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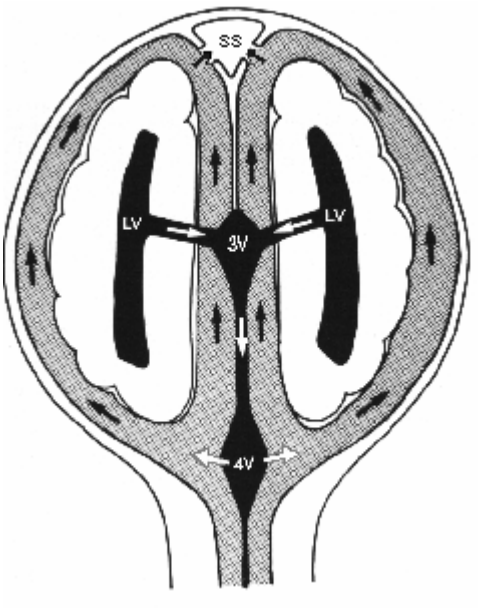
Fetal Anatomy: Intracranial Anomalies

Hydrocephalus

Hydrocephalus is commonly defined as an increased intracranial content of cerebrospinal fluid (CSF). Even though many disorders of the CNS share this condition, the term "hydrocephalus" is generally used to refer to a situation in which an abnormal accumulation of CSF results in enlargement of the ventricular system. The adjacent figure shows the origin, circulation, and drainage of CSF. CSF is formed mainly at the level of the choroid plexuses inside the ventricular system and flows slowly from the lateral ventricles to the third ventricle and from there to the fourth ventricle. At this level, CSF passes through the foramina of Luschka and Magendie inside the subarachnoid space that externally bathes the cerebral structures. Flowing along the subarachnoid cisterns, the fluid is then reabsorbed by the granulations of Pacchioni that are mainly distributed along the superior sagittal sinus.



Schematic representation of the circulation of cerebrospinal fluid. The fluid is formed mainly inside the ventricular system by the choroid plexuses. It then flows slowly from the lateral ventricles (LV) to the third ventricle (3V) and fourth ventricle (4V). At this level it escapes into the subarachnoid space (shaded area) and flows toward the superior sagittal sinus (SS) where it is resorbed.

In the majority of cases, congenital hydrocephalus is the consequence of an obstruction along the normal pathway of the CSF (obstructive hydrocephaly). Hydrocephalus is one of the most common congenital anomalies, with an incidence of 0.3 to 0.8 per 1000 births.

The diagnosis of hydrocephalus has traditionally relied on the demonstration of enlarged lateral ventricles. Several nomograms have been developed to quantify the dimensions of the lateral ventricles. The LVW: HW (lateral ventricular width: head width) ratio is the parameter most frequently used for this assessment. However, several false negative diagnoses in early pregnancy have been reported and they raise questions about the sensitivity of the measurement of the LVW: HW ratio in diagnosing early or mild ventricular dilatation. Morphologic, rather than purely biometric, criteria have been suggested for the early detection of hydrocephalus, including the simultaneous visualization of the

medial and lateral wall of the lateral ventricle and the anterior displacement of the choroid plexus. Recently, measurement of the atria of the lateral ventricle has been suggested. At present, the problem of early detection of hydrocephalus remains unsolved.

Associated Anomalies

Hydrocephalus is commonly associated with other congenital anomalies. Associated intracranial anomalies have been reported in 37 percent of hydrocephalus cases. They include hypoplasia of the corpus callosum, cephalocele, arteriovenous malformation, and arachnoid cyst. Extracranial anomalies were present in 63 percent of cases and included meningomyelocele, renal anomalies (bilateral or unilateral renal agenesis, dysplastic kidneys), cardiac anomalies (ventricular septal defect, tetralogy of Fallot), gastrointestinal anomalies (colon and anal agenesis, malrotation of the bowel), cleft lip and palate, Meckel syndrome, gonadal dysgenesis, sirenomelia, arthrogryposis, and dysplastic phalanges. Chromosomal anomalies were present in 11 percent of cases, including trisomy 21, balanced translocation, and mosaicism.

Prognosis

The three major forms of hydrocephalus are **aqueductal stenosis, communicating hydrocephalus, and Dandy-Walker syndrome.** Because the sonographic appearance and prognosis of each variety differ, they are discussed separately.

Prognostic figures reported in each section are derived from pediatric series, and therefore they should be used with caution in counseling obstetric patients. Furthermore, because it is not always possible to identify the specific type of hydrocephalus, some general information about prognosis and obstetrical management guidelines will be addressed.

There is only one study that examines the prognosis of infants with hydrocephalus diagnosed in utero. In this report, 37 infants with a heterogeneous group of disorders having ventriculomegaly in common (uncomplicated hydrocephaly, myelomeningocele, intracranial teratoma, Meckel syndrome) were followed for 7 to 60 months. Immediate neonatal death (in less than 24 hours) was associated with the presence of other congenital anomalies, namely intracranial teratoma, thanatophoric dysplasia with cloverleaf skull, cebocephaly, sirenomelia, Meckel syndrome, tetralogy of Fallot, and arthrogryposis multiplex congenita. Among the survivors, a poor mental score was associated with the presence of other anomalies, such as cephalocele, intraventricular cyst with agenesis of corpus callosum, arachnoid cyst with agenesis of corpus callosum, microcephaly, and ring chromosome 18. On the other hand, all cases with normal intelligence did not have associated anomalies or they had meningomyelocele. Therefore, the most important prognostic consideration is the presence and nature of the associated anomalies.

Pediatric data suggest that a correlation exists between cortical mantle thickness before shunting and long-term intellectual performances. Thickness of less than 1 cm has been associated with a poor outcome. However, this

correlation is imperfect and excellent neurologic outcomes have been observed after early shunting with mantle thickness of less than 1 cm. This parameter, therefore, should not be used for obstetrical management decisions.

1. Aqueductal Stenosis

Synonyms

Stenosis of the aqueduct of Sylvius and aqueduct stenosis.

Definition

Aqueductal stenosis is a form of obstructive hydrocephalus caused by narrowing of the aqueduct of Sylvius.

Incidence

Aqueductal stenosis is the most frequent cause of congenital hydrocephaly. It has been reported to account for 43 percent of the cases studied. Male to female ratio is 1 .8.

Etiology

Aqueductal stenosis is a heterogeneous disease for which genetic, infectious, teratogenic, and neoplastic causes have been implicated. The relative contributions of these factors have been determined from autopsy studies. Histologic evidence of inflammation (gliosis) have been found in approximately 50 percent of the cases studied. Toxoplasmosis, syphilis, cytomegalovirus, mumps, and influenza virus have caused aqueductal stenosis in mammals. In cases without evidence of inflammation, the disease appears to be the consequence of maldevelopment for an unknown reason. This maldevelopment is histologically expressed by forking or simple narrowing of the aqueduct. Genetic transmission has been postulated to account for some of these cases. Many familial studies have demonstrated that aqueductal stenosis can be inherited as an X-linked recessive trait. Sex-linked transmission was thought to be a rare cause of the disease, because only 1 case was found among 200 siblings of probands with hydrocephalus. However, it has been suggested that this mode of inheritance involves 25 percent of affected male infants. The possibility of a coexistent polygenic pattern of inheritance has been suggested by case reports of families in which both females and males were affected.

Teratogenic agents, such as radiation, have been implicated in animal models, but the relevance of these observations to humans is uncertain. Such tumors as gliomas, pinealomas, meningiomas, and other conditions (neurofibromatosis and tuberous sclerosis) may cause aqueductal stenosis by a compressive mechanism. However, the prevalence of these entities in the prenatal period is extremely low. It has also been suggested that communicating hydrocephalus may lead to secondary aqueductal stenosis, causing white matter edema and extrinsic compression.

Embryology

The aqueduct of Sylvius is the portion of the ventricular system that connects the third and fourth ventricles (Fig. 1—30). The aqueduct develops from a narrowing of the primitive ventricular cavity between the prosencephalon and rhomboencephalon at about the sixth week (conceptional age).

Pathology

Aqueductal stenosis may result from an inflammatory process or a developmental anomaly. “Gliosis” is the term used to describe the inflammatory reaction seen in the CNS. A mononuclear microglial response and a repair process conducted by astrocytes characterize this reaction. Malformations include forking, narrowing, and the presence of a transverse septum. Forking describes the substitution of the aqueduct by multiple narrow channels. Narrowing may be of variable degree and is usually accompanied by an irregular outline of the ependymal wall. When a septum is responsible for the stenosis of the aqueduct, it is usually located in its posterior portion.

Narrowing is the most common finding in hereditary cases. Aqueductal stenosis is associated with a variable degree of dilatation of the lateral and third ventricles. Knowledge about the pathogenesis of congenital obstructive hydrocephaly is largely incomplete. Studies performed in experimental animals and based on biopsies of brain tissue obtained in children at the time of shunting seem to demonstrate the following sequence of events. Initially, there is disruption of the ependymal lining, followed by edema of the white matter. This phase has been considered reversible. Later, there is astrocyte proliferation and fibrosis of the white matter. The gray matter seems to be spared during the initial phase of the process.

Associated Anomalies

Other congenital anomalies occur in 16 percent of infants with aqueductal stenosis. Bilateral thumb deformities of flexion and adduction have been seen in 17 percent of the sex-linked inherited type.

Diagnosis

A diagnosis of aqueductal stenosis is suggested by enlargement of the lateral ventricles (which can be either symmetrical or slightly asymmetrical) and of the third ventricle in the presence of a normal fourth ventricle Unfortunately, this finding is nonspecific, since many cases of communicating hydrocephaly may have similar appearances, and the differential diagnosis between these two conditions may be impossible. Careful scanning of the fetal spine is recommended in order to rule out a coexistent spinal defect.

2. Communicating Hydrocephalus

Synonym

External hydronephrosis

Definition

Communicating hydrocephalus is a form of enlargement of the ventricle and subarachnoid system by an obstruction to CSF flow outside the ventricular system.

Etiology

In most cases, the etiology is unknown. Communicating hydrocephalus is found in infants with spinal defects and has also been seen in association with obliteration of the superior sagittal sinus, subarachnoid hemorrhage, absence of Pacchioni granulations, and choroid plexus papilloma. Subarachnoid hemorrhage is probably the most common cause of infantile communicating hydrocephalus, but it is probably rare in the prenatal period. Familial transmission is rare; only 1 affected individual was found among 154 siblings of 77 probands.' However, the recurrence rate quoted for this condition is 1 to 2 percent, which is higher than the incidence in the general population.'

Pathology

The basic cause of communicating hydrocephalus is either a mechanical obstruction outside the ventricular system or an impaired reabsorption of cerebrospinal fluid. This leads to dilatation of the subarachnoid space and later to the dilatation of the ventricular system. Over time, the enlargement of the subarachnoid space may become less prominent, and ventriculomegaly may be the only finding. In fact, most patients with communicating hydrocephalus show only triventricular hydrocephalus without overt enlargement of the subarachnoid space and fourth ventricle. The pathophysiology of the disappearance of cisternal dilatation is not clear. However, it has been suggested that the increased intracranial pressure may eventually lead to obstruction of the aqueduct, resulting in hydrocephalus.

Diagnosis

Communicating hydrocephalus causes tetraventricular enlargement (dilatation of the lateral, third, and fourth ventricles). However, because the enlargement of the fourth ventricle is often minimal, the main problem arises with the differential diagnosis from aqueductal stenosis. The dilatation of the subarachnoid cistern is pathognomonic of communicating hydrocephaly. This is most easily demonstrated at the level of the subarachnoid space overlying the cerebral convexities and interhemispheric fissure. Unfortunately, in a large number of cases, this image is rarely detected, making it impossible to differentiate it from aqueductal stenosis. In one longitudinal study of infants

developing communicating hydrocephaly, isolated dilatation of the subarachnoid space was seen prior to ventriculomegaly. Therefore, the visualization of such a finding in a fetus is an indication for follow-up examinations.
The natural history of communicating hydrocephalus is unknown. Some cases are diagnosed in utero, whereas others are not recognized until infancy

Prognosis
Data concerning the survival and intellectual performance of infants with isolated congenital communicating hydrocephaly are limited, since many studies are probably biased because of the inclusion of infantile forms. The outcome appears to be much better than with other types of hydrocephaly. In an old series of 35 treated infants, the mortality rate was 11 percent. Eighty-four percent of the survivors developed a normal intelligence In a more recent series of 9 treated infants, no deaths were observed, and the mean IQ was 101 (SD = 19). If communicating hydrocephaly is associated with either a neural tube defect or a choroid plexus papilloma, the prognosis is different.

Hydrocephalus - Summary of Sonographic Findings

1st trimester:

* CSF seen in lateral ventricle totally surrounding and compressing choroid plexus.

2nd/3rd trimester:

Normal ventricular configuration, just dilated
*Presence of excess fluid in lateral ventricles with an axial atrial measurement exceeding 10mm.
*Dangling choroid plexus
*Observe brain echogenicity. Dense texture may suggest intrauterine infection.
*Associated sonographic findings may include: polyhydramnios, abnormal fetal lie, hepatomegaly and fetal ascites with associated infection, meningomyelocele, other intracranial abnormalities including Dandy-Walker, encephalocele, intracranial tumor.

Filly's Rule: If the atrium of the lateral ventricle and the cisterna magna both measure less that or equal to 10mm, there is a 95% negative predictive value for ANY central nervous system anomaly.

3. Dandy-Walker Malformation

Synonym

Dandy-Walker syndrome.

Definition

Dandy-Walker malformation (DWM) is characterized by the association of (1) hydrocephalus of variable degree, (2) a cyst in the posterior fossa, and (3) a defect in the cerebellar vermis through which the cyst communicates with the fourth ventricle.

Incidence

DWM accounts for 12 percent of all cases of congenital hydrocephalus. However, this figure may represent an underestimation of the real incidence because cases without hydrocephalus and without significant symptoms have also been reported.

Etiology

Unknown. DWM may occur as a part of Mendelian disorders, such as Meckel syndrome and Warburg syndrome. It has been found in chromosomal aberrations, such as Turner syndrome, and triploidy. Environmental factors, such as viral infections, alcohol, and diabetes, have been suggested as playing a role in its etiology. When DWM is not associated with mendelian disorders, the recurrence risk is 1 to 5 percent. In rare cases, the disease is probably inherited as an autosomal recessive trait, with a recurrence risk of 25 percent. A cerebral anomaly similar to DWM, Joubert syndrome, is also inherited as an autosomal recessive trait.

Embryology

According to the original theory of Dandy and Walker, atresia of the foramina of Luschka and Magendie would lead to dilatation of the ventricular system. However, Benda subsequently observed that (1) the foramina of Luschka and Magendie are not atretic in all cases and (2) it is difficult to understand how atresia of these foramina (which are not normally patent until the fourth month of gestation) would lead to cerebellar vermis hypoplasia. It is now commonly accepted that DWM is a more complex developmental abnormality of the rhomboencephalic midline structures. Gardner et al. have proposed that the malformation is due to an imbalance between the CSF production in the lateral and third ventricles and in the fourth ventricle. The overproduction of CSF at the level of the fourth ventricle would lead to early dilatation and herniation of the rhomboencephalic roof. Dilatation would be maximal at the level of the fourth ventricle, resulting in compression and secondary hypoplasia of the cerebellar vermis. The enlargement of the fourth ventricle would be responsible for the cyst seen in the posterior fossa.

Pathology

The three pathologic features are hydrocephalus, a cerebellar vermis

defect, and a retrocerebellar cyst. The vermian defect is variable, ranging from complete aplasia to a small fissure. The retrocerebellar cyst is internally lined by ependyma and is of variable size. Although hydrocephalus has been classically considered to be an essential diagnostic element of DWM, recent evidence suggests that it is not present at birth in most patients, but it develops usually in the first months of life. This is relevant for prenatal diagnosis because the only detectable signs in these fetuses would be the posterior fossa abnormalities. Depending on whether the foramina of Luschka and Magendie are open or closed, the malformation would be classified as "communicating" or "noncommunicating." This classification is relevant because the noncommunicating forms are associated with variable degrees of hydrocephaly

Associated Anomalies

DWM is frequently associated with other CNS abnormalities. Clinical studies have found an incidence of 50 percent of associated anomalies. Agenesis of the corpus callosum has been reported to occur in between and 17 percent of patients studied. Pathologic studies have demonstrated an incidence of cerebral defects as high as 68 percent. However, it should be stressed that most of these anomalies (polymicrogyria, agyria, microgyria, malformation of the inferior olives) are not sonographically detectable in utero. Other anomalies include encephaloceles, polycystic kidneys, and cardiovascular defects (mainly ventricular septal defects).

Diagnosis

The diagnosis of DWM should be considered whenever a cystic mass is seen in the posterior fossa. The differential diagnosis includes an arachnoid cyst and dilatation of the cisterna magna. A defect in the vermis, through which the cyst communicates with the fourth ventricle, is pathognomonic of DWM. Such a finding is well documented in both computed tomographic and ultrasound studies in the postnatal period, and it can be demonstrated in the fetus as well. The defect may vary in size from a small fissure to a large tunnel with widely separated cerebellar hemispheres. Extreme care is necessary because, in some cases, the superior vermis is intact and the defect can only be demonstrated by careful examination of the inferior vermis. Differentiation from an arachnoid cyst or enlarged cisterna magna may be difficult, however. This difficulty can be encountered even in the neonatal period despite the use of computed tomography. There is controversy in the radiologic literature about the optimal means of making a diagnosis. Some authors are concerned about the limitations of computed tomography and recommend that a pneumoencephalogram be performed.[1] Other authors believe that pneumoencephalography may be misleading and recommend contrast studies (metrimazide, radionucleotides) when noncontrast computed tomography is equivocal.

Traditionally, DWM has been considered a cause of intrauterine hydrocephalus. However, the evidence indicates that this association is not

frequent in the fetus.[23,32] Therefore; we recommend a careful study of the posterior fossa as part of a routine survey of the intracranial anatomy.

Dandy Walker - Summary of Sonographic Findings

*Posterior fossa cyst continuous with 4th vent.
*Posterior fossa enlargement
*Cerebellar vermian dysgenesis

Cystic Intracranial Abnormalities

Hydranencephaly

Synonyms

Hydrocephalic anencephaly, hydroencephalodysplasia, hydromerencephaly, and cystencephaly.

Definition

Hydranencephaly describes a condition in which most of the cerebral hemispheres are absent and are replaced by CSF.

Epidemiology

Hydranencephaly is found in 0.2 percent of infant autopsies. Approximately 1 percent of infants thought to have hydrocephalus by clinical examination are later found to have hydranencephaly.

Etiology

Hydranencephaly does not seem to be a developmental anomaly but rather the result of a destructive intrauterine insult of vascular or infectious origin. Vascular occlusion of the internal carotid artery cuts the blood supply to the cerebral hemispheres and causes extensive necrosis. Myers has successfully created hydranencephaly in monkeys by either bilateral occlusion of the carotid artery and jugular vein in utero or by incomplete placental abruption. This view is supported by observations of absence, thrombosis, and vasculitis of the cerebral vessels in hydranencephalic infants. Infection may cause hydranencephaly either by a necrotizing vasculitis or by local destruction of brain tissue. In these cases, dilatation of the ventricular system will occur, filling the intracranial cavity. Some authors have expressed the view that hydranencephaly may be considered as an extreme form of pseudo-porencephaly. Familial cases are rare.

Pathology

There is variability in the extent of destruction of the cerebral hemispheres. Destruction may be complete or may spare portions of the temporal and occipital cortex. The brain stem is present, although the thalami and cerebellum may be smaller than normal. The head is filled with CSF, which is contained in a cavity lined by leptomeninges. Macrocrania may develop. The falx cerebri may be absent or incomplete.

Diagnosis

A positive diagnosis can be made by identifying a large cystic mass filling the entire intracranial cavity or by detecting the absence or discontinuity of the cerebral cortex and of the midline echo. The ultrasound appearance of the brain stem protruding inside the cystic cavity is quite characteristic.

The most common diagnostic problem is the differentiation among hydranencephaly, extreme hydrocephalus, and porencephaly. In porencephaly, some spared cortical mantle is usually seen. Extreme hydrocephalus may be difficult to differentiate from those cases of hydranencephaly in which the falx is present, even in the neonatal period. The most important clue is the typical appearance of the thalami and brain stem, which bulge inside the fluid-filled intracranial cavity when hydranencephaly is present. In extreme hydrocephalus, these structures are surrounded by cortex and do not acquire such an appearance. The presence of even minimal frontal cerebral cortex indicates extreme hydrocephalus instead of hydranencephaly.

Pathologists can make a differential diagnosis between hydranencephaly and hydrocephalus by examining the lining of the cystic structures. While leptomeninges will be found in hydranencephaly, ependyma lines the ventricular system in hydrocephalus.

Hydranencephaly - Summary of Sonographic Findings

water, no brain

*Macrocephaly

*Large anechoic areas in cranial vault surrounding midbrain and basal anglia

*Absent falx and cortical mantle

*Variable presence of 3rd vent

*Tentorium separating a normal posterior fossa from anterior and middle cranial fossae

*Polyhydramnios

*Occasionally small portions of occipital lobes

Prognosis

Data on the neurologic performance of hydranencephalic infants is scanty. Some infants with hydranencephaly have severe neurologic abnormalities at birth and die. Abnormalities include seizures, myoclonus, and respiratory failure. Chronic survival (up to 3.5 years) occurs in some cases and seems to depend on an intact hypothalamus capable of thermoregulation. These infants have no intellectual function.

Holoprosencephaly

Definition

Holoprosencephaly is a complex developmental abnormality of the brain arising from failure of cleavage of the prosencephalon. The condition termed "holoprosencephaly" includes cyclopia, cebocephaly, ethmocephaly, median cleft, and holotelencephaly.

Epidemiology

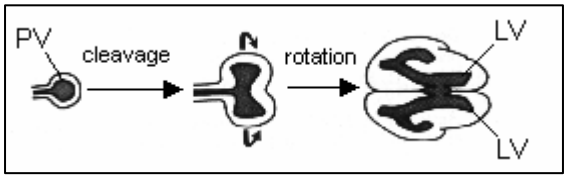
The incidence of holoprosencephaly is not known because milder forms without facial defects may be unrecognized unless appropriate diagnostic investigation is undertaken. Cyclopia has been reported to occur in 1:40,000 births, whereas cebocephaly and median cleft lip occur at a rate of 1:16,000 births. The disease may be more frequent in abortuses; Matsunaga and Shiota report an incidence of 0.4 percent of induced abortions. This observation suggests a high fatality rate

Etiology

Chromosomal abnormalities (primarily trisomy 13, trisomy 18, and trisomy 13/15) are found in association with holoprosencephaly. Other abnormalities include deletions and ring chromosomes (mainly 18). Teratogenic agents, such as veratrum alkaloids and radiation, have induced holoprosencephaly in animals. Ingestion of salicylates in pregnancy has also been reported in relation to holoprosencephaly. Several studies have indicated a familial tendency, with both autosomal dominant with variable penetrance and autosomal recessive transmission. An association with diabetes and maternal infections during pregnancy has been suggested but not proven. The empirical recurrence risk in the absence of chromosomal abnormalities has been estimated to be 6 percent. In the presence of an abnormal karyotype, the recurrence risk depends on the chromosomal aberration. A primary trisomy is associated with a less than 1 percent chance of recurrence. If the parents are carriers of a balanced translocation, the recurrence risks are much greater

Embryology

Holoprosencephaly is the result of a failure of cleavage of the prosencephalon. The prosencephalon is the most rostral of the three primitive cerebral vesicles and gives rise to the cerebral hemispheres and diencephalic structures (including neurohypophysis, thalami, third ventricle, and optic bulbs). This differentiation process is thought to be induced by the prechordal mesenchymal interposed between the roof of the mouth and the prosencephalon. The same tissue is responsible for the normal development of the median facial structures (forehead, nose, interorbital structures, and upper lip).



Normal development of the prosencephalon. PV, primitive ventricular cavity; LV, lateral

An interference with the activity of the prechordal mesenchyma would lead to

defects in areas, brain and face. The cerebral anomalies are due to varying degrees of failure of cleavage of the prosencephalon, with incomplete division of the cerebral hemispheres and underlying structures.

The facial anomalies encompass a broad range of defects that are due to aplasia or varying degrees of hypoplasia of the median central structures.

Pathology

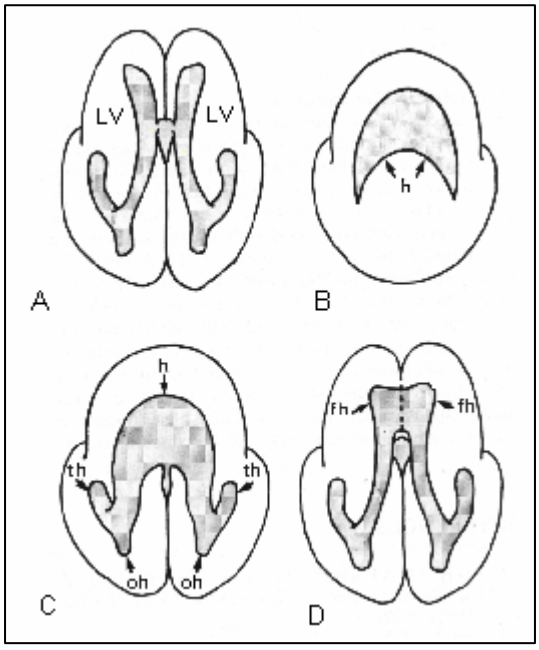
The most relevant classification of holoprosencephaly for antenatal diagnosis is that suggested by DeMyer, which recognizes three types: alobar, semilobar, and lobar according to the degree of incomplete division of the prosencephalic derivatives.

In the most severe form (alobar holoprosencephaly), there is an absence of the interhemispheric fissure, a single primitive ventricle, fused thalami, absence of the third ventricle, neurophypophysis, and olfactory bulbs. Failure of inward rotation of the primitive cerebral hemispheres prevents the thin membranous roof of the ventricular cavity from being enfolded within the brain. Because of an increase in CSF, the membrane may balloon out to form a cyst between the cerebral convexity and the calvarium (so-called dorsal sac). According to the degree of failure of rotation, alobar holoprosencephaly is commonly subdivided into three types: pancake, cup, and ball varieties.

In semilobar holoprosencephaly, the two cerebral hemispheres are partially separated posteriorly, but there is still a single ventricular cavity. Alobar and semilobar holoprosencephaly might be associated with either microcephaly or macrocephaly.

In lobar holoprosencephaly, the interhemispheric fissure is well developed anteriorly and posteriorly, but there is a certain degree of fusion of structures, such as the lateral ventricles and the cingulate gyrus and absence of the cavum septum pellucidum.

The facial defects have been categorized into five different types.



A. Schematic drawing of axial sections of the normal neonatal brain. B. Alobar holoprosencephaly. There is absence of division of the cerebral hemispheres and a single primitive ventricular cavity. C. Semilobar holoprosencephaly. There is an incipient separation of the hemispheres in the occipital areas and partial development of the occipital and temporal horns of the ventricles. D. Lobar holoprosencephaly. Note the almost complete separation of the cerebral hemispheres. The ventricles are almost totally separated, except for the frontal portion and are generally mildly dilated. LV, lateral ventricles; h, holoventricle; OH, occipital horn; TH, temporal horn; FH, frontal horn.

Diagnostic Criteria

The antenatal diagnosis of holoprosencephaly has been reported on several diagnostic criteria vary depending on the type of holoprosencephaly. In the alobar and semilobar varieties, the single most valuable finding is the identification of a single sickle-shaped ventricle. In an

axial scan, this primitive ventricular cavity is lined anteriorly by a crescent-shaped cortex with no discernible inter-hemispheric fissure and posteriorly by the bulblike undivided. In the alobar variety, the presence of a dorsal sac can be easily recognized either in an axial scan above the level of the thalami or in a coronal scan, which would demonstrate the continuity between this structure and the single ventricle. The semilobar variety is recognized in the neonatal period by observing well-developed occipital horns and an incomplete inter-hemispheric fissure, but it is yet to be demonstrated that ultrasound can differentiate the semilobar from the alobar type of holoprosencephaly in utero. The lobar form is a serious diagnostic challenge because the interhemispheric fissure is well formed and the lateral ventricles are separated, with the exception of the frontal portions. It has not been identified in the fetus. Fusion of the frontal horns could probably be recognized by ultrasound. In all forms of holoprosencephaly, the posterior fossa contents are normal.

The facial findings are further diagnostic hints. The presence of hypotelorism, cyclopia, absence of orbits and nose, identification of a proboscis, and cleft palate or lip strengthens the diagnosis based on CNS findings. On the other hand, if any of the aforementioned facial features are serendipitously encountered , a careful examination of the intracranial contents is indicated.

Holoprosencephaly - Summary of Sonographic Findings

* Fetal cranium appears as a large cystic space with a mantle of peripheral cerebral tissue
* Presence of a single midline ventricle
* Craniofacial abnormalities including: proboscis, severe hypotelorism, cyclopia
* Appearance varies with severity of malformation

Non-Cystic Intracranial Abnormalities

Agenesis of the Corpus Callosum

Epidemiology

There is a discrepancy in the reported incidence between autopsy series and those based on pneumoencephalographic studies. In one autopsy study, the frequency was about 1:19 (5.3 percent). On the other hand, one radiologic series based on 6450 pneumo -encephalograms found an incidence of 0.7 percent.

Etiology

Agenesis of the corpus callosum (ACC) can occur in chromosomal abnormalities, such as trisomy 13 and trisomy 18 (as part of the holoprosencephalic sequence) and translocations (2 to a chromosome B). Familial occurrence has been documented, suggesting a marked genetic heterogeneity with autosomal dominant, autosomal recessive, and X-linked inheritance. ACC has also been described in the median cleft face syndrome, in the Aicardi syndrome (seizures, chorioretinal lacunae, mental retardation,

microcephaly, vertebral anomalies; sex-linked dominant inheritance), Andermann syndrome (mental retardation, progressive motor neuropathy; autosomal recessive transmission), F.G. syndrome (mental retardation, macrocephaly, hypotonia), and acrocallosal syndrome (mental retardation, macrocephaly, polydactyly; autosomal recessive transmission). An association with tuberous sclerosis, mucopolysaccharidosis, basal cell nevus syndrome, maternal toxoplasmosis, and maternal rubella has been reported.

Embryology

The corpus callosum is a white matter structure that connects both cerebral hemispheres. Its presence is important in coordinating information and exchanging sensorial stimuli between the two hemispheres. The corpus callosum is derived from the lamina terminalis in the portion of the neural tube cephalic to the rostral neuropore. Until the fourth month of gestation, only the most rostral part of the corpus callosuin is formed. The caudal portion develops only after the 5th month. The insult responsible for ACC or varying degrees of hypoplasia of the corpus callosum is not known. Logically, an early insult may lead to complete agenesis, whereas a later one will lead to partial agenesis

Pathology

The defect may be complete or partial. In partial ACC, the posterior portion is missing. As a consequence of the absence of the corpus callosum, the two lateral ventricles are set apart, and the third ventricle may sometimes be displaced upward. In most cases, there is stable, non-progressive dilatation of the lateral ventricles (atria and occipital horns). The reason for this enlargement is not known. There is no evidence of obstruction along the CSF pathways, since there is neither increased intra-ventricular pressure or progressive ventriculomegaly.

Associated Anomalies

ACC is frequently associated with other anomalies of the CNS and of other organs, including holoprosencephaly, Dandy-Walker malformation, microcephaly, macrocephaly, median cleft syndrome, and cardiovascular, gastrointestinal, and genitourinary anomalies. ACC may be a part of Mendelian syndromes.

Diagnosis

In the newborn, ACC can be diagnosed by both computed tomography and sonography through the demonstration of (1) increased separation of the lateral ventricles, (2) enlargement of the occipital horns and atria, and (3) upward displacement of the third ventricle. These findings can also be demonstrated in utero. The increased separation of the normal-sized bodies and the enlargement of the atria and occipital horns of the lateral ventricles result in a typical ultrasound image. Upward displacement of the third ventricle is a very specific sign. When ACC is suspected, orbital measurements should be made, and the fetal face should be examined because of the possible association of this condition with the hypertelorism median cleft syndrome.[8] Investigation of the

posterior fossa is also recommended because of the frequent association with Dandy-Walker malformation.

Agenesis of Corpus Callosum - Summary of Sonographic Findings

*Absent cavum septi pellucidi
*Lateral ventricles displaced upward and outward
*Enlarged occipital horn
*Upward displacement of the lateral ventricles
*3rd ventricle displaced superiorly

Prognosis

The corpus callosum is phylogenetically a recent structure, and its absence is not essential for life functions. Patients with ACC may have neurologic problems, such as seizures, intellectual impairment, and psychosis. However, these conditions are believed to be caused by associated cerebral anomalies. Isolated ACC may be either a completely asymptomatic finding or revealed during the course of a neurologic examination by subtle deficits, such as inability to match stimuli using both hands (e.g., individuals are unable to discriminate differences in temperature, shape, weight in objects placed in both hands). In our own series of nine cases of ACC identified in utero, severe associated anomalies were found in three (Dandy-Walker malformation, microcephaly, diaphragmatic hernia). Of the remaining six, one infant is affected by moderate paraparesis and five are developing normally.

Intracranial tumors

Intracranial tumors include epidermoid, dermoid, teratoma, germinoma, medulloblastoma, tuberous sclerosis (Bourneville's disease), neurofibromatosis (Von Recklinghausen's disease), and systemic angiomatosis of the central nervous system and eye (Von Hippel-Lindau's disease).

Incidence

Fetal intracranial tumors are rare. There are obvious difficulties in assessing the incidence of congenital brain neoplasms, because some lesions are asymptomatic or become symptomatic during childhood, adolescence, or even adulthood. Malignancies of the CNS were found to account for 0.04 to 0.18 percent of the total deaths of infants under 1 year of age. It should be stressed that only a very small portion of brain tumors in children seem to arise during fetal life. In a series of 730 neoplasms diagnosed between 1 and 16 years of age, only 56 (7.8 percent) were thought to be congenital.

Etiology

Embryonic tumors are thought to derive from embryologically displaced cells. Brain tumors have been produced in animals by the use of chemical and viral teratogens. The relevance of these experiments to human brain neoplasms is unclear.

Pathology

There are several classifications of congenital brain tumors. Epidermoid tumors (also known as “cholesteatomas”) derive from epithelial cells and frequently appear as cystic lesions, containing a leaf-like material, that originate from the desquamation of the internal epithelial lining. They are most cornmonly located at the level of the cerebellopontine are characterized by the presence of desquamated epithelium, sebaceous secretions, and hair. They are often connected with the skin surface by a dermal sinus and usually occur in the posterior fossa. Teratomas are tumors derived from the three embryonic layers. They may contain well-differentiated structures, such as hair, bone, or muscle, or undifferentiated structures. In the latter case, they have a tendency toward malignancy. Teratomas usually occur in the pineal region, the suprasellar region, or the fourth ventricle.

Germinomas originate from germ cells and are usually solid lesions occurring in the pineal and suprasellar regions. Tumors originating from differentiated germ cells include choriocarcinoma (trophoblastic cells), endodermal sinus tumor (yolk sac), embryonal carcinoma, and teratoma. Medulloblastoma only arises in the posterior fossa. It is a very malignant lesion that appears as a soft, friable mass often with internal necrosis.

Craniopharyngioma is the most frequent supratentorial tumor in children. It derives from remnants of the craniopharyngeal duct, consists of both cystic and solid components, and occurs in the suprasellar region. Among the tumors that derive from ependymal cells, the one that is most frequently congenital in origin is the choroid plexus papilloma

Tuberous. sclerosis, neurofibromatosis, and systemic angiomatosis of the CNS and eye are autosomal dominant diseases that are characterized by the presence of intracranial tumors. In tuberous sclerosis, multiple neuroglial nodules occur in the cerebral cortex or ventricular system. Neurofibromatosis is associated with brain tumors, such as acoustic neurinoma, multiple meningioma, and glioma. Systemic angiomatosis of the CNS and eye is characterized by the presence of cerebellar hemangioblastoma. The colloid cyst of the third ventricle is thought to derive from the epithelium that forms the roof of the thela choroidea and is located in the anterior portion of the third ventricle.

Intracranial tumors frequently cause obstruction to the normal flow of CSF within the ventricular system and are, therefore, often found in association with obstructive hydrocephalus. Choroid plexus papilloma may cause hydrocephalus by overproduction of cerebrospinal fluid.

Diagnosis

Experience in the prenatal diagnosis of brain neoplasms is limited, because of the rarity of these lesions. Cystic tumors and teratomas are usually characterized by complete loss of the normal intracranial architecture. A brain tumor should be suspected when mass-occupying lesions, cystic areas, or solid areas are seen or when there is a change in shape or size of the normal anatomic structures (e.g., a shift in the midline). In some cases, the lesion appears as a low echogenic structure, and it may be difficult to recognize.[8,9] Hydrocephalus is frequently

associated with brain tumors and may be the presenting sign. Although ultrasound can detect some fetal intracranial tumors, it does not allow a specific diagnosis of the histological variety. Identification of brain neoplasm associated with tuberous sclerosis, neurofibromatosis, and systemic angiomatosis of the CNS and eye can be attempted in the patients at risk.

Intracranial Tumors - Summary of Sonographic Findings

*Loss of normal intracranial architecture
*Presence of a space-occupying lesion with changes in normal anatomic structures and anatomic relationships
*Histological diagnosis cannot be made with ultrasound

Prognosis

Prognosis depends on a number of factors, including the histologic type and the size and location of the lesion. Congenital intracranial teratomas are usually fatal. The limited experience with the other neoplasms in prenatal diagnosis precludes the formulation of prognostic considerations.