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ORIGINAL ARTICLE

Diagnosis of Acrania Before 11 Weeks

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Abstract To review embryonic skull shape and brain anatomy by sonography during late embryonic and early fetal periods. We examined embryos/fetuses of 8–11 weeks between March 2015 and February 2018, the period corresponds to CRL 16–44 mm and also corresponds to late embryonic and early fetal periods by transvaginal and transabdominal sonography. We assessed shape of the skull and intracranial brain vesicles. Additionally, embryonic brain anatomy was also assessed by three-dimensional ultrasound. We found 12 abnormal cases, 5 cases between CRL 16–30 mm and 7 cases between CRL 31–44 mm. We followed all cases between 11 and 13 weeks and confirmed acrania with loss of variable amount of brain tissues. Acrania–Exencephaly–Anencephaly sequence can be diagnosed before 11 weeks. Sonographer should be familiar and proper knowledge of brain embryology and anatomy is key to diagnose.

Keywords Acrania · Exencephaly · Anencephaly · Brain vesicles

Introduction

CNS malformation are amongst the most frequently detected anomalies and most of them are lethal or if survived, carry poor prognosis. Anencephaly results from failure of closure of anterior portion of neural tube during early embryogenesis. 1st trimester evaluation of CNS is difficult as this system evolves considerably over gestation.

Method

We examined pregnant women before nuchal translucency scan by transvaginal and transabdominal sonography between March 2015 and February 2018. We included embryos and fetuses of 8–11 weeks according to post menstrual age in our study. This period of 8–11 weeks corresponds to CRL 16–44 mm and it is late embryonic and early fetal period. We assessed the shape of skull and intracranial brain vesicles. Any abnormalities of the shape of the skull like irregularity, shortening, elongation, lobulation, hyperextension, etc. were noted. Also, we assessed overall shape of the embryo. Embryonic brain cavities (vesicles) were also assessed. Additionally, embryonic brain anatomy was also assessed by three-dimensional ultrasound. All cases were followed again at 11–14 weeks.

Result

We found 12 cases of abnormal shape of skull, five cases with CRL between 16 and 30 mm and seven cases with CRL between 31 and 44 mm (Fig. 1). Four embryos/fetuses with elongated head shape, three with shape irregularity, one short, two bilobed, one broad head shape and one short and hyperextended head (Table 1). Overlapping of abnormal shape was common. Abnormalities of intracranial brain vesicles with abnormal cystic brain spaces were noted in few cases. Echogenicity into amniotic fluid compared to clear chorionic cavity fluid was

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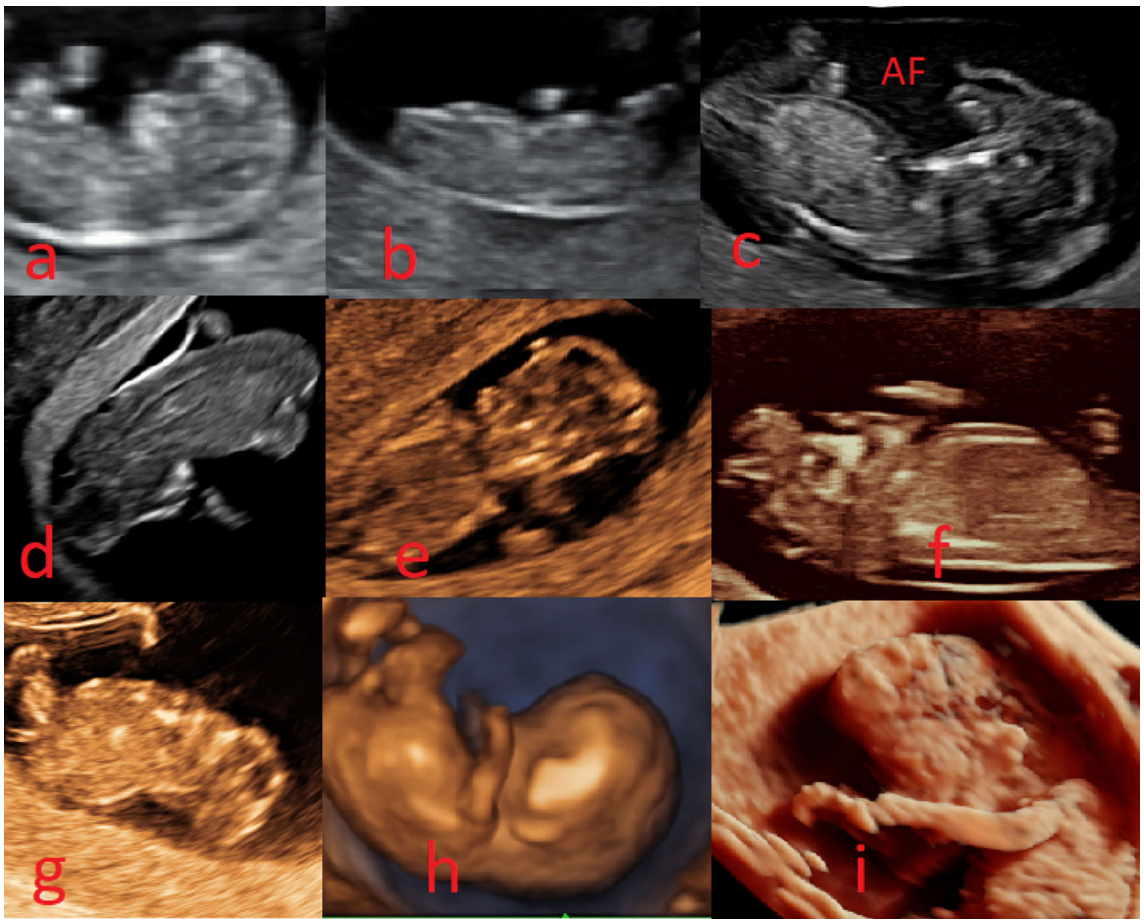

Fig. 1 Sonographic images of embryos/fetuses. **a** Normal embryo at CRL 32 mm; **b–g** are anencephaly. **b** Elongated; **c** irregular, note the turbid amniotic fluid (AF); **d** unrecognized cystic area in the brain; **e** broad in coronal section; **f** irregular and lobulated; **g** hyperextended and short; **h** 3 D ultrasound image of normal embryo; **i** 3 D ultrasound image of anencephaly

Table 1 12 cases of anencephaly

S. no	CRL (mm)	Shape of the head	Additional findings
1.	18.9	Elongated posterior	Echogenic amniotic fluid
2.	19.5	Bilobed and cystic areas	–
3.	26.9	Cystic areas in brain	–
4.	28.8	Elongated, irregular	–
5.	29.0	Irregular and hyperextended	Spine short
6.	31.6	Irregular	Broad on coronal section
7.	34.0	Elongated and cystic area	–
8.	34.6	Short	Echogenic amniotic fluid
9.	38.8	Elongated	–
10.	40.0	Irregular	Broad on coronal section
11.	41.2	Lobulated and irregular	–
12.	43.0	Irregular	–

noted into 2 cases. We followed all cases between 11 and 13 weeks and we confirmed acrania with loss of variable amount of brain tissues.

Discussion

As mentioned by Hans et al. [1], neurulation is the process by which neural tube is formed during stage 10 of embryogenesis that takes place around 22–23 days.

Embryologists have classified embryo development into 23 carnegie stages, ending at 10 post menstrual week with completion of embryonic period.

Of the two modes of bone formation, flat bones of the skull are derived by intramembranous ossification. The mesenchymal cells are derived from neural crest and paraxial mesoderm. These cells then encircle the brain and form most of the flat bones of the skull. Ossification centres of frontal, temporal, supraoccipital region occur at around 31–32 mm of CRL and ossification of the skull should be visible from 11 weeks. Calcification of the skull is complete by 10–11 weeks and the diagnosis might be missed if the fetus is examined at gestational age less than 11 weeks. It should always be detected after 11 weeks.

Most of the anencephaly shows a multifactorial pattern of inheritance, with interaction of multiple genes as well as environmental factors.

Neural tube defects (NTDs) are the second most frequent congenital structural anomalies. The most severe of these defects is the sequence of acrania, an abnormality incompatible with the life. Kandasamy et al. [2] studied incidence of neural tube defects and accordingly overall incidence of NTDs is 2.79/1000 births, significantly reduced from 11.42/1000 births due to pre conceptional and 1st trimester folic acid supplementation and prenatal screening. It has variation in occurrence rate according to geographic area. Sharada [3] studied NTDs in India and according to them spina bifida and anencephaly are two most common NTDs.

The cranial abnormality may extend inferiorly to the cervical region as spina bifida. The head may be hyperextended or flexed.

Acrania is absence of calvarium that leads exposure of the brain tissue to the amniotic fluid. This is called exencephaly. Exencephaly is the lack of bones of the skull cap. The brain is covered only with soft meninges. This prolonged exposure of the developing brain to the amniotic fluid and repeated mechanical and chemical trauma in utero results in anencephaly. In exencephaly, there is a large amount of recognizable neural tissue, but in anencephaly the cerebral hemispheres are replaced by a mass of brain remnant. Absence of calvarium and loss of brain tissue result into decrease of actual CRL of anencephaly fetuses. Also, degraded brain tissues into amniotic fluid give echogenic appearance of the fluid into amniotic cavity and clear into chorionic cavity.

Acrania is considered as primary event, this leads to exencephaly and later leads anencephaly. So, anencephaly occurs in 3 phases: first the cranial part of the neural tube fails to close, second the developed brain parts protrude and are exposed to the amniotic fluid and at last degeneration of the exposed part results into anencephaly.

By sonography, 1st anencephaly fetus was diagnosed by Campbell and colleagues in 1972 at 17 weeks.

In the second-trimester, the typical appearance of anencephaly is the ‘frog’s eyes’ sign, because of the absence of cerebral tissue visible cephalad to the orbits. In the first trimester, the main difference is the presence of cerebral tissue, and, with the fetus in the sagittal view, the absence of cranium may not be noted. In the coronal section, the cerebral lobes are seen as two semi-circular structures above the orbits floating in amniotic fluid, the appearance best described as the ‘Mickey Mouse’ sign. Chatzipapas et al. [4] described ‘Mickey Mouse’ sign for early diagnosis of anencephaly as fetal face in coronal section appears as mickey mouse between 11 and 14 weeks with sensitivity of 100%. The cerebral hemispheres, the basal ganglia and the hypothalamus are absent. If the cerebellum is present, it is imperfect. The eyes are usually protuberant because of inadequate bony orbits.

According to Tanaka et al. [5], during the 6th week of gestation, three primary brain vesicles are formed: the forebrain or prosencephalon, the midbrain or mesencephalon and the hindbrain or rhombencephalon. During the 7th week of gestation, the forebrain partly divides into two vesicles, the telencephalon and the diencephalon, and the hindbrain partly divides into the metencephalon and the myelencephalon. As a result, there are five secondary brain vesicles.

As Hans et al. [1] mentioned in clinical neuroembryology, in half of the embryos studied at 7 weeks, three primary brain vesicles are visualized, representing the unpartitioned prosencephalon, mesencephalon and rhombencephalon. Also, in half of the embryos studied at week 7, in most embryos at week 8 and in all fetuses after week 8, five secondary brain vesicles (telencephalon, diencephalon, mesencephalon, metencephalon and myelencephalon) are visualized.

Sonoembryology has a great potentiality in the detection of central nervous system maldevelopment. Ritsuko et al. [6] described the role of 3D sonography as this offers a better quality of imaging. Familiarity with these structures and their normal variants is essential for prenatal ultrasound studies. Examination of these brain vesicles can be useful to enhance the diagnosis of brain malformations. In cases of acrania, proper identification of these brain vesicles is difficult.

As Miguelez et al. [7] described signs of acrania prior to 11 weeks and are abnormal shape of the head in sagittal and coronal sections. The smooth contour of the cranium is lost. The head may be elongated, short, irregular, broad (coronal section), lobulated or bilobed (Fig. 2) and this sign is key sign to diagnose acrania. Examination of the brain vesicles may give some clue. Echogenic appearance of the amniotic fluid compare to chorionic fluid is indirect

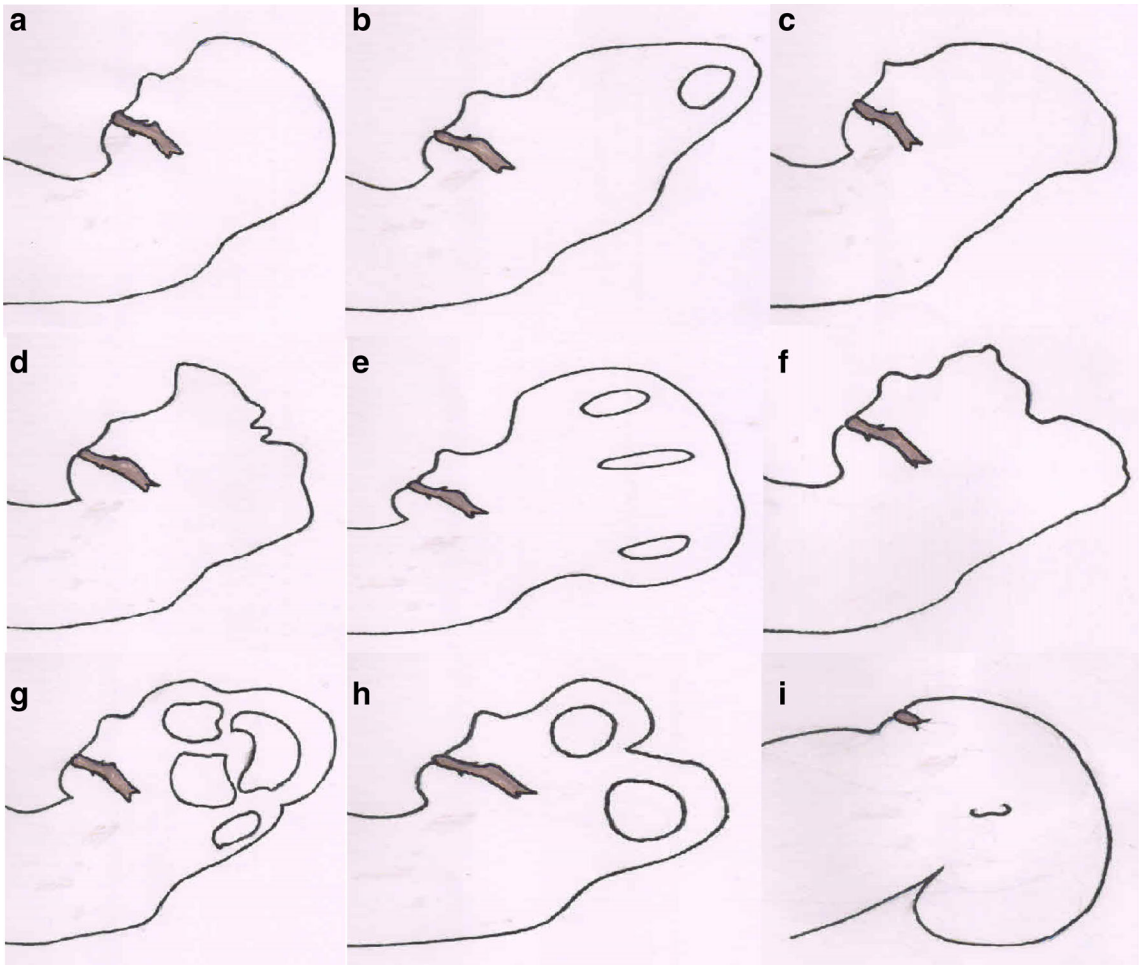

Fig. 2 Schematic drawing of different shapes of anencephaly before 11 weeks. **a** Normal, **b** elongated, **c** elongated posteriorly, **d** irregular and lobulated, **e** broad, **f** irregular and lobulated, **g** irregular cystic spaces, **h** bilobed, **i** iniencephaly

hint and not always present. Embryo with iniencephaly additionally has hyperextended head with or without short spine.

Conclusion

Acrania–Exencephaly–Anencephaly sequence can be diagnosed before 11 weeks. Ultrasound technology has reached a level where the diagnosis of embryonic brain malformations can be made. With advanced technology and better knowledge of sonoembryology, these open NTDs can be diagnosed during embryonic period. In the era of NIPT, early diagnosis of this lethal malformation is rewarding.

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Compliance with Ethical Standards

Conflict of interest The author declares that he has no conflict of interest.

References

1. Donkelaar H, Lammens M, Hori A. Clinical neuroembryology: development and developmental disorders of the human central nervous system. 2nd ed. Berlin: Springer; 2014. p. 12–4.
2. Kandasamy V, Subramanian M, Sivaanandam R. A study on the incidence of neural tube defects in a tertiary care hospital over a period of five years. J Clin Diagn Rese. 2015;9(7):QC01–4.
3. Menasinkai Sharada B. A study of neural tube defects. J Anat Soc India. 2010;59(2):162–7.
4. Chatzipapas IK, Whitow BJ, Economides DL. The 'Mickey Mouse' sign and the diagnosis of anencephaly in early pregnancy. Ultrasound Obstet Gynecol. 1999;13:196–9.
5. Tanaka H, Hata T. Intrauterine sonographic measurement of the embryonic brain mantle. Ultrasound Obstet Gynecol. 2009;34:47–51.
6. Pooh RK, Kurjak A. 3D/4D sonography moved prenatal diagnosis of fetal anomalies from the second to the first trimester of pregnancy. J Matern Fetal Neonatal Med. 2012;25:433–55.
7. Miguelez J, Hisaba W, Boute T. Case report: diagnosis of 3 cases of anencephaly/exencephaly at 8–10 weeks. Ultrasound Obstet Gynecol. 2014;44:207.