of the thoracic cavity [5]. The term is derived from the Greek ''ektopos,'' meaning ''out of position,'' and the Latin ''cordis,'' meaning ''heart.'' Anatomy scholars have offered subclassifications of this anomaly for almost 2 centuries [6–8]. Based on these schema and their extensive experience with sternal defects, Shamberger and Welch [9] suggested the use of the following 3 nonoverlapping categories of ectopia cordis: thoracic, cervical, and thoracoabdominal.

Thoracoabdominal ectopia cordis is the most common type, frequently associated with the eponym Cantrell's syndrome, and is characterized by thoracoabdominal location of the heart with an intact pericardial sac. Thoracic ectopia cordis describes the displacement of the heart outside the thoracic cavity through a sternal defect [9]. In partial thoracic ectopia cordis, the heart is visibly pulsating under the skin. However, in complete thoracic ectopia cordis, the naked heart resides outside the thoracic cavity without an overlying pericardial sac. Associated intracardiac defects are present in the majority of cases. Surgical correction must include coverage of the naked heart, relocation of the heart to the thoracic cavity, repair of associated intracardiac defects, and reconstruction of the sternum [10]. While the condition portends a poor prognosis, the success of surgical intervention depends largely on the degree of associated intracardiac defects. Cervical ectopia cordis is distinguished from the thoracic subtype by the degree of superior displacement of the heart. Often there is fusion of the apex of the heart and the mouth. Additional craniofacial abnormalities are frequently observed [9]. To our knowledge, this condition is universally fatal—no attempts at surgical repair have been reported.

The prognosis of ectopia cordis depends on its classification and associated intracardiac anomalies [11]. Reports of successful repair of thoracic ectopia cordis are rare, the cervical type is universally fatal, and the thoracoabdominal type has a higher rate of successful repair but also has a high mortality rate [9,11]. The etiology of ectopia cordis remains unknown, but failure of closure of the ventral wall in the developing embryo is the leading explanatory hypothesis [12]. There are descriptions of ectopia cordis with chromosomal abnormalities, but there is no known genetic etiology in humans.

Pentalogy of cantrell

In 1958, Cantrell and Ravitch proposed a pentalogy of ventral midline defects known as Cantrell's syndrome, or Cantrell's pentalogy. The defects include (1) a supraumbilical abdominal wall defect; (2) a defect of the lower sternum; (3) a deficiency of the anterior diaphragm; (4) a defect in the diaphragmatic pericardium; (5) and congenital intracardiac defects [13]. In the original description of the syndrome, Cantrell and colleagues [13] stated that intracardiac lesions are an integral component of the syndrome, but varying degrees of expression are expected. Later, Toyama [14] presented a series of cases of incomplete expression of Cantrell's pentalogy, including cases with less than 5 of the associated anomalies, many lacking associated intracardiac defects. Further descriptions of the spectrum of Cantrell's pentalogy suggest that a wide range of cases with ventral wall defects can be described as having complete or incomplete expression of the syndrome. In addition, several reports [15,16] demonstrate an association with cleft lip/palate. This association prompted the astute observation that the ventral midline components of Cantrell's pentalogy and frontonasal dysplasia may represent one developmental field [17].

Limb-body wall complex

Limb-body wall complex was described by Van Allen and colleagues, in 1987 [18] as a complex with 2 or more of the following: (1) exencephaly/encephalocele with facial clefts, (2) thoraco- and/or gastroschisis, and (3) limb defect. Recently, LBWC was reviewed by Hunter and colleagues [19], who suggested an etiology similar to that of ectopia cordis, gastroschisis, and bladder exstrophy. Hunter and colleagues state that the limb deficiency is likely a secondary complication of the primary embryological defect that occurs in the first 6–10 weeks of gestation [19]. Along these lines, Martínez-Frías [20] proposed that the limb deficiency is not an integral component of the complex and has suggested the term body wall complex, defined as a thoraco- or gastroschisis without associated exencephaly or limb deficiency. As is the case with gastroschisis, LBWC has a strong association with young maternal age.

DISCUSSION

The case presented here notably shares characteristics of all the entities described above, yet no single entity completely describes the pathology we encountered. We reviewed the literature in search of similar cases that may help classify this combination of anomalies.

In 1986, Bair and colleagues [21] reviewed a series of 24 cases in which a prenatal ventral wall defect was diagnosed radiographically between 1977 and 1985. Of these 24 cases with ventral wall defects, 5 involved ectopia cordis. Of the cases with ectopia cordis, 4 were diagnosed with omphalocele, and 1 was diagnosed with gastroschisis [21].

Khoury and colleagues [5] reviewed a series of 4 cases of ectopia cordis, derived from the Metropolitan Atlanta Congenital Defects Program between 1968 and 1986. In this series, there were 2 cases of ectopia cordis combined with gastroschisis. In one case, the maternal age was 20 years and the associated defects were amniotic bands, gastroschisis, ectopia cordis, hypoplasia of sternum, agenesis of gallbladder, scoliosis, lordosis, loss of fingertips, fusion of fingers, patent ductus arteriosus, and skin tags. In the other case, similar to the one presented here, the associated defects were reported as gastroschisis combined with ectopia cordis [5].

In 1991, Meyer and colleagues [22] reported a case with multiple congenital anomalies including ectopia cordis, diaphragmatic hernia, and gastroschisis, with exstrophy of the liver, intestines, kidneys, and bladder. Scoliosis and bilateral multicystic kidneys were also present. Though the entities cyllosomas, amniotic band syndrome, and pentalogy of Cantrell were suggested in the differential diagnosis, the authors favored a diagnosis of ''thoracic ectopia cordis with abdominal wall defect.''

Medina-Escobedo and colleagues [16] described a series of 4 cases of ectopia cordis in 1991. These cases were collected by the National Institute for Pediatrics in Mexico City over a 20-year period. In this series, 3 of the cases had an associated abdominal wall defect and were described in the context of Cantrell's syndrome. The authors describe the 1st case as an incomplete form of the syndrome—the patient had craniofacial abnormalities, thoracic ectopia cordis, and complex cardiac defects, yet no abdominal or diaphragmatic defects were present. The 2nd case was a quintessential example of Cantrell's syndrome. The neonate showed a supraumbilical abdominal wall defect, inferior sternal defect, diaphragmatic defect, a pericardial defect, and various intracardiac anomalies. The 3rd case was also classified as a complete form of Cantrell's syndrome, featuring gastroschisis, a total sternal defect, a pericardial defect, a diaphragmatic defect, and multiple intracardiac anomalies.

In 1999, Daum and Zachariou [23] published a technique for surgical correction of sternal clefts. In a series of 8 cases from their institution, they described one with ectopia cordis and total ventral schisis. The patient was considered inoperable.

More recently, in 2010 Baral and colleagues [24] reported a case of thoracoabdominal ectopia cordis with omphalocele. They considered it a case of Cantrell's syndrome because of the associated sternal defect, pericardial defect, associated intracardiac anomalies, and defect in the ventral diaphragm.

Ventral wall defects arise as a result of abnormalities in the closure of the ventral wall during the 4th week following fertilization. Duhamel [25] suggests that the differential rates of cell proliferation and movement of the lateral folds may be targets for teratogenic effects. In addition, the fusion process of these folds may be vulnerable to disruption that leads to malformation of the ventral body wall. Vascular disruption has been

suggested as a potential mechanism in the pathogenesis of ventral body wall defects. According to the hypothesis by Hoyme and colleagues[26], intrauterine interruption of the omphalomesenteric artery may result in gastroschisis. This hypothesis has been criticized, however, based on a lack of embryological evidence [27]. Murine investigations into the genetics of body wall defects have shown that mutations in *Hoxb2, Hoxb4, Tcfap2a, Tgfβ2,* and *Tgfβ3* genes can result in ventral wall closure defects [12]. Additional investigation is required to further understand malformations in the ventral body wall of humans. While the details of the pathogenesis are largely unknown, ventral wall defects do have a well-known association with young maternal age. Gynecological immaturity and nutritional status are proposed hypotheses for this association [28]. Nevertheless, the precise mechanisms underlying the development of ventral wall defects have yet to be elucidated.

In this report, we present a 24-weeks gestation age phenotypic male fetus with ventral body wall defect and associated extrusion of the heart, liver, stomach, intestines, and spleen. The abdominal herniation is to the right of the umbilicus, and no intact peritoneal sac is present, constituting gastroschisis. Above the diaphragm, the heart is present outside the thorax, with herniation through a cleft sternum. Notably, no pericardial sac is present. According to the classification schema described by Shamberger and Welch [9], this constitutes complete thoracic ectopia cordis. Structural cardiac abnormalities are required to meet criteria for Cantrell's syndrome. While a small (1–2-mm) perimembranous VSD is present in our case, defects of this site and size are uncommonly of clinical significance and, in most instances, close spontaneously [29]. Although tempting to qualify elegant nomenclature that unifies these anomalies, such as ''partial or incomplete Cantrell's pentalogy'' or ''LBWC'' (or perhaps just ''body wall complex''), we feel this case may be best described as a thoracoabdominal ventral wall defect with complete thoracic ectopia cordis and gastroschisis.

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