A Pattern of Malformations in the First Trimester Ultrasound

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Section 2 – Answer

Case

A 33-year-old woman, primigravida, with a medical history of euthyroid autoimmune thyroiditis, was referred to our prenatal diagnostic center due to suspicion of multiple malformations detected during an ultrasound performed at her obstetric appointment at 11 weeks of gestational age. The obstetric ultrasound showed a thickened nuchal translucency, an encephalocele [Figure 1], and a midline defect, including an omphalocele and ectopia cordis [Figures 2 and 3].

Chorionic villus sampling was performed. Genetic analysis revealed a normal karyotype (46, XY) and an array of CGH findings.

What is your initial diagnostic hypothesis?

Interpretation

The ultrasound abnormalities were suggestive of a pentalogy of Cantrell (PoC). The diagnostic hypothesis and its prognosis were explained to the couple, who opted for elective termination of the pregnancy at 12 weeks of gestational age.

Subsequent anatomopathological examination described a male fetus with a long midline thoracoabdominal supraumbilical defect starting at the xiphoid process of the sternum and associated with ectopia cordis and exteriorization of the abdominal organs: liver and bowel [Figure 4]. A partial atrioventricular defect and a single umbilical artery, in a short umbilical cord (UC), were also described, as well as a cleft palate and low-set ears [Figure 5].

In addition, microcephaly with frontonasal and right ocular dysplasia, ipsilateral microphthalmia, and frontal encephalocele [Figure 5] were observed, all attributed to the presence of an amniotic band, histologically documented [Figures 1 and 5].

Based on the described anomalies, the final diagnosis was the co-occurrence of a pentalogy – or more precisely, a hexalogy – of Cantrell and amniotic band syndrome (ABS), likely of sporadic origin and associated with a low risk of recurrence in future pregnancies.

A few months later, the woman experienced a new spontaneous pregnancy, which progressed without complications, resulting in the delivery of a healthy newborn.

Discussion

The syndrome of Cantrell *et al*. was first described in 1958 as a pentalogy that included congenital defects involving the abdominal wall, sternum, diaphragm, pericardium, and heart.[1] Its estimated incidence is 1 in 5.5 million live births, with a male-to-female ratio of 1.35:1.[2]

Cantrell *et al*. suggested that the defects associated with PoC originate during the embryonic period, as early as days 14–18 of development, due to a failure of mesodermal fold migration to the midline (resulting in sternal and abdominal defects) and incomplete development of the septum transversum (causing pericardial and anterior diaphragmatic abnormalities).[1,2] Given the pathophysiologic disruptions so early in fetal development, numerous congenital defects can complement the classic manifestations of PoC.[1,2]

In 1972, Toyama advocated a broader classification of the syndrome, which encompassed patients with variable expression of the defects.[3] A short UC and a single umbilical artery, as described in this case, are among the most frequently observed anomalies and likely contributed to the emergence of the term "hexalogy" in later descriptions.[4,5]

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Abbreviations

ABS	Amniotic Band Syndrome
AWD	Abdominal Wall Defect
PoC	Pentalogy of Cantrell
UC	Umbilical Cord

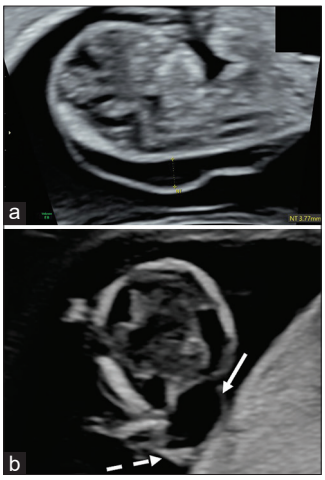

Figure 1: Obstetric ultrasound showing a thickened nuchal translucency in a sagittal section (a) and an encephalocele (b, full arrow) in a transverse section of the fetal head. Although not initially suspected during the ultrasound, we hypothesize that the amniotic band diagnosed during the anatomopathological examination may be partially seen on this image (b, dashed arrow)

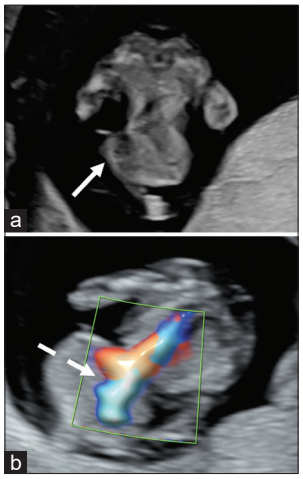

Figure 3: Obstetric ultrasound: transverse section of the midline defect (a, full arrow) and ectopia cordis (b, dashed arrow) without (a) and with (b) color Doppler

The differential diagnosis of this type of fetal malformations can be challenging. When in the presence of a complex abdominal wall defect (AWD), one must consider not only the possibility of a PoC but also of ABS, body stalk anomaly, and limb body wall complex.[6]

Although ABS is a major differential diagnosis of PoC, the co-occurrence of these two conditions has only seldom been reported in the literature.[6-8] In this case, the craniofacial

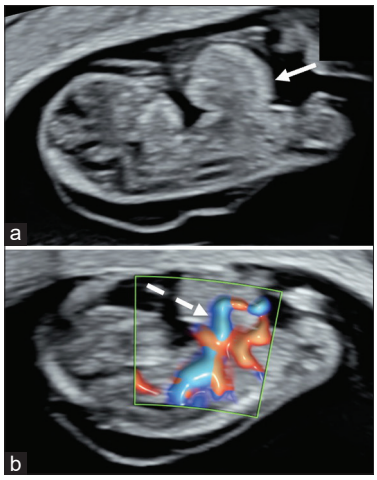

Figure 2: Obstetric ultrasound: midline sagittal section of the fetal body showing a midline defect with omphalocele (a, full arrow) and ectopia cordis (b, dashed arrow), as evidenced with the use of color Doppler

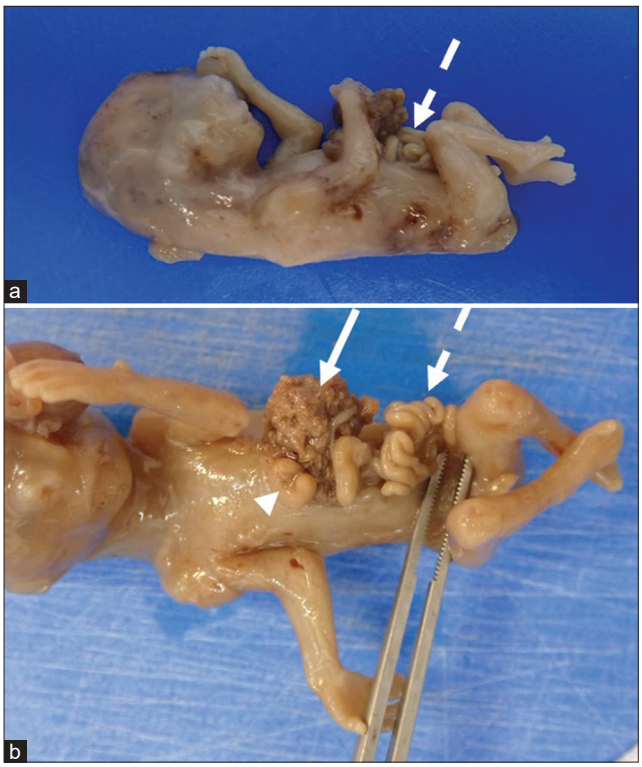

Figure 4: Anatomopathological examination of the fetus showing a long midline thoracoabdominal supraumbilical defect, beginning at the xiphoid process of the sternum, associated with ectopia cordis (b, arrowhead) and exteriorization of the abdominal organs – liver (b, full arrow) and bowel (a and b, dashed arrow). These findings corroborated the ultrasound-based hypothesis of the pentalogy of Cantrell

abnormalities were attributed to the presence of an amniotic band. However, ABS rarely causes AWDs as severe as the one in this fetus. The localization of the AWD above the UC insertion, as well as the association with defects of the sternum, diaphragm, pericardium, heart, and UC, supports the diagnosis of a hexalogy of Cantrell with concurrent ABS.

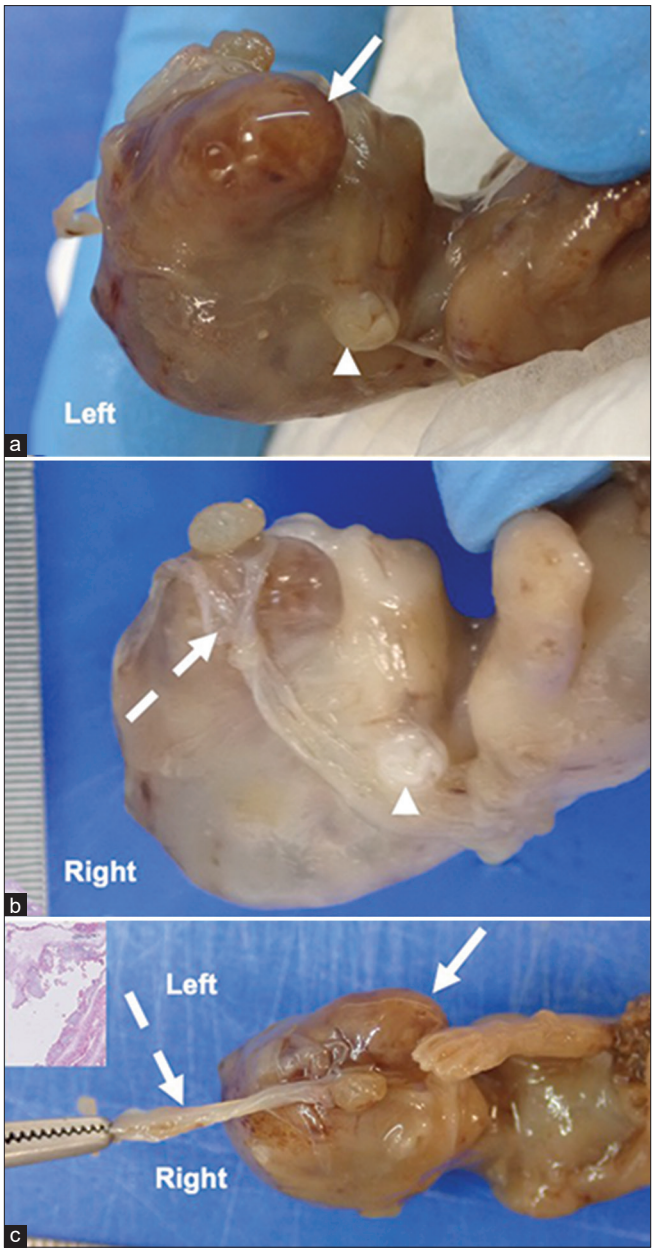

Figure 5: Anatomopathological examination of the fetal head showing microcephaly with frontonasal and right ocular dysplasia, ipsilateral microphthalmia, and a frontal encephalocele (a and c, full arrow). All these anomalies were attributed to an amniotic band (b and c, dashed arrow), which was histologically documented (c, top left corner). The presence of low-set ears was also noted (a and b, arrowhead)

In PoC, even considering all the major advances in diagnosis and surgical techniques, the survival rate remains as low as 37%. The presence of ectopia cordis significantly worsens the prognosis, with mortality rates reported as high as 100%.[2,9,10] Early detection and accurate characterization of fetal malformations are critical to provide adequate parental counseling regarding prognostic implications.[2,6] The sporadic nature of most cases of PoC can offer reassurance to couples regarding the low recurrence risk in future pregnancies.[1,2,10]

Ethics statement

This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and its amendments. The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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