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Case Series

Radiology Section

Acrania-Exencephaly-Anencephaly Sequence on Antenatal Scans

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ABSTRACT

Acrania-Exencephaly-Anencephaly sequence is the progression from an absent cranial vault (acrania) showing relatively normal appearing exposed brain (exencephaly) to no recognisable brain parenchymal tissue (anencephaly). The study presents different cases of acrania, exencephaly and anencephaly along with their imaging features on Two Dimensional (2D) Ultrasonography (US) and additional benefits of using Three Dimensional (3D)/Four Dimensional (4D) ultrasonography to aid in the diagnosis. Over a span of one year, seven patients with abnormal foetuses were scanned during the first trimester or at 18-20 weeks of gestation using both 2D and 3D/4D volumetric probes. The International Society of Ultrasound in Obstetrics and Gynaecology (ISUOG) practice guidelines were adopted for appropriateness. Specific imaging features seen on 2D US helps early diagnosis and high detection rate of this rare type of Neural Tube Defect (NTD) malformation. A 3D/4D US can also detect foetal acrania, exencephaly and anencephaly as early as 2D scan and in addition can illustrate findings with different modes of reconstruction, which 2D US cannot. Hence, 3D/4D US may contribute to early detection of foetal acrania-exencephaly-anencephaly sequence.

Keywords: Anomaly scan, Central nervous system scan, Four dimensional ultrasound, Level II scan, Neural tube defects, Three dimensional ultrasound, Two-dimensional ultrasound

INTRODUCTION

This case series comprises, of seven antenatal patients with foetuses having either acrania, exencephaly or anencephaly. Study was approved by the Institutional Review Board of Sri Guru Ram Das Institute of Medical Sciences and Research. Informed consent was obtained from all patients included in the study. All scans were performed according to the ISUOG guidelines for first trimester scan and anomaly scan for appropriateness. Over a span of one year (between March 2019 to February 2020), seven patients presented either during the first trimester scan or anomaly scan and showed abnormal foetus with acrania-exencephaly-anencepahly sequence. Voluson E8 (GE Medical Systems) US system having a high frequency 5-9 MHz transabdominal/transvaginal 2D and 3D/4D volumetric probes (RIC 5-9W and RAB 4-8L) were used. All the 2D and 3D volume datasets were acquired digitally when the foetuses were at rest. The foetuses were preferentially scanned in the sagittal and coronal plane with a variable sweep time of 8-15 seconds for volume acquisition. Surface rendering in the multiplanar mode was utilised as standard for better 3D visualisation.

CASE SERIES

CASE 1

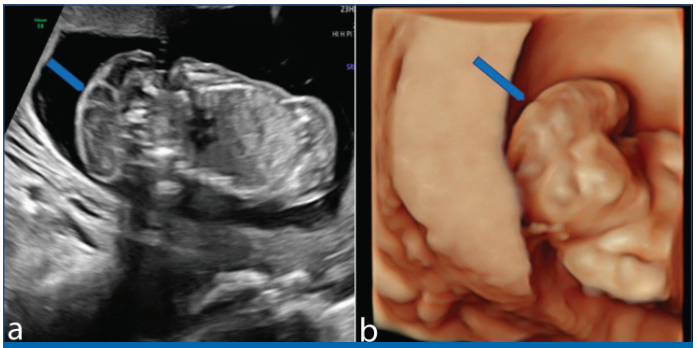
A 30-year-old non-diabetic, non-alcoholic primigravida with normal obstetric examination came for foetal sonography. A single live foetus was demonstrated with variable presentation. Liquor was adequate (AFI of 13) with closed internal os. Placenta was anterior, along the body of uterus and upper in position. Femur length and abdominal circumference were matching with menstrually calculated gestational age of about 16 weeks. A 2D and 3D US showed irregular brain matter covered by meninges but without the echogenic rim of skull, suggesting absence of foetal skull vault. This was a case of acrania with exencephaly [Table/Fig-1,2a,b].

CASE 2

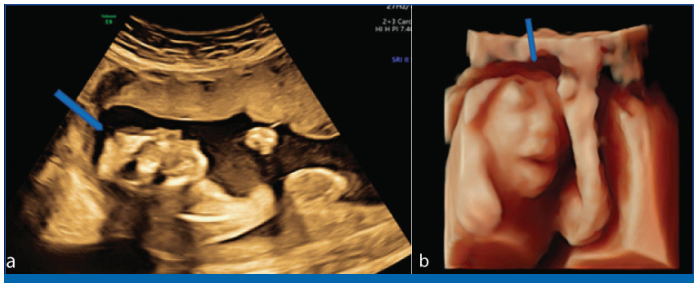
A 28-year-old gravid female came for level II anomaly scan at 19 weeks 5 days of gestation. A single live foetus was seen with variable presentation. Liquor (AFI of 15) showed increased echogenicity. Placenta was anterior, along the body of uterus and upper in position. Femur length and abdominal circumference were matching with menstrually calculated gestational age. US showed foetal orbits with non-visualisation of foetal forehead. The foetal brain and cranial vault were not seen [Table/Fig-3a,b]. Foetal spine was not well visualised at the time of scan. Foetal thorax appeared smaller in size. Foetal nose, lips and limbs appeared grossly normal. This was a case of acrania with anencephaly [Table/Fig-1].

Patients	Features
Case 1	Acrania with Exencephaly on 2D/3D Scan
Case 2	Acrania with Anencephaly on 2D/3D Scan
Case 3	Mickey Mouse sign in Anencephaly on grey scale
Case 4	Acrania with Exencephaly on 2D/3D Scan
Case 5	Acrania with Anencephaly on 2D/3D Scan showing Frog Eye sign on grey scale
Case 6	Acrania and Exencephaly with associated Spina Bifida
Case 7	Acrania with Exencephaly and Polyhydramnios showing increased echogenicity of the liquor

[Table/Fig-1]: Salient features of the cases.



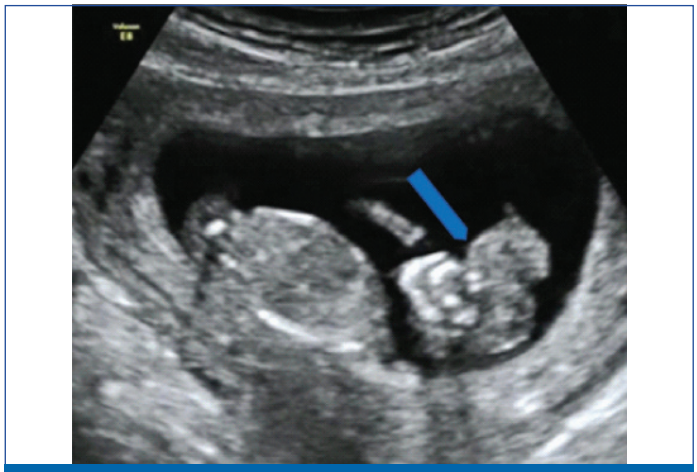
[Table/Fig-2]: (a) 2D, (b) 3D ultrasonographic images showing absence of foetal skull vault with disorganized brain tissue herniating out, suggestive of acrania with exencephaly.



[Table/Fig-3]: (a) 2D, (b) 3D ultrasonographic images showing absence of skull vault with absence of brain tissue, suggestive of acrania with anencephaly.

CASE 3

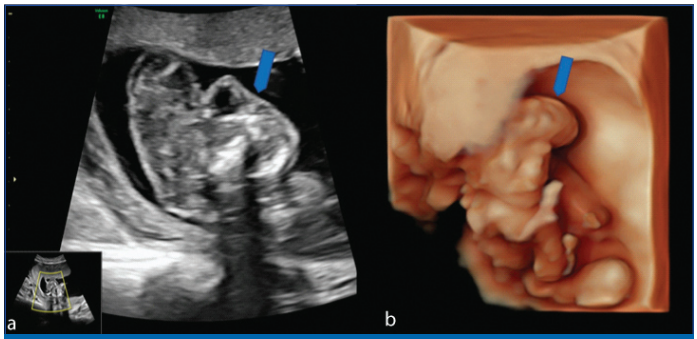
A 31-year-old gravid female presented for primary 1st trimester scan at 11 weeks 3 days of gestation. A single live foetus was seen with variable presentation. A 2D US on grey scale revealed a bilobular face giving a typical mickey mouse appearance with absence of cranial vault [Table/Fig-1,4].



[Table/Fig-4]: 2D Ultrasound performed at 11 weeks and 3 days showing a bilobular face giving typical 'mickey mouse' appearance on grey scale.

CASE 4

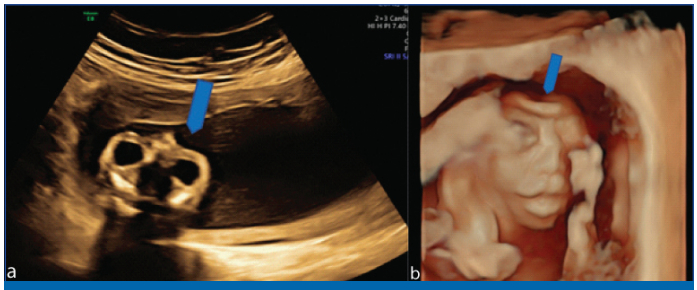
A 26-year-old gravid female presented anomaly scan at 19 weeks 3 days of gestation. A single live foetus was seen with variable presentation. Placenta was posteriorly located along the left lateral wall of uterus. Femur length and abdominal circumference were corresponding to the menstrually calculated gestational age. A 2D and 3D US on grey scale revealed non-visualisation of foetal calvaria with disorganised brain parenchyma [Table/Fig-5a,b]. There was associated polyhydramnios (AFI of 25.5) with increased echogenicity of the liquor [Table/Fig-1].



[Table/Fig-5]: (a) Ultrasonographic image on gray scale showing absence of echogenic rim of skull with disorganised brain matter covered by meninges. (b) Lack of the calvarium with disorganised brain tissue contrasted against the ossified spine on sonogram.

CASE 5

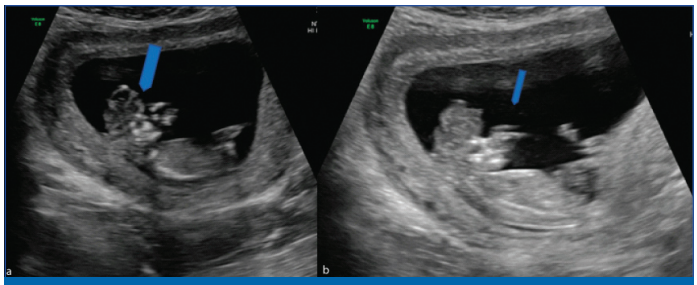
A 29-year-old gravid female for level II anomaly scan at 19 weeks 3 days of gestation. A single live foetus was seen with variable presentation. Liquor showed increased echogenicity. Placenta was posterior and upper in position. US showed prominent foetal orbits with non-visualisation of foetal forehead giving a characteristic frog eye sign. The foetal brain and cranial vault were not seen [Table/Fig-6a,b]. Foetal spine was not well visualised at the time of scan. Foetal thorax appeared smaller in size. Foetal nose, lips and limbs appeared grossly normal. This was a case of acrania with anencephaly showing typical frog eye sign on grey scale [Table/Fig-1].



[Table/Fig-6]: (a) 2D Ultrasonographic image showing protruding orbital structures - frog eye sign. (b) 3D/4D Ultrasonographic image showing absence of calvaria and brain tissue, suggestive of acrania with anencephaly.

CASE 6

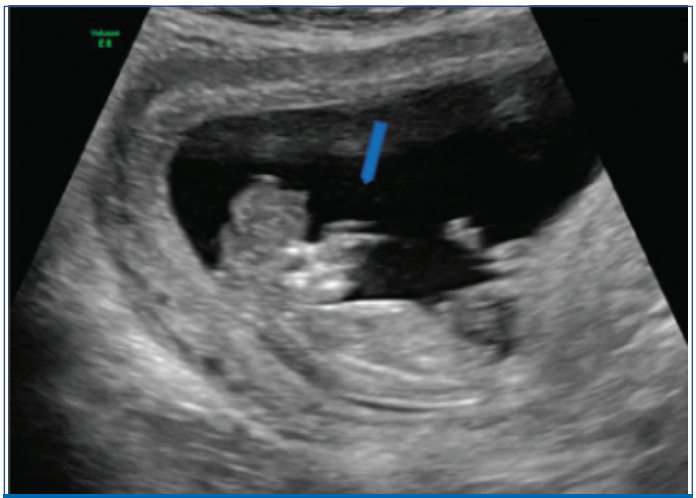
A 31-year-old primigravida female presented at 18 weeks 6 days of gestation for anomaly scan. A 2D US showed splaying of the vertebrae which was suggestive of spinal bifida [Table/Fig-7a] along with absence of cranial vault and disorganised brain tissue, suggestive of exencephaly [Table/Fig-1,7b].



[Table/Fig-7]: (a) Grey scale ultrasound image showing spina bifida. (b) 2D ultrasonography in the same foetus showing disorganised brain tissue with absence of cranial vault.

CASE 7

A 27-year-old gravid female came presented for 1st trimester scan at 11 weeks 5 days of gestation. A single live foetus was seen with variable presentation. A 2D US on grey scale revealed acrania with exencephaly along with polyhydramnios and increased echogenicity of the amniotic fluid [Table/Fig-1,8].



[Table/Fig-8]: Foetus with acrania with exencephaly showing polyhydramnios with increased echogenicity of the liquor.

DISCUSSION

Central Nervous System (CNS) malformations comprises of many important diseases in child neurology. NTDs occur as a result from failure of spontaneous closure of the neural tube between the 3rd and 4th week of foetal life. NTDs are the most common

cause of congenital anomalies of the CNS [1]. US examination plays an important role in the detection of these anomalies in the 1st as well as 2nd trimester of pregnancy. With the advent of newer technology in foetal imaging, role of 3D/4D US has become pivotal for overall evaluation of foetal CNS. A 3D/4D US imaging also aids in the diagnosis of congenital CNS anomalies as it provides better visualisation and good quality images [2]. US is an established imaging modality in the evaluation of foetal well-being performed in routine obstetric practice. It helps in identification of congenital anomalies and foetal malformation in pregnant women. A standardised protocol in the sonographic evaluation of the developing foetus is necessary for an early prenatal diagnosis of congenital malformations. US examination performed using a frequency probe has a higher sensitivity of around 60% in high risk pregnancies with a detection rate of almost 100% in diagnosing congenital anomalies such as acrania [3].

Acrania is a lethal and rare congenital anomaly which is characterised by a partial or complete absence of cranium. A very few cases of isolated acrania without anencephaly has been reported and its true incidence is not known. No significant increase in incidence in subsequent pregnancies is seen [4]. Exencephaly refers to complete but abnormal development of brain tissue and it can usually be seen with isolated acrania. Membranous flat bones are affected in acrania. It starts with the closure of anterior neuropore after 4th week of gestation. The normal mesenchymal migration under the calvarial ectoderm does not occur as it remains membranous instead of forming the epidermis. This leads to nondevelopment of calvarial bones of the skull, related underlying musculature and dura mater. Due to the absence of induction from the neurocranium of the brain, parenchyma is unable to differentiate into two cerebral hemispheres. The cerebellum, brainstem and the cranial nerves appear relatively normal. However, the outer globe and diencephalon is appearing abnormally small [5]. Antenatal US allows an early diagnosis of acrania from 11 weeks onwards as the ossification of the foetal cranium begins after 9 weeks. It is also important to look for frontal bone ossification in the axial and coronal planes while evaluating a case for acrania. Maternal serum alfa-feto proteins are elevated and also aid in diagnosis [6]. In present case series, foetal acrania was detected earliest at 11 weeks 1 day. The maternal alfa feto proteins were elevated in 4 cases who came for level II/anomaly scan. In the remaining cases, the test was not performed. Johnson SP et al., first described the serial progression from exencephaly to anencephaly [7].

Acrania when noted at an early stage shows the disorganised brain tissue detectable just above the orbits which are referred to as exencephaly [8]. Anencephaly on the other hand occurs as a result of failed closure of the midbrain and forebrain, but with normal fusion at the level of the hindbrain and the cervical cord region [9]. It has been demonstrated that about 12-25% of these cases also have other associated structural abnormalities, with 1-5% being aneuploidy [10-12]. The most severe form of cranial NTD is anencephaly which is characterised by lack of cortical brain tissue along with absence of the cranial vault. Incidence of anencephaly is around 1:1000 and it shows a female predilection with a Female:Male ratio of 4:1. Acrania anencephaly sequence is the serial progression from a relatively normal looking exposed brain (exencephaly) with an absent cranial vault (acrania) to no recognisable brain tissue (anencephaly) [13,14]. At birth, the diagnosis is made due to obvious malformation of the cranial vault. Therefore, it is of paramount importance to screen the foetus antenatally for early detection. Failure of closure of the antral end of the neural tube which usually occurs by day 24 of embryonal life results in anencephaly.

Anencephaly can be detected on high resolution ultrasonography by 11 weeks of gestation. US is a cost-effective, non-invasive and quick method to detect anencephaly. It has an accuracy of almost 100% at 14 weeks of gestation. In present study, 2D and 3D/4D ultrasonography was easily able to detect all the cases of acrania with anencephaly in both early first trimester scans and level II scans.

There is a 2.5% risk of recurrence of a NTD in future pregnancies. However, folic acid therapy is helpful in reducing the risk of recurrence. Folic acid was not taken by any of the seven patients in their 1st trimester. All the patients were advised to take folic acid therapy for subsequent pregnancies. Tonni G et al., reported early 3D US diagnosis of acrania/exencephaly sequence in a foetus with a diagnosis of tetraploidy established by coelocentesis [15]. They concluded that 3D US was helpful in the early prenatal diagnosis of acrania - exencephaly sequence. They also showed that 3D US was useful in excluding other associated congenital malformations such as iniencephaly and/or alobar holoprosencephaly. A 3D US during the first trimester scan is very helpful to display the coronal or sagittal planes, because these planes may be difficult to achieve using conventional 2D US [16-19]. In present study, only a single case of spinal bifida having acrania with exencephaly was seen during the 2nd trimester anomaly scan.

A training program for the definition and detection of the various types of NTDs along with specific knowledge of foetal development according to the Carnegie Classification are important in understanding the underlying pathogenesis and achieving accurate and precise diagnoses in clinical practice [20-23].

CONCLUSION(S)

Acrania-exencephaly-anenecephaly sequence shows characteristic ultrasonographic features on 2D as well as 3D/4D US. However, the diagnosis of the acrania-exencephaly-anencephaly sequence is very difficult at lower gestational ages, and most cases remain undetected at an early stage of pregnancy. A 3D/4D US provide additional benefits compared to 2D ultrasonography in the form of better visualisation of and depiction of the defects at both early and relatively late stages of gestation. A 3D/4D ultrasonography can also illustrate findings with different modes of reconstruction, which 2D US cannot. Hence, 3D/4D US may contribute to early detection of foetal acrania-exencephaly-anencephaly sequence.

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