NORMAL SONOGRAPHIC ANATOMY

The fetal brain undergoes major developmental changes throughout pregnancy. Fetal neurosonography demands a thorough knowledge of ontogeny of the brain. If one is unaware of the normal developmental changes of the brain, both missed as well as false positive diagnosis will be the result.1

Transvaginal high-resolution sonography reveals surprising details of the fetal anatomy. At 7 weeks of gestation, a sonolucent area is seen in the cephalic pole, presumably representing the fluid-filled rhombencephalic vesicle. At 9 weeks, demonstration of the convoluted pattern of three primary cerebral vesicles is feasible. From 11th week, the brightly echogenic choroid plexuses filling the large lateral ventricles are the most prominent intracranial structures.2 In the early second trimester, the lateral ventricles and choroid plexuses decrease in size relative to the brain mass (Figs 1 and 2).

Examination of the fetal brain can essentially be carried out by two transverse planes, commonly referred to as the transventricular and the transcerebellar plane (Fig. 3). The transventricular plane (Fig. 4), obtained by a transverse scan at the level of the cavum septum pellucidum, will demonstrate lateral borders of the anterior (or frontal) horns, medial and lateral borders of the posterior horns (or atria) of lateral ventricles, choroid plexuses and Sylvian fissures. It is used to measure the biparietal diameter, head circumference and the width of ventricles. The transcerebellar (or suboccipito-bregmatic) view allows examination of the mid brain and posterior fossa. This view is used for measurement of the transverse cerebellar diameter and the width of cistern magna.
Fig. 2: Transverse views of the cephalic pole normal embryos at 7 to 12 weeks. At 7 weeks, the rhombencephalic vesicle is the dominant structure. At 9 weeks the prosencephalic vesicle is seen in front of the rhombencephalon. At 12 weeks the cerebral hemispheres have greatly developed, and it is possible to appreciate the midline as well as the large echogenic choroid plexus filling the cavity of the ventricles.

Fig. 3: The two axial planes recommended for the standard sonographic examination of the fetal brain.

Fig. 4: Transventricular view showing the cavum septum pellucidum and the thalami.

Fig. 5: Schematic representation of the scanning planes commonly used for the evaluation of fetal cerebral anatomy.

Fig. 6: Transabdominal axial view demonstrating the circle of Willis.
Additional scanning planes along with different orientations may be required from time to time to better define subtle details of intracranial anatomy better in selected cases. Reverberation artifacts usually obscure the cerebral hemisphere close to the transducer. Visualization of both cerebral hemispheres would require sagittal and coronal planes that are often difficult to obtain and may require vaginal sonography (Fig. 5). Color Doppler sonography helps in the diagnosis of lesions (Fig. 6).

Luckily, unilateral cerebral lesions are rare and often associated with a shift in the midline echo. Therefore, we adhere to the approach that in standard examination only one hemisphere is seen, and symmetry is assumed unless otherwise proven.

A sagittal and coronal view of the entire fetal spine should be obtained in each case. In the sagittal plane, the normal spine has a ‘double railway’ appearance and it is possible to appreciate the intact soft tissues above it. In the coronal plane, three ossification centers of the vertebra form three regular lines that tether down into the sacrum. These views are used to assess the integrity of the vertebrae (to rule out spina bifida) and the presence and regularity of the whole spine (to rule out sacral agenesis and scoliosis) (Fig. 7).

**NEURAL TUBE DEFECTS**

These include anencephaly, spina bifida and cephaloceles. In anencephaly, there is absence of the cranial vault (acrania) and telencephalon with secondary degeneration of the brain. Cephaloceles (encephalocele) are cranial defects, usually occipital, with herniated fluid-filled or brain-filled cysts. In spina bifida, the neural arch, usually in the lumbosacral region, is incomplete with secondary damage to the exposed nerves.

**Prevalence**

This is subject to large geographical and ethnic variations. In the United Kingdom, the prevalence is about 5 per 1,000 births. Anencephaly and spina bifida, with an approximately equal prevalence, account for 95% of the cases and cephaloceles for the remaining 5%.

**Etiology**

Chromosomal abnormalities, single mutant genes, and maternal diabetes mellitus or ingestion of teratogens, such as antiepileptic drugs, are implicated in about 10% of the cases. However, the precise etiology for the majority of these defects is unknown. When a parent or previous sibling has had a neural tube defect, the risk of recurrence is 5 to 10%. Periconceptual supplementation of the maternal diet with folate reduces by about half the risk of developing these defects.

**Diagnosis**

The diagnosis of anencephaly during the second trimester of pregnancy is based on the demonstration of absent cranial vault and cerebral hemispheres. However, the facial bones, brain stem and portions of the occipital bones and midbrain are usually present. Associated spinal lesions are found in up to 50% of cases. In the first trimester, the diagnosis can be made after 11 weeks when ossification of the skull normally occurs. Anencephaly is considered to be the final stage of acrania, as a consequence of disruption of abnormal brain tissue unprotected by the calvarium (Figs 8 and 9). In the first trimester, the pathognomonic feature is acrania, the brain being either entirely normal or at varying degrees of distortion and disruption. Most anencephalics have normal eyes. The orbits are often shallow causing protrusion of the eyes. The forebrain is then replaced by an angiomatous mass with multiple cavities containing CSF.3

Diagnosis of spina bifida requires 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 whereas in spina bifida the arch is “U” shaped and there is an associated bulging meningocele (thin-walled cyst) or myelomeningocele (Fig. 10). The extent of the defect and any associated kyphoscoliosis are best assessed in the longitudinal scan (Fig. 11).

The diagnosis of spina bifida has been greatly enhanced by the recognition of associated abnormalities in the skull and brain. These abnormalities are secondary 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).4 A variable degree of ventricular enlargement is present in virtually all cases of open spina bifida at birth, but in only about 70% of cases in the midtrimester.
Encephaloceles are recognized as cranial defects with herniated fluid-filled or brain-filled cysts. They are most commonly found in an occipital location (75% of the cases) but alternative sites include the frontoethmoidal and parietal regions (Fig. 12).

**Prognosis**

Anencephaly is fatal at or within the hours of birth. In cephalocele, the prognosis is inversely related to the amount of herniated cerebral tissue. Overall the neonatal mortality is about 40% and more that 80% of survivors are intellectually and neurologically handicapped. In spina bifida, the surviving infants are often severely handicapped with paralysis in the lower limbs and double incontinence. Despite the associated hydrocephalus requiring surgery, intelligence may be normal.\(^5\)

**Fetal Therapy**

There is some experimental evidence that *in utero* closure of spina bifida may reduce the risk of handicap because the amniotic fluid in the third trimester is thought to be neurotoxic.

**VENTRICULOMEGALY AND HYDROCEPHALUS**

In hydrocephalus, there is pathological increase in the size of cerebral ventricles.

**Prevalence**

Hydrocephalus is found in about 2 per 1,000 births. Ventriclemegaly (lateral ventricle diameter of 10 mm or more at the level of the glomus of choroid plexus) is found in 1% of pregnancies at the 20 to 23 week scan. Therefore, the majority of fetuses with ventriculomegaly do not develop hydrocephalus.

**Etiology**

This may result from chromosomal and genetic abnormalities, intrauterine hemorrhage or congenital infection, although many cases have as clearcut etiology yet no. With time, it has become increasingly clear that a variable degree of enlargement of the ventricles is shared by a wide variety of anomalies different
from obstructive hydrocephalus, and that ventriculomegaly can be regarded as a general marker of abnormal brain development.

**Diagnosis**

Fetal hydrocephalus is diagnosed sonographically, by the demonstration of abnormally dilated lateral cerebral ventricles.6 Certainly before 24 weeks and particularly in cases of associated spina bifida, the head circumference may be small rather than large for gestation. A transverse scan of the fetal head at the level of the cavum septum pellucidum will demonstrate the dilated lateral ventricles, defined by a diameter of 10 mm or more at the level of glomus of choroid plexus. The choroid plexuses, which normally fill the lateral ventricles, are surrounded by fluid. A distinction is usually made between mild, or borderline, ventriculomegaly (diameter of the posterior horn 10-15 mm) and overt ventriculomegaly or hydrocephalus (diameter greater than 15 mm)7 (Figs 13A and B).

**Prognosis**

Fetal or perinatal death and neurodevelopment in survivors are strongly related to the presence of other malformations and chromosomal defects. Although mild, also referred to as borderline, ventriculomegaly is generally associated with a good prognosis, affected fetuses form the group with the highest incidence of chromosomal abnormalities (often trisomy 21). In addition in a few cases with apparently isolated mild ventriculomegaly, there may be an underlying cerebral maldevelopment (such as lissencephaly) or destructive lesion (such as periventricular leukomalacia). Recent evidence suggests that in about 10% of cases there is mild to moderate neurodevelopmental delay.

**Fetal Therapy**

There is some experimental evidence that in utero cerebro spinal fluid diversion may be beneficial. However, attempts in the 1980s to treat hydrocephalic fetuses by ventriculoamniotic shunting have now been abandoned because of poor results mainly because of inappropriate selection of patients. It is possible that intrauterine drainage may be beneficial, if all intracrania and extracerebral malformations and chromosomal defects are excluded, and if serial ultrasound scans demonstrate progressive ventriculomegaly.

**HOLOPROSENCEPHALY**

This is a spectrum of cerebral abnormalities resulting from incomplete cleavage of the forebrain. There are three types of abnormalities according to the degree of forebrain cleavage. The alobar type, the most severe, is characterized by a monoventricular cavity and fusion of the thalami. In the semilobar type, there is 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 absence of the septum pellucidum. The first two types are often accompanied by microcephaly and facial abnormalities.8

**Prevalence**

Holoprosencephaly is found in about 1 per 10,000 births.

**Etiology**

Although 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. The etiology is unknown in many cases. The risk of recurrence for sporadic, nonchromosomal holoprosencephaly, the empirical recurrence risk is 6%.

**Diagnosis**

In the standard 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 partial segmentation of the ventricles. The alobar and semilobar types
are often associated with facial defects, such as hypotelorism or cyclopia, facial cleft and nasal hypoplasia or proboscis (Fig. 14).

**Prognosis**

Alobar and semilobar holoprosencephaly are lethal. Lobar holoprosencephaly is associated with mental retardation.

**AGENESIS OF CORPUS CALLOSUM**

The corpus callosum is a bundle of fibers that connects the two cerebral hemispheres. It develops at 12 to 18 weeks of gestation. Agenesis of the corpus callosum may be either complete or partial (usually affecting the posterior part).

**Prevalence**

Agenesis of the corpus callosum is found in about 5 per 1,000 births.

**Etiology**

Agenesis of the corpus callosum may be due to maldevelopment or secondary to a destructive lesion. It is commonly associated with chromosomal abnormalities (usually trisomies 18, 13 and 8) and more than 100 genetic syndromes.

**Diagnosis**

The corpus callosum is not visible in the standard transverse views of the brain but agenesis of the corpus callosum may be suspected by the absence of cavum septum pellucidum and the ‘teardrop’ configuration of the lateral ventricles (enlargement of the posterior horns). Agenesis of the corpus callosum is demonstrated in the mid-coronal and mid-sagittal views, which may require vaginal sonography (Fig. 15).

**Prognosis**

This depends on the underlying cause. In about 90% of those with apparently isolated agenesis of the corpus callosum development is normal.

**DANDY-WALKER COMPLEX**

The Dandy-Walker complex refers to a spectrum of abnormalities of the cerebellar vermis, cystic dilation of the fourth ventricle and enlargement of the cisterna magna. The condition is classified into (a) Dandy-Walker malformation (complete or partial agenesis of the cerebellar vermis and enlarged posterior fossa), (b) Dandy-Walker variant (partial agenesis of the cerebellar vermis without enlargement of the posterior fossa), and (c) mega-cisterna magna (normal vermis and fourth ventricle).

**Prevalence**

Dandy-Walker malformation is found in about 1 per 30,000 births.

**Etiology**

The Dandy-Walker complex is a non-specific endpoint of chromosomal abnormalities (usually trisomy 18 or 13 and triploidy), more than 50 genetic syndromes, congenital infection or teratogens such as warfarin, but it can also be an isolated finding.

**Diagnosis**

Ultrasonographically, the contents of the posterior fossa are visualized through a transverse suboccipitobregmatic section of the fetal head. In the Dandy-Walker malformation, there is cystic dilatation of the fourth ventricle with partial or complete agenesis of the vermis (Figs 16A and B). In more than 50% of the cases, there is associated hydrocephalus and other
extracranial defects. Enlarged cisterna magna is diagnosed if the vertical distance from the vermis to the inner border of the skull is more than 10 mm.12

Prenatal diagnosis of isolated partial agenesis of the vermis is difficult and a false diagnosis can be made prior to 18 weeks gestation, when the formation of the vermis is incomplete and anytime in gestation, if the angle of insonation is too steep.

**Prognosis**

Dandy-Walker malformation is associated with a high postnatal mortality (about 20%) and a high incidence (more than 50%) of impaired intellectual and neurological development. Experience with apparently isolated partial agenesis of the vermis or enlarged cisterna magna is limited and the prognosis for these conditions is uncertain.

**DESTRUCTIVE CEREBRAL LESIONS**

These lesions include hydranencephaly, porencephaly and schizencephaly. In hydranencephaly, there is absence of the cerebral hemispheres with preservation of the midbrain and cerebellum. In porencephaly, there are cystic cavities within the brain that usually communicate with the ventricular system, the subarachnoid space or both. Schizencephaly is associated with clefts in the fetal brain connecting the lateral ventricles with the subarachnoid space.

**Prevalence**

Destructive cerebral lesions are found in about 1 per 10,000 births.

**Etiology**

Hydranencephaly is a sporadic abnormality that may result from widespread vascular occlusion in the distribution of internal carotid arteries, prolonged severe hydrocephalus, or an overwhelming infection, such as toxoplasmosis and cytomegalovirus. Porencephaly may be caused by infarction of the cerebral arteries or hemorrhage into the brain parenchyma. Schizencephaly may be a primary disorder of brain development or it may be due to bilateral occlusion of the middle cerebral arteries.

**Diagnosis**

Complete absence of echoes from the anterior and middle fossa distinguishes hydranencephaly from severe hydrocephalus in which a thin rim of remaining cortex and the midline echo can always be identified. In porencephaly, there is one or more cystic area in the cerebral cortex, which usually communicates with the ventricle. The differential diagnosis is from intracranial cysts (arachnoid, gliopendymal) that are usually found either within the scissures or in the midline, and compress the brain. In schizencephaly, there are bilateral clefts extending from the lateral ventricles to the subarachnoid space, and is usually associated with absence of the cavum septum pellucidum13 (Fig. 17).

**Prognosis**

Hydranencephaly is usually incompatible with survival beyond early infancy. The prognosis in porencephaly is related to the size and location of the lesion and, although, there is increased risk of impaired neurodevelopment, in some cases development is normal. Schizencephaly is associated with severe neurodevelopmental delay and seizures.

**DISORDERS OF NERVE CELL PROLIFERATION**

A. **Microcephaly**: Microcephaly means small head and brain.

**Prevalence**

Microcephaly is found in about 1 per 1,000 births.

**Etiology**

This may result from chromosomal and genetic abnormalities, fetal hypoxia, congenital infection, and exposure to radiation or other teratogens, such as maternal anticoagulation with warfarin. It is commonly found in the presence of other brain abnormalities, such as cephalocele and holoprosencephaly.

**Diagnosis**

The diagnosis is made by the demonstration of brain abnormalities, such as holoprosencephaly. In cases with apparently isolated microcephaly, it is necessary to demonstrate progressive decrease in the head to abdomen circumference ratio to below the 1st centile with advancing gestation.14 Such diagnosis may not be apparent before the third trimester. In microcephaly, there is a typical disproportion between the size of the skull and face. The brain is small with the cerebral
hemispheres affected to a greater extent than the midbrain and posterior fossa. Demonstration of a sloping forehead also increases the index of suspicion (Fig. 18).

Prognosis
This depends on the underlying cause, but in more than 50% of cases, there is severe mental retardation.

B. Megalencephaly: Megalencephaly means large head and brain.

Prevalence
Megalencephaly is a very rare abnormality.

Etiology
This is usually familial with no adverse consequence. However, it may also be the consequence of genetic syndromes, such as Beckwith-Wiedemann syndrome, achondroplasia, neurofibromatosis, and tuberous sclerosis. Unilateral megalencephaly is a sporadic condition.

Diagnosis
The diagnosis is made by the demonstration of a head to abdomen circumference ratio above the 99th centile without the evidence of hydrocephalus or intracranial masses. Unilateral megalencephaly is characterized by macrocrania, a shift in the midline echo, borderline enlargement of the lateral ventricle and a typical gyri of the affected hemisphere.15

Prognosis
Isolated megalencephaly is usually an asymptomatic condition. Unilateral megalencephaly is associated with severe mental retardation and untreatable seizures.

INTRACRANIAL HEMORRHAGE IN UTERO
Hemorrhage may be seen in a typical subependymal or intraparenchymal location.

Etiology
1. Sudden changes in the cerebral blood pressure leading to ruptured capillaries in the germinal matrix or capillary venous junction.
2. Perinatal asphyxia, known to induce fluctuation in blood pressure.16

ARTERIOVENOUS MALFORMATION
VEIN OF GALEN ANEURYSM
This is a midline aneurysmal dilation of the vein of Galen due to an arteriovenous malformation with major hemodynamic disturbances.

Prevalence
Vein of Galen aneurysm is a rare abnormality.

Etiology
Vein of Galen aneurysm is a sporadic abnormality.

Diagnosis
The diagnosis is made by the demonstration of a supratentorial midline translucent elongated cyst. Color Doppler demonstrates active arteriovenous flow within the cyst. There may be associated evidence of high-output heart failure17 (Fig. 19).

Prognosis
In the neonatal period, about 50% of the infants present with heart failure and the rest are asymptomatic. In later life hydrocephalus and intracranial hemorrhage may develop. Good results can be achieved by catheterization and embolization of the malformation.

CHOROID PLEXUS CYSTS
These cysts, usually bilateral, are in the choroid plexuses of the lateral cerebral ventricles.

Prevalence
Choroid plexus cysts are found in about 2% of fetuses at 20 weeks of gestation but in more than 90% of cases, they resolve by 26 weeks.

Etiology
The choroid plexus is easily visualized from 10 weeks of gestation when it occupies almost the entire hemisphere. Thereafter and until 26 weeks, there is a rapid decrease in both the size of the choroid plexus and of the lateral cerebral ventricle in relation to the hemisphere. Choroid plexus cysts contain cerebrospinal fluid and cellular debris.

Diagnosis
Single or multiple cystic areas (greater than 2 mm in diameter) in one or both choroid plexuses18 (Fig. 20).

Prognosis
They are usually of no pathological significance, but they are associated with an increased risk for trisomy 18 and possibly...
trisomy 21. In the absence of other markers of trisomy 18, the maternal age-related risk is increased by a factor of 1.5.

ARACHNOID CYSTS

Arachnoid cysts are fluid-filled cyst contained within the arachnoid space.

Prevalence

Arachnoid cysts are extremely rare.

Etiology

Unknown infectious process has been hypothesized but it is unlikely that this may explain the congenital cysts.

Diagnosis

Arachnoid cysts appear on antenatal ultrasound, as sonolucent lesions with a thin regular outline and containing no blood flow, do not communicate with the lateral ventricles and anyhow are not associated with the loss of brain tissue (Fig. 21). They occur most frequently in the area of cerebral fissure and midline. Large cyst may cause significant mass effect and the distinction from porencephaly may be difficult. Interhemispheric cysts associated with agenesis of the corpus callosum most likely are not arachnoid cysts, but rather glioependymal cysts.

Prognosis

Large cysts may cause intracranial hypertension and require neurosurgical treatment. However, a normal intellectual development in the range of 80 to 90% is reported by most series. Spontaneous remission has been described both in the postnatal as well as in the antenatal period. Glioependymal cyst, that should be suspected in the cases with associated agenesis of corpus callosum, probably reflects a greater degree of derangement in the development of the brain and this may be reflected in worse outcome.

CONCLUSION

Modern ultrasound equipments yield a unique potential for evaluation of normal and abnormal fetal CNS very early in pregnancy. It should be stressed, however, that some cerebral anomalies are the consequence of disruptions or are characterized by intrauterine development. Counseling the parents and deciding on a sensible obstetric management are frequently difficult.

REFERENCES