# Prenatal Diagnosis and Management of Congenital Abnormalities of Central Nervous System

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Among the congenital anomalies, central nervous system malformations are the most commonly seen ones whose antenatal sonographic diagnosis is very important. Sixteen cases, attempted to Karaelmas University Obstetrics Clinic, diagnosed as having central nervous system anomaly were presented. Ultrasonographic screening is a noninvasive method that should be recommended to all pregnant women. Second trimester ultrasonography is generally performed between 20-22 gestational weeks in order to detect fetal structural defects. In the early antenatal period the ultrasonographic diagnosis of major and minor anomalies will provide the chance of giving genetic counseling to families.
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**Key Words:** Central nervous system anomaly, Prenatal diagnosis, Ultrasonography

Central nervous system (CNS) anomalies are seen approximately 1/100 incidence second only to cardiovascular system anomalies. Fetal CNS is known to undergo major developmental changes throughout the gestation and some time after gestation. Therefore it is crucial to have a working knowledge of CNS embryology in order to perform prenatal ultrasonographic diagnosis of CNS abnormalities. Besides its frequency, most congenital CNS anomalies are usually carrying poor prognosis. Therefore CNS examination should be examined in all diagnostic ultrasonographic studies. Since associations with other congenital and genetic abnormalities antenatal diagnosis and genetic counseling are also necessary.[1]

CNS is the first organ system begins to develop in embryo. It is also the last one that completes development postnatally. For these reason teratogenic effects, maternal diseases and infectious causes could affect CNS at almost any time throughout the pregnancy. After the completion of early development of brain, most of the abnormalities were already established. Therefore it is also important to know etiologic causes and eliminate them prenatally to prevent CNS abnormalities. Current technology enables only early diagnosis of congenital abnormalities. Therefore elimination of CNS abnormalities generally depends on early diagnosis and termination of pregnancy in severe CNS malformations.[1]

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In this review we report most recent diagnoses of CNS abnormalities in our clinic and discuss their management with the current guidelines.

**CASES**

**Case 1: Arnold Chiari (Chiari II)**

Twentythree year-old G: 2 P: 0 A: 1 woman without any significant obstetric risk factor was followed until 20th week of gestation. Ventriculomegaly, lemon sign, spina bifida located in the lumbar region was detected with second trimester ultrasonographic examination. Interventricular distance mas measured as 12 mm. After counseling the parents with the presumptive diagnosis of Chiari type II (Arnold Chiari) malformation termination of pregnancy was decided. Pregnancy was terminated in another institution due to insurance problems.

**Case 2: Arnold Chiari (Chiari II)**

Twentyfour year-old G: 1 P:0 pregnant woman referred with the diagnosis of hydrocephalus at 21st week of gestation. Ultrasonographic scan revealed spina bifida at sacral region, ventriculomegaly, and lemon sign in the cranial region (Figure 1A-B). Corpus callosum couldn't be visualized and interventricular distance was measured 14 mm. Intrauterin growth restriction was also diagnosed in this fetus. Pregnancy was terminated with the diagnoses of Chiari II malformation (Arnold Chiari) diagnoses. Further follow-up and termination of pregnancy was performed in referring center.

**Case 3: Choroid Plexus Cysts**

During routine follow-up of uncomplicated pregnancy of 29 year-old G2P1L1 patient bilateral multiple choroid plexus cyst was detected at 18 weeks of gestation (Figure 2A). Ultrasonographic examination of other organ systems was normal. Previous nuchal translucency (performed at 13th weeks of gestation) was 1.5 mm. Triple screening was also within normal range. Amniocentesis was performed and resulted as normal. At 38th gestational weeks, the female baby was born without any complication.

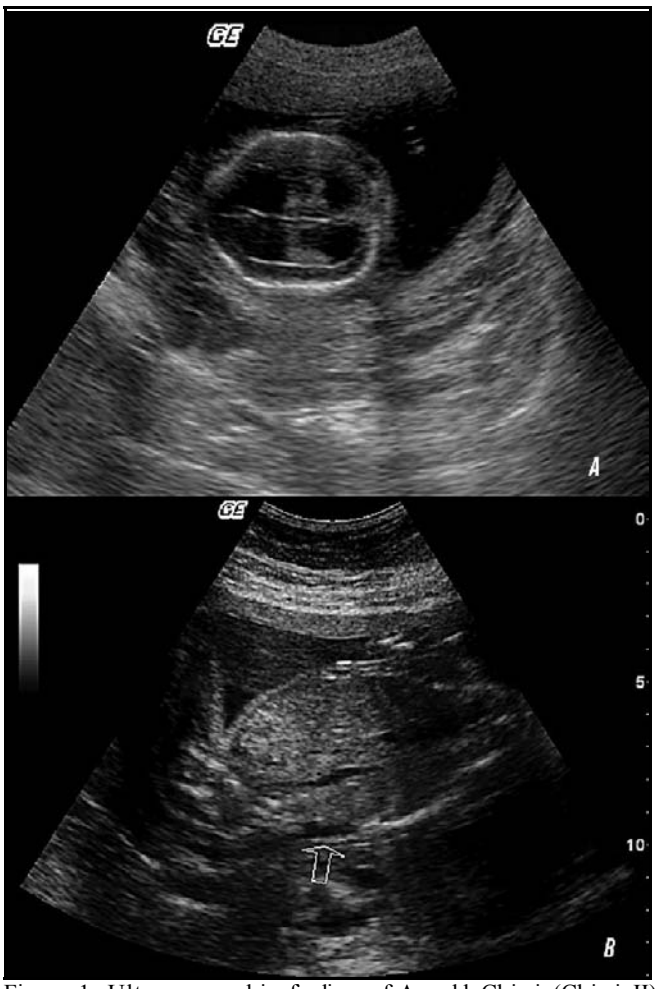


Figure 1. Ultrasonographic finding of Arnold Chiari (Chiari II) malformation A: Ventriculomegaly, lemon sign B: Spina bifida located in the lumbar region.

**Case 4: Dandy-Walker Syndrome**

A late admission pregnancy was referred to our clinic from a clinic in rural area with the diagnosis of hydrocephalus. 32 year-old women with 37-week gestation according to last menstrual period were hospitalized after ultrasonographic detection of posterior fossa cyst, severe ventriculomegaly and hypoplasia of cerebellar vermis (Figure 2B). Agenesis of corpus callosum was also detected. Neurosurgical consultation was ordered with prenatal diagnosis of Dandy-Walker syndrome. After planned caesarean section at 38-week of gestation the diagnosis of Dandy-Walker syndrome was confirmed with cranial magnetic resonance imaging. Ventriculoperitoneal shunt was implanted by neurosurgical department.

**Case 5: Hemivertebra**

Hemivertebra was detected in 26 year-old women during routine ultrasonographic examination at 20$^{th}$ week of gestation. Level of vertebral abnormality was reported at T12-L1 and no other associated abnormality was detected (Figure 2C-D). After genetic consultation karyotype analysis was performed with amniocentesis. Karyotype was found to be normal. After discussion with family about possible outcomes pregnancy was continued.

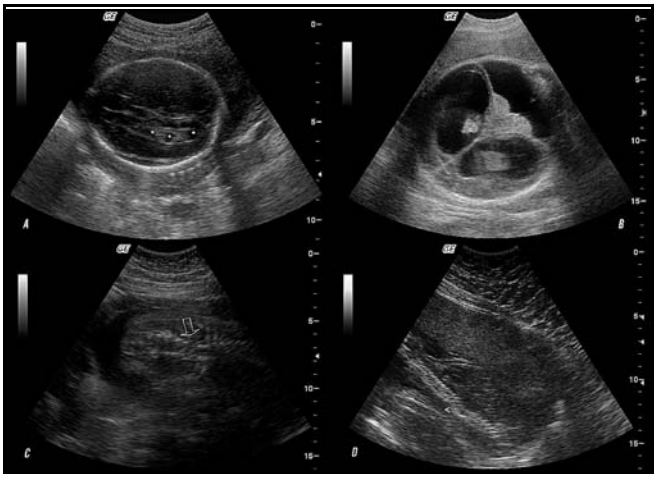


Figure 2. Ultrasonographic Finding of Dandy-Walker Syndrome, Choroid Plexus Cyst, Hemivertebra (A Multiple Choroid Plexus Cysts;B- Dandy-Walker Syndrome- ventriculomegaly and hypoplasia of cerebellar vermis; C Hemivertebra at T12-L1 region).

**Case 6: Ventriculomegaly, spina bifida**

Twentytwo year-old G 3 P 1 A 1 pregnant woman referred with the diagnosis of ventriculomegaly at 28th week of gestation. Ultrasonographic scan revealed ventriculomegaly (figure 3A), (interventricular distance was measured 20.5 mm), and spina bifida located in the lumbar region (Figure 3B). Pregnancy was terminated with the diagnoses of ventriculomegaly and spina bifida.

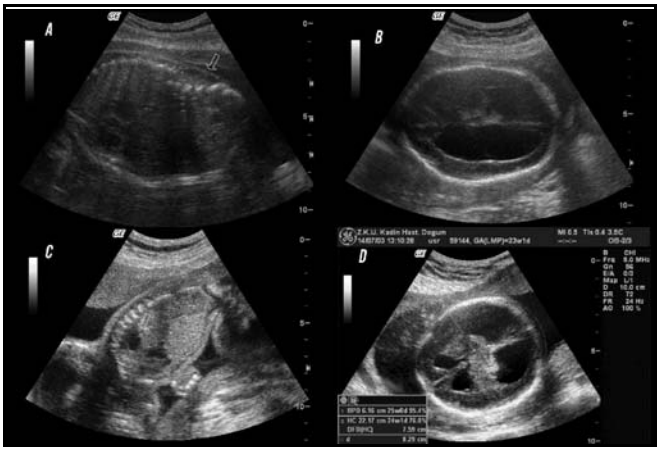


Figure 3. Ultrasonographic Finding of A Ventriculomegaly; B Spina bifida located in the lumbar region; C Diaphragmatic hernia; D Hydrocephalus and ventriculomegaly.

**Case 7: Hydrocephalus, diaphragmatic hernia**

Twentynine year-old G 5 P 3 D/C1 pregnant woman referred to our obsterics outpatient clinic with the diagnosis of hydrocephalus at 21$^{st}$ week of gestation. Ultrasonographic examination revealed as diaphragmatic hernia (Figure 3C),

hydrocephalus, ventriculomegaly (Figure 3D), (interventricular distance was measured as 22 mm), and polyhdramnios. Pregnancy was terminated and fetus was diagnosed as hydrocephalus, diaphragmatic hernia and polyhdramnios.

**Case 8: Anencephaly, spina bifida, cleft lip**

Twenty year-old G 1 P0 pregnant woman referred with the diagnosis of anencephaly at 21st week of gestation. Ultrasonographic examination revealed anencephaly, spina bifida located in the lumbatoroca-servical region and cleft lip (Figure 4A) .Pregnancy was terminated with the diagnoses of anencephaly, spina bifida and cleft lip.

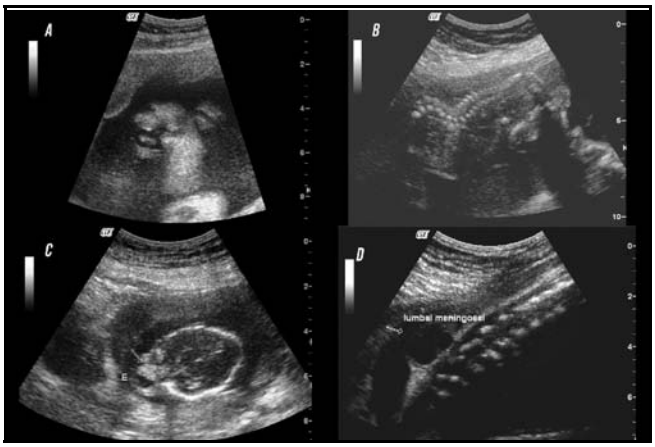


Figure 4. Ultrasonographic finding of A Cleft Lip; B Anencephaly and Spina Bifida; C Occipital Encephalocel; D Lumbosacral Meningocele Sac.

**Case 9: Iniencephaly, spina bifida**

Nineteen year-old G 1 P0 pregnant woman referred with the diagnosis of anencephaly at 15st week of gestation. Ultrasonographic scan revealed iniencephaly, spina bifida located in the lumbotorocaservical region. Pregnancy was terminated with the diagnoses of iniencephaly, spina bifida. Autopsy was identical with intrauterine diagnosis

**Case 10: Acrania and gastroshisis**

Twentyseven year-old G 1 P0 pregnant woman attended to our outpatient clinic of obsterics. Ultrasonographic scan revealed acrania and gastroshisis at 16th week of gestation. Pregnancy was terminated with the diagnoses of acrania.

**Case 11: Bilateral ventriculomegaly**

Nineteen year-old G1 P0 pregnant woman referred with the diagnosis of bilateral ventriculomegaly at 31st week of gestation. Ultrasonographic scan revealed bilateral ventriculomegaly, (interventricular distance was measured riht 15.9 mm, left 18.2 mm).After discussion with family about possible outcomes pregnancy was continued. At 40th gestational weeks, the female baby was born without any complication. Postpartum neurological examination was normal.

**Case 12: Hydrocephalus, lumbosacral myelomeningocele**

A late admission pregnancy was referred to our clinic from a clinic in rural area with the diagnosis of hydrocephalus. Thirty-eight year-old women was at 32 gestationional week. Ultrasonographic scan revealed hydrocephalus (biparietal diameter 93 mm, cortical thickness 7.5 mm) and lumbosacral myelomeningocele. Planned caesarean section was made at 38-week of gestation. One day after; ventriculoperitoneal shunt was implanted and meningocele sac was closed by neurosurgical department.

**Case 13: Hydrocephalus, corpus callasum agenesis, spina bifida**

Thirty five years old pregnant women G2P1A1 with the pre-diagnosis of neural tube defect was attended to our outpatient clinic of obstetrics. Ultrasonographic examination was revealed as hydrocephaly, corpus callasum agenesis, spina bifida and microgynati at 22nd week of gestation age. Termination was advised and 520 gr ex male fetus was born.

**Case 14: Anencephaly, spina bifida**

Thirty one years old twin pregnancy G3P2 L2 was referred as one fetus with anencephaly and the other one with normal appearance at 18th weeks of gestation. Utrasonograpic examination was revealed as dichorionic-diamniotic twin pregnancy. Intraabdominal ascites, pericardial effusion, anencephaly and spina bifida (Figure 4B) was diagnosed in one of the twin. The other twin was normal in appearance. The fetus with anomaly was terminated. The normal fetus was born at 38th of gestational age with caesarean section.

**Case 15: Occipital encephalocel**

Twenty years old pregnant women G2P1 was admitted to our outpatient clinic of obstetrics at the 16th weeks of gestation. Ultrasonographic examination was revealed as occipital encephalocel (Figure 4C), small mouth and jaw, and cardiac hyperechogenic focus. After the family counseling, termination was made.

**Case 16: Lumbosacral meningocele**

Thirty three years old woman G7P3A3 was admitted our hospital at the 37th gestational week. At sonographic examination, lumbosacral meningocele sac (Figure 4D) was diagnosed. Caesarian section was made with indication of fetal stress. The meningocele was repaired at 40th postpartum day by neurosurgery department.

## Discussion

Central nervous system abnormalities were seen in 1-3% of live births.[1] However this rate increases to 40% in stillbirths. Etiology of developmental abnormalities ranges from genetic causes to environmental factors that affect develop-

ment. Most of the abnormalities related with development neural tube occur in the first 28 days of gestation. On the other hand abnormalities related with the cellular proliferation and migration usually takes place after 28th day of gestation.

Incidence of fetal ventriculomegaly changes from 0.3/1000 to 1.5/1000 in some series. The term fetal ventriculomegaly defines an abnormal finding irrespective of etiology. Therefore includes numerous pathologies with heterogeneous etiologies. In general mechanism that leads to development of ventriculomegaly might be secondary to following: obstruction of normal circulation of cerebrospinal fluid, hypersecretion of CSF, defective filtration, and abnormal development of intracranial structures.

The most common cause of fetal hydrocephalus is obstruction of CSF circulation. Hydrocephalus could be classified according to level of obstruction: noncommunicating intraventricular hydrocephalus (aqueductal stenosis, Dandy-Walker malformation, intracranial mass) and communicating-extraventricular hydrocephalus (Chiari malformation, encephalocele, fibrosis secondary to intracranial hemorrhage).Throughout the gestation fetal brain and lateral ventricles undergo structural changes that cause different ultrasonographic appearance at different gestational weeks. Therefore in order to prevent false positive diagnosis size and shape of ventricles at specific time period should be known.[2,3] Atrial measurements in axial plane are the simplest and best method for diagnosis of ventriculomegaly. Measurements up to 10 mm are interpreted as normal. In the absence of associated abnormalities measurements between 10-14 mm are considered intermediate and follow-up is required. Fetal or perinatal death and neurodevelopment in survivors are directly related to the presence of other malformations and chromosomal defects. Although mildventriculomegaly is generally associated with a good prognosis, affected fetuses form the group with the highest incidence of chromosomal abnormalities (often trisomy 21). Fifteen mm and greater measurements are diagnosed as ventriculomegaly.[4] Most common causes of fetal ventriculomegaly are aqueductal stenosis (33-43%), Chiari II malformation (25-30%), Dandy-Walker syndrome and corpus callosum agenesis (7-10%) 5.

After 2nd week of gestation neural plate and neural tube begins development from ectoderm. Forebrain (proencephalon), midbrain (mesencephalon) and hindbrain (rhombencephalon) are formed at 25-28 days of gestation in the rostral part of neural tube. These parts differentiate into prosencephalon, telencephalon and diencephalon after 6th week of development. These structures later form cortex, hemispheres, thalamus and hypophysis. Inner parts of mesencephalon originate from mesencephalon. Rhombencephalon gives rise to pons, cerebellum and medulla oblongata.[6]

During the period of 2-5th weeks in which dorsal induction takes place anencephaly, myelocele, Arnold-Chiari I-II malformations may develop. Similarly ventral induction takes place during the period of 5-10th weeks of gestation. Dandy-Walker malformation, holoprosencephaly, cerebellar hypoplasia, Arnold-Chiari IV malformations might develop during this period of development.[6,7]

## CHIARI MALFORMATIONS

Prof. Hans Chiari is a german pathologist, first defined the malformation. It is defined as a neuronal migration defect characterized by cerebellar displacement. According to severity it is divided into 4 types. These types are not related embryologically and anatomically. Chiari II, III and IV are life threatening abnormalities that are typically diagnosed antenatally. However Chiari I malformation might not be diagnosed until 24.9±15.8 weeks of gestation.[8]

### Chiari I malformation

The malformation is defined as greater than 5 mm downward herniation of cerebellar tonsils through foramen magnum.[9] Hydrocephalus seen in 90% of patients and in 30-40% associated with syrenomelic cavity. In this spectrum this is the mildest form of anomaly. Cerebellar tonsils and sometimes medulla might elongate towards the lower limit of foramen magnum. Posterior fossa is small and clivus is short. There is a relation between size of posterior fossa and cerebellar ectopy.[6]

### Chiari II malformation (Arnold-Chiari malformation)

In addition to Chiari I there is caudal displacement of 4th ventricle. It is most commonly seen abnormality. Fourth ventricle frequently located below medulla oblangata, posterior to spinal cord as a cystic structure.[10,11] Size of posterior fossa is small and cisterna magna is flattened. Due to lower displacement of cervical spinal cord upper cervical nerve roots tensioned in their foramina.[12] A characteristic folding in cervicomedullary junction is seen in 70% of cases. Lumbar myelocele and similar congenital abnormalities might be associated. Meningomyelocele is seen in 80% of patients and might cause hydrocephalus.[13] Hydrocephalus risk is proportional to degree of rostral location.[6]

### Chiari III malformation

It is characterized by the herniation of all posterior fossa structures and brain stem into encephalocele. This is an uncommon form of this malformation.[14]

### Chiari IV malformation

It is characterized by hypoplasia of cerebellum. Some authors consider this entity as a variant of Dandy-Walker malformation.[15]

## DANDY-WALKER COMPLEX

Dandy-Walker syndrome is a complex cerebellar vermis anomaly that is characterized by cystic dilatation of 4th ventricle and enlargement of cisterna magna. Dandy-Walker

complex is divided into three groups: first, Dandy-Walker malformation (partial or total agenesis of cerebellar vermis, cystic dilatation of posterior fossa and hydrocephalus).[16] Second, Dandy-Walker variant (partial agenesis of cerebellar vermis and cystic dilatation of fourth ventricle without enlargement of posterior fossa).[17] Third, Mega cisterna magna (cystic dilatation of fourth ventricle without dilatation of posterior fossa and normal cerebellar vermis).

Dandy-Walker malformation is seen in 1/30,000 live births. Hydrocephalus might be absent at birth and might develop later in life. Dilatation of lateral ventricle is not the same extent as dilatation of 4th ventricles. Most commonly associated abnormality is the absence of corpus callosum.[18] Ultrasonographic diagnosis depends on the demonstration of dilated 4th ventricle and associated total or partial vermal agenesis.[15,19,20] Diagnosis of mega cysterna magna is attributed by means of measurement of the distance between cerebellar vermis and inner border of occipital bone greater than 10 mm.

**HEMIVERTEBRA**

Hemivertebra or butterfly shaped vertebra is developed secondary to a defect in the formation of vertebral segment. Hemivertebra creates a bridge in the vertebral column that causes bending in the opposite direction. However hemivertebra located in the lower lumbar and sacral levels does not cause a deformity. Prenatal ultrasonographic findings include asymmetric vertebral body in sagittal or coronal planes and focal defect in the vertebral colon in either sides of axial plane.[21] Since vertebral anomalies can frequently be seen in association with VATER or VACTERL syndromes, all other organ systems must be investigated carefully when such anomalies are encountered.[22] Prenatal diagnosis of vertebral anomalies could help earlier recognition of problems like scoliosis or kyphoscoliosis and planning for treatment.[23]

**CHOROID PLEXUS CYST**

These cysts are usually bilateral and located in the choroid plexus in the lateral cerebral ventricle. These sonolucent areas are actually developing fetal choroid plexus and do not contain any cystic areas. Generally these cysts are detected in 16-18 weeks of gestation.[24] Prevalence is about 2% in 20 weeks of gestation. Most of these cysts (90%) resorbed until 26 weeks of gestation.25 Ultrasonographic detection of single cyst greater than 2 mm diameter or multiple cysts is a significant finding. Cysts might be multiloculated and borders might be irregular. Larger cysts might cause ventricular dilatation.[26]

Isolated choroid plexus cysts are seen in 1% of all pregnancies. Chromosomal abnormalities are seen in 1-2% of these cases.[27,28] Choroid plexus cysts are frequently seen in trisomy 18 (Edward's syndrome), trisomy 21 (Down syndrome) and other chromosomal abnormalities.[29] Risk of trisomy 18 is increased in patients with choroid plexus cyst associated other congenital abnormalities. Therefore careful ultrasonographic examination and karyotype analysis are required in fetuses with choroid plexus cyst.[30,31]

In conclusion widespread use of prenatal ultrasonography enabled early diagnosis of congenital fetal central nervous system abnormalities. Craniospinal abnormalities are most frequent diagnoses. In suspected cases serial determination for measurement might be required. Associated congenital abnormalities might indicate a karyotype examination due to increased risk of chromosomal abnormalities. In mild defects careful consultation with family is necessary. In this report we presented our experience with consecutive diagnoses of 5 patients with ultrasonographic detection of fetal central nervous system abnormalities.

**NEURAL TUBE DEFECTS**

The prevalence of neural tube defects which include anencephaly, spina bifida and cephalocele is about 5 per 1.000 births. Encephaloceles are cranial defects, frequently occipital, with herniated fluid-filled or brain-filled cysts. In spina bifida the neural arch, commonly in the lumbosacral region, is incomplete with resulting damage to the exposed nerves. In anencephaly, the cranial vault is absent (acrania) with secondary degeneration of the brain.[32] The exact etiology for the majority of these defects is unknown. Chromosomal abnormalities, single mutant genes, and maternal diabetes mellitus or ingestion of teratogens, such as antiepileptic drugs, are concerned in about 10% of the cases. The risk of recurrence is about 5-10%. The diagnosis of anencephaly is revealed as absent cranial vault and cerebral hemispheres. But, the facial bones, brain stem and portions of the occipital bones and mid brain are frequently present. Spinal lesions are found in up to 50% of cases of anencephaly.[32]

Diagnosis of spina bifida necessitates the systematic examination of each neural arch from the cervical to the sacral region both transversely and longitudinally. In the transverse scan the normal neural arch appears as a closed circle with an intact skin covering, but in spina bifida the arch is "U" shaped and an associated bulging meningocele (thin-walled cyst) or myelomeningocoele are found. The diagnosis of spina bifida has been significantly increased by the recognition of related abnormalities in the skull and brain. These anomalies are resulting to the Arnold-Chiari malformation and include frontal bone scalloping (lemon sign), and obliteration of the cisterna magna with either an "absent" cerebellum or abnormal anterior curvature of the cerebellar hemispheres (banana sign).[33]

Anencephaly is fatal. In cephalocele the prognosis is inversely related to the amount of herniated cerebral tissue; the neonatal mortality is about 40% and more that 80% of survivors are intellectually and neurologically handicapped. In spina bifida the survivors are strictly handicapped, with

paralysis in the lower limbs and double incontinence; despite the associated hydrocephalus requiring surgery, intelligence may be normal.[34]

**AGENESİS OF CORPUS CALLOSUM**

The corpus callosum is a bundle of fibers, joins the two cerebral hemispheres. It develops at 12-18 weeks of gestation. Agenesis of the corpus callosum is established in about 5 per 1.000 births, it may be either complete or partial (usually affecting the posterior part). Agenesis of the corpus callosum may be due to maldevelopment or resulting to a destructive lesion. It is usually coupled with chromosomal abnormalities (usually trisomies 18, 13 and 8) and more than 100 genetic syndromes. In about 90% of those with isolated agenesis of the corpus callosum, development is normal.[35]

**HOLOPROSENCEPHALY**

This is a spectrum of cerebral abnormalities resulting from partial cleavage of the forebrain and found in about 1 per 10,000 births. Three types according to the degree of forebrain cleavage are present. The alobar type, which is the most rigorous, is characterized by a monoventricular cavity and fusion of the thalami. Semilobar type is characterized by partial segmentation of the ventricles and cerebral hemispheres posteriorly with incomplete fusion of the thalami. In lobar holoprosencephaly there is normal separation of the ventricles and thalami but deficiency of the septum pellucidum. The first two types are usually accompany by microcephaly and facial abnormalities.[36] Even though in many cases the cause is a chromosomal abnormality (usually trisomy 13) or a genetic disorder with an autosomal dominant or recessive mode of transmission, in many cases the etiology is unidentified. For sporadic, non-chromosomal holoprosencephaly, the empirical reappearance risk is 6%. In the transverse view of the fetal head for measurement of the biparietal diameter there is a single dilated midline ventricle replacing the two lateral ventricles or incomplete segmentation of the ventricles. The alobar and semilobar types are frequently coupled with facial defects, such as hypotelorism or cyclopia, facial cleft and nasal hypoplasia or proboscis.[37]

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