The Prevalence of Fetal Neural Abnormalities Detected By Ultrasonography in Southeast Part of Turkey

Ayhan ÖZKUR[1], Selim KERVANCIOĞLU[1], Ebru DİKENSOY[2], Aylin AKÇALI[3], Reşat KERVANCIOĞLU[1]

Metin BAYRAM[1]

Gaziantep, Turkey

OBJECTIVE: The aim of this study was to determine the prevalence of fetal neural abnormalities detected by prenatal ultrasonography in a university hospital in Turkey, and to review the points critical on the diagnosis of each fetal neural abnormality.

STUDY DESING: This is a single center retrospective study. The prenatal ultrasonographic imaging of all the women referred to Department of Radiology of Gaziantep University Medical School, between January 2000 and March 2006, for fetal ultrasonography were reviewed. Fetal ultrasonographies were performed with high resolution sonography devices and all the fetal neural abnormalities were recorded.

RESULTS: A total of 32 (0.85%) fetuses with neural abnormalities among 3782 fetal ultrasonographies were detected. Of these 32, six were also confirmed to have fetal neural abnormality by using fast obstetric magnetic resonance imaging. The identified fetal neural abnormalities were as follows: seven Chiari II (0,18%), one Chiari III (0,02%), three Meckel-Gruber syndrome (0,08%), eight anencephaly (0,21%), two schizencephaly (0,05%), two colpocephaly (0,05%), two choroid plexus cysts (0,05%), one arachnoid cyst (0,02%), two Dandy-Walker Malformation with occipital encephalocele (0,05%) and one thoracal meningomyelocele (0,02%).

CONCLUSIONS: The results of this study showed that the overall prevalence of fetal neural abnormalities in the Department of Radiology in Gaziantep University is relevant to current medical literature. However, the prevalence of schizencephaly is remarkably higher than previously reported, which is thought to be due to high sensitivity of high resolution sonography devices used in this study.

Key Words: Prenatal diagnosis, Neural abnormalities, Ultrasonography

Gynecol Obstet Reprod Med;16:1 (12-17)

Introduction

The congenital anomalies of the central nervous system (CNS) occur in approximately 1% of all pregnancies.[1] Modern high-resolution ultrasound equipment yields a unique potential in evaluating normal and abnormal anatomy of the fetal neural axis at very early stages of development.[2] Identification of selected anomalies, such as chiari malformation, schizencephaly, anencephaly and arachnoid cyst, remains a challenge in many cases.

We aimed to determine the prevalence of fetal neural abnormalities diagnosed by sonographic investigation in a tertiary health center in Turkey.

Gaziantep University Faculty of Medicine [1]Department of Radiology, [2]Department of Obsterics and Gynecology, [3]Department of Neurology, Gaziantep

Address of Correspondence: Ayhan Özkur
Gaziantep University Faculty of Medicine
Department of Radiology, Gaziantep
ayhanozkur@yahoo.com

Submitted for Publication: 13.08.2009
Accepted for Publication: 08.12.2009

Material and Method

This is a single center study in which all the prenatal obstetric ultrasonographic imagings obtained in between January 2000 and March 2006 in the Department of Radiology at Gaziantep University Hospital were reviewed retrospectively.

Gaziantep University is a 400 bed, tertiary referral center caring for about 1.5 million people in the South-eastern region of Anatolia.

Ultrasonographic examinations were performed by three different experienced sonographers using 3.5 or 5 MHz transducers and three different high resolution sonography devices (Sonoline Elegra, Siemens, Erlangen, Germany; Sonoline Antares Siemens, Erlangen, Germany; and Applio 80, Toshiba, Tokyo Japan). Sonographic examinations were included a detailed search for associated central nervous system (CNS) and extra-CNS anomalies.

In six of the cases, magnetic resonance imaging was performed for the further confirmation of the diagnoses. Prenatal MRI (Philips 1.5-T Gyroscan Intera; Netherlands) using a balanced fact-field-echo T2-weighted sequence (TR, 4.5 ms; TE,

2.2 ms; time of acquisition, 18 s; flip angle, 60◦; field of view, 270×270 mm; matrix, 256×256) was performed in some of the cases. The Synergy body phased-array coil was used in all cases. Oral sedation or gadolinium based contrast material was not used in any cases.

In each case, the prenatal sonographic findings were compared with the results of postnatal clinical examination and autopsy findings in non-surviving infants.

Results

A total of 3782 fetal ultrasonographies performed between January 2000 and March 2006 found in the archive of the Radiology Department of Gaziantep University were reevaluated. The overall prevalence of the fetal neural abnormalities was detected to be 0.85%. The mean maternal age was 29.2 years (range between 15-41 years) and the mean gestational age at first sonographic suspicion of fetal abnormality was 19 weeks (ranged between 15-36 weeks).

The demographics and the ultrasonographic findings of the fetuses were summarized in table 1. We determined seven Chiari II (0,18%), one Chiari III (0,02%), three Meckel-Gruber syndrome (0,08%), eight anencephaly (0,21%), two schizencephaly (0,05%), two colpocephally (0,05%), two choroid plexus cysts (0,05%), one arachnoid cyst (0,02%), two Dandy-Walker Malformation with occipital encephalocele (0,05%) and one thoracal meningomyelocele (0,02) (table 2).

The lemon sign (scalloping of the frontal bones) were observed in five and corpus callosum agenesis were observed in one of the Chiari II cases, respectively (table 3).

Table 1: Distribution of central nervous system anomalies

Chiari II	7 cases (21,8%)
Chiari III	1 case (3.1%)
Occipital encephalomyelocele	3 cases (9,3%)
thoracal meningomyelocele	1 case (3.1%)
Dandy-Walker Malformation + 4.ventriculocele	2 cases (6.2%)
Meckel-Gruber syndrome	3 cases (9,3%)
anencephaly	8 cases (25%)
schizencephaly	2 cases (6,2%)
choroid plexus cysts	2 cases (6.2%)
Arachnoid cyst	1 case (3.1%)
colpocephaly	2 cases (6,2%)

Table 2: Distribution of maternal and gestational age with central nervous system pathology excluding Chiari II

Maternal age	Gestational week	anomalies	
35 years	15 weeks	Anencephally	
41	22	Anencephally	single UA, hydrocephaly, gibbus
22	19	Anencephally	
40	19	Anencephally	
34	20	Anencephally	
20	15	Anencephally	
23	14	Anencephally	kifoscoliosis
24	20	Anencephally	gibbus,
17	29	Schizencephally	unilateral openloop
24	22	Schizencephally	unilateral openloop
35	17	Choroid plexus cyst	(7 mm- regression at 26. gestational week)
26	22	Choroid plexus cyst	
24	23	Arachnoid cyst	
25	25	Bilateral ventriculomegaly (4 cm) ,	IUGR
27	25	Bilateral ventriculomegaly (4cm)	
21	23	Bilateral ventriculomegaly (1,5 cm)	
17	23	Thoracal meningomyelocele	
26	15	Dandy-Walker malformation+ encephalocele	
40	20	Dandy-Walker malformation+ encephalocele	
31	22	Chiari III (occipital encephalomyelocele)	

UA: uterine artery, IUGR: intrauterine growth retardation

Table 3: Distribution of Chiari II Anomalies

Maternal age	Fetal age	affected area	lemon sing	hydrocephally	other
29 years	30 weeks	Lomber MMC 4 x 2 mm	+	+	
23	28	Lomber MMC		+	
29	21	Sacral MMC	+	+	
26	19	Lumbosacral MMC 5x4 cm	-	colpocephally	
35	25	Lumbosacral MMC4x1x1,5cm	+	+	Corpus callosum agenesis
27	19	Lumbosacral MMC 1,5x0,7cm	+	+	Bilateral hydronephrosis Pleural effusion
26	20	Lomber MMC	+	+	

MMC: meningomyelocele

Six of the fetuses had sonographic extra-CNS anomalies: renal anomaly (three cases), and single umbilical artery (one case). Two of the fetuses had intrauterine growth retardation (IUGR), combined with oligohydramnios in one case.

Twenty five of the cases were detected at second trimester, and seven of the cases were detected at third trimester. Twenty-nine of the pregnancies with no chance of survival such as anencephaly were terminated after parental permissions were obtained. In one of the cases with coroid plexus cyst, detected at seventeenth week, a marked regression of the cyst was observed at the twenty-sixth week and a healthy baby was delivered in term with no detectable abnormality. Two of the fetuses with arachnoid cyst and coroid plexus cyst were persisted ultrasonographically until delivery, which were performed in term with no fatality.

Discussion

Retrospective evaluation of fetal ultrasonography records performed between January 2000 and March 2006 in Gaziantep University Hospital showed that the prevalence of fetal neural abnormalities is 0.85%, which is similar to 1% reported in the world literature.[1-3]

Modern high-resolution ultrasound equipment yields a unique potential in evaluating normal and abnormal anatomy of the fetal neural axis at very early stages of development.[2] However, identification of selected anomalies, such as Chiari malformation, schizencephaly, anencephaly and arachnoid cyst, remains a challenge in many cases.

The prevalence of anencephaly detected in the six years of duration in this study was 0,21% (eight cases). Anencephaly is the most common abnormality affecting the central nervous system and results from failure in closure of neural tube's rostral portion. Its diagnosis in the first trimester is very critical [4,5] Characteristic finding of anencephaly on ultrasonography is flat appearances of brain remnant. When brain remnant appears an irregular bulging structure the term exencephaly is usually preferred.[6] Four out of eight fetuses in this study were diagnosed as exencephaly (Figure 1 a-d).

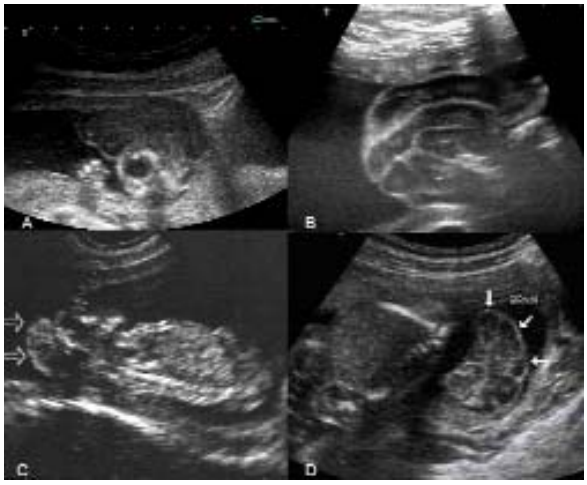

Figure 1a-d. a, Sonogram of fetal head and orbit, b, the disorganization of the anatomy of the brain is clearly seen and it is not covered by skull bones of exencephalic fetus, c, sagittal sonogram of the other case at 15 weeks gestation with anencephaly , d, the thin membrane (arrows) that covers the brain can be easily identified.

A total of seven Chiari II (0,18%) and one Chiari III (0,02%) abnormalities were detected among 3782 fetal ultrasonography during six years of period in this study. Chiari malformations include a group of pathogenetically interrelated abnormalities. Chiari I is the mildest form, which is characterized by caudal extension of the cerebellar tonsils below the foramen magnum, so called tonsillar ectopia.[7,8] Detection of Chiari I malformation by fetal ultrasonography is a challenge. There was no Chiari I malformation detected in this study probably due to diagnostic difficulty.

Chiari II is a more complex malformation in which there are myelomeningoceles, commonly in the lumbosacral region, hydrocephalus, and hypoplasia of the posterior fossa and associated supratentorial findings. All the seven fetuses with Chiari II malformations in this study had lomber or sacral meningomyelocele, and hydro or colpocephally. Four of the

cases with Chiari II malformations had also ultrasonographic findings relevant with "lemon sing" (Figure 2a-d). Other ultrasonographic findings detected in the cases with Chiari II malformations were as follows: corpus callosum agenesis in one case, intrauterine growth retardation from placental insuffiency (uterine artery peak systole / end diastole ratio 2, 7) in one case, and bilateral hydronephrosis in one case.

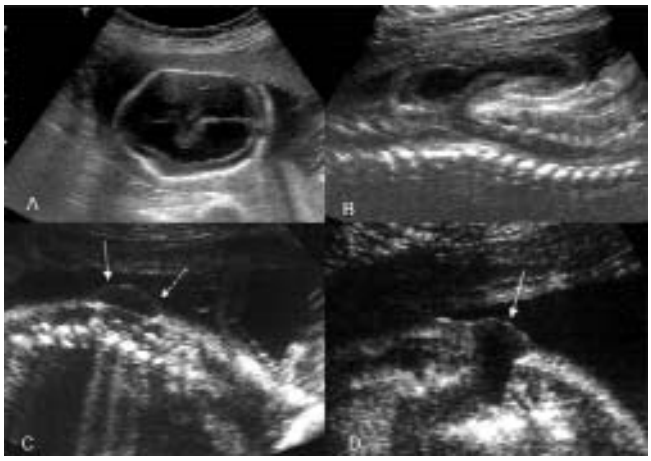

Figure 2a-f: a, b, Chiari II malformation. "Lemon sign" Note the unusual shape of the frontal skull (arrow) c, sagittal and d, axial view, large lomber myelomeningocele at 25 weeks, e, saggital and f, axial view myelomeningocele at 21 weeks gestation.

Chiari III malformation is an extremely rare anomaly. To our knowledge there have been only 22 cases reported in the English medical literature.9,10 Pathogenesis of the malformation is not fully clarified. One fetus in this study was diagnosed as having Chiari III malformation. This case had occipital bone defect and encephalomyelocele on the ultrasonography. We found three different fetuses (0,08%) with occipital encephalomyelocele in this study (figure 3a-d).

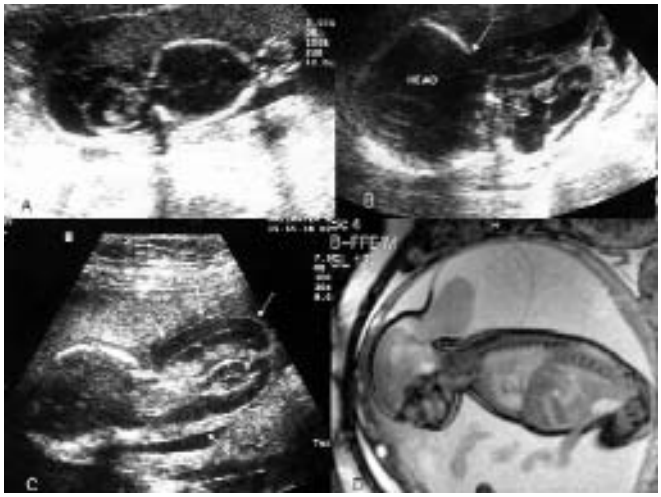

Figure 3a-d: a-c, sonogram demonstrated an occipital bone defect with encephalomyelocele sac at three different gestations and d, saggital plane balance-fast field echo (B-FFE) MR imaging of occipital encephalomyelocele

The detected prevalence of schizencephaly in six years was 0,05% (two cases) in the present study. Schizencephaly is a rare central nervous system malformation. It is one of the least common causes of a cerebrospinal fluid containing abnormalitiy in fetus. Larger lesions are easier to detect by using ultrasonography. However, abnormalities of neuronal migration can only be diagnosed by fetal MRI.[11-13] The diagnosis of schizencephaly in two cases in this study was also confirmed by MRI, which however, provided no additional information to ultrasonographic findings. Both of them had unilateral schizencephalic cleft on the right lateral ventricle (Figure 4 a-d).

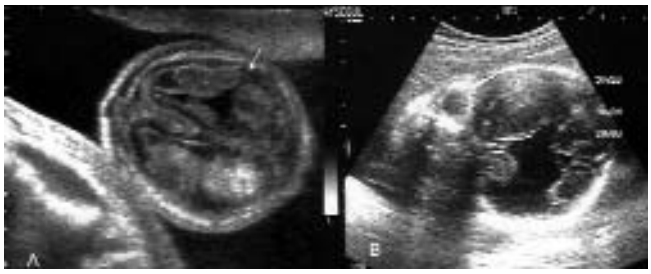

Figure 4a-d: a, Axial US image shows a focal small schizencephalic defect in a 22-week gestation preterm infant. b, coronal US scan in the other case shows an open lip schizencephalic cleft c, axial US scan angled more anteriorly than b shows unilateral cleft. d, coronal B-FFE-weighted MR image shows the right cleft, the defect extends from the ventricle to the pial surface . This appearance could misdiagnosed with porencephaly

The detected prevalence of Meckel-Gruber syndrome in the present study was 0,08% (three fetuses) (Figure 5a-c).

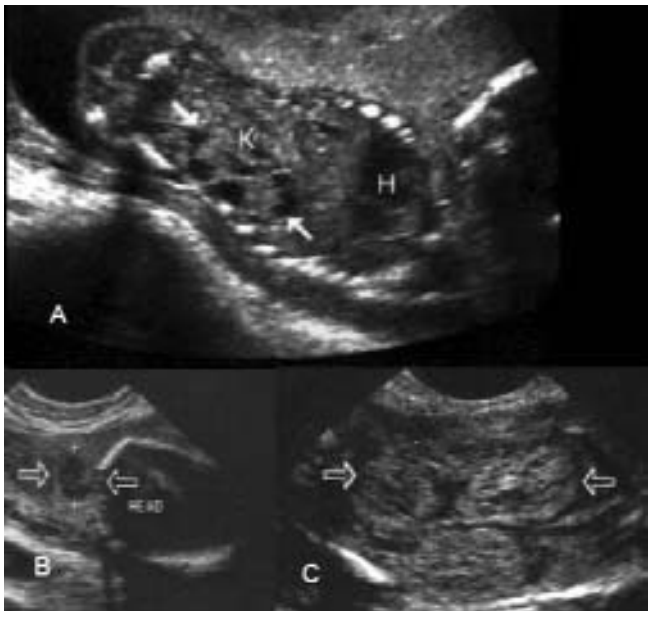

Figure 5a-c: a, Small occipital encephalocele at 21 weeks. b, associated with unilateral multycystic dysplastic kidney and c, infantile type polycystic kidney(arrows) in other case, in a Meckel-Gruber syndrome

Meckel-Gruber syndrome, an autosomal recessive disorder characterized by renal cystic dysphasia, encephalocele and polydactyly.[14,15] The detected abnormalities on ultrasonographic examination in the two cases in the present study showed herniation of the occipital horn through a skull defect to the amniotic cavity and bilateral enlarged kidneys with the renal parenchyma replaced by numerous tiny cysts, suggesting polycystic kidneys. One fetus was with lumbosacral meningomyelocele and unilateral multicytic displastic kidney (Table 4).

Table 4. Distribution of occipital encephalomyelocele

Maternal age	Fetal age	
21 years	27 week	Occipital encephalomyelocele, Hydrocephaly, thoracal MMC(2x1mm)
37	15	Occipital encephalomyelocele
30	20	Occipital encephalomyelocele (2 cm defect 4,5x3cm)

MMC: meningomyelocele

Two fetuses (0,05%) with Dandy-Walker (DW) complex were detected in this study. (Figure 6 a-c).DW complex is defined by a triad of malformations: cystic dilatation of the fourth ventricle, complete or partial agenesis of the cerebellar vermis, and an enlarged posterior fossa with displacement of the tentorium and torcular and lateral sinus.[16-18]

Only one fetus (0,03%) with arachnoid cyst and two fetuses (0,05%) with Choroid plexus cysts (CPC) were found in this study. Arachnoid cysts are benign developmental anomalies that occur in the cerebrospinal axis in relation to the arachnoid membrane. It appears as a transonic nonvascular round-shaped mass, which may occasionally have septa. The location of these masses is more often supratentorial than infratentorial. If the cyst is in the quadrigeminal plate area may simulate a Galenic arterio-venous malformation, Doppler helps to make the differentiation (Figure 7).

CPC are usually a few millimeters in diameter and are commonly located within the body of the plexus. Isolated CPC occur in about 1% of all pregnancies.[19-20] CPC resolve by 26–28 weeks. One of the two CPC in the present study was resolved in the third trimester.

In conclusion, the prevalence of fetal neural abnormalities detected by ultrasonograhic examination in the Department of Radiology in Gaziantep University is similar to world literature. Since detection of such abnormalities is operator and technology dependent, we believe that the continuing development in the medical technology will lead an increase in the prevalence of such fetal abnormalities.

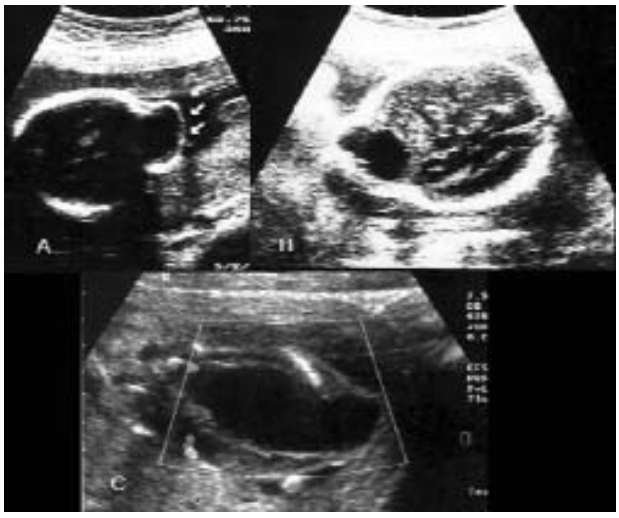

Figure 6 a-c: a, Saggital and b, axial US images show Dandy-Walker malformations and occipital encephalocele. Note abnormal cerebellar vermis in association with a posterior fossa cyst (arrow) c, the other case of DWM.

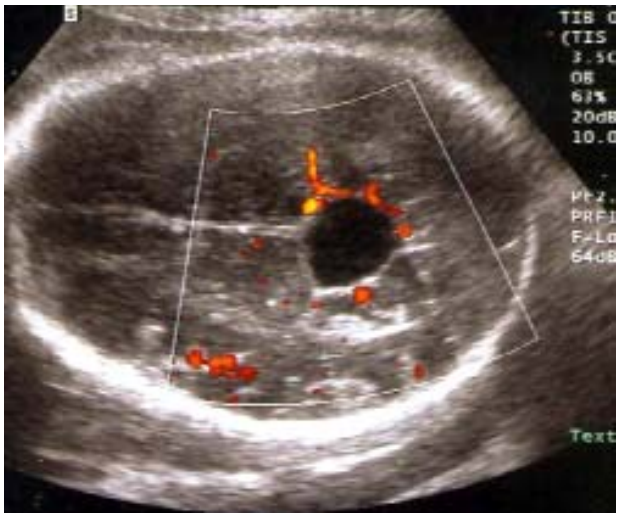

Figure 7: Axial US image shows a arachnoid cyst and this appearance could not be differentiated from a Galenic arteriovenous malformation and Doppler helps make the differentiation.

Güneydoğu Anadolu Bölgesi'nde Ultrasonografi ile Belirlenen Fetal Nöral Anomalilerin Prevalansı

AMAÇ: Bu çalışmanın amacı, Türkiye'de bir Üniversite hastanesinde prenatal ultrasonografi ile belirlenen fetal nöral anomalilerin prevalansını belirlemekti.

GEREÇ VE YÖNTEM: Bu bir tek merkezli retrospektif çalışmadır.Prenatal ultrasonografik görüntülerin tamamı Gaziantep Üniversitesi Tıp Fakültesi Radyoloji Anabilim Dalı'na Ocak 2000 ve Mart 2006 tarihleri arasında gönderilen gebelerin ultrasonografilerinin geriye dönük olarak araştırılması ile elde

edildi.Fetal ultrasonografiler yüksel rezolusyonlu cihazlarla yapıldı ve tüm fetal nöral anomaliler kaydedildi.

BULGULAR: Yapılan 3782 adet fetal ultrasonografi arasında 32 tane (%0,85) fetus nöral anomaliliydi. Bu 32 hastanın, 6 tanesinin nöral anomalisi hızlı obstetric manyetik rözenans görüntülemesi kullanılarak doğrulandı.Belirlenen fetal nöral anomaliler; yedi Chiari II (%0,18), bir Chiari III (%0,02), üç Meckel-Gruber sendromu (%0,08), sekiz anensefali (%0,21), iki şizensefali (%0,05), iki kolposefali (%0,05), iki koroid pleksus kisti (%0,05), bir araknoid kist (%0,02), iki oksipital ensefalosel ve Dandy-Walker malformasyonu (%0,05) ve torakal meningomyelosel (%0,02).

SONUÇ: Bu çalışmanın sonuçları gösterdi ki, Gaziantep Üniversitesi Radyoloji Anabilim Dalı'nda fetal nöral anomalilerin genel olarak prevalansı mevcut tıp literatürü ile uyumluydu. Bununla birlikte, şizensefali prevalansının belirgin derecede yüksek olduğu daha önce rapor edilmişti ve bunun çalışmada kullanılan yüksek rezolusyonlu yüksek sensitiviteli ultrasonografi cihazlarına bağlı olduğu düşünülmüştü.

Anahtar Kelimeler: Prenatal tanı, Nöral anomaliler, Ultrasonography

References

1. Myrianthopoulos NC. Epidemiology of central nervous system malformations. In: Vinken PJi Bruyn GW, eds. Handbook of clinical Neurolgy. Amsterdam: Elsevier; 1977;139-71.
2. Filly RA, Cardoza JD, Goldstein RB, et al. Detection of fetal central nervous system anomalies. A practical level of effort for a routine sonogram. Radiology 1989;172: 403.
3. Fleischer AC, Manning FA, Jeanty F, Romero R. Sonography in Obstetric and Gynecology, principles and practice. Connecticut, Appleton and lange, 1996;375-93
4. Chen CY, Chen FH, Lee CC, Lee KW, Hsiao HS. Sonographic characteristics of the cavum velum interpositum. AJNR Am J Neuroradiol 1998;19:1631-5.
5. Fong KW, Toi A, Salem S, Hornberger LK, Chitayat D, Keating SJ, Mc Auliff F, Johnson SA. Detection of fetal structural abnormalities with US during early pregnancy. Radiographics 2004;24:157-174.
6. Aubry MC, Aubry JP, Dommergues M. Sonographic prenatal diagnosis of central nervous system abnormalities. Childs Nerv Syst 2003;19:391-402.
7. Cama A, Tortori-Donati P, Piatelli GL, Fondelli MP, Andreussi L. Chiari complex in children: neuroradiological diagnosis, neurosurgical treatment and proposal of a new classification (312 cases). Eur JPediatr Surg 1995;5 (Suppl 1): 35-8.
8. Barkovich AJ. Pediatric neuroimaging. Philadelphia: Lippincott Williams and Wilkens, 2000; 327-37.
9. Sirikci A, Bayazit YA, Bayram M. The Chiari III malformation: an unusual and asymptomatic variant in an 11-year old child. Eur J Radiol 2001 Sep; 39 (3):147-50.
10. Çakırer S. Chiari III malformation: varieties of MRI appearances in two patients. Clin Imaging 2003 Jan-Feb;27 (1) :1-4.
11. Oh KY, Kennedy AM, Frias AE Jr, Byrne JL. Fetal schizencephaly: pre- and postnatal imaging with a review of the clinical manifestations. Radiographics 2005; 25(3): 647-57.
12. Huang WM, Monteagudo A, Bennett GL, Fowkes ME, Timor-Tritsch IE. Schizencephaly in a dysgenetic fetal brain: prenatal sonographic, magnetic resonance imaging, and postmortem correlation. J Ultrasound Med 2006;25 (4):551-4.
13. Lituania M, Passamonti U, Cordone MS, Magnano GM, Toma P. Schizencephaly: prenatal diagnosis by computed sonography and magnetic resonance imaging. Prenat Diagn 1989;9(9):649-55.
14. Ergur AT, Tas F, Yildiz E, Kilic F, Sezgin I. Meckel-gruber syndrome associated with gastrointestinal tractus anomaly. Turk J Pediatr 2004;46(4):388-92.
15. Balci S, Teksen F, Dokmeci F, Cengiz B, Comert RB, Can B, Ozdamar S. Prenatal diagnosis of Meckel-Gruber syndrome and Dandy-Walker malformation in four consecutive affected siblings, with the fourth one being diagnosed prenatally at 22 weeks of gestation. Turk J Pediatr 2004; 46 (3): 283-8.
16. Phillips JJ, Mahony BS, Siebert JR, Lalani T, Fligner CL, Kapur RP. Dandy-Walker Malformation Complex: Correlation Between Ultrasonographic Diagnosis and Postmortem Neuropathology. Obstet Gynecol 2006; 107 (3): 685-693.
17. Teksam M, Ozyer U, McKinney A, Kirbas I, Cakir B. Fetal MRI of a severe Dandy-Walker malformation with an enlarged posterior fossa cyst causing severe hydrocephalus. Fetal Diagn Ther 2005;20 (6):524-7.
18. van Baalen A, Versmold H. Choroid plexus cyst: comparison of new ultrasound technique with old histological finding. Arch Dis Child 2004;89:426.
19. Osborn AG, Blaser SI, Salzman KL, et al. Diagnostic imaging: brain. Part I, sections 1-7. Salt Lake City, Utah: Amyrsis, 2004
20. Sahinoglu Z, Peker H, Etker S, Celayir A, Cesur S. Difficulties in perinatal diagnosis of fetal thoracic foregut cysts: report of two cases.J Obstet Gynaecol. 2005 Feb; 25(2):211-4.