

Complete Pentalogy of Cantrell with craniorachischisis: a case report

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Summary

Background: Pentalogy of Cantrell is a rare malformation syndrome consisting of a specific combination of ventral midline defects, uncommonly found to be associated with other anomalies.

Case: We report a case of complete Pentalogy of Cantrell with craniorachischisis diagnosed in-utero at 19 weeks of gestation through antenatal ultrasonography. Fetal autopsy following termination of the pregnancy confirmed the presence of the sonographically detected malformations and also revealed associated transposition of great vessels (TGV) in the fetus.

Conclusion: Co-occurrence of such ventral and dorsal midline defects suggests the possibility that common genetic and environmental factors influence the early stages of development of the ventral as well as dorsal embryonic midline.

Key words: Pentalogy of Cantrell, craniorachischisis.

Introduction

Pentalogy of Cantrell (PC) is a rare syndrome consisting of a specific combination of five congenital anomalies – a defect of the lower sternum, a deficiency of the anterior diaphragm, a defect in the diaphragmatic pericardium, a midline supraumbilical abdominal wall defect and an intracardiac abnormality, first described by Cantrell and colleagues in 1958 (1). We report here an antenatally diagnosed case of complete Pentalogy of Cantrell with associated craniorachischisis and transposition of great vessels (TGV).

Case report

A 28 year old primigravida, was referred to our centre at a gestational age of 19 weeks, for a fetal anomaly scan. An ultrasonogram done outside, prior to referral, at 18 weeks of gestation, had shown evidence of an anterior abdominal wall defect in the fetus. The marriage was non-consanguineous, neither spouse had any significant medical or surgical illness and there was no history of any congenital malformations, genetic diseases, recurrent pregnancy losses or early childhood deaths in their respective families. This pregnancy was a spontaneous conception. The first trimester of the pregnancy was uneventful with no history suggestive of any teratogenic exposure.

Transabdominal ultrasonography demonstrated a single live fetus corresponding to a gestational age of 19 weeks. The fetal heart, great vessels, liver, stomach and intestinal loops were found to be lying outside the thoraco-abdominal cavity, encased in a fluid filled sac. The great vessels appeared to be parallel to each other. Spinal dysraphism was present. A disorganized mass of cerebral tissue arising from the base of the cranium with absence of the flat bones of the calvaria, was also visualized. There were no cardiac septal defects. Facial structures appeared to be normal. No limb reduction defects were noted. Amniotic fluid was slightly increased in amount.

The couple, on being conveyed the ultrasonogram findings, opted to terminate the pregnancy. The fetus was female. Fetal autopsy demonstrated the presence of exencephaly continuous with the spinal dysraphism, defect of the lower sternum, defect of the anterior diaphragm and supraumbilical portion of the anterior abdominal wall and a ruptured omphalocele with eventration of the thoracic and abdominal viscera (heart, great vessels, right lung, liver, stomach and small intestine) (Fig. 1). Examination of the fetal heart revealed the presence of an uncorrected transposition of the great vessels, but there were no other intracardiac anomalies. Contractures of both the elbow joints and a soft tissue band across the left elbow joint were also noted (Fig. 2). Standard cytogenetic analysis of the fetal cord blood revealed a normal 46,XX female karyotype.

Discussion

Cantrell's pentalogy is a rare condition with an incidence of less than 1 in 100,000 with a 2:1 male predominance (2). The complete pentalogy is very rare, while variants with incomplete expression lacking one or more of the defects in the heart, anterior diaphragm, diaphragmatic pericardium and/or lower sternum are reported more often (2). Neural tube defects that have been described in



Figure 1. Fetus showing anencephaly, spinal dysraphism, anterior abdominal wall defect and sternal defect.

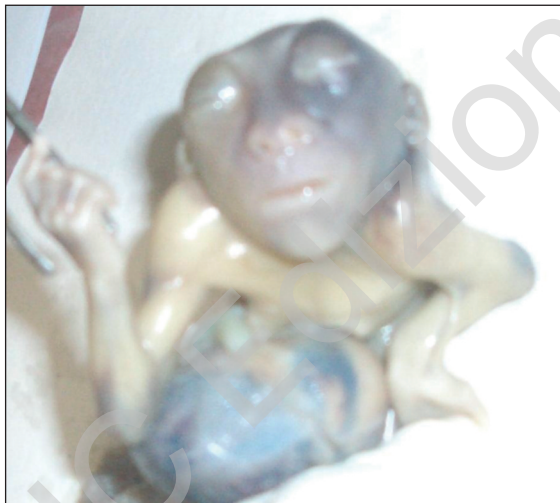


Figure 2. Fetus showing contracture of both elbow joints.

association with PC include encephalocele (especially occipital), meningomyelocele, anencephaly, exencephaly, spina bifida and craniorachischisis (3-5). There are only 3 previous reports in literature of cases with Pentalogy of Cantrell with associated craniorachischisis (6-8). Both the cases reported by Polat et al. had incomplete expression of the syndrome with absence of intracardiac anomalies while our case was unusual in that there was a complete Pentalogy of Cantrell with presence of all 5 components of the pentad, in addition to a complete craniorachischisis. Intracardiac anomalies are one of the 5 defects that constitute the classic pentad

and various cardiac malformations have been described in association with PC. The PC case we have reported here is one of those few cases in which transposition of great vessels has been found.

The exact aetio-pathogenesis of PC remains unclear and it is believed to be of sporadic occurrence. Cantrell et al. had proposed that this entity results from failure of development of a lateral mesodermal segment at 14 -18 days of embryonic life which in turn would cause failure of development of the transverse septum of the diaphragm and a failure in the ventromedial migration of the paired mesodermal folds of the upper abdomen (1). Carmi and Boughman, following their personal observation and review of literature, found that apart from the ventral midline defects that constitute PC, other midline anomalies such as cleft lip/palate and neural tube defects may be associated with PC and hence suggested that Cantrell's pentalogy represents the most severe expression of anomalies in the ventral midline developmental field (3).

Our case also had an additional midline defect in the form of craniorachischisis along with the classic pentad of ventral midline defects. Craniorachischisis is a malformation in which an open cranial defect (anencephaly/exencephaly) is continuous with a complete spinal dysraphism and represents a complete failure of neurulation. It is believed to result from dysmorphogenesis occurring no later than 20-22 days after conception, which coincides with the occurrence of PC on the embryologic time line, the latter being determined at approximately 14 - 18 days after conception (1, 3).

It has been suggested that the embryonic midline is a developmentally vulnerable or 'weakly buffered' developmental field susceptible to the actions of various dysmorphogenetic forces. It is likely that different combinations of the pentad anomalies and additional midline defects represent different phenotypic outcomes of embryogenetic insults occurring within this embryonic midline developmental field. These insults could be varied such as mechanical disruption via amniotic bands, single gene mutations, chromosomal abnormalities (particularly trisomy 18) and disruptive vascular events (3).

Gene expression studies in mouse and/or human embryonic tissues have shown that a number of genes are involved in the normal development of midline structures including the *SHH*, *BAPX1*, *BMP2*, *MID1* and *MID2* genes. Of these the *BMP2* (Bone morphogenetic protein 2) gene in particular appears to be a likely candidate gene for Pentalogy of Cantrell as a recent study by Singh et al. showed that specific alleles associated with reduced expression of this gene in mouse embryonic models, produced a lethal phenotype with defects in cephalic neural tube closure and ventral abdominal wall closure (9). The role of each of the midline genes and of *Bmp2* in particular in the causation of Cantrell's pathology needs to be investigated further.

Conclusion

Co-occurrence of such ventral and dorsal midline defects suggests the possibility that common genetic and environmental factors influence the early stages of development of the ventral as well as dorsal embryonic midline.

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