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Evaluation and prevalence of major central nervous system malformations: a retrospective study

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ABSTRACT

OBJECTIVE: Central nervous system (CNS) anomalies are the most common abnormalities of all malformations and can be diagnosed on routine prenatal ultrasonography (US). We aimed to find out fetal CNS anomaly rate in our clinic which is the referral center in the region.

METHODS: This is a retrospective study of 15000 pregnant women who were scanned for routine obstetric follow-up from January 2012 to July 2013 in our referral center. We diagnosed CNS anomalies in 41 fetuses by using high resolution ultrasound unit with 3.5 MHz transabdominal and 6 MHz transvaginal transducers.

RESULTS: CNS anomalies included 12 Chiari malformations, 2 Dandy-Walker malformations (DWM), 1 variant of Dandy-Walker syndrome (DWS), 3 iniencephalies, 15 anencephalies, 1 alobar holoprosencephaly, 2 isolated hydrocephalies, 3 hydrocephalies with cerebellar hypoplasia, 1 occipital encephalocele, 1 lumbosacral myelomeningocele accompanied with microcephaly. There were some associated anomalies in the groups that included club-foot deformities in 6 cases, ventricular septal defect (VSD) in 2 cases, polycystic kidney in 2 cases, scoliosis in 1 case, hypoplasic left ventricle in 1 case; alone atrium, single umbilical artery, echogenic focus, hydronephrosis and cleft lip and palate in the same case, and omphalocele in one.

CONCLUSION: Prognosis and early detection of CNS abnormalities have become an important issue because the most serious complications of major CNS anomalies are disability and getting bedridden and this situation is inevitably related to health economy. On the other hand prognosis of the fetus and family counseling is another important issue. Parents should decide whether to continue their pregnancies or not.

Key words: Anencephaly; Chiari; fetal anomaly; prenatal ultrasonography.

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Central nervous system (CNS) anomalies are the most common abnormalities of all malformations and can be diagnosed on routine prenatal ultrasonography (US). Thanks to recent advances in ultrasound technology including the development of high-resolution transducers, improvements in color Doppler signal processing and new scanning techniques, structural and vascular abnormalities in the fetuses can be visualized [1]. Ultrasound examination is used as the first choice modality to detect fetal CNS malformations. It has been established in several studies that accuracy of US detection varies from 92% to 99.7% for CNS abnormalities [2]. Routine anomaly scan has become a part of current obstetric follow up. CNS malformations were defined as any abnormality visualized on head and spine evaluation. Goetzinger et al showed that some of the CNS abnormalities could be associated with chromosomal abnormalities [1]. For this reason, common CNS abnormalities such as choroid plexus cysts and ventriculomegaly were not included in this study because they may not be considered as malformations.

Prognosis and early detection of CNS abnormalities have become an important issue because the most serious complications of major CNS anomalies are disability and getting bedridden and inevitably, this situation is related to health economy. On the other hand prognosis of the fetus and family counseling is another important issue. Parents should decide whether to continue pregnancy or not.

The aim of this study was to determine CNS anomaly rate in our clinic.

MATERIALS AND METHODS

This is a retrospective study of 15000 pregnant women who were scanned for routine obstetric follow-up from January 2012 to July 2013 in our referral center. In our department, anomaly scanning is performed by expert radiologists between 11 and 14 weeks and between 20 and 24 weeks of gestation and additionally, in the third trimester if it is clinically required. We diagnosed CNS anomalies in 42 fetuses by using high resolution ultrasound unit with 3.5 MHz transabdominal and 6 MHz transvaginal transducers (Toshiba Xzario Shimuishigami, Otawara-Shi, Tochigi, Japan). Each ultrasound scan took approximately 20 minutes. Fetuses' brains and spinal canals were all scanned in axial, coronal and sagittal sections through transventricular, transcerebellar, transthalamic and spinal canal planes.

Major structural abnormalities like anencephaly, and holoprosencephaly were diagnosed in the first trimester and terminated with the approval. By considering this issue, we classified the cases with CNS abnormalities into two main groups. The first group contained the fatal abnormalities which were diagnosed in the first trimester and then terminated (Table 1). In the second group, the fetuses with mild abnormalities were followed up until their birth when the parents decided to give birth (Table 2). In the first group, however, postmortem findings and ultrasound images were compared. In the second group, cranial ultrasound or cranial magnetic resonance imaging (MRI) findings after birth were compared with the pediatricians' feedback and the

Table 1. Fatal abnormalities in the first group

Abnormalities	Number
Anencephaly	15
Iniencephaly	3
Alobar holoprosencephaly	1
Hydrocephaly with cerebellar hypoplasia	3
Occipital encephalocele	1

Table 2. Mild abnormalities in the second group

Abnormality	Number
Chiari malformations	12
Dandy-Walker syndrome	2
Variant of Dandy-Walker syndrome	1
Isolated hydrocephaly	2
Lumbosacral myelomeningocele accompany with microcephaly	1

comparison of prenatal USG findings and postnatal physical examination findings were compared. Other fetal structural abnormalities evaluated routinely included cardiac, genitourinary, musculoskeletal systems anomalies. Maternal age, and drugs used were not taken into consideration.

Our research is a retrospective scanning study. We aimed to find out fetal CNS anomaly rate in our clinic which is the referral center in the region.

RESULTS

In the current study, in sonographic examination of 15000 pregnant women, CNS anomalies were detected in 41 fetuses and some fetuses had more than one anomaly. The mothers' age ranged between 18 and 39 years. Major CNS anomalies were as follows: Chiari malformations, 12; Dandy-Walker Syndrome, 2; variant of Dandy-Walker Syndrome, 1; iniencephaly, 3; anencephaly, 15; alobar holoprosencephaly, 1; isolated hydrocephaly, 2; hydrocephaly with cerebellar hypoplasia, 3; occipital encephalocele, 1; lumbosacral myelomeningocele accompany with microcephaly, 1.

Nineteen of the 23 cases in Group 1 were terminated with the parents' approval. These cases were 14 anencephalies (Figure 1), 1 alobar holoprosencephaly, 3 iniencephalies, 1 hydrocephaly with cerebellar hypoplasia. In 4 of the 23 cases, parents did not accept the termination of their pregnancy. Two of these 4 cases were hydrocephaly with cerebellar hypoplasia (Figure 2), and they were in utero ex in the 20th and 22th weeks of gestation. The other two of the 4 cases were occipital encephaloceles and anencephalies. Two cases were born at term but died soon.

Eleven of the 18 cases in Group 2 were born at term and operated by a neurosurgeon. These cases had Chiari malformations (n=7/12) (Figure 3), Dandy-Walker syndrome (1/2), isolated hydrocephaly (2/2)lum-bosacral myelomeningocele accompanied with microcephaly (n=1). The two of the other three cases in Group 2 had Dandy-Walker syndrome (n=1), and variant of Dandy-Walker Syndrome (n=1) that were born at term without being operated and then followed up. Five of the

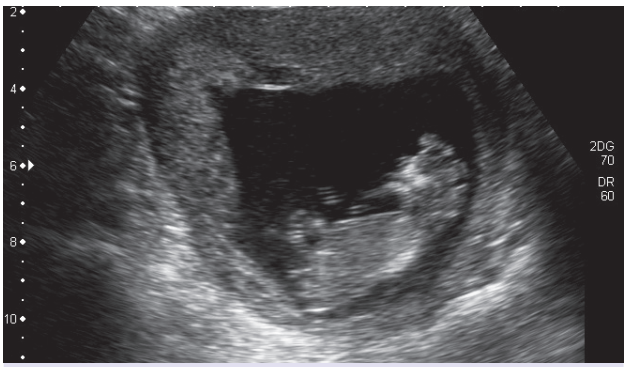

Figure 1. Fetus with anencephaly.

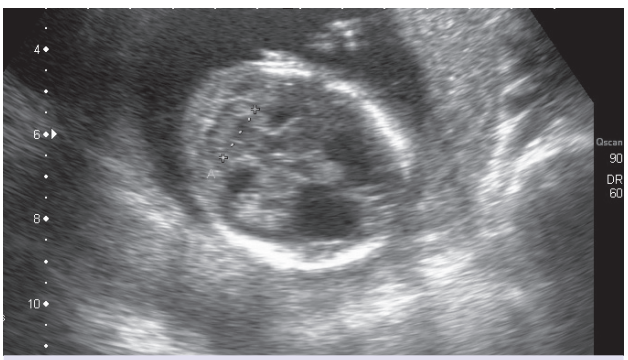

Figure 2. 18 weeks fetus with hydrocephaly and cerebellar hypoplasia available.

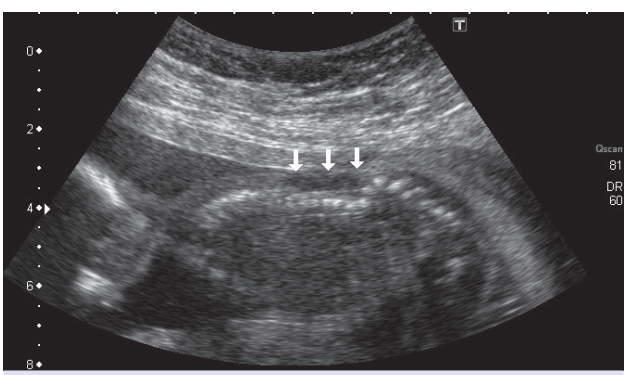

Figure 3. Chiari malformation in the fetus, there is seen apparent neural tube defects.

12 Chiari malformations were terminated with the parents' approval. Among these cases, there were four cases with relative marriage. Two of them were Chiari malformation, one of them was isolated hydrocephaly and one of them was anencephaly.

There were some associated anomalies in the groups that included club-foot deformity in six cases; ventricular septal defect (VSD) in two cases; polycystic kidney in two cases; scoliosis in one cases; hypoplasia left ventricule, in one case; alone atrium, single umbilical artery, echogenic focus, hydronephrosis and cleft lip and palate in the same case, and omphalocele in one case.

Polycystic kidney was seen in one anencephaly case and in one Dandy-Walker case. Six clup foot was seen in four Chiari cases, one with L-S meningomyelocele accompanied with microcephaly and one with iniencephaly case. VSD was seen in two fetuses in one anencephaly and in the other one alobar holoprosencephaly. Only one fetus with scoliosis had Chiari malformation. One Chiari case had left hearth hypoplasia. The only case with alobar holoprosencephaly had echogenic focus, single atrium, VSD, cleft lift-palate, hydronephrose and single umblical artery. Six meningocele, one scolosis and four clup foot deformity cases were seen out of twelve Chiari cases. One of the three fetuses with iniencephaly had omphalocele and clup foot deformity. One anencephaly case had policlistic kidney, hydronephrose and anhydramnios Lumbosacral meningomyelocele accompanied with microcephaly had interhemispheric cyst.

DISCUSSION

CNS malformations are the most common congenital abnormalities. Neural tube defects are the most frequent CNS malformations and the ratio is about 1–2 cases out of 1000 births. The incidence of anencephaly case depends on geographical distribution and it might be between one out of a hundred births and one out of a thousand births [3]. In our study, there were 41 central nervous system malformations on ultrasound in 15000 pregnant women. The incidence in our study was 0.28%. Similarly, Onkar et al. reported that the incidence of central nervous system malformations on ultrasound was 0.31% [4]. In their study there was a high correlation between autopsy and postnatal examination findings with ultrasound findings. The sum of the Occipital encephalocele, L-S meningomiyelocele and Chiari 2 cases in our clinic were found meaningful by the frequency of neural tube defects. In addition to that, the incidence of the anencephaly case is also meaningful. The incidence of hidrocephaly cases without neural tube defect is 1 out of 2000 [5]. In our clinic, in 5 cases seen out of 15000 patients the incidence of alobar holoprosencephaly was 1 out of 10000, however, it was reported as 1 out of 250 and generally seen as sporadic [6]. No underlying reason was determined in our case as well Dandy-Walker malformation is a rare abnormality of the CNS with a reported incidence of 1 in 25,00-35,00 live births and a slight female predominance [7]. Also iniencephaly is a very rare anomaly. According to us, the reason why we have relatively more cases in our clinic for those two anomalies are due to its being a referral center. The incidence of intracranial abnormalities with an intact neural tube is uncertain as probably most of these escape detection at birth and only become manifest in later life. Early diagnosis of fetal malformations has been a goal in fetal medicine for a long time [8].

The assessment of fetal anatomy has always been part of this early scan and in recent years significant improvements have been seen in ultrasound technology [9, 10]. The first trimester ultrasound examination can detect the majority of anencephalies [11]. In our research, all of the anencephalies (15 cases) and iniencephalies (3 cases) were detected at the first trimester. Cyr et al. [12] described the sonographic appearance of the fetal rhombencephalon in 25 fetuses aged between 8 and 10 gestational weeks. Blaas et al. [13, 14] were able to demonstrate the development of the fetal brain from 7 to 12 weeks. Since the beginning of these studies, improvements in ultrasound equipment with increasingly widespread availability have allowed the investigation of the fetal brain in a much larger population, during the routine first-trimester scanning [12-14]. Detailed screening of CNS has become available through high-resolution vaginal ultrasound probes and the development of a variety of 3-dimensional (3D) ultrasound modalities. Since three dimensional and doppler ultrasound scan have not clearly demonstrated their superiority over the routine two dimensional ultrasound imaging, prenatal ultraso-

nography has been based on two dimensional techniques. The early development of the central nervous system (CNS), as described by embryologists and anatomists in modern embryological textbooks, is compared with sonoanatomic descriptions from two-dimensional (2D) and three-dimensional (3D) ultrasound studies, week by week in the first trimester [15] color and power Doppler ultrasound scan may be used mainly to identify and cerebral vessels and 3D ultrasound can help detect the lesions with complex anatomy [15].

Structures that should be noted in the routine examination of central nervous system include the head shape, lateral ventricles, cerebellum, cisterna magna, cavum septi pellucidum, corpus collosum and spine. The parameters affecting ultrasound examination are gestational age, fetal position, obesity and amnion fluid index.

MRI is a potential screening tool in the second trimester of pregnancies in fetuses at risk for brain anomalies and helps in describing new brain syndromes with in utero presentation [16]. In recent years fetal MRI has emerged as a promising new technique that may add important information in selected cases mainly after 20-22 weeks [17]. We reinforced our diagnosis with two fetal MRI cases with caudal regression syndrome and cerebellar hypoplasia with hydrocephaly. MRI can provide additional information that cannot be obtained by US and is invaluable in CNS anomaly evaluation, airway management, and planning for postnatal intervention [18].

In the current study, we performed standard two dimensional imaging and established major CNS anomalies like anencephaly, iniencephaly etc. at first trimester. Most cases were detected at the first or the second trimester. CNS malformations are major anomalies. Therefore, we tried to draw attention to early diagnosis because therapeutic abortion of the major CNS anomalies is of great importance to the health economy.

In conclusion, the most common CNS anomalies in our clinic are Chiari malformation and anencephaly. Half of the cases (25 cases) were terminated with the parents' approval and most of the cases were detected at the first trimester. From our experience, using standard two dimensional ultrasound to determine CNS anomalies is an adequate choice and the investigation of the fetal CNS during the first trimester scanning has become widespread with the improvements in ultrasound equipment.

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