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Case Report

The sequence of acrania–exencephaly–anencephaly (AEAS)- An infrequent case report

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ABSTRACT

Acrania–exencephaly–anencephaly sequence has an incidence of 3.6–5.4 for 10,000 live births and has been reported in literature. Exencephaly, described here is a defect of the neural tube which occurs due to the absence of closure of the neural fold. The main diagnostic ultrasound features include that are characterized by acrania, decreased size of cranial pole in comparison with the chest, irregular cranial surface, with increased amniotic fluid echogenicity due to the damaged brain tissue. Associated with amniotic band syndrome, Pentalogy of Cantrell, limb anomalies and ventral body wall defects. It is incompatible with life. Conducting programs training the budding neuro-sonographers about the knowledge in detection, diagnosis of NTD according to the Carnegie Classification is crucial to look forward in pathogenesis and application in the clinical scenario.

1. Introduction

NTDs include a broad spectrum of anomalies ranging from spina bifida to anencephaly.[1] Acrania–exencephaly–anencephaly sequence has an incidence of 3.6–5.4 for 10,000 live births and is specialized by the absence of scalp along with cranial cavity leading to the exposure of neural tissue and protruding eyeballs. This, being a precursor of anencephaly, lies along a spectrum i.e, acrania [absent cranium]-exencephaly [amorphous brain mass]- anencephaly [no recognizable brain tissue]—sequence {AEAS}.[2] Embyrological development of brain is disrupted leaving behind the area cerebro- vasculosa with a flattened remnant consisting of anarchic outgrowth of brain tissue as a mixed tissue of ependymal[3] (AEAS).

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2. Case Presentation

28-year-old G2P1L1, educated postgraduate, BMI-32, home-maker. No significant surgical history. No h/o teratogenic drugs intake. Family h/o diabetes. Her glycosylated hemoglobin was 9.2. Fasting and postprandial was 122/167 mg/dl. She was started on human mixtard insulin and medical nutritional therapy. Counselled regarding the risk of congenital malformations and need for adequate glycemic control. Married since 5 years and had a vacuum delivery 4 years ago with a living child. She was on regular follow up after dating scan which was corresponding to gestational age. On N T scan, the cranial vault (bony calvarial ossification) of the fetus was absent. Irregular outlined brain parenchyma was seen protruding freely into amniotic fluid. Facial views revealed frog-like appearance with prominent bulging eyeballs, compatible with diagnosis of acrania – exencephaly sequence (Figures 1 and 2). Femur

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length, abdominal circumference were normal. Normal chest, adequate outflow tracts and intact diaphragm were noted. Discussed with the radiology, blood- bank and maternofetal unit and decision was taken to terminate the pregnancy due to its incompatibility with life with maternal consent. Mifepristone 200 mg oral given, intravaginal misoprostol 800 mcg placed for cervical ripening 48 hours later and after 8 hours, a fetus with acrania-exencephaly without any other obvious major malformations was expelled. Aborted fetal autopsy examination showed around 12 weeks gestation, male weighing 110 gm, crown to heel length 14.3 cm. Placenta was morphologically normal. She was discharged after adequate counselling within 48 hours.

O/E- fetal cranium was absent. Fetal facial features were normal. The cranial defect measured 2.1 × 1.9 cm. The cervical, thoracic, lumbar spine appeared normal. The inter and intra-orbital distance, nasal bone, lips were normal. The intra abdominal organs were normal. The extremities were normal. Final impression given was acrania– exencephaly.

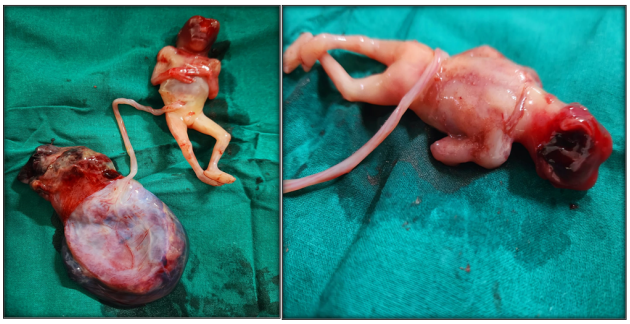

Figure 1: *Fetus with acrania -exencephaly – anencephaly-sequence seen with the placenta, note the absence of defects in the midface, abdomen, genitals and extremities. This was taken with the permission of the mother*

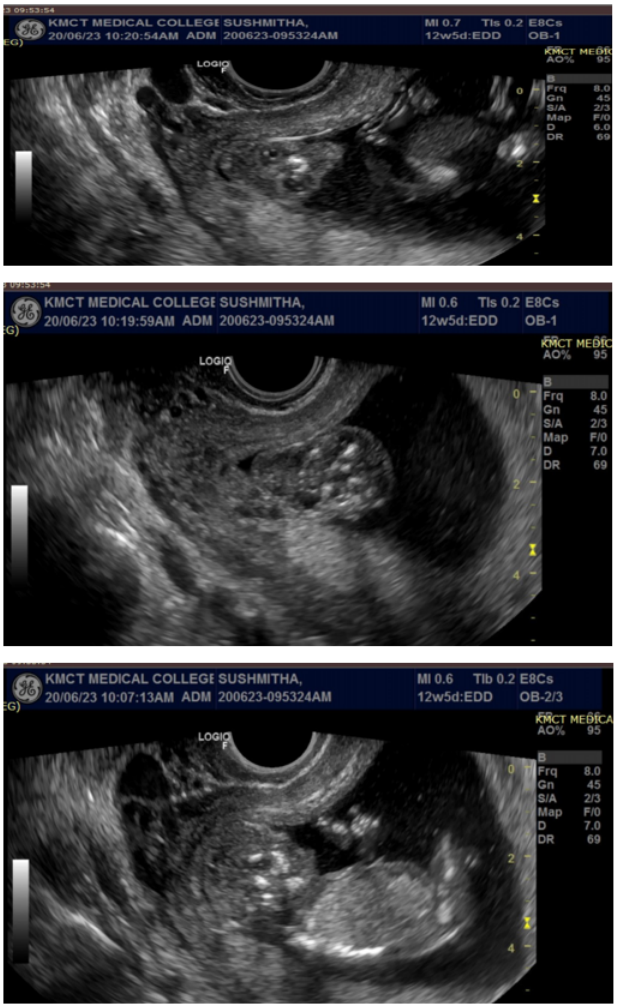

Figure 2: Fetus with acrania, note the absence of occipital bone and cerebral hemispheres

3. Discussion

Embryology: Failed mesenchymal differentiation is said to cause AEAS. During the 4^{th} week of fetal life, dysgraphia can be due to the defect in the migration of the membranous segment of the neurocranium.

Dual elements comprising fetal neurocranium are the base bones originating from the chondrocranium and the remaining membranous flat bones leading to the vault of the brain. At 4 weeks of gestation, acrania is characterized as absent closure of the neuropore.[4,5] In Acrania, facial features and skull base are preserved, central nervous system damage occurs after formation of the retinal cusps, hence the retina and eyes are developed[4] and with an incidence of ~1:1000 pregnancies.

Precursor cell differentiation is the causative factor for lack of cortical tissue apart from failure of neural tube closure.

Exencephaly where the sole layer of vascular epithelium covering the anarchic neural mass undergoes gradual degradation by the dual mechanical power along with the liquor amnii leads to progressive dissolution of the brain matter converting into anencephaly from 14 weeks of gestation. As they share the same etiology, the recurrence risk is same as for other any NTD(2.5%). International Society of Ultrasound in Obstetrics and Gynecology[6] (ISUOG) suggests early sonography during the first trimester. There has to be clear visualization and demarcation of the head of the fetus, cranial bone development appropriate for that gestational age with location of the choroid-plexus and ventricles of the brain. The median age of USG diagnosis has decreased from 15 weeks (2006) to 13 weeks (2020) due to technology and neuro-expertise.

Table 1:

Feature	Exencephaly	Anencephaly	Acrania
Cerebrum	large brain tissue which is poorly arranged	Flattened remains involving anarchic outgrowth of neural tissue along with the cells of ependyme, plexus of the choroid and cells lining the meningeal epithelium.	Deformed and is present
Covering of extracranial nervous tissue	Vascular layer of epithelium	Angiomatous stroma	Thick membrane
Calvarium	Absent above the level of orbits	Supra-orbital part, there is no calvarium	Absent
Base of the skull	No defect	No defect	Has a defect and is not there.
Facial features	Not affected	Deformed	Not affected

4. Radiology

1. The main diagnostic ultrasound features include that are characterized by acrania, decreased size of cranial pole in comparison with the chest, irregular cranial surface, with increased amniotic fluid echogenicity due to the damaged brain tissue. The special Mickey Mouse sign is due to the semicircular form on either side which float above the face of fetus mimicking the rounded Mickey Mouse like ears. Progressing in the next few weeks (second – trimester), further loss of cranial tissue causes frog -face sign (absence of recognizable tissue superior to the level of fetal orbits) and increased amniotic fluid echogenicity ensue.[7]
2. Transvaginal approach fastened the earliest diagnosis by 9 weeks and 3 days and 10 weeks.
3. Moreover, sonographical presence of high amniotic fluid echogenicity at 11–14 weeks, marks AEAS in 90% cases.[8,9] The characteristic fetal MRI for exencephaly include (i) supra-orbitally no calvarium and scalp, (ii) skull which is unflawed and standard development of the face (eyes, nose, and mouth) (iii) disruption of parenchyma of brain with poor demarcation of landmarks, (iv) fragmentary membranous or bleary matter covering the brain tissue, (v) disproportion of the cerebellum and brain stem.[10]

• With the aid of 3 D USG,[11] early detection by 8 weeks has been described.

Maternal pregestational diabetes and pre-pregnancy obesity have been clearly established. Glucose homeostasis dysregulation and high glycemic levels lead to disturbed milieu. Genetic, environmental and ethnic factors predispose to this condition. The first stage of mal-development sequence is Acrania, that takes place 18–20 days post-fertilization. Evolution from exencephaly to anencephaly by Wilking S et al. has been described.[12] Structural non-NTD anomalies, which are mostly consistent with limb body wall complex are seen in up to 25% cases. Genetic factors (10%) often predispose with trisomy 18 being frequent aberration. Amniotic band syndrome, Pentalogy of Cantrell, limb anomalies and ventral body wall defects could make it lethal and incompatible with survival.[13,14] Aneuploidy is seen in about 2% of cases.

1. In the back-drop of multifetal/ twin gestation, discordancy in the echogenicity of amniotic fluid could be an early predictor of this acrania-exencephaly-anencephaly sequence. TRAP with MCMA twin has also been described. Large encephalocele, microcephaly, amniotic band syndrome, craniopagus parasiticus are differential diagnosis of the same.

Hendricks et al. showed that the neural tissue is covered by a vascular epithelial layer. Shallow flat, anarchic gyri and sulci are typical in Exencephaly. The cranial mass remaining is dysplastic, with absent or poor neuronal differentiation. Cortical matter is sparse.[15] Absent closure of the midbrain and forebrain, but with regular fusion at the level of the hindbrain and the cervical cord characterizes as anencephaly.

5. What Options are Available Next?

1. Prognostication cannot be done with genetic testing. Hence prenatal sampling with chromosomal microarray analysis (CMA) should be offered when exencephaly-anencephaly sequence (AEAS) is suspected which describes information pertaining to the risk of recurrence and prenatal diagnosis as a part of pre-conceptional counselling.
2. 4 mg of folate should be recommended in pre-pregnancy to reduce the recurrence risk of NTD.
3. For couple who are not willing for any tests in prenatal diagnosis, testing in postnatal phase as well as termination of pregnancy is helpful than cell-free DNA screening.
4. Conducting programs training the budding neuro-sonographers about the knowledge in detection, diagnosis of NTD according to the Carnegie

Classification is crucial to look forward in pathogenesis and application in the clinical scenario.[16]

6. Declaration of Patient Consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/ her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

7. Source of Funding

Nil.

8. Conflict of Interest

None declared.

9. Ethical approval

Not required.

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