The Role of Magnetic Resonance Imaging in the Diagnosis of Fetal Malformations

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Abstract: Even if ultrasonography still remains the primary prenatal investigation technique for the assessment of fetal development, magnetic resonance imaging (MRI) plays an important role for the study of fetal morphology and pathology.

MRI has been shown to be particularly useful for the evaluation of the central nervous system (CNS), the latter being a common site of pathology such as cerebral and spinal malformations.

MRI is contributive in defining fetal neck, thoracic, abdominal, and pelvic masses. This can be especially helpful when differing opinions exist as to the etiology of a mass.

Ultrasonography, a non-invasive, low cost, real time technique, still represents the investigation of choice in prenatal screening, not only regarding the CNS. Nevertheless several cases need a diagnostic complement by means of MRI, that increases the diagnostic potential of ultrasound.

The additional information from MRI is important in prenatal counseling, delivery planning and planning for pre- or postnatal intervention.

Key words: Magnetic resonance imaging, congenital anomalies, prenatal diagnosis, pregnancy, fetus.

INTRODUCTION

Even if ultrasonography still remains the primary prenatal investigation technique for the assessment of fetal development, nowadays magnetic resonance imaging (MRI) plays an important role for the study of fetal morphology and pathology. MRI has been shown to be particularly useful for the evaluation of the central nervous system (CNS), the latter being a common site of pathology such as cerebral and spinal malformations that are frequently detected on prenatal screening ultrasound. Due to its easiness to perform and possibility of producing multiplanar images and obtaining easy-to-reproduce anatomical planes, MRI represents the investigation of choice in sonographic uncertain cases or in some fetomaternatal conditions that may hinder a correct visualization of the fetus by means of ultrasound (maternal obesity, oligohydranmios, low position of the fetal head, advanced skull ossification). The absence of bone artefacts allows to accurately evaluate the cerebral cortex and the overlying subarachnoid spaces. Moreover the reproducibility of the technique makes it possible to repeat the examination every time a pathologic condition needs to be monitored in time.

Although the harmlessness of MRI still has to be proven and no harmful effects are described so far on the fetus (studies on potential harmful effects on the fetal hearing depending on the scanner noisiness are in progress), fetal MRI is usually performed as a second choice investigation, when indicated by the sonographer, only starting from 18 weeks of pregnancy, the fetal morphogenesis being ended and the fetal dimensions allowing to obtain a sufficient spatial and contrast resolution.

The disadvantages of MRI mainly depend on the high costs (that considerably overcome those of ultrasonography), on the scant literature related to its relatively recent applicability and which is limited to a few ultraspecialistic centers and on the scarcity of controlled studies, especially referring to fetal lesions acquired during late pregnancy.

Technique

The need for eliminating fetal and maternal movements in order to obtain images of sufficient diagnostic quality has been representing a sometimes insurmountable limit to perform fetal MRI. Fetal sedation by means of curare used to be indispensable during the first clinical applications of MRI because of the length of spin echo sequences lasting 4 to 10 minutes. When such invasive techniques were abandoned fetal immobility was later obtained by either oral or intravenous administration of benzodiazepines to the mother. Thanks to the advent of ultrafast imaging (echo planar and single shot fast spin echo techniques), high definition images of the fetus can now be obtained in less than one second with no need for invasive techniques and thus eliminating the problem of fetal movements; T1-weighted
sequences only still require relatively long acquisition times (about 18 seconds) and remain sensitive to fetal and maternal movements. Ultrafast imaging is a prerogative of fetal cerebral tissue and highly performing gradients. The combination of 1.5 T magnets and multiple torso/phased array coils is associated with high signal homogeneity and very good spatial and contrast resolution both in fetal brain and spine.

The MRI examination is performed, after centering the anatomical region of interest, both with T1-weighted (T1W) and T2-weighted (T2W) sequences, acquired while the mother is freely breathing on the three spatial planes according to the fetal anatomy. To study the brain and the spinal cord, contiguous slices respectively 3 and 2 mm thick are obtained, with no gap interposition.

The good quality of images is favored by the cephalic presentation of the fetus, a condition in which the transmission of maternal respiratory movements to the fetal head is reduced.

Ultrafast T2W sequences (single shot FSE), thanks to the excellent signal to noise ratio (SNR) and the extremely good contrast resolution (depending on the high water content of fetal brain), represent the basis of fetal MRI: such sequences are primarily meant to outline the anatomy and to study the cerebral sulci, besides being useful in biometric analysis. Each individual slice is acquired separately with a duration of about 400 ms, so that these sequences are not particularly affected by fetal movements. New generation MRI equipments allow to perform 3D T2W acquisitions with a substantial reduction of the examination time. Several anatomical structures such as the corpus callosum, the cavum of the septum pellucidum, the vermis and the cerebellar hemispheres can be easily pointed out by T2W sequences. On the other hand there are lesions, such as small calcifications and some types of hemorrhagic lesions, and the cerebral myelination pattern that they cannot accurately assess.

Fast gradient echo sequences with low flip angles are used to obtain T1W images. They are characterized by longer acquisition times than the former sequences and they are often sensitive to movement artefacts; also they are less indicated for the study of the cerebral anatomy, but they find indication in the evaluation of cerebral myelination, in the detection of intra and pericerebral hemorrhage, calcifications (subependimal nodules of tuberous sclerosis), lipomatous tissue (corpus callosum lipomas).

Gradient echo T2* sequences are able to depict hemosiderin deposits and calcific tissues as areas of signal loss, due to paramagnetic interferences; also they easily outline osseous and osteocartilaginous structures: nevertheless these sequences have a low SNR with a poor definition of the anatomy and of the cerebral parenchyma.

Angiographic images can be obtained when suspecting a vascular malformation.16 Diffusion weighted images (DWI) (echo planar imaging) can visualize the cytotoxic and/or vasogenic edema resulting from recent ischemic lesions, and they can furthermore provide important informations for the evaluation of pre-myelinated white matter bundles and cortex, earlier than with conventional sequences. The purpose of diffusion tensor imaging is to study the water diffusion within the cerebral tissue by measuring the apparent diffusion coefficient (ADC) and the fractional anisotropy (FA). For this purpose multishot echo-planar imaging (EPI) techniques with diffusion gradient (amplitude: 30 mT/m, b: 600 s/mm²) are applied in six non-collinear axis to obtain transverse sections of the fetal brain (acquisition time of about 1 minute). The parameters ADC and FA are then measured in different anatomical regions, such as the corpus callosum, the frontal white matter, the basal ganglia, the cerebral peduncles.

MR spectroscopy,17 even though successfully applied, requires fetal immobility through maternal sedation, resulting in non-routinary application. Spectroscopic studies are based on the variation of the resonance frequency of a nucleus according to the molecular structure. Hydrogen, consisting of one proton only, is the most studied nucleus. It is possible to determine the concentration of several biologic molecules contained in a given tissue by studying the amplitude of the different spectroscopic frequencies emitted by a small volume of such tissue. The molecules of interest in the CNS include: N-acetyl-aspartate (a marker of neurons and axons density), creatine (a marker of cellular metabolic energy), coline (a marker of cell membrane integrity and myelination) and lactate (a marker of anaerobic metabolism).

A spectroscopy pattern showing reduced N-acetyl-aspartate levels and increased lactate levels is highly suggestive of impaired neural development.

Functional MRI18 is a relatively new technique which gives information on the pre- and poststimulus blood flow to various parts of the brain. When an external stimulus causes increased neuronal activity in one part of the brain there is increased blood volume to this site. Functional MRI can identify the brain response to various stimuli by estimating the amount of oxyhemoglobin in venous blood at different sites. This technique may allow to identify fetal brain dysfunction even in absence of anatomical anomaly.

Since gadolinium is able to pass through the placental filter entering repeatedly the fetal circulation, paramagnetic contrast agents are not at the moment used in fetal MRI.

Examination Protocol

Fetal MRI is performed by a standardized protocol, by using 4-5 mm thick slices orientated parallel and perpendicular to the brainstem. If necessary the examination can be complemented with more slices of lower thickness aimed to the region of interest orientated in the different spatial planes.
CNS Normal Anatomy

The normal anatomy of a developing fetal brain is characterized by considerable morphologic changes involving the volume and shape of the ventricles, the contraction of the pericerebral liquoral spaces, the reduction of the germinative matrix, the development of cerebral sulci. The gyration pattern becomes almost completely visible only at gestation week 34-35. Subarachnoid spaces usually remain wide, especially in the parieto-occipital region. The maturation process underlying neuronal migration and cerebral myelination is characterized by several MR signal changes occurring simultaneously. Such changes reflect modifications in the water content and cellular density, especially evident in the brainstem at gestation week 20, of the germinative matrix and of the white matter, where the intermediate zone formed by migratory neurons can be visible until week 30.

MR signal changes can be already identified at 20 weeks of pregnancy in the posterior limb of the internal capsule and in the optic tracts, and in the semioval centers at gestation week 35. Considering MR analysis, it is important to point out how the normal multilaminar presentation of fetal brain and the regular sequential appearance of the fissures and cerebral sulci represent essential parameters of a normal CNS development. On the other hand, when such patterns are modified, they can be sign of severe pathologic events.

Fetal MRI should be essentially considered as a complementary and supplementary investigation technique in the assessment of the fetus in the second and third trimester, particularly when facing ultrasonography limits and doubtful cases.

Fetal biometry on MRI is strictly related to ultrasonographic biometry and it can be used to obtain supplementary information on the fetal CNS. A biometric study includes the measuring of several anatomical structures, for example: fronto-occipital diameter, biparietal osseous and cerebral diameter, corpus callosum length, lateral ventricles, III and IV ventricles, interhemispheric distance, anteroposterior and cranio-caudal interopercular distances, vermis height and anteroposterior diameter, vermis surface, transverse cerebellar diameter. Such measures are obtained directly during the examination and then compared to statistical data.

The study of gyration aims to the assessment of the sulci. They can only be called sulci when they are clearly identifiable as real depressions on the cerebral surface. Cerebral sulci are divided into primary and secondary, the latter arising as ramifications from the first and being more easily assessed in later stages of the fetal development. The central, pre and postcentral sulci can be studied in axial sections at the vertex. The sulci of the internal surface and of the basis of the cerebral hemispheres can be better assessed in sagittal and coronal sections (cingulate sulcus, marginal, callosal, internal parieto-occipital fissure, calcarine fissure). The hippocampal fissure and the collateral and external occipito-temporal sulci are better identified in coronal sections, as well as the superior and inferior temporal and occipital sulci and the intraparietal sulcus. The Sylvian fissure and its opercularization are evaluated in the three orthogonal planes.

Study of myelination: cerebral myelination can be assessed in axial sections by T1W sequences where it shows high signal intensity. Myelination of several structures can be evaluated: the pons tegmen, the cerebellar vermis and cerebral peduncles, the internal capsule and basal ganglia. DWI can also be used.

CNS Anomalies

Ventriculomegaly: is defined by the evidence of a ventricular atrium width of more than 10 mm and it can have a malformative, obstructive or clastic origin (Fig. 1). In 70-84% of cases is associated with chromosomal anomalies and with other organs and CNS malformations (neural tube defects, agenesis of the corpus callosum, Dandy-Walker malformation, cortical dysplasias, gyration anomalies). It can also be associated with subependimal and intraventricular hemorrhages and porencephaly. The prognosis of isolated ventriculomegaly is favorable, while in case of ventriculomegaly with associated CNS malformations the probability of late psychomotor development increases. The detection of the latter is therefore of critical importance and fetal MRI represents the reference technique for such purpose: the literature reports that fetal MRI has detected CNS malformation associated with ventriculomegaly in 40-50% of the cases and such anomalies were not previously diagnosed by ultrasonography (Fig. 2).

Agenesis of the corpus callosum. Complete or partial, this malformation has been reported both in asymptomatic patients and in association with various neurological deficits (psychomotor delay, epilepsy). In about 85% of cases it is associated with other CNS malformations, such as Dandy-Walker, Chiari II, cortical dysplasias, oloprosencephaly,
The Role of Magnetic Resonance Imaging in the Diagnosis of Fetal Malformations

callosal agenesis can now be diagnosed by ultrasound, both with indirect signs and with a direct visualization of the lack of the corpus callosum.

In some cases of partial agenesis and/or of inadequate visualization of the corpus callosum caused by oligohydramnios or maternal obesity, the diagnosis can only be confirmed by a fetal MRI examination. Sometimes a particularly flexed or deflexed position of the fetal head and some positions of the maternal pelvis make a fetal MRI necessary to complement an ultrasonographic suspect. Ultrasonographic suspicious findings can be represented by a lack in the visualization of the septum pellucidum, by a widening of occipital horns and atria in a typical teardrop configuration, by an upward positioning of the III ventricle or a radial convergence of the mesial cerebral sulci towards the III ventricle. In such cases fetal MRI allows a direct or indirect visualization of the corpus callosum (Fig. 3) after 20 weeks of pregnancy in sagittal and coronal sections, but above all it allows to detect the absence of the corpus callosum besides the possibly associated ultrasound invisible CNS anomalies.

The posterior fossa malformations that can be diagnosed by fetal MRI include the Dandy-Walker complex (Dandy-Walker malformation and Dandy-Walker variant), the mega cysterna magna, the Blake’s pouch, arachnoid cysts, cerebellar malformations (hypoplasia and dysplasia), and the Chiari II malformation.

In the Dandy-Walker malformation MRI shows a cystic dilatation of the IV ventricle, a widening of the posterior fossa with high confluence of the sinuses, a hypoplasia or agenesis of the inferior cerebellar vermis, which appears anticlockwise rotated (Figs 4 and 5). In the Dandy-Walker malformation variant, in which the posterior fossa shows normal dimensions, the only finding can be an abnormal widening of the Magendie foramen associated with a slight anticlockwise rotation of the vermis. The Blake’s pouch cyst is characterized by an expansion of the IV ventricle in association with supratentorial hydrocephalus. Although the classic Dandy-Walker

Figs 2A and B: Untreated Toxoplasma infection at 31 weeks of pregnancy. Hydrocephalus with small iuxtaependymal cysts (arrow). Slight expansion of the periencephalic liquoral spaces. (A and B) axial sections

Figs 3A and B: Agenesis of the corpus callosum at 33 weeks of pregnancy. Parallel course of the lateral ventricles, with colpocephalic configuration, telencephalic pseudocyst and eversion of the cingulate gyrus and coronal sections, but above all it allows to detect the absence of the corpus callosum besides the possibly associated ultrasound invisible CNS anomalies.

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Figs 4A and B: Dandy-Walker malformation at 29 weeks of pregnancy. Anticlockwise rotation of the cerebellar vermis and communication of the IV ventricle with a large liquoral retrocerebellar “cyst” with associated internal theca scalloping. Note the enlarged posterior fossa. Upward displacement of the torcular Herophili. (A) sagittal section, (B) coronal section

Figs 5A and B: Dandy-Walker malformation at 18 weeks of pregnancy. The anticlockwise rotated vermis, appearing hypoplastic in its inferior portion, and the cystic IV ventricle are easily visualized. (A) sagittal section, (B) coronal section
malformation can be easily diagnosed by ultrasound, sometimes the differential diagnosis between a less severe variant of the malformation and a mega cisterna magna or an arachnoid cyst (conditions in which the agenesis/hypogenesis of the cerebellar vermis is not described) can be very difficult, especially in presence of an advanced cranial ossification of the fetus that hinder a correct ultrasonographic assessment of the posterior fossa. In such cases MRI is very important because it can accurately describe the morphology and position of the cerebellar vermis and the relationship between the posterior fossa cyst and the IV ventricle.

Once the presence of a Dandy-Walker complex malformation is verified, MRI is necessary for accurately searching the signs of the most frequently associated malformations (agenesis of the corpus callosum, polymicrogyria, neurons heterotopia, occipital cephalocele). This is very important for the prognosis, because a strict relation between associated malformations and psychomotor development delays has been demonstrated.

**Abnormal proliferation and migration of neurons and cortical organization anomalies.** The diagnostic potential of MRI in this field is very high compared to ultrasound.\(^2\) The etiologic spectrum of such pathologies is extremely broad: genetic, infectious, metabolic, toxic, ischemic, traumatic. The resulting lesions, independently form the underlying cause, are similar in all cases and they substantially differ from one another depending on the time elapsed from the injury and on the affected anatomical structure.

**Microcephaly** may arise from several familiar, infective, toxic and metabolic causes. It can be primitive or associated with other malformations, such as holoprosencephaly and lissencephaly. In cases of primitive microcephaly presenting with simplified gyration pattern (microlissencephaly), the lesions seem to be caused by a defect in the neuronal proliferation of the germinative matrix or by an excessive cellular death program, with a subsequent reduction of glioneuronal units and reduction of the amount of white matter (Fig. 6). These are cases in which MRI plays a determinant role not only for the detection of microcephaly but above all for the analysis of cortical gyration, that is simplified when only the primary sulci are visible, and they have a widened and flattened unusual appearance. The secondary sulci, usually already visible at gestation week 24, are absent. The most appropriate time for the execution of MRI should be gestation week 30-34, which is not too early for the secondary sulci not to have appeared yet, nor too late, when the liquoral spaces appear reduced in thickness. Both in the cases of macrocrania and of macrencephaly or megalencephaly (increase of the cerebral volume), MRI allows an accurate assessment of the relations among the theca, the cranial base and the cerebral structures, because it is able to accurately visualize the pericerebral liquoral spaces. Besides it allows to identify other possibly associated abnormalities, especially hydrocephalus.

![Figs 6A to F](image)

Figs 6A to F: Microlissencephaly associated with midline malformation (Dandy-Walker) at 28 weeks of pregnancy. Fetal MRI shows a very small agyric brain, enlargement of the subarachnoid space, with a thin cortex in a micrencephalic fetus. Moreover, other associated anomalies are detected: Dandy-Walker malformation, hypoplastic cerebellum and brainstem: (A, B) sagittal sections; (C, D) coronal sections; (E, F) axial sections
In the cases of hemimegalencephaly, a condition in which a cerebral hemisphere or part of it grows in excess, possibly associated with areas of pachygyria, lissencephaly, polymicrogyria, heterotopia and gliosis, MRI can accurately detect anatomical asymmetries because it allows to simultaneously visualize both hemispheres and to acquire biometric measures, whatever the position of the fetus is.

The term *complete lissencephaly* or agyria (type I lissencephaly) refers to a complete absence of sulci; *pachygyria*, or incomplete lissencephaly, is characterized by shallow and smooth sulci and thickening of the cortex. Type I lissencephaly, observed in patients with mutation of genes DCX and LIS1, at histology shows a four layered cortex, in which the most internal and thick layer is made of neurons that have interrupted their physiological migration process between gestation week 12 and 16. A deletion of the gene LIS1 has been observed in all patients with Miller-Dieker syndrome, characterized by lissencephaly and facial anomalies. MRI accurately highlights the typical “8” configuration of the brain due to an absent opercularization of the Sylvian fissures and to an abnormally thick internal cortical layer (Fig. 7).

The most common form of lissencephaly is type II lissencephaly (cobblestone lissencephaly). It has been observed in several syndromes (Walker-Warburg syndrome, congenital Fukuyama muscular dystrophy, cerebro-oculo-muscular syndrome) deriving from deficits of proteins involved in muscular contraction and in CNS development. In the Fukuyama syndrome, the deficit of merosin affects the migration of oligodendrocytes precursors, with a resulting altered myelination process, associated with alteration of the final migration stage and of cortical organization. In this type of lissencephaly the cortex has an aberrant appearance, lacking the normal lamination. In the Walker-Warburg syndrome, in which dilatation of ventricles, posterior fossa anomalies (similar to Dandy-Walker), ocular abnormalities and cephalocele are also observed, MRI allows an accurate assessment of the posterior fossa structures.

Fetal MRI imaging is also superior to ultrasound in identifying *schizencephaly*, *polymicrogyria* and *grey matter heterotopia*. Subependymal heterotopia is characterized by nodules that are isointense to the germinal matrix and located along the ventricular walls. They cannot be reliably distinguished from subependymal nodules seen in tuberous sclerosis; therefore, it is important to search for other signs of tuberous sclerosis, such as cortical hamartomas (which are hypointense compared to normal unmyelinated white matter on SSFSE images) and cardiac rhabdomyomas. Schizencephaly appears as a grey matter-lined cleft extending from the ventricles to the subarachnoid space. Polymicrogyria appears as a localized or generalized absence of the normal sulcation with multiple abnormal infoldings of the affected cortex.

In holoprosencephaly MRI can be useful to recognize the lobar forms, especially when the fusion of the frontal lobes is so slight that it cannot be detected by ultrasound. In such cases MRI is indicated on the basis of extracerebral findings such as hypotelorism, microcephaly, labio-palatal schisis. Fetal MRI allows a detailed prenatal evaluation of the upper lip and palate for the diagnosis of cleft lip and cleft palate. The identification of a secondary palate is particularly important because it is not often adequately seen by ultrasound. The knowledge of the appearance of isolated cleft secondary palate may enable prospective diagnosis of this anomaly by MRI.

Figs 7A to C: Miller-Dieker syndrome (confirmed by DNA analysis) at 34 weeks of pregnancy. Lissencephaly with verticalization of the Sylvian cisterns and slight ventriculomegaly associated with hypomyelination. (A) axial section, (B) coronal section, (C) posterior coronal section
Although the sensitivity and specificity of MRI in the detection of cleft lip and palate and cleft secondary palate have not been determined yet, we can easily predict a very useful application of fetal MRI in the analysis and vigilance of fetal facial anomalies due to a combination of the improving visualization of several bony structures and of facial soft-tissue.29

Fetal Cephalocele

Cephaloceles are defined as a herniation of intracranial contents through a bony defect in the skull. Herniation of the meninges alone is termed meningocele and if there is brain tissue present as well, encephalocele.

An encephalocele may simply result from a cranial defect, or it may occur concurrently along with other more complex brain anomalies.

The contents of an encephalocele often undergo significant rotation and distortion. The so-called “Chiari III malformation” specifies a cerebellar herniation through a cervico-occipital defect.

The exquisite contrast resolution of MRI should allow easy differentiation between a CSF filled herniation and one filled with brain parenchyma, especially at the skull base.

MRI allows better evaluation of the brain structure and the skull defect, providing additional information for prenatal counseling, delivery planning and planning for postnatal intervention30 (Figs 8-10).

Spinal malformations. One of the major indications for fetal MRI is the study of spinal osseous abnormalities detected by ultrasound. MRI can contribute to point out and analyze rare anomalies of the spinal cord, such as diastematomyelia and segmentary dysgenesis, that are not always detected by ultrasound. Nevertheless, the most common spinal anomaly seen on ultrasound is myelomeningocele. Myelomeningocele is always associated with Chiari II malformation and MRI is able to demonstrate the reduced dimensions of the posterior fossa, the downward displacement of the sinuses confluence and of the trunco-cerebellar structures, the degree of vermis herniation in the foramen magnum (directly dependant on the severity of the malformation) and the frequently associated CNS malformations (anomalies of the corpus callosum, cortical dysplasias).

Brain injury. It represents one of the most common indication for fetal MRI.31,32 Regarding brain injury it is necessary to state in advance that harmful events occurring very early can interfere with the normal development of the nervous structures, and may result in real malformative conditions. MRI, due to its anatomical accuracy and its capability of tissue differentiation, plays an important role in the diagnosis of this type of lesions (Figs 2, 11 and 12). The destruction of fetal brain can be caused by several conditions: hypoxia, congenital infections (especially toxoplasmosis and cytomegalovirus), vascular and cardiac malformations, pregnancies with high risk for fetal brain damage (toxic and coagulative risk factors, maternal hypoxia, mechanic factors), hereditary metabolic defects (especially mitochondrial pathologies), tumors (Figs 13-17).

In hemorrhagic lesions MRI, allowing to simultaneously visualize the whole brain and liquoral spaces, is more helpful, compared to ultrasound, in the detection of intraventricular bleedings and especially, thanks to the high contrast resolution,
The Role of Magnetic Resonance Imaging in the Diagnosis of Fetal Malformations

Figs 11A to D: Complicated malformation of the midline associated with a clastic lesion involving the cerebral hemispheres at 22 weeks of pregnancy. It might be referred to corpus callosum agenesis associated with a large telencephalic pseudocyst, that has progressively expanded determining a maturation arrest of the rostro-mesial portion of the cerebral hemispheres: (A, B) sagittal sections; (C, D) axial sections.

Fig. 12: Same case of the Figure 11: autopsy findings

Figs 13A and B: Hemorrhagic cyst of the choroid plexus (arrow) at 30 weeks of pregnancy. (A) sagittal section, (B) coronal section

Figs 14A and B: Hemorrhage of the choroids plexus at 36 weeks of pregnancy. The bleeding is extended to the adjacent parenchyma with associated hydrocephalus. (A) fetal MRI coronal section. (B) the neonatal ultrasonographic examination shows a large hypoechoic area representing the resulting involutive-malacic lesion

Figs 15A and B: Cerebral hemorrhage at 30 weeks of pregnancy. A nucleo-capsular lesion, of desomogenous signal, mostly hypointense, is seen associated with dilatation of the adjacent ventricular spaces. (A) axial section, (B) coronal section

of juxtaventricular and intraparenchimal hemorrhages, even the small ones.

T2* sequences allow to identify occult bleedings caused by underlying vascular malformations and capillary telangiectasias. Indirect signs of cerebral edema caused by
ischemia are seen on MRI as a reduction of the pericerebral spaces and ventricles and, although more rarely, as a reduced visualization of the cortical-subcortical junction. Direct signs of acute ischemic lesion should be seen as focal changes of the white matter signal but, due to the physiological high water content of unmyelinated brain, the differentiation between normal white matter and ischemic lesions can be very difficult or even impossible.

On the other hand focal ischemic lesions are easily identified when they show a cavitated configuration as they appear more hyperintense in T2 than edema and gliosis.

Cerebral tumors and arachnoid cysts: the contribute of MRI in these cases is limited, apart from the possibility of a more accurate localization of the tumoral or cystic lesion and of its relation with the adjacent anatomical structures (Figs 18 and 19).
**Vascular malformations**: The most common are the aneurysm of the vein of Galen (Vein of Galen aneurysmal malformation – VGAM),\textsuperscript{16} dural sinus malformation (DSM) (Fig. 20), and pial arteriovenous fistulas.

The role of MRI, besides that of a possible use of angiographic sequences, mainly consists in the assessment of the cerebral parenchyma and in the identification of associated ischemic and hemorrhagic lesions, that can be related to a negative prognosis. Ischemic and hemorrhagic lesions show different characteristics depending on when they occurred, and may appear with different patterns such as periventricular leukomalacia, focal atrophy, cortical necrosis, stenogyria.

**Chest Anomalies**

Lesions of considerable dimensions such as lymphangiomas are commonly deforming the neck and extending to the mediastinum, while lesions occupying the anterolateral region of the neck that are often represented by teratomas may cause compression and dislocation, with severe obstruction of the airways.\textsuperscript{33} The fetal airways are seen as high signal intensity areas due to the presence of fluid in the tracheobronchial tree.

The normal fetal lung on T2-weighted images is homogeneous, and has moderate signal intensity. With fetal lung maturation, increased alveolar fluid production results in higher signal intensity. Low signal intensity of lungs may be suggestive of pulmonary hypoplasia; MRI can also accurately determine the volume of the lungs.\textsuperscript{34-36}

Fetal pulmonary hypoplasia occurs as a result of several disorders, including bilateral renal agenesis, congenital diaphragmatic hernia (CDH), pleural effusions, thoracic masses, skeletal dysplasia and preterm premature rupture of the membranes. Magnetic resonance spectroscopy of fetal lungs has also been attempted.\textsuperscript{37} The rationale is to noninvasively assess the relative concentrations of phosphatidylcholine (lecithin) and other phospholipidic components of the surfactant. There are several technical limitations left that need to be overcome before magnetic resonance spectroscopy becomes routinely available for this purpose. Once such problems are solved, this may get round the need for amniocentesis to assess the maturity of lungs.

The main thoracic anomalies for which MRI is performed are CDH (Figs 21 and 22) congenital cystic adenomatoid malformations\textsuperscript{38} (Figs 23 and 24) and bronchopulmonary sequestration, bronchogenic cyst (Fig. 25) and tracheal bronchial atresia.\textsuperscript{39}

Congenital diaphragmatic herniations, with an incidence of 1/2400-3000 live births, includes a group of diaphragmatic defects...
Figs 21A to C: Diaphragmatic hernia at 27 weeks of pregnancy. The left hemithorax appears almost completely occupied by the abdominal viscera, herniated through a mid-posterior diaphragmatic defect. (A,B) sagittal sections (C) coronal section

Figs 22A and B: Eventration of the diaphragm at 27 weeks of pregnancy. On the left side the diaphragm and the underlying abdominal viscera appear elevated in a dome-shaped configuration. (A) coronal section, (B) paramedian sagittal section

Figs 23A to C: Cystic adenomatoid malformation (macrocystic type) at 26 weeks of a twin pregnancy. The inferior lobe of the right lung is mainly involved, the lesion showing a bunch-shaped configuration. (A) sagittal section (B) coronal section (C) axial section

Figs 24A and B: Hybrid form of congenital cystic adenomatoid malformation (CCAM) and bronchopulmonary sequestration (BPS) with subdiaphragmatic involvement at 22 weeks of pregnancy. Area of hyperexpansion of the right inferior lobe with tendency to transdiaphragmatic extension (arrow). (A) sagittal section (B) coronal section

Figs 25A to C: Bronchogenic cyst at 27 weeks of pregnancy. Large fluid-filled lesion of the right lung at the confluence of the lobes. (A) coronal section, (B) sagittal section, (C) axial section

in which some portions of the abdominal content protrude into the chest cavity, through a posterolateral defect in 95% of cases. MRI enables the recognition of small parts of herniated liver. The diaphragmatic defect can be difficult to detect by ultrasound when the stomach lies in its normal position. It can be accurately diagnosed by MRI before birth in almost 60% of cases. This has two major advantages: the exclusion of commonly associated defects and the possibility to plan the delivery in appropriate facilities for neonatal intensive care and for surgical repair of the defect. Despite recent advances in postnatal care, the mortality rate of patients with congenital diaphragmatic hernia remains high: most of these patients die from respiratory failure due to pulmonary hypoplasia.

In the cases of isolated congenital diaphragmatic herniation the lung-to-head-ratio (LHR) is probably the most efficient sonographic predictor of outcome. MRI could also be useful as an additional tool for the quantitative and qualitative evaluation of the fetal lungs, with FLV measurements. Good agreement between lung volumes measured by MRI and those measured by 3D ultrasonography is demonstrated.

Traditionally, MRI produces static images and is inferior to ultrasound in assessing cardiac anomalies. Newer MRI techniques include rapid hybrid sequences able to produce cine images of the cardiac motion.
Gastrointestinal Anomalies

Fetal gastrointestinal tract disorders are usually diagnosed by ultrasound. Small bowel dilatation, polyhydramnios and hyperechoic intestine are the most common findings that may identify a gastrointestinal malformation. However, many of these findings are not specific, may occur late in pregnancy, and may be related to transient normal variants or functional obstruction. MRI provides a complete visualization of the fetal GI tract showing its specific signals and may locate the level of bowel obstruction, and detect a microcolon. It is helpful in identifying intra-abdominal hemorrhage.

MRI appears to be accurate for establishing or ruling out a prenatal diagnosis of esophageal atresia, and should be considered in fetuses who are at high risk based on ultrasound findings.

Esophageal and gastric duplication can be detected by MRI (Figs 26 and 27). The stomach and gallbladder are readily identified due to a bright signal on T2W images. The colonic haustral pattern is visible after 25 weeks. The main cause of proximal bowel obstruction are duodenal (Fig. 28) and jejunal atresia; the causes of distal bowel obstruction include ileal atresia, meconium ileus and small left colon syndrome. Intestinal atresia presents on MRI with three signs: proximal intestinal dilatation, abnormal signal of the content and microcolon.

MRI shows a very thin rectum, of much reduced diameter and with abnormal signal.

Abdominal wall defects are usually detected by ultrasound, but MRI is useful in case of gastroschisis to diagnose the associated intra-abdominal bowel obstruction (Fig. 29).
Genitourinary Anomalies

The application of MRI in urinary pathology is based on the high signal intensity of the urine within the excretory system and on the possibility of always visualizing the urinary bladder, which constitutes a very good reference point.

Anomalies of the genitourinary system are common. Sonography is an excellent tool for the assessment of the fetal genitourinary tract. However, some factors, including the patient's body habitus and oligohydramnios, often prevent an optimal assessment of anomalies of the genitourinary system using sonography. MRI is extremely useful in evaluating suspected anomalies and it is especially valuable for the imaging of fetuses with abnormalities of the genitourinary system that have resulted in oligohydramnios and in whom lethal pulmonary hypoplasia is suspected. Fetal MR urography performed using T2W sequences, especially in coronal sections, can show both the ureters and their size, and the ectopic position of kidneys. MRI can accurately identify the different forms of renal cystic disease, especially when the diagnosis is not confirmed on ultrasound. Multicystic dysplastic kidneys appear as enlarged kidneys with randomly scattered cysts of different size (Fig. 34). Prenatal diagnosis of autosomal recessive polycystic kidney disease is usually performed by sonography.

Prenatal diagnosis of fetal renal masses can be performed by ultrasound and MRI (Fig. 35).

The diagnosis of cloacal malformations is difficult by means of ultrasound; MRI may demonstrate a moderately dilated rectum with an abnormal fluid signal. The rectum appears to be normally located under the bladder neck, but it is separated...
from the bladder by a low signal structure corresponding to a
dilated genitourinary tract.

**Sacrococcygeal Teratoma**

Although rare, sacrococcygeal teratoma is the most common
tumor of the fetus and neonate, with a reported incidence of 1/
35,000-40,000 live births.

It has been considered either a neoplasm composed of
tissues arising from all three germ layers or a neoplasm composed
of a wide variety of tissues foreign to the anatomic site in which
they arise.

It is now generally accepted that these tumors originate
from totipotent cells from Hansen’s node or primitive germ cells
during their migration from the yolk sac to the genital ridge and
escape the normal inductive influences.

The natural history of prenatal diagnosed sacrococcygeal
teratomas differs from that of the postnatally diagnosed ones.
Malignant degeneration, the primary cause of death in postnatal
sacroccigial teratoma, is rare in utero. Prenatal assessment
of the fetus is critical for counseling and prenatal/postnatal management.

Also, with the development of in utero treatment for sacrococcygeal teratoma it is important to select appropriate candidates for fetal surgery.

Because of the acoustic shadowing due to the fetal pelvic bones, sonography cannot always define the most cephalic extent of sacrococcygeal teratomas. MRI is superior to sonography in assessing the intrapelvic and/or intraspinal extent of the tumor and in evaluating the possible compression effects on the pelvic organs by the tumor. MRI is also able to assess the content of sacrococcygeal teratoma. Both on ultrasound and on MRI it may appear cystic, solid or mixed and it may contain typical patterns secondary to areas of tumor necrosis, cystic degeneration, internal hemorrhage and calcification. The prognosis of prenatally detected sacrococcygeal teratomas seems to be related non only to the size of the mass but also to its content. Fetuses with predominantly solid and highly vascularized masses have a poorer prognosis than fetuses with tumors that are mainly cystic and avascular. The presence of hemorrhage in the tumor can be detected by MRI with T1W or echo-planar sequences, and an evaluation of the possible fetal anemia should be promptly made. MRI is also an extremely valuable tool in the assessment of the compression or involvement of the adjacent organs, conditions that favor the morbidity of sacrococcygeal teratoma. MRI helps in the prenatal planning of the intervention being, therefore, very useful for a comprehensive prenatal counseling.

The Future of Fetal MRI

Ultrasonography, a non invasive, low cost, real time performable technique, still represents the investigation of choice in prenatal screening, not only regarding the CNS. Nevertheless several cases need a diagnostic complement by means of MRI, that increases the diagnostic potential of ultrasound with important results for a better management of the time, place and modalities of delivery, for the application of in utero treatments and for the formulation of a genetic advice. While on one side several multidisciplinary groups, specifically dedicated to the study of fetomaternal pathology, are forming and are acquiring experience, on the other side, thanks to the continuous technological progress of MRI, new technical application are being considered for the nearby future. This is particularly true regarding diffusion imaging, for the quantitative analysis of cerebral development in a non-invasive way, both in pathology and in normal intrauterine development.

The application of diffusion imaging could be useful to identify ischemic lesions that are not pointed out by conventional sequences, to study the cerebral microstructure and myelination, to differentiate between intra and extracellular cerebral edema and to study placental anomalies. Besides, some cerebral lesions caused by metabolic diseases or by a decreased oxygen supply could be detected by protonic MRI spectroscopy on the basis of the altered cerebral tissue metabolism.

Thanks to spectroscopy and MR angiography some crucial points of the fetomaternal unit (such as apparently isolated ventriculomegalias detected on ultrasound, high risk of fetal anomalies in mothers with an already affected fetus or child, reduced intrauterine growths, the course and monitoring of hydrocephalus and posterior fossa anomalies associated with myelomeningocele in the Chiari II syndrome) will be better managed.

REFERENCES

The Role of Magnetic Resonance Imaging in the Diagnosis of Fetal Malformations


75


