Fetal Neurosonography: Ultrasound Findings in Different Types, Associated Syndromes and Impact on Fetal Outcome

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Abstract

Objective: The aim of this study is to show the ultrasound findings in different fetal brain anomalies and specify those which may raise the suspicion of associated extra cranial anomalies.

Patients and Method: 60 pregnant women with suspected CNS fetal anomalies by 2D US were examined over a period of 18 months starting from November 2010 until May 2012. Fetal gestation ranged from 8-39 weeks with a 26 wks mean age. In all patients 2D, 3D and 4D ultrasound as well as fetal Doppler study were performed. Follow-up was done for all cases.

Results: The most common anomaly seen was acrania (27%), followed by hydrocephalus (20%) and encephaloceles (18%). Associated syndromes or anomalies were found in 22 (37%) cases. Major anomalies which are incompatible with fetal life were diagnosed as early as 10 gestational weeks by using 3D and 4D ultrasound.

Conclusion: The ability to simultaneously view and review a brain volume in all three scanning planes, by ‘navigating’ back and forth through the digitally stored data was found to be clinically important. It can be also used for teaching purposes especially in those with little experience in ultrasound, as the image with 3D is more distinct and clear.

Key Words: Prenatal ultrasound – 3D/4D ultrasound – Congenital brain anomalies – Fetal CNS – Hydrocephalus.

Introduction

CENTRAL nervous system (CNS) malformations constitute a broad range of congenital anomalies. Almost all of them result in severe and irreversible neurological defects, and many cannot support life [1]. Ultrasound (US) detection of prenatal central nervous system (CNS) anatomic anomalies is very important in making decision about therapeutic termination. It is a non-invasive technique, which is more acceptable by patients. Several studies have shown an accuracy of 92% to 99.7% for US detection of CNS anatomic anomalies [2].

3D/4D ultrasonography has been used as an adjunctive imaging modality to 2D ultrasonography. Thus, the current paradigm consists of performing 3D/4D ultrasonography as part of a target scan, after an initial diagnostic impression has been established by 2D ultrasonography [3].

Several previous studies [4,5] have shown the advantage of using 3D ultrasound in the prenatal diagnosis of brain anomalies. Thus our study shows the ultrasound findings in different fetal brain anomalies and specifies those which may raise the suspicion of associated extra cranial anomalies. This study provides a rather wide scale of fetal brain anomalies as well as associated syndromes or anomalies.

Material and Methods

Patients:

60 pregnant women with suspected fetal brain anomalies were prospectively studied over a period of 18 months starting from November 2010 until May 2012. Fetal gestation ranged from 8-39 weeks with a 26 wks mean age. Gestational age was calculated according to the date of the last menstrual period. Maternal age ranged from 18-40 years (mean age was 28 years). In all patients 2D/3D as well as 4D ultrasound and fetal Doppler study were performed.

Full personal, family and maternal history was taken with special emphasis on presence of previous family history of congenital anomalies, drug intake or infection during pregnancy, positive consanguinity, maternal diabetes and Rh incompatibility.
The study protocol was approved by the ethical committee in Medical School, Kasr El Aini Hospital, Cairo University. Verbal consent was obtained from all participants.

**Ultrasonography:**

2D gray-scale and fetal Doppler studies, 3D and 4D pelvic Ultrasound was performed in all second and third trimester cases using 5-9 MHz 3D probe on Voluson pro 730 General Electric machine.

Transvaginal US was done in first trimester pregnancies (8-12 weeks gestational age) as well as cases with impacted cephalic fetal presentation. Automatic volume acquisition was performed and all the data were saved on the magneto-optical disks. The image analyses were done off-line in 3D, while in 4D the volume was taken on real time. Surface mode was used for assessment of the superficial structure of the fetal cranial bone and facial features. Multiplanar image analysis was used for the assessment of the intracranial morphological development. 3D color/angio mode was used for the demonstration of the brain circulation.

**US studies were reviewed and reported by experienced sonographers in prenatal US. The following parameters were assessed in each fetus:**

- Calculation of gestational age, fetal number, position, viability and biophysical profile.
- Measurements of biparietal diameter, size of the lateral ventricular atria, sizes of the third and fourth ventricles, thickness of the frontoparietal cortical mantle and size of the posterior fossa including the cerebellum.
- Regarding the placenta: Chrionicity, position, thickness, grading, and presence of abruption or retro-placental hematoma.
- Liquor: Amount, turbidity, presence or absence of amniotic septum. Amount of amniotic fluid was calculated using four quadrants amniotic fluid index.
- Assessment of lung volume, whether it is normal or hypoplastic [6].
- Assessment of abnormal uterine and adnexal lesions.
- Full anomaly scan for all systems in addition to assessment of abnormal neural translucency in early pregnancy.
- Color, pulsed Doppler & spectral analysis were done for umbilical artery, fetal middle cerebral artery & ductus venosus in fetuses with low biophysical profile.
- 4D US: Smooth surface mode for assessment mainly of facial features and deformity. Cine views were taken to see limitation of movement associated with some anomalies.

Follow-up was done for all cases and the diagnosis was confirmed either by postnatal CT, MRI, prenatal MRI or autopsy. Follow-up of fetal outcome was done in viable births.

**Results**

60 pregnant women suspected to have fetal brain anomalies at 8-39 weeks gestation were prospectively examined. The maternal age ranged from 18-40 yrs (mean age 28) years.

56 (93%) were singletons while 4 were twins (7%); two DCDA and the other two were MCMA.

The most common anomaly seen was acrania (28%), followed by encephaloceles (18%) and hydrocephalus (15%) as seen in Table (1).

<table>
<thead>
<tr>
<th>Types of anomalies</th>
<th>No of cases</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acrania</td>
<td>16</td>
<td>27</td>
</tr>
<tr>
<td>• Exencephaly,</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>• Anencephaly</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Hydrocephalus</td>
<td>12</td>
<td>20</td>
</tr>
<tr>
<td>Encephaloceles</td>
<td>11</td>
<td>18</td>
</tr>
<tr>
<td>(10 occipital and 1 front parietal)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tonsillar herniation</td>
<td>7</td>
<td>11</td>
</tr>
<tr>
<td>Microcephaly</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>Alobar Holoprosencephaly</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Vermian agenesis</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Unilateral ventriculomegaly</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Choroid plexus cyst</td>
<td>1</td>
<td>1.6</td>
</tr>
<tr>
<td>Arachnoid cyst</td>
<td>1</td>
<td>1.6</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>60</strong></td>
<td><strong>100</strong></td>
</tr>
</tbody>
</table>

Associated syndromes or anomalies were found in 22 (37%) cases (Table 2).

Including Meckel gruber syndrome (n=10), Pentology of Cantrell (n=2), Meningoceles (n=6), facial anomalies (n=2), Dandy walker malformation (n=1), micromelia (n=1).

27 cases were primigravida, the others were multigravida with 15 having previous unexplained miscarriages.
Table (2): Associated anomalies and Syndromes.

<table>
<thead>
<tr>
<th>CNS anomalies</th>
<th>No</th>
<th>Associated anomalies</th>
<th>Syndromes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exencephaly</td>
<td>2</td>
<td>Omphalocele, ectopia cordis, single umbilical artery</td>
<td>Pentology of cantrell</td>
</tr>
<tr>
<td>Alobar Holoprosencephaly</td>
<td>1</td>
<td>- Midline defect (fused central mass, small proboscis instead of nose, cleft lip) hypoplastic lungs, clinched hands, extended LL</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>- Cyclops, Polydactaly</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>- Dandy walker malformation</td>
<td></td>
</tr>
<tr>
<td>Occipital encephalocele</td>
<td>6</td>
<td>- Bilateral autosomal recessive polycystic kidneys</td>
<td>Meckel Gruber Syndrome</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Anhydramnious, Hypoplastic lungs, Hypognathia</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Bilateral autosomal recessive polycystic kidneys,</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Oligohydramnious, Hypoplastic lungs, Biliary radicle dilatation</td>
<td></td>
</tr>
<tr>
<td>Anencephaly</td>
<td>1</td>
<td>- Bilateral autosomal recessive polycystic kidneys</td>
<td>Meckel Gruber Syndrome</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>Oligohydramnious, Hypoplastic lungs</td>
<td></td>
</tr>
<tr>
<td>Microcephaly</td>
<td>1</td>
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<tr>
<td></td>
<td>1</td>
<td>Anhydramnious, Hypoplastic lungs</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Thickened neural translucency</td>
<td></td>
</tr>
<tr>
<td>Tonsillar herniation</td>
<td>5</td>
<td>- Spinal meningocele</td>
<td>Chiari II</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Occipital meningocele</td>
<td>Chiari III</td>
</tr>
</tbody>
</table>

Most of the pregnant females (70%) had one or more risk factor for congenital anomalies; mainly positive consanguinity (42 cases), intake of drugs specially clomid for infertility patients (21 cases). Positive family history of unexplained abortion or congenital anomalies was found in 23 cases. 65% of those with detected brain anomalies showed abnormal ventricular atrium measurements ranging between 14-22mm while 78% showed abnormal biparietal diameter (smaller biparietal diameter in encephalocele & microcephaly, large BPD in hydrocephalus).

The cisterna magna was small in cases of chiari malformation and occipital encephalocles, while it was enlarged with reduced volumetric measurements of the cerebellum in vermian agenesis and dandy walker malformation.

Acrania was the commonest anomaly detected in our study (16 cases) accounting for 27% of the cases (Fig. 1).

10 cases showed anencephaly of which two were anencephaly in one of twins while six showed exencephaly. Most cases were isolated, only four cases (23.5%) had associated anomalies of Meckel Gruber syndrome (1 case), micromelia (1 case) and pentology of Cantrell (2 cases) as shown in Table (2).

Eleven cases of encephaloceles were diagnosed in our study, 10 of which were occipital (Fig. 2) and one was frontoparietal. They presented the second most common anomaly in our study (20%). Occipital encephaloceles had the second highest incidence of associated anomalies since 8 of the occipital encephaloceles (80%) were part of Meckel Gruber syndromes, while only 20% were isolated anomalies.

All cases (100%) with tonsillar herniation and small posterior fossa showed associated spinal or occipital meningoceles as part of chiari II or III syndromes.

Alobar holoprosencephaly cases showed associated anomalies mainly facial and extremities in all 3 of them.

Hypoplastic lungs were diagnosed in all cases of Meckel Gruber syndromes and alobar holoprosencephaly (1 case). Oligohydranminos or anhydraminos was detected in 24 cases all of them showed sluggish fetal movement on 4D ultrasound. Polyhydranminos was found in only 2 cases.

18 patients with lethal anomalies (Acrania and 2 cases of MGS) had undergone termination of pregnancy, 13 had intrauterine fetal death and six cases were still born. All of them were autopsied and the diagnosis was confirmed.

The other cases reached full term pregnancy and delivered viable babies. They were followed by postnatal MRI or CT giving similar diagnosis as the prenatal US.
Fig. (1): Fetus at 19 GA with acrania. 3D US showing fetal face with no calvarium, note the overlying fetal brain floating in liquor (arrow).

Fig. (2): A- 2D axial scan of fetal head revealed a large occipital meningiocele (arrow) with 3.6cm bone defect, note the deformed brain inside, head in microcephalic (BPD 40mm corresponds to 18 weeks) B- Sagittal 4D image confirming 2D findings microcephalic skull, abnormal facies, hypognathia, occipital encephalocele (arrow).

Discussion

The detection of fetal anomalies was one of the earliest uses and remains a pivotal application of prenatal ultrasound. Prenatal recognition of birth defects is generally regarded as being advantageous and desirable because care of handicapped and disable persons is a serious healthcare burden on communities.

Applications of 3D ultrasonography continue to evolve as this technology becomes increasingly available in clinical practice [7].

This study shows different types of fetal congenital brain anomalies, their ultrasound findings and incidence of associated extracranial anomalies. We provided a relatively wide scale of different anomalies than those reported in previous studies [2,8].

By using 3D and 4D ultrasound we were able to detect exencephaly at 10 weeks of gestation, alobar holoprosencephaly at 12 weeks and anencephaly at 11 weeks. Which was earlier than those stated by Tahmasebi et al. [2].

Since the most powerful single observation for the detection of fetal brain abnormalities is measurement of the ventricular atrium [9], we found that 65% of the fetuses had abnormal ventricular atrium which made us search for further anomalies in the brain.

Evaluation of the cisterna magna was done to identify fetuses with abnormal posterior fossa without ventricular dilatation as demonstrated by Goldstein et al. [10]. In addition the use of 3D multiplanar US enabled us to obtain volumetric data regarding the cerebellum and vermis.

Anencephaly is the most common anomaly affecting the central nervous system and results from failure of closure of the rostral portion of the neural tube [11]. We reported 10 cases of anencephaly (17%) showing an amorphous brain mass with no recognizable cranial bones (Fig. 1).

Encephaloceles account for the third most common anomaly in this study (18%). Antenatal diagnosis of an encephalocele is based on sonographic identification of brain tissue adjacent to the fetal head because of herniation through a defect in the calvarium [12]. We were able to detect the site and size of the calvarial defect along with the content of the meningiocele, such information is crucial for patient’s management (Fig. 2).
The presence of an occipital encephalocele should alert us to search for other anomalies since 80% of our cases were part of MGS. Thus full scanning of the abdomen specially the kidneys is mandatory. Also the presence on an occipital encephalocele or meningocele may raise the possibility of chiari III syndrome so proper scanning of the cerebellum and tonsils is of great importance.

Numerous abnormalities associated with Meckel-Gruber syndrome were previously reported in the literature [13]. We presented ten cases of Meckel-Gruber syndrome (MGS) showing oligo or anhydraminos, bilateral autosomal recessive polycystic kidneys, brain anomalies including; occipital encephalocele, microcephaly and anencephaly. All cases had sluggish fetal movement on 4D ultrasound.

Mortality rate of MGS was 100% either by intrauterine fetal death or death immediately after delivery, showing agreeable results with Carter S [14].

Aqueductal stenosis is responsible for approximately 20% of cases of hydrocephalus [18]. Four of 12 hydrocephalic cases were diagnosed as aqueductal stenosis due to presence of supratentorial hydrocephalus with no evident dilatation of the forth ventricle as was seen in the coronal and sagittal 3D US planes (Fig. 3).

In one of the cases additional prenatal MRI was done to exclude tonsillar herniation as the fetal gestational age was 38 wks and the head was impacted in the pelvis making visualization of the cerebellum and cisterna magna difficult. Postnatal CT was done as a proof of diagnosis showing total agreement.

The intrauterine detection of hydrocephalus enabled us to choose the optimum method for delivery according to the size of the calvarium and more over allowed for early management. Shunt tubes were introduced postnatal as soon as possible to improve the fetal outcome.

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Reliable identification of holoprosencephaly is important, since affected fetuses have a uniformly poor outcome [16]. Ultrasound revealed a fetus complicated with single ventricle (without cortical mantle), complete absence of the falx and fused thalami denoting alobar type of holoprosencephaly. In the present study alobar holoprosencephaly was associated with a high frequency of extra-CNS anomalies (100%) mainly facial and 100% fetal mortality either by termination of pregnancy or IUFD (Figs. 4,5).

The use of 3D US enabled us to measure the posterior fossa in fetuses with Chiari malformations revealing a small posterior fossa, caudal displacement of posterior fossa structures, and almost complete obliteration of the cisterna magna. Those with Chiari II had lumbar meningoceles while Chiari III had associated occipital cephalocele.

A high percentage of associated anomalies were found in this study reaching 37% of the cases. Therefore the presence of fetal brain anomalies should alert us to search for other associated anomalies to exclude syndromal conditions.

Baba et al. [17] demonstrated that real-time-processible 3D US is useful for evaluating fetal abnormalities particularly for abnormalities of the face, ears, fingers, and anatomic axis. We used the 3D surface mode and more over the 4D US to evaluate associated facial anomalies which were clearly visualized in cases of holoprosencephaly where we detected presence of midline defect in two cases and Cyclops in another two (Figs. 4,5). Anomalies as clinched hand, hypognathia and extended LL where also demonstrated.

Correa et al., [18] found that the use of volume datasets obtained transabdominally (as in the current study) is feasible for examination of the fetal brain.

We agree with Kalache et al. [19] who stated that three-dimensional Multi-Slice View can deliver informative images of the region of interest regardless of fetal position. It is particularly helpful for evaluation of complex fetal anomalies. The use of 4D ultrasound enabled us to obtain real time images detecting the fetal movement and its facial features accurately.

Fig. (3): 2D coronal image showed supratentorial hydrocephalus at 37 weeks gestational age denoting aqueductal stenosis.
Fig. (4): 33 weeks GA fetus with alobar holoprosencephaly.
A: 2D axial. B: Sagittal image of fetal head showing smaller head (BPD 26 weeks), single ventricle, fused thalami, no falx detected.
C: 4D sagittal image dilated ventricle, fused central mass (white arrow).
D: 4D surface mode image showing associated mid facial defect, small proboscis instead of nose (arrow head), cleft lip (black arrow).

Fig. (5): Another case of holoprosencephaly 4D images showing associated anomalies A- Cyclops: One eye in middle.
B- Polydactyly.
The ability to simultaneously view and review a brain volume in all three scanning planes, by ‘navigating’ back and forth through the digitally stored data was found to be clinically important. It can be also used for teaching purposes especially in those with little experience in ultrasound, as the image with 3D is more distinct and clear.

The presence or absence of fetal congenital brain anomalies is very important in making the decision of termination or continuation of the pregnancy; hence it should be discovered as early as possible. We stated that major anomalies which are incompatible with fetal life can be diagnosed as early as 10 gestational weeks.

References