52 Assessment of fetal brain abnormalities

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INTRODUCTION

Recent advanced ultrasound imaging technologies such as high-frequency transvaginal scanning and three-dimensional (3D) sonography have been remarkably improved, and introduction of those technologies in clinical practice has contributed to prenatal evaluation of fetal central nervous system (CNS) development and assessment of CNS abnormalities in utero.

Sonographic assessment of the fetal brain in the sagittal and coronal sections requires an approach through anterior/posterior fontanelle and/or the sagittal suture. Transvaginal sonography of the fetal brain opened a new field in medicine, “neurosonography” (1). Transvaginal approach to the normal fetal brain during the second and third trimesters was introduced in the beginning of 1990s. It was the first practical application of 3D CNS assessment by two-dimensional (2D) ultrasound (2). Transvaginal observation of the fetal brain offers sagittal and coronal views of the brain (3–6) through the fontanelles and/or the sagittal suture as ultrasound windows. Serial oblique sections (1) via the same ultrasound window reveal the intracranial morphology in detail. This method has contributed to the prenatal assessment of congenital CNS anomalies and acquired brain damage in utero. Furthermore, the brain circulation demonstrated by transvaginal power Doppler was first reported in 1996 (7,8); brain vascularity and blood supply have become clearly detectable afterward.

Three-dimensional ultrasound is one of the most attractive modality in a field of fetal ultrasound imaging. Automatic scan by dedicated 3D transducer produces motor-driven automatic sweeping and is called as a fan scan. With this method, a shift and/or angle change of the transducer is not required during scanning and scan duration needs only several seconds. After the acquisition of the target organ, multiplanar imaging analysis and tomographic imaging analysis are possible. Combination of both transvaginal sonography and 3D ultrasound (9–19) has been a great diagnostic tool for evaluation of 3D structure of fetal CNS. Recent advanced 3D ultrasound equipments have several useful functions as follows:

- Surface anatomy imaging
- Bony structural imaging of the calvaria and vertebrae (13,14)
- Multiplanar imaging of the intracranial structure
- Tomographic ultrasound imaging of fetal brain in the any cutting section (Fig. 1)
- Thick slice imaging of the intracranial structure
- Simultaneous volume contrast imaging of the same section or vertical section of fetal brain structure
- Volume calculation of target organs such as intracranial cavity, ventricle, choroid plexus, and intracranial lesions (20–25)

- Three-dimensional sono-angiography of the brain circulation (3D power Doppler) (8)

Fetal neuroimaging with advanced 3D technology is an easy, noninvasive, and reproducible method. It produces not only comprehensible images but also objective imaging data. Easy storage/extraction of raw volume data set enables easy off-line analysis and consultation to neurologists and neurosurgeons.

VENTRICULOMEGALY AND HYDROCEPHALUS

“Hydrocephalus” and “ventriculomegaly” are both the terms used to describe dilatation of the lateral ventricles. However, those two should be distinguished from each other. Hydrocephalus signifies dilated lateral ventricles resulted from increased amount of cerebrospinal fluid (CSF) inside the ventricles and increased intracranial pressure, while ventriculomegaly is the dilatation of lateral ventricles without increased intracranial pressure, due to cerebral hypoplasia or CNS anomaly such as agenesis of the corpus callosum (26,27). Of course, ventriculomegaly can sometimes change into hydrocephalic state. In sonographic imaging, those two intracranial conditions can be differentiated by visualization of subarachnoid space and appearance of choroid plexus. In normal condition, subarachnoid space, visualized around both the cerebral hemispheres, is well preserved during pregnancy. Choroid plexus is a soft tissue and is easily affected by intracranial pressure. Obliterated subarachnoid space and dangling choroid plexus are observed in the case of hydrocephalus. By contrast, the subarachnoid space and choroid plexus are well preserved in cases of ventriculomegaly. It is difficult to evaluate subarachnoid space in the axial plane because the subarachnoid space is observed in the parietal side of the hemispheres. It is suggested that the evaluation of enlarged ventricles should be done in the parasagittal and coronal views by transvaginal approach to the fetal brain or 3D multidimensional analysis (Fig. 2). As a screening examination, the measurement of atrial width (AW) is useful with a cutoff value of 10mm (28,29). In normal fetuses, blood flow waveforms of dural sinuses, such as the superior sagittal sinus, vein of Galen, and straight sinus have pulsatile pattern (30). However, in cases with progressive hydrocephalus, normal pulsation disappears and blood flow waveforms become flat pattern (30). Intracranial venous blood flow may be related to increased intracranial pressure.

Variety of Mild Ventriculomegaly with AW 10–15mm

Mild ventriculomegaly is defined as of a width of the atrium of the lateral cerebral ventricles of 10 to 15mm. It has been reported that mild ventriculomegaly with AW 10 to 15mm resolves in 29%, remains stable in 57%, and progresses in 14% of the cases during pregnancy (31). In cases of

Figure 1 Tomographic ultrasound imaging by three-dimensional transvaginal sonography. Normal brain at 20 weeks (left) and 31 weeks (right) on the coronal cutting sections. Note the changing cortical development between those two different gestational stages.

Figure 2 Hydrocephalus (left) and ventriculomegaly (right). Tomographic ultrasound imaging of X-linked hydrocephalus at 21 weeks (left) and ventriculomegaly at 25 weeks (right). Note the obliterated subarachnoid space in the hydrocephalic case compared with normal subarachnoid space in the ventriculomegaly case.

ventriculomegaly with AW of 10 to 13mm at referral, the ultimate fetal outcome and prognosis depends on associated abnormalities.

Generally, in cases of mild fetal ventriculomegaly with a normal karyotype and an absence of malformations, the outcome appears to be favorable (32). Piliu and his colleagues (33) reviewed 234 cases of borderline ventriculomegaly including an abnormal outcome in 22.8% and concluded that borderline ventriculomegaly carries an increased risk of cerebral maldevelopment, delayed neurologic development, and, possibly, chromosomal aberrations. Isolated mild ventriculomegaly with AW of 10 to 12mm may be normal variation. Signorelli and colleagues (34) described that their data of normal neurodevelopment between 18 months and 10 years after birth in cases of isolated mild ventriculomegaly (AW of 10–12mm) should provide a basis for reassuring counseling. Ouahba and colleagues (35) recently reported the outcome of 167 cases of isolated mild ventriculomegaly and concluded that in addition to associated anomalies, three criteria are often associated with an unfavorable outcome: AW greater than 12mm, progression of the enlargement, and asymmetrical and bilateral ventriculomegaly.

Moderate to Severe Ventriculomegaly and Hydrocephalus with AW>15mm

The term of “hydrocephalus” does not identify a specified disease, but is a generic term that means a group of pathologic conditions due to abnormal circulation of CSF. Treatment method of hydrocephalus should be selected according to age of onset and symptoms. Congenital hydrocephalus is classified into three categories by causes that disturb CSF circulation pathway: simple hydrocephalus, dysgenetic hydrocephalus, and secondary hydrocephalus (15,26).

1. Simple hydrocephalus

Simple hydrocephalus, caused by developmental abnormality that is localized within CSF circulation pathway, includes aqueductal stenosis, atresia of foramen Monro, and maldevelopment of arachnoid granulation.

2. Dysgenetic hydrocephalus

Dysgenetic hydrocephalus indicates hydrocephalus as a result of cerebral developmental disorder in early developmental stage and includes hydranencephaly, holoprosencephaly, porencephaly, schizencephaly, Dandy-Walker malformation, dysraphism, and Chiari malformation.

Figure 3 Encephalocele. Tomographic ultrasound imaging (upper) and MR imaging (lower) in a case of encephalocele at 28 weeks of gestation.

3. Secondary hydrocephalus

Secondary hydrocephalus is a generic term indicating hydrocephalus caused by intracranial pathologic condition, such as brain tumor, intracranial infection, and intracranial hemorrhage.

In cases with progressive hydrocephalus, there may be seven stages of progression: (i) increased fluid collection of lateral ventricles, (ii) increased intracranial pressure, (iii) dangling choroid plexus, (iv) disappearance of subarachnoid space, (v) excessive extension of the dura and superior sagittal sinus, (vi) disappearance of venous pulsation, and finally (vii) enlarged skull (24). In general, both hydrocephalus and ventriculomegaly are still evaluated by the measurement of biparietal diameter and AW in transabdominal axial section.

Although all cases have similar ventricular appearance, the causes of ventriculomegaly vary, such as Chiari type II malformation, aqueductal obstruction, and amniotic band syndrome (ABS). In the case of ABS, amniotic band attached to the scalp resulted in partial cranial bone defect and a small cephalocele, which may have caused Monro obstruction and enlarged ventricles.

From our data of 23 ventriculomegaly cases with AW > 15 mm (27), 9 cases (39.1%) had no other CNS abnormality, but 2 out of those 9 were complicated with chromosomal aberration. Four cases out of seven without any complication had favorable postnatal prognosis after ventricular-peritoneal shunting procedure. Among the rest of 14 cases with other CNS abnormalities, holoprosencephaly was detected in 5 cases and myelomeningocele in 5 cases (27).

NEURAL TUBE DEFECTS

Cranium Bifidum

Cranium bifidum is classified into four types of encephaloschisis (including anencephaly and exencephaly), meningocele, encephalomeningocele, encephalocystocele, and cranium bifidum occultum. Encephalocele occurs in the occipital region in 70% to 80%. Acrania, exencephaly, and anencephaly are not independent anomalies. It is considered that dysraphia (absent cranial vault, acrania) occurs in very early stage and disintegration of the exposed brain (exencephaly) during the fetal period results in anencephaly. Encephalocele (Fig. 3) is often observed in the median section and in the parieto-occipital part. ABS should be differentiated from acrania during early pregnancy, because ABS has completely different pathogenesis from acrania/exencephaly. In cases of ABS, cranial destruction occurs secondary to an amniotic band; similar appearance is often observed.

Spina Bifida

Spina bifida aperta, manifest form of spina bifida, is classified into four types: meningocele, myelomeningocele, myelocystocele, and myeloschisis. In myelomeningocele, the spinal cord and its protective covering (the meninges) protrude from an opening in the spine. In meningocele, the spinal cord develops normally but the meninges protrude from a spinal opening. The most common location of the malformations is the lumbar and sacral areas of the spinal cord. Chiari type II malformation and secondary hydrocephalus/ventriculomegaly are mostly, and scoliosis or kyphosis occasionally, associated with open spina bifida. Surface anatomy of the fetus and appearance of clubfoot, which occasionally manifests early in

Figure 4 Myelomeningocele. Two-dimensional (2D) ultrasound of myelomeningocele (upper left) and myelomeningocele with kyphosis (lower left), 3D ultrasound (middle), and MRI (right). Right upper MRI shows Chiari type II malformation (arrows). Clear visualization of spinal cord protrusion is obtained by 2D ultrasound and MRI. The 3D ultrasound images show the bony structure that helps to determine the level of spina bifida and lower extremity appearance.

mid-gestation as a complication of spinal bifida, are easily demonstrable by using 3D ultrasound. The 3D ultrasound with maximum mode can demonstrate bony structure (Fig. 4) and is helpful to detect the spinal levels of lesion and to predict neurologic prognosis. Although most myelomeningoceles are demonstrated as a protruding swelling, fetal back appears flat in the type of myeloschisis; therefore, open spina bifida may be often overlooked. Because more than 80% of cases of open spina bifida are associated with ventriculomegaly due to Chiari type II malformation, demonstration of ventriculomegaly is usually the first observable sign leading to the detailed examination of spine and the subsequent diagnosis of spinal bifida.

PROSENCEPHALIC DEVELOPMENTAL DISORDER

Holoprosencephaly

Holoprosencephalies are classified into three varieties: alobar, semilobar, and lobar types. Facial abnormalities such as cyclopia, ethmocephaly, cebocephaly, flat nose, cleft lip, and palate are invariably associated with holoprosencephaly and extracerebral abnormalities. Facial abnormalities are often associated with holoprosencephaly.

Agenesis of the Corpus Callosum

Absence of the corpus callosum (AOCC) is divided into complete agenesis, partial agenesis, or hypogenesis. Chromosomal aberration or syndromic diseases may occasionally be related to agenesis of the corpus callosum. Colpocephalic ventriculomegaly with disproportionate enlargement of trigones, occipital horns and temporal horns, and superior elongation of the third ventricle is usually observed. Inter-hemispheric cyst is often associated with AOCC and some cases are with pericallosal lipoma. Complete AOCC is

demonstrated in the coronal and sagittal sections by sonography and fetal MRI. Typical shape of enlarged ventricles associated with AOCC is colpocephaly with large occipital horns. Typical radiated formation of brain vessels in the sagittal section is demonstrated by color Doppler study. As the corpus callosum is depicted after 17 or 18 weeks of gestation by ultrasound, it is impossible to diagnose agenesis of the corpus callosum prior to this age (36).

POSTERIOR FOSSA ANOMALY

Chiari Malformation

Chiari classified anomalies with cerebellar herniation in the spinal canal into three types by contents of herniated tissue: contents of type I is a lip of cerebellum; type II part of cerebellum, fourth ventricle and medulla oblongata, and pons; and type III large herniation of the posterior fossa. Thereafter, type IV with just cerebellar hypogenesis was added. However, this classification occasionally leads to confusion in neuroimaging diagnosis. Therefore, at present, the classification as below is advocated: type I not associated with myelomeningocele, type II (schematic picture is shown in Fig. 5 upper left) associated with myelomeningocele, type III associated with cephalocele or craniocervical meningocele, and type IV associated with marked cerebellar hypogenesis and posterior fossa shrinking. Chiari malformation occurs according to i) inferior displacement of the medulla and the fourth ventricle into the upper cervical canal, ii) elongation and thinning of the upper medulla and lower pons and persistence of the embryonic flexure of these structures, iii) inferior displacement of the lower cerebellum through the foramen magnum into the upper cervical region, and iv) a variety of bony defects of the foramen magnum, occiput, and upper cervical vertebra (37). Hydrocephalus is caused by

Figure 5 Chiari type II malformation. Schematic picture of Chiari type II malformation (upper left). Elongation and stenosis of the aqueduct and fourth ventricle in the specimen from aborted fetus at 21 weeks (upper middle) are shown. Lower brain images are lemon sign and banana sign from the left. Arrowheads indicate indentations of lemon-shaped skull and banana-shaped cerebellum. Lower middle picture shows the lemon sign on the autopsy of an aborted fetus. Right sagittal ultrasound images show normal cerebropinal structure, Chiari type II malformation without kink, and Chiari II with medullary kink from above.

obstruction of fourth ventricular outflow or associated aqueductal stenosis. Eighty-eight percent of fetuses with open spina bifida develop ventriculomegaly, by 21 weeks of gestation in the majority of cases (38). As prenatal neuroimaging of Chiari malformation, lemon and banana signs (39) are circumstantial evidences of Chiari malformation, which are easily demonstrated in the early second trimester. Lemon sign indicates deformity of the frontal bone, and banana sign indicates abnormal shape of cerebellum without cisterna magna space (Fig. 5, lower). Herniation of the cerebellar tonsil and medulla oblongata and medullary kink are demonstrable (Fig. 5, right). Small clivus–supraocciput angle is seen in cases of Chiari malformation (40).

DANDY WALKER MALFORMATION, DANDY WALKER VARIANT, MEGACISTERNA MAGNA

During development of the fourth ventricular roof, a delay or total failure of the foramen of Magendie to open occurs, allowing a buildup of CSF and development of the cystic dilation of the fourth ventricle. Despite the subsequent opening of the foramina of Luschka (usually patent in Dandy–Walker malformation), cystic dilatation of the fourth ventricle persists and CSF flow is impaired. At present, the term “Dandy–Walker complex” by Barkovich et al. (41) is used to indicate a spectrum of anomalies of the posterior fossa that are classified by axial CT scans as it follows. Dandy–Walker malformation, Dandy–Walker variant, and megacisterna magna seem to represent a continuum of developmental anomalies of the posterior fossa (41). Figure 6 (upper) shows the differential diagnosis of hypoechoic lesion

of the posterior fossa, and typical sonographic images of Dandy–Walker malformation are shown in the lower part of Figure 6.

- *(Classic) Dandy–Walker malformation:* cystic dilatation of fourth ventricle, enlarged posterior fossa, elevated tentorium, and complete or partial agenesis of the cerebellar vermis.
- *Dandy–Walker variant:* variable hypoplasia of the cerebellar vermis with or without enlargement of the posterior fossa.
- *Megacisterna magna:* enlarged cisterna magna with integrity of both cerebellar vermis and fourth ventricle.

NEURONAL PROLIFERATION DISORDER

Microcephaly

Microcephaly is defined as a head circumference that is more than two standard deviations below the normal mean for age, sex, race, and gestation. Infections such as with rubella, cytomegalovirus, varicella (chicken pox) virus, and toxoplasmosis, radiation, medications, chromosome abnormalities, and genetic diseases may cause microcephaly. Occasionally, microcephaly occurs with late onset during pregnancy (42).

NEURONAL MIGRATION DISORDERS

Neuronal migration disorders are caused by the abnormal migration of neurons in the developing brain and nervous system. Neurons must migrate from the areas where they are born to the areas where they will settle into their proper neural

Figure 6 Differential diagnosis of hypoechoic lesion of the posterior fossa (upper) and typical sonographic images of Dandy–Walker malformation (lower). Abbreviation: C, cerebellum. Asterisks indicate cystic dilatation of the fourth ventricle.

circuits. Neuronal migration, which occurs as early as the second month of gestation, is controlled by a complex assortment of chemical guides and signals. When these signals are absent or incorrect, neurons do not end up where they belong. This can result in structurally abnormal or missing areas of the brain in the cerebral hemispheres, cerebellum, brainstem, or hippocampus, including schizencephaly, porencephaly, lissencephaly, agyria, macrogyria, pachygyria, microgyria, micropolygyria, neuronal heterotopias (including band heterotopia), agenesis of the corpus callosum, and agenesis of the cranial nerves. Symptoms vary according to the specific disorder and the degree of brain abnormality and subsequent neurologic losses, but often feature poor muscle tone and motor function, seizures, developmental delays, mental retardation, failure to grow and thrive, difficulties with feeding, swelling in the extremities, and a smaller than normal head. Most infants with a neuronal migration disorder appear

normal, but some disorders have characteristic facial or skull features.

Lissencephaly

Lissencephaly is very rare and characterized by a lack of gyral development and divided into two types.

Lissencephaly type I shows a smooth surface of the brain and cerebral wall is similar to that of an approximately 12-week-old fetus (43). *Isolated lissencephaly* (Fig. 7) or *Miller–Dieker syndrome* is associated with additional craniofacial abnormalities, cardiac anomalies, genital anomalies, sacral dimple, creases, and/or clinodactyly. *Lissencephaly type II* shows cobblestone appearance. *Walker–Warburg syndrome* with macrocephaly, congenital muscular dystrophy, cerebellar malformation, and retinal malformation or *Fukuyama congenital muscular dystrophy* with microcephaly and congenital muscular dystrophy has been proven.

Figure 7 Changing appearance of Sylvian fissure in the anterior coronal section (upper) and abnormal Sylvian fissure in cases of migration disorder (lower). At 20 weeks of gestation, bilateral Sylvian fissures (arrowheads) appear to be indentations (left). With cortical development, Sylvian fissures are formed during the latter half of second trimester (middle) and become as lateral sulci. Sylvian fissure appearance is one of the most reliable ultrasound markers for the assessment of cortical development. Lower MR images show coronal cutting sections of various migration disorders after 30 weeks of gestation: Isolated lissencephaly, cobblestone lissencephaly, and pachygyria from left.

Recently, classification has been made based on associated malformations and etiologies.

- Classic lissencephaly (previously known as type I lissencephaly)
 - Lissencephaly due to LIS1 gene mutation
 - Type I isolated lissencephaly
 - Link to chromosome 17p13.3 and chromosome Xq24-q24
 - Miller–Dieker syndrome link to chromosome 17p13.3
 - Lissencephaly due to doublecortin gene mutation
 - Lissencephaly type I, isolated, without other genetic defects
- Lissencephaly X-linked with AOCC (ARX gene)
- Lissencephaly with cerebellar hypoplasia
 - Norman–Roberts syndrome (mutation of reelin gene)
- Microlissencephaly (lissencephaly and microcephaly)
- Cobblestone lissencephaly (previously known as type II lissencephaly)
 - Walker–Warburg syndrome, HARD(E) syndrome
 - Fukuyama syndrome linked to chromosome 9q31, fukutin (44)
 - Muscle–eye–brain disease

A few reports of prenatal diagnosis of lissencephaly have been published (45–47). It was described that without previous history of an affected child, lissencephaly probably cannot be reliably made until 26 to 28 weeks of gestation (48). However, from recent study in the assessment of Sylvian fissure appearance during pregnancy, there might be a potential of earlier diagnosis of migration disorders (49).

Schizencephaly

Schizencephaly is a disorder characterized by congenital clefts in the cerebral mantle, lined by pia-ependyma, with

communication between the subarachnoid space laterally and the ventricular system medially. Of that 63% is unilateral and 37% bilateral. Frontal region is 44% and frontoparietal is 30% (43). Schizencephaly is associated with ventriculomegaly, microcephaly, polymicrogyria, gray matter heterotopias, dysgenesis of the corpus callosum, absence of the septum pellucidum, and optic nerve hypoplasia.

OTHER CONGENITAL ANOMALIES

Arachnoid Cyst, Interhemispheric Cyst

Congenital or acquired cyst, with prevalence of 1% of intracranial masses in newborns, is lined by arachnoid membranes and filled with fluid collection, which is of the same characteristic as the CSF. The number of cysts is mostly single, but two or more cysts can be occasionally observed. Location of arachnoid cyst is various, and it is said that approximately 50% of cysts occurs from the Sylvian fissure (middle fossa), 20% from the posterior fossa, and 10% to 20% each from the convexity, suprasellar, interhemisphere, and quadrigeminal cistern in the pediatric field. Interhemispheric cysts are commonly associated with agenesis or hypogenesis of the corpus callosum. Callosal agenesis with interhemispheric cyst is classified as two types (50). Type I cysts appear to be an extension or diverticulum of the third or lateral ventricles, whereas type 2 cysts are loculated and do not communicate with the ventricular system. Prenatal neuroimaging examples of interhemispheric cyst, middle fossa arachnoid cyst, and suprasellar arachnoid cyst are shown in Figure 8. As intrauterine spontaneous resolution or changing cyst size is often seen during fetal period, serial scanning is important. Detection in the first trimester was

Figure 8 Prenatal neuroimaging of interhemispheric cyst, middle fossa arachnoid cyst, and suprasellar arachnoid cyst. Abbreviations: USG, ultrasonography; MRI, magnetic resonance imaging.

reported (51). Prognosis is generally good. Many are asymptomatic and remain quiescent for years, although others may expand and cause neurologic symptoms by compressing adjacent brain, development of ventriculomegaly, and/or expanding the overlying skull.

Brain Tumors

Brain tumors are divided into *teratomatous*, most are the commonly reported brain tumors, and *nonteratomatous*. Nonteratomatous tumors includes *neuroepithelial tumor*, such as medulloblastoma, astrocytoma, choroid plexus papilloma, choroid plexus carcinoma, ependymoma, ependymblastoma, and *mesenchymal tumor* such as craniopharyngioma, sarcoma, fibroma, hemangioblastoma, hemangioma, and meningioma, and *others* such as lipoma of the corpus callosum, subependymal giant-cell astrocytoma associated with tuberous sclerosis (often accompanied by cardiac rhabdomyoma) (52). Depending on the site and vascularity, these tumors may lead to macrocrania or local skull swelling, epignathus, secondary hydrocephalus, intracranial hemorrhage, intraventricular hemorrhage, polyhydramnios, and heart failure by high-cardiac output (53) or hydrops. Intracranial masses with solid, cystic, or mixture pattern with or without visualization of hypervascularity can be detected by ultrasound and fetal MRI. Brain tumor should be considered in cases with unexplained intracranial hemorrhage.

Craniosynostosis

Craniosynostosis is the premature closure of cranial suture, which may affect one or more cranial sutures. Simple sagittal synostosis is most common. Various cranial shapes depend on affected suture(s).

Sagittal suture	Scaphocephaly or dolichocephaly
Bilateral coronal suture	Brachycephaly
Unilateral coronal suture	Anterior plagiocephaly
Metopic suture	Trigonocephaly
Lambdoid suture	Acrocephaly
Unilateral lambdoid suture	Posterior plagiocephaly
Coronal/lambdoid/metopic or squamous/sagittal suture	Cloverleaf skull
Total cranial sutures	Oxycephaly

Craniosynostosis due to specific syndromes (syndromic craniosynostosis) is usually associated with additional specific features and therefore correct differentiation between these conditions is possible. Examples include *Crouzon syndrome* (acrocephaly, synostosis of coronal, sagittal and lambdoid sutures and ocular proptosis, maxillary hypoplasia), *Apert syndrome* (brachycephaly, irregular synostosis, especially coronal suture and midfacial hypoplasia, syndactyly, broad distal phalanx of thumb, and big toe), *Pfeiffer syndrome* (brachycephaly, synostosis of coronal and/or sagittal sutures

Figure 9 Three-dimensional B-flow detection, color Doppler image, and MRI of vein of Galen aneurysmal malformation.

and hypertelorism, broad thumbs and toes, and partial syndactyly), and *Antley-Bixler syndrome* (brachycephaly, multiple synostosis, especially of coronal suture and maxillary hypoplasia, radiohumeral synostosis, choanal atresia, arthrogryposis). Abnormal craniofacial appearance can be detected prenatally by 2D/3D ultrasound (26,54–56).

VEIN OF GALEN ANEURYSMAL MALFORMATION

It is a congenital malformation of blood vessels of the brain. The main structure is direct arteriovenous fistulas in which blood shunts from choroidal and/or quadrigeminal arteries into an overlying single median venous sac. Vein of Galen aneurysm is not “aneurysm” but “arteriovenous malformation (AVM).” Vein of Galen aneurysmal malformation (VGAM) is a choroidal type of AVM involving the vein of Galen forerunner. This is distinct from an AVM with venous drainage into a dilated, but already formed, vein of Galen (57). Associated anomalies are cardiomegaly, high cardiac output, secondary hydrocephalus, macrocrania, cerebral ischemia (intracranial steal phenomenon), and subarachnoid/cerebral/intraventricular hemorrhages. The 3D B-flow detection, color Doppler image, and MRI of VGAM are shown in Figure 9.

Pericallosal Lipoma

Intracranial lipomas are congenital malformations composed of mature adipocytes. They are usually located in the midline, particularly in the pericallosal region, a hemispheric location accounting for only 3% to 7% of cases. Two morphologic types of pericallosal lipoma have been described (58,59).

Tubulonodular type with generally greater than 2cm in diameter (often smaller than 2cm in fetal period) has a high incidence of corpus callosum dysgenesis, frontal lobe anomalies, and frontal encephaloceles. *Curvilinear type*, which comprises thin, posteriorly situated lipomas curving around the splenium, is generally associated with a normal corpus callosum and otherwise has a low incidence of associated anomalies. High echogenic mass can be easily demonstrated by ultrasound. Several reports on prenatal diagnosis have been published (60–62).

ACQUIRED BRAIN ABNORMALITIES IN UTERO

In terms of encephalopathy or cerebral palsy, “*timing of brain insult, antepartum, intrapartum, or postpartum?*” is one of the serious controversial issues including medico-socio-legal-ethical problems (15). Although brain insults may relate to antepartum events in a substantial number of term infants with hypoxic-ischemic encephalopathy, the timing of insult cannot always be certain. It is a difficult task to provide a precise prediction of subsequent development of cerebral palsy after a given antepartum event or complication. Fetal heart rate monitoring cannot reveal the presence of encephalopathy, and neuroimaging by ultrasound and MR imaging is the most reliable modality for disclosure of silent encephalopathy. In many cases with cerebral palsy with acquired brain insults, especially term-delivered infants with reactive fetal heart rate tracing and good Apgar score at delivery, recent imaging studies have confirmed the presence of brain insult in utero, suggesting that the majority of cerebral palsy are of antepartum rather than intrapartum in origin.

Figure 10 Intracerebral hemorrhage at 32 weeks of gestation. Transvaginal three-dimensional tomographic ultrasound images show unilateral ventriculomegaly due to cerebral hemorrhage and fresh intracerebral hemorrhage (arrows), which is going to change into porencephaly.

Intracranial Hemorrhage

Intracranial hemorrhage includes subdural hemorrhage, primary subarachnoid hemorrhage, intracerebellar hemorrhage, intraventricular hemorrhage, and intraparenchymal hemorrhage other than cerebellar hemorrhage (63). Hydrocephalus, hydranencephaly, porencephaly, and/or microcephaly are possible secondary complications, which are often detectable by imaging studies. Unilateral ventriculomegaly due to cerebral hemorrhage and fresh intracerebral hemorrhage is shown in Figure 10. The hyperechoic lesion is changing into porencephaly in a short period.

Porencephaly

Porencephaly or porencephalic cyst is defined as fluid-filled spaces replacing normal brain parenchyma and may or may not communicate with the lateral ventricles or subarachnoid space. The causes may be ischemic episode, trauma (64), demise of one twin, Intracerebral hemorrhage, and infection of cytomegalovirus (65). Some cases in utero have been reported (66,67). Porencephalic cyst never causes a mass effect, which is observed in cases with arachnoid cyst or other cystic mass lesions. This condition is acquired brain insult and differentiated from schizencephaly of migration disorder.

FETAL PERIVENTRICULAR LEUKOMALACIA

Multifocal areas of necrosis are found deep in the cortical white matter, which are often symmetrical and occur adjacent to the lateral ventricles. Periventricular leukomalacia (PVL) represents a major precursor for neurologic and intellectual impairment, and cerebral palsy in later life. About

25% to 75% of premature infants at autopsy are complicated with periventricular white matter injury. However, clinically, incidence may be much lower. About 5% to 10% of infants have less than 1500g birth weight. In term infants, PVL is very rare.

CONCLUSIONS

Recent advances of imaging technology have provided us objective neuroimaging diagnosis as shown in this article. Longitudinal and careful evaluation of neurologic short-term/long-term prognosis should be required according to precise prenatal diagnosis, for proper counseling and management based on accurate evidence.

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