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5, 4, 3, 2, 1: embryologic variants of pentalogy of Cantrell

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ABSTRACT

Background: The purpose of this study was to evaluate our experience with pentalogy of Cantrell and the various embryologic variants.

Materials and methods: Patient charts and diagnostic imaging studies of all fetuses evaluated at Texas Children's Fetal Center for pentalogy of Cantrell between April 2004 and June 2014 were reviewed retrospectively. Data collected from patient charts included demographic information, clinical presentation, fetal and postnatal imaging findings, operative treatment, pathologic evaluation, and outcomes.

Results: There were 10 patients who presented with embryologic variants of pentalogy of Cantrell over a 6-y period. Two cases displayed the full range of embryologic defects observed, and eight cases exhibited variants of the classic pentalogy. Sternal and pericardial defects were each present in 40% of patients. Additional anomalies present included pulmonary hypoplasia, pulmonary artery stenosis, and chromosomal abnormalities. Four patients presented with diaphragmatic defects but no defect in the pericardium, and one patient presented with a defective pericardium but no associated diaphragmatic defect, suggesting highly specific losses of somatic mesoderm during embryologic development. One patient was lost to follow-up, and a second patient underwent termination of pregnancy. Five of the remaining eight patients survived, one of which had the full range of embryologic defects and now attends preschool but requires speech and occupational therapy. The remaining surviving patients have developed without serious sequelae.

Conclusions: This report highlights the spectrum of anomalies observed in the pentalogy of Cantrell and demonstrates that these fetuses can survive but with substantial morbidity.

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1. Introduction

The pentalogy of Cantrell is a rare congenital syndrome characterized by five anomalies: intracardiac abnormalities, defects of the diaphragmatic pericardium, lower sternum, anterior diaphragm, and supraumbilical abdominal wall [1]. The expression of these defects is variable, with previous studies citing the presence of a complete pentalogy and the associated severity of intracardiac defects as the most important prognostic factor [2–4]. Additionally, although not part of the classic pentalogy, some severe cases have been associated with herniation of the heart through the diaphragmatic defect resulting in ectopia cordis [5]. Although the pathogenesis of the pentalogy has yet to be fully elucidated, Cantrell *et al.* [1] suggested that the syndrome is caused by an embryologic failure of the lateral mesoderm to properly develop into the transverse septum of the diaphragm and the mesodermal fold of the abdomen to migrate ventromedially. Consequently, organs may eviscerate through the midline defects, most commonly through the supraumbilical abdominal wall and anterior diaphragmatic defects. Here, we report 10 new cases: two cases of the complete pentalogy and eight unique embryologic variants of the classic pentalogy of Cantrell.

2. Methods

After approval from the Institutional Review Board of Baylor College of Medicine (Protocol# H-26143), the medical records and diagnostic imaging studies of all fetuses evaluated at Texas Children's Fetal Center for pentalogy of Cantrell between April 2004 and June 2014 were reviewed retrospectively. All patients referred to the fetal center underwent comprehensive ultrasounds, magnetic resonance imaging (MRI), and/or echocardiography using a previously described protocol [6]. Data collected from patient charts included demographic information, clinical presentation, fetal and postnatal imaging findings, operative treatment, pathologic evaluation, and outcomes. Specifically, imaging findings were evaluated for the presence or absence of omphalocele, diaphragmatic hernia, sternal defects, intracardiac defects, and defects of the pericardium. The presence or absence of ectopia cordis was also assessed. Giant omphaloceles were characterized as defects involving >50% of the liver within the hernia sac. Combined data were evaluated in light of embryologic variants seen in the pentalogy of Cantrell. As is the practice in our fetal center, each diagnosis had been discussed in depth with the parents and evaluated in a multidisciplinary fashion with all medical teams involved for clinical input, including but not limited to pediatric surgeons, maternal fetal medicine specialists, cardiologists, neonatologists, and our ethics committee.

3. Results

There were 10 patients who presented with embryologic variants of pentalogy of Cantrell over a 6-y period (Tables 1 and 2). Two cases displayed the full range of embryologic defects observed, and eight cases exhibited variants of the classic pentalogy. All but one patient who underwent repair of an omphalocele defect did so using the paint-and-wait strategy, or a delayed-type closure, involving daily application of silver sulfadiazine and eventual fascial closure as this type of closure has been associated with better outcomes at our own institution. All congenital diaaphragmatic hernia repairs were performed open.

3.1. *Patient 1*

A healthy 27-y-old G_1P_0 female was referred at 24 6/7-wk gestational age after detection of an omphalocele at 15 wk. Imaging revealed a giant omphalocele containing liver and bowel, a Morgagni-type (anterior) diaphragmatic hernia with herniation of stomach, spleen and colon through the defect, a left hydrothorax with mediastinal shift, a ventricular septal defect, and pulmonary hypoplasia (Fig. 1). Amniocentesis was normal for a 46XY karyotype. A prenatal diagnosis of pentalogy of Cantrell was made and the prognosis was discussed with the parents. Elective delivery was at 37 wk. Initial examination was significant for the presence of a large omphalocele with evisceration of the liver, stomach and bowel, a congenital diaphragmatic hernia,

Table 1 – Five anomalies associated with pentalogy of Cantrell, the number of patients within each variant and the outcome for each variant.

N = 10	Omphalocele	Diaphragmatic hernia	Sternal defect	Cardiac defect	Pericardial defect
Number of patients with defect	9	7	4	9	4
Number of pentalogy components present	1/5	2/5	3/5	4/5	5/5
Number of patients within each variant group	—	2	5	1	2
Outcome	—	1 survived, 1 lost to follow-up	3 survived, 1 death, 1 termination of pregnancy	1 death	1 survived, 1 death