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CASE REPORT

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A Recurrent Case of Pentalogy of Cantrell: A Rare Case with Sonological Findings and Review of Literature

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Summary

Background: Pentalogy of Cantrell (POC) is an extremely rare and complex congenital anomaly. Ultrasound is a valuable, safe, nonionizing, cost effective, widely available, and easily reproducible imaging tool and is indispensible in the diagnosis of POC. Despite the rarity of POC, it is imperative for a radiologist to be aware of its wide spectrum of presentation on ultrasound in first trimester of gestation. Most reported cases in literature till now have been sporadic. In this paper, we aimed to report for the first time in literature, a recurrent case of POC detected in the first trimester in a mother whose previous pregnancy also was terminated in the second trimester medically due to the ultrasound diagnosis of POC. We also discuss the role of ultrasound and other imaging modalities in a case of POC as well as the differential diagnoses which can mimic POC.

Case Report: A 23-year-old G2P0A1 (Gravida2, para0, abortion1) woman with a gestational age of around 12 weeks was referred for a routine first trimester ultrasound scan. The antenatal ultrasound scan showed a single, live, intrauterine gestation corresponding to a gestational age of 11 weeks and 5 days. The fetal heart was visualized outside the chest through a defect in the lower sternum in association with anterior diaphragmatic and ventral abdominal wall defects suggestive of thoraco-abdominal variety of ectopia cardis. There was a membrane covered, midline, abdominal wall defect at the base of the umbilical cord insertion containing the herniated abdominal organs including the liver, bowel loops and the ectopic cardia. There was a breach in the normal outline of the lower sternum indicating a sternal deficiency. The fetal pericardium was absent. The nuchal translucency was grossly increased. Pentalogy of Cantrell was diagnosed on ultrasound and the patient was explained about the poor prognosis of this condition. An informed consent was obtained after she opted for medical termination of pregnancy. The autopsy confirmed all the above mentioned ultrasound features.

Conclusions: Pentalogy of Cantrell (POC) is an extremely rare and complex syndrome of numerous fetal anomalies but should always be borne in the mind during the ultrasound evaluation of either of an omphalocele, ectopia cordis, distal sternal defect, pericardial defect, anterior diaphragmatic defect or intracardiac anomalies. Ultrasound is a valuable, safe, nonionizing, cost effective, widely available, and easily reproducible imaging tool for diagnosis of POC. Ultrasound should always be the primary mode of diagnosis in POC because although Magnetic resonance imaging (MRI) can help in better delineation of fetal anomalies, it does not significantly alter the course of the pregnancy or the management of POC.

MeSH Keywords: Congenital Abnormalities • Pentalogy of Cantrell • Ultrasonography, Doppler

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Background

Pentalogy of Cantrell (POC) is an extremely rare and complex congenital anomaly with an estimated incidence of 5.5 per million births. Ultrasound is a valuable, safe, nonionizing, cost effective, widely available, and easily reproducible imaging tool and is indispensible in the diagnosis of POC. Despite the rarity of POC, it is imperative for a radiologist to be aware of its wide spectrum of presentation on ultrasound in first trimester of gestation. The aetiopathogenesis of this syndrome is still not completely understood and most reported cases in literature till now have been sporadic. In this paper, we aimed to report for the first time in literature, a recurrent case of POC detected in the first trimester in a mother whose previous pregnancy also was terminated in the second trimester medically due to the ultrasound diagnosis of POC. We also discuss the role of ultrasound and other imaging modalities in a case of POC as well as the differential diagnoses which can mimic POC.

Case Report

A 23-year-old G2P0A1 (Gravida2, para0, abortion1) woman with a gestational age of around 12 weeks was referred to our Department of Radiodiagnosis for a routine first trimester ultrasound scan. She had a non consanguineous married life of 3 years and 4 months. The patient and her husband had no present or past history of any significant medical illness. The patient gave history of Pentalogy of Cantrell in the fetus from her previous pregnancy, detected at a gestational age of 24 weeks and 1 day. The pregnancy was then terminated medically after counseling of the couple regarding the implications of this congenital anomaly and the poor prognosis. There was an interval of around 2 years between the present gestation and the previous medically induced abortion. Like the previous pregnancy, the patient denied exposure of any form to teratogenic substances like ionizing radiation, medications, alcohol, tobacco, cocaine, lead, lithium, phenytoin, warfarin or valproic acid during present gestation. This pregnancy was also a spontaneous conception. Clinically, the course of her first trimester was uneventful. General physical examination revealed a regular pulse of 86 beats per minute and blood pressure of 118/90 mm Hg. Hemoglobin was 12.4 gm%. She was negative for HIV and HBsAg serology.

B-mode real time transabdominal as well as transvaginal sonography and Doppler evaluation of the fetus was performed on GE VOLUSON 730 PRO machine (GE healthcare, Milwaukee, USA) equipped with a 14 MHz, broad spectrum, microconvex transvaginal transducer and a 5 MHz curvilinear array, transabdominal transducer. All sonograms obtained were saved in a picture archiving and communication system.

The antenatal ultrasound scan showed a single, live, intrauterine gestation of crown rump length (CRL=5.5 cms) corresponding to a gestational age of 11 weeks and 5 days. The yolk sac measured 4.7 mm in diameter, and was normal in size and shape. The fetal heart rate was 170 beats per minute. However, the fetal heart was visualized outside the chest (Figure 1) through a defect in the lower sternum in association with anterior diaphragmatic and ventral

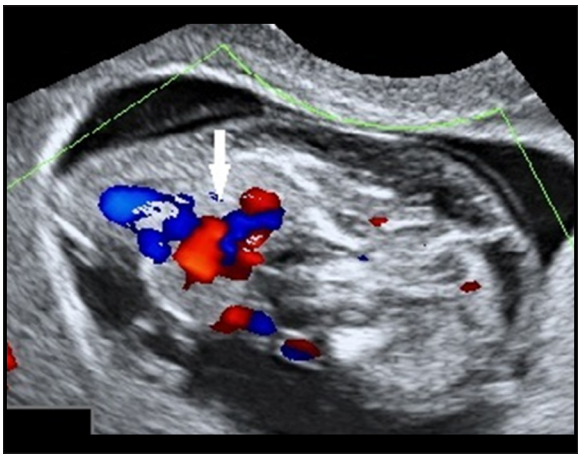

Figure 1. Gray scale transvaginal ultrasound image of the fetus in a sagittal section showing abnormally positioned fetal heart outside the chest through a defect in the lower sternum in association with anterior diaphragmatic and ventral abdominal wall defects suggestive of thoraco-abdominal variety of ectopia cordis (white, filled arrow).

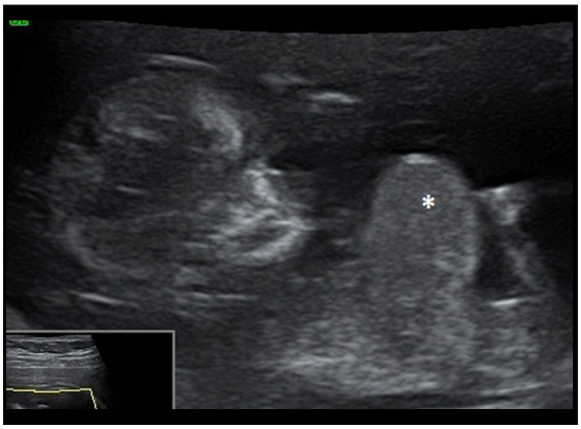

Figure 2. Gray scale transabdominal ultrasound image of the fetus in a sagittal section showing a membrane covered, midline, abdominal wall defect at the base of the umbilical cord insertion containing the herniated abdominal organs including the liver, bowel loops and the ectopic cardia suggestive of an omphalocele (asterix).

abdominal wall defects suggestive of thoraco-abdominal variety of ectopia cardis. There was a membrane covered, midline, abdominal wall defect at the base of the umbilical cord insertion (Figure 2) containing the herniated abdominal organs including the liver, bowel loops and the abovementioned ectopic cardia. All these herniated contents were not free flowing within the amniotic fluid as they were contained by the peritoneal membrane. The thoracic cavity appeared to be smaller than normal for the gestational age. There was a breach in the normal outline of the lower sternum indicating a sternal deficiency. The fetal pericardium was absent. The nuchal translucency was grossly increased, measuring around 5.4 mm (Figure 3). There was no evidence of cystic hygroma, encephalocele, cranioschisis or anencephaly. The volume of amniotic fluid was normal for the gestational age. There was no evidence of ascites or pleural effusion.

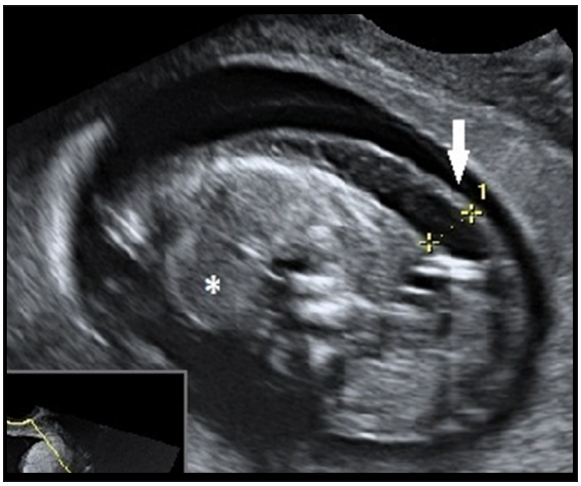

Figure 3. Gray scale transvaginal ultrasound image of the fetus in a sagittal section showing grossly increased nuchal translucency, measuring around 5.4 mm (white, filled arrow). An omphalocele (asterix) is also noted.

After explaining the poor prognosis of this condition to the patient, an informed consent was obtained after she opted for medical termination of pregnancy. The autopsy confirmed all the above mentioned ultrasound features.

Discussion

Pentalogy of Cantrell (POC) is an extremely rare and severe congenital anomaly, first reported by James R Cantrell in 1958 [1]. This syndrome has an estimated incidence of 5.5 per million births with a 2:1 male to female predominance [2,3]. This syndrome consists of a midline anterior ventral wall defect, a defect of anterior diaphragm, a cleft distal sternum, a defect of apical pericardium with communication into the peritoneum, and an intracardiac defect [4]. The major hallmark of POC is an omphalocele associated with ectopia cardis [5]. Toyama classified POC into three different types in 1972, wherein all the five defects were present in class I, four defects including ventral abdominal wall and intracardiac defects were present in class II, and a partial expression of this syndrome, always including a sternal defect was present in class III [4].

The aetiopathogenesis of this syndrome is still not completely understood. There seems to be a developmental arrest in the thoracoabdominal wall closure in the primordial lateral mesoderm tissue during embryonic stage [2]. The developmental failure involving this mesoderm between 14 and 18 days of gestation results in failure of transverse septum of diaphragm and of the ventromedial migration of the paired mesodermal folds of the upper abdomen [5]. This corresponds with the time period for differentiation of somatic and spalnchnic mesoderm. Ventral diaphragmatic defects are caused by the failure of the transverse septum to complete the process of flexion or ventral folding. Disrupted mesoderm development involving failure of ventral migration results in ventral abdominal wall and sternal defects [6]. Most cases of POC are sporadic. Few POC cases associated with trisomy 18 and X-linked inheritance have also been reported previously [7]. This syndrome is considered to be of heterogeneous origin caused by numerous factors including gene mutation, chromosomal abnormalities, physical and chemical teratogens [8]. Some investigators have proposed BMP2 (bone morphogenetic protein 2) gene mutations as a likely cause of this condition since these genes are responsible for the normal development of midline structures [3,9]. Also, more recently, the role of ALDH1A2 (Aldehyde Dehydrogenase 1 family, member A2), which is located in chromosome 15 has been implicated in the causation of POC. ALDH1A2 encodes the enzyme retinaldehyde dehydrogenase type 2, which is critical for the conversion of vitamin A into all trans-retinoic acid. Retinoic acid is a very vital morphogen for organogenesis including its important role in the pleuroperitoneal folding in diaphragm embryogenesis [3,10].

Apart from the midline anterior ventral wall defect, a defect of anterior diaphragm, a cleft distal sternum, a defect of apical pericardium with communication into the peritoneum, and an intracardiac defect, POC is known to be associated with numerous other anomalies like cleft lip, cleft palate, encephalocele, hydrocephalus, craniorachischisis, thoracoabdominal organ abnormalities include pulmonary hypoplasia, adrenal hypoplasia, gallbladder agenesis, single renal agenesis, polysplenia, malrotation of the colon, herniation of bowel into pericardium, bladder exstrophy, undescended testes and bilateral inguinal hernia, and limb defects include club foot, absence of tibia, radius and hypodactyly [3,11]. The intracardiac anomalies in POC comprise of ventricular septal defects, Ebstein's anomaly, truncus arteriosus, transposition of great vessels, single atrium, atrioventricular canal, an atrial septal defect, a left ventricular diverticulum, tetralogy of Fallot, a double-outlet right ventricle, and hypoplastic left heart syndrome [3,12].

The case discussed in our report was a class III type of POC as there was presence of a midline anterior ventral wall defect with an associated omphalocele, a defect of anterior diaphragm and a cleft distal sternum with associated thoracoabdominal ectopia cordis and absence of the pericardium. We could not assess for any intracardiac defect as the fetus in our report was at a very early stage of gestation (11 weeks and 5 days).

Ultrasound is a valuable, safe, nonionizing, cost effective, widely available, and easily reproducible imaging tool and is indispensible in the diagnosis of POC [13]. Although three-dimensional sonography has an advantage over two-dimensional sonography in the better depiction and visualization of the various fetal anomalies, two-dimensional ultrasound is also equally efficient in an early stage of gestation like the first trimester as in our study. An omphalocele can be detected sonologically when multiple bowel loops with or without the liver herniate into a membrane-covered defect with the insertion of the umbilical cord directly into the omphalocele. As a result, the abdominal circumference will be corresponding to a lower gestational age than the accurate gestational age. Ectopia cordis can be confirmed on Doppler evaluation when the position of the heart is visualized partially or completely outside the thoracic cavity. This condition is classified into 4 types based on the position of the heart. In cervical ectopic cardia (3% of cases of ectopia cordis), the heart is displaced superiorly into the area of the neck. In the thoracic variety of ectopia

cordis (60% of cases of ectopia cordis), the heart protrudes anteriorly through a sternal defect. In the thoraco-abdominal variety of ectopia cordis (7% of cases of ectopia cordis), the heart is displaced outside the chest through a defect in the lower sternum in association with diaphragmatic and ventral abdominal wall defects. In the abdominal variety of ectopia cordis (30% of cases of ectopia cordis), the heart is displaced inferiorly into the abdomen through a defect in the diaphragm [12]. In POC, the sternal defect can be visualized as a partial or complete breach in the continuity of the fetal sternum towards its distal or the lower aspect that can be adequately assessed in the sagittal plane on ultrasound. The anterior diaphragmatic defect can be detected in both the coronal as well as sagittal planes when there is a breach in its continuity along its anterior aspect.

MRI helps in a better identification of the fetal anomalies [1]. Unlike ultrasound, it is not operator dependent. Also, it can be very helpful in cases where there is severe oligohydramnios, thus preventing adequate visualization of the fetal parts on ultrasonography. Fetal MRI along with prenatal echocardiography allows optimal assessment of cases with Cantrell syndrome. These modalities may improve our view of prognosis, but they are more crucial for preoperative planning after the first trimester for cases deciding to continue the pregnancy [4]. 3D CT reconstruction also helps in important structural information, measurements and visualization of critical anatomic details in a case of POC which has been decided to be terminated medically [2].

POC is a complex syndrome with a very poor prognosis and medical termination of the pregnancy is advised in most of these cases. In few cases where medical termination of pregnancy is not opted, the management mainly depends on the severity of the intracardiac anomalies and the size and contents of the omphalocele defect. Surgical correction of the abdominal wall defect is done in less complicated cases. In complicated cases of POC with ectopia cordis, surgical correction is often difficult due to hypoplasia of the thoracic cage and inability to enclose the ectopic heart [3].

The main differential diagnosis of POC is the omphalocele-exstrophy-imperforate anus-spinal defects complex (OEIS complex), which comprises of omphalocele, bladder exstrophy/cloacal exstrophy, an imperforate anus and spinal anomalies like kyphoscoliosis or hemivertebrae. However, OEIS can be easily differentiated from POC as the location and internal anatomy of the cardia as well as the sternal and diaphragmatic anatomy is normal in OEIS complex. Isolated cardiac ectopy, ectopia cordis associated with amniotic band syndrome body stalk abnormality and isolated omphalocele can also be easily differentiated from the more complex POC.

Conclusions

Pentalogy of Cantrell (POC) is an extremely rare and complex syndrome of numerous fetal anomalies but should always be borne in the mind during the ultrasound evaluation of either of an omphalocele, ectopia cordis, distal sternal defect, pericardial defect, anterior diaphragmatic defect or intracardiac anomalies. Ultrasound is a valuable, safe, nonionizing, cost effective, widely available, and easily reproducible imaging tool for diagnosis of POC. There is a wide spectrum of ultrasound associations of POC including neural, pulmonary, gall bladder, splenic, adrenal, renal and vesical involvement. Ultrasound should always be the primary mode of diagnosis in POC because although Magnetic resonance imaging (MRI) can help in better delineation of fetal anomalies, it does not significantly alter the course of the pregnancy or the management of POC.

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