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CASE REPORT

Trisomy 18 Syndrome with Incomplete Cantrell Syndrome

Yi-Jen Hou[1,2], Fong-Lin Chen[3], Yan-Yan Ng[1], Jui-Ming Hu[1], Suh-Jen Chen[1,2], Jia-Yuh Chen[1,2], Pen-Hua Su[1,2]*

[1]*Department of Pediatrics, Division of Neonatology, Chung Shan Medical University Hospital, Taichung, Taiwan*
[2]*Department of Pediatrics, Division of Genetics, Chung Shan Medical University Hospital, Taichung, Taiwan*
[3]*Department of Pediatrics, Division of Cardiology, Chung Shan Medical University Hospital, Taichung, Taiwan*

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The pentalogy of Cantrell was first described in 1958 by Cantrell and coworkers, who reported five cases in which they described a pentad of findings including a midline supraumbilical thoracoabdominal wall defect, a defect of the lower sternum, abnormalities of the diaphragmatic pericardium and the anterior diaphragm, and congenital cardiac anomalies. Trisomy 18 has an incidence of about 0.3 per 1000 newborns. We present a case of trisomy 18 with incomplete Cantrell syndrome. The patient presented with hypogenesis of the corpus callosum, vermian-cerebellar hypoplasia (Dandy-Walker variant), ventricular septal defect, dextrocardia, patent ductus arteriosus, a defect of the lower sternum, a midline supraumbilical abdominal wall defect with omphalocele, congenital left posterior diaphragmatic hernia (Bochdalek hernia), micrognathia, low-set and malformed ears, rocker-bottom feet, dorsiflexed hallux, hypoplastic nails, short neck, and wrist deformity. Trisomy 18 syndrome was unusually combined with the pentalogy of Cantrell. We present this case because of its rarity and high risk of mortality.

1. Introduction

In 1958, Cantrell et al[1] described a rare congenital syndrome involving the abdominal wall, sternum, diaphragm, pericardium, and heart. The characteristics included a midline supraumbilical abdominal wall defect, a defect of the lower part of the sternum, abnormalities of the anterior diaphragm and diaphragmatic pericardium, and a congenital heart malformation. Previously, patients with this combination of anomalies were considered to have a form of ectopia cordis. Byron[2] was the first to suggest a distinction between the other categories of ectopia cordis and those associated with abdominal wall defects.

Cantrell presented five patients and identified a further 16 who had previously been described by Major.[3] Cantrell and co-workers postulated that these malformations resulted from developmental failure of a segment of the mesoderm at a very early

*Corresponding author. Division of Genetics, Department of Pediatrics, Chung Shan Medical University Hospital, 110 Chien-Kuo North Road, Section 1, Taichung 402, Taiwan.
E-mail: jen@csh.org.tw

period in embryonic life.[1] Since then, cases of children displaying all five characteristics, considered by some to represent the full spectrum of the syndrome, have been reported in the literature, while less severe cases are more appropriately regarded as incomplete forms of the pentalogy of Cantrell. The full pentalogy is rare, and its pathogenesis has not been fully elucidated. It occurs sporadically as an isolated event, but has also been recorded in families,[4,5] in patients with triploidy,[6,7] and in patients with trisomy 18.[8–11]

Trisomy 18 has an incidence of approximately 0.3 per 1000 newborns.[12,13] The structural abnormalities described in this condition can be detected prenatally by ultrasonography, as early as the first trimester.[14] Several defects occur in the majority of prenatally detected cases of trisomy 18 with incomplete Cantrell syndrome. The prognosis for these patients depends on the severity of the cardiac anomalies, extracardiac defects, and other associated anomalies.

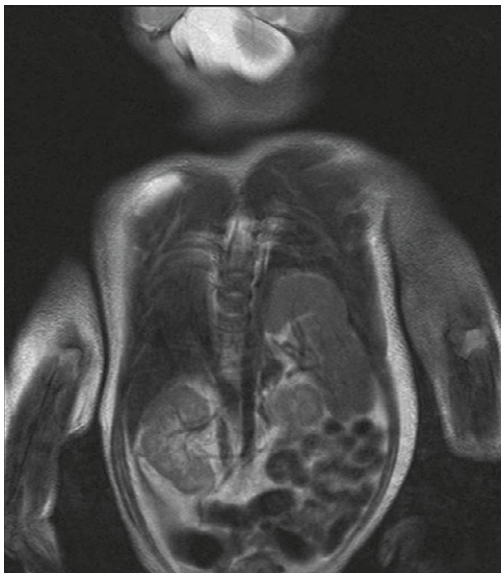

Figure 1 Chest magnetic resonance imaging shows congenital left posterior diaphragmatic hernia (Bochdalek hernia).

2. Case Report

This male patient was born on May 22, 2007 by cesarean section at Chung Shan Medical University Hospital to a gravida 2, para 1, female at 41 weeks' and 5 days' gestation. He had multiple congenital anomalies. The family history was unremarkable, except for his elder sister who had a right inguinal hernia, status post repair, at age 3 years, and controlled epilepsy.

After birth, an omphalocele was immediately apparent. The sternum was short, and a pulsatile structure extending into the epigastrium was present ventral to the xiphoid process. A grade IV systolic ejection murmur was heard over the left upper sternal border. The neonate had wide fontanelles and cranial sutures, a short nose with upturned nares, a wide nasal bridge, low-set malformed ears, micrognathia, a short neck, and a concealed penis. A chest roentgenogram showed cardiomegaly and dextrocardia. Echocardiography showed a huge patent ductus arteriosus, an atrioventricular canal, a ventricular septal defect, bilateral ventricular hypertrophy, and right ventricular dilatation. Chest computerized tomography (CT) and magnetic resonance imaging (MRI) (Figure 1) revealed a congenital left posterior diaphragmatic hernia (Bochdalek hernia) and three-dimensional CT of the chest showed a defect of the inferior sternum (Figure 2). Brain ultrasound revealed hypogenesis of the corpus callosum. Brain MRI showed vermian-cerebellar hypoplasia (Dandy-Walker variant). Renal ultrasound findings were normal. The neurologic assessment demonstrated generalized hypotonia. Flexion

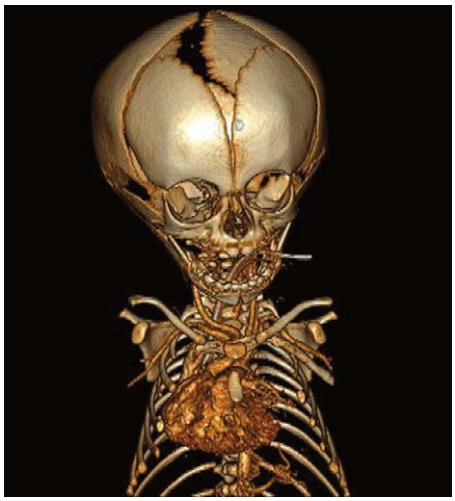

Figure 2 Three-dimensional computerized tomography of the chest reveals an inferior sternal defect and dextrocardia.

contractures of multiple joints, arthrogryposis of the wrist, clenched hands, and an increased number of simple arches on the fingertips, rocker-bottom feet, a dorsiflexed hallux and hypoplastic nails were also noted.

Because of multiple congenital anomalies, respiratory failure and general cyanosis, he was admitted to our neonatal intensive care unit for treatment and underwent surgical repair of the omphalocele on the first day of life. The karyotype of the proband was 47XY,+18. His parents declined further treatment on the 12th day of life. He developed bradycardia followed by cardiac arrest and died on July 6, 2007.

3. Discussion

Trisomy 18 syndrome is not usually combined with the pentalogy of Cantrell. The occurrence of all five characteristic anomalies occurs rarely, and is considered by some to be the full spectrum of the syndrome, with less severe cases considered to represent incomplete forms of the pentalogy. The complete syndrome is characterized by two major defects: (1) ectopia cordis, and (2) an abdominal wall defect, most commonly an omphalocele, but gastroschisis may also be present. The other three defects of the pentalogy involve disruption of all the interposing structures, i.e., the distal sternum, the anterior diaphragm, and the diaphragmatic pericardium.

Variants of the pentalogy of Cantrell have been described by Toyama.[6] He suggested the following classifications: (1) certain diagnosis, when all five defects are present; (2) probable diagnosis, when four defects, including intracardiac and ventral abdominal wall defects, are present; and (3) incomplete, when variable combinations of defects are present, but always include an abnormality involving the sternum. The pathogenesis of Cantrell syndrome has not been elucidated. Cantrell et al[1] suggested a developmental failure of a segment of the lateral mesoderm around embryonic days 14–18. The diaphragmatic and pericardial defects are closely related to either total or partial developmental failure of the transverse septum, whereas the cardiac abnormalities result from faulty development of the epimyocardium. The sternal and abdominal wall defects represent faulty migration of these mesodermal primordial structures. The failure of this process is believed to be due to: (1) vascular dysplasias resulting in a vascular steal phenomenon; (2) mechanical teratogenesis following rupture of the amnion, tearing and adherence to the amnion, tissue band adherence causing pressure necrosis and incomplete morphogenesis, or mechanical compression secondary to rupture of the chorion or the yolk sac; (3) gene alterations, either idiopathic or due to viral infection, in the early first trimester; or (4) maternal drug ingestion.

Barrow et al[15] tested this hypothesis by administering B-aminopropionitrile to female rats to induce ectopia cordis and gastroschisis. The time of the insult needed to be between days 14 and 15 of gestation, when splanchnic and parietal mesoderm are still undifferentiated and when an insult can affect the heart and pericardium (splanchnic), as well as the abdominal wall and diaphragm (parietal mesoderm).[15] Further, although definite and uniform chromosomal abnormalities have not been described in the pentalogy, a possible genetic cause has been suggested by its occurrence in one set of monozygotic twins with lumbosacral meningomyelocele and other associated major anomalies.[16] It has also been recorded in families,[4,5] and in patients with triploidy,[6,7] and with trisomy 18.[8–11] Therefore, even when the pentalogy of Cantrell occurs sporadically as an isolated event, the family should receive genetic counseling.

The syndrome has been diagnosed prenatally,[15,17,18] but as the defects range from subtle to severe, the ability to make an ultrasound diagnosis varies. Even at birth, the full extent of the syndrome may not be apparent, as the sternal defect may be minor, without true ectopia cordis. In the present case, a small open sternal defect was contiguous with the upper portion of the small omphalocele, but the heart and bowel did not protrude through these defects. In the prenatally detected cases that have been reported, ectopia cordis was present.

We present this case of trisomy 18 with incomplete pentalogy of Cantrell in which an omphalocele was detected prenatally as an isolated defect at 38 weeks' gestation. The poor prognosis may be related to the extent of the ventral wall and cardiac defects. We therefore conclude that trisomy 18 with pentalogy of Cantrell is represented by a spectrum of congenital anomalies, from fatal to nonfatal, which need to be adequately evaluated to provide appropriate prenatal counseling and postnatal management of the individual cases. The ultrasonographer should be alerted to check carefully for other markers of these syndromes. If a diagnosis is made by ultrasound, then amniocentesis for chromosomal analysis is recommended. Termination of pregnancy can be considered if an ultrasound diagnosis is made early enough in the pregnancy. In patients choosing to continue the pregnancy, no data have suggested improved or changed outcomes with cesarean delivery.[15] After delivery, repair of the omphalocele should not be delayed. Repair of the sternal, diaphragmatic and pericardial defects can be attempted at the same time. Surgical correction is often difficult because of hypoplasia of the thoracic cage and inability to enclose the ectopic heart. Some affected infants have respiratory insufficiency, secondary to pulmonary hypoplasia. Recognition and treatment of any intracardiac anomaly is important, as congenital heart disease is a source of major morbidity in infants surviving the neonatal period.[19]

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