MAGNETIC RESONANCE IMAGING: CLINICAL UTILITY IN THE EVALUATION OF FETAL CENTRAL NERVOUS SYSTEM

Resonancia magnética: Utilidad clínica en la valoración del sistema nervioso fetal

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SUMMARY
Magnetic Resonance Imaging (MRI) is a valuable complementary technique to prenatal ultrasound. It is useful in the detection and characterization of the fetal central nervous system (CNS) anomalies, partly due to the use of ultrafast sequences to reduce acquisition times. This is a revision article that shows representative cases by the authors. We include a woman in the second and third trimester of pregnancy, referred for an MRI due to a suspicion of fetal CNS anomaly during the ultrasound, and images of normal fetal brains, in pregnant women referred for a suspicion of placenta accreta.

RESUMEN
La resonancia magnética (RM) es una valiosa técnica complementaria de la ecografía prenatal, útil en la detección y caracterización de anomalías del sistema nervioso central (SNC) fetal. En parte, gracias al uso de secuencias ultrarrápidas que reducen los tiempos de adquisición. Este es un artículo de revisión que presenta casos representativos de los autores. Incluye gestantes en el segundo y tercer trimestres de edad gestacional (EG), remitidas por sospecha ecográfica de anomalía del SNC fetal; e imágenes de cerebros fetales normales, de gestantes remitidas por sospecha de acretismo placentario.

Introduction
Fetal development anomalies are found between 2 and 3% of pregnancies (1). Magnetic resonance (MR) is not a routine tool for the screening of fetal malformations, but it has proven to be a valuable complement to the ultrasound in the evaluation of the fetal central nervous system (CNS). The MRI enables the direct visualization of the developing cerebral parenchyma, and a superior representation of the processes of sulcation, the formation of convolutions and myelination (2). Therefore, it is not a technique which is susceptible to the same limiting factors as the ultrasound (3,4), and it helps to identify patients who will benefit from an early prenatal intervention (5,6).

Safety in fetal MRI
The current data has not conclusively proven harmful effects of the 1.5 tesla (T) MRI in utero during fetal or post-natal development (7-12). Despite the achieved results in several publications, some articles (3, 4) and guides of the scientific community (13) recommend not to perform an MRI during organogenesis. In our institutional protocol, we wait until after the 20th week...
of pregnancy to reduce technical difficulties, given the size and the excessive movement of the fetus.

During pregnancy, gadolinium is considered a class C medication (14). Some studies have proven that chelates cross the placenta and enter fetal circulation, remaining there for an unspecified period of time. Because of this, the average biological age in the fetus is unknown (15,16).

**Indications**

The most common reference diagnosis for the MRI of fetal CNS is ventriculomegaly. The MRI shows an important advantage in the visualization of the posterior fossa, and in the characterization of cystic lesions (17). Similarly, it is very sensitive in the determination of intra-cranial hemorrhage. Hemoglobin can be detected in sequences in T2* gradient-echo sequences (GRE), as a signal loss due to the local magnetization of iron (18). In addition, it is useful in the screening of families with known genetic disorders, fetal malformations in previous pregnancies; fetuses with cardiac rhabdomyoma, due to its association with tuberous sclerosis (19); complications of twinning monochorionic pregnancies (20,21), destructive encephalic lesions, congenital infections (22-24), intracranial and sacrococcygeal tumors (25,26), among others (27).

**Exploration techniques**

In our institution, the MRI of fetal CNS is performed with 1.5 T equipment. The use of magnetic fields with greater “magnetic field measure” (teslaje) requires studies for their validation. The exploration begins by placing the pregnant woman in a supine position, with previous bladder emptying, and fasting during 4 hours. This study lasts approximately 20 minutes, but this factor varies according to the number of sequences. A multi-channel surface antenna is used. After obtaining the weighted localizing images with T2 information, continuous images with a width of 1 mm are acquired, using ultra-fast single shot spin echo techniques (SENSE, HASTE, ssFSE, ssTSE), and balanced sequences (BFFE) weighted in T2 in the three levels of the fetal neuroaxis. Additionally, axial images with T1 information are obtained, as well as GRE, diffusion (DWI) and apparent diffusion coefficient (ADC) (28-33). Spectroscopy due to resonance is part of the routine in some centers. Its application is limited to the third trimester, when the fetal head is larger and fits in the maternal pelvis due to the excessive movement of the fetus.

**Evaluation of the fetal central nervous system**

The knowledge of the anatomy of the fetal CNS and its development are essential aspects in the interpretation of images. The formation of fetal CNS includes stages which are characterized by its complexity. Following is our suggestion of a systematic order for the evaluation of fetal CNS:

- **Cortical development:** This stage begins during the seventh week of GA (gestational age). It includes the proliferation, differentiation, neuronal migration, and cortical organization processes, which are influenced by specific molecular ligands, cellular recognition, formation of synaptic connections, etc. (2)
- **Sulcation** is a well-established criteria used to determine the maturity of the fetal brain (35). The brain furrows appear in an organized manner, as surface invaginations which progressively deepen. Before 18 weeks of GA, the fetal brain is agyric (3). The furrows of the medial surface of the hemisphere appear earlier than those of the lateral convexity (table 1 and figure 1).

**Table 1. Gestational age when the primary furrows are visible in the MRI**

<table>
<thead>
<tr>
<th>Furrows or ridges</th>
<th>MRI (weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Findings</td>
<td>Visible for the first time</td>
</tr>
<tr>
<td>Parieto-occipital</td>
<td>18-19</td>
</tr>
<tr>
<td>Calcarine</td>
<td>18-19</td>
</tr>
<tr>
<td>Cingulum</td>
<td>24-25</td>
</tr>
<tr>
<td>Central</td>
<td>26-27</td>
</tr>
<tr>
<td>Of convexity</td>
<td>26-27</td>
</tr>
</tbody>
</table>


- **Cerebral parenchyma:** A typical multi-layer pattern in the cerebral parenchyma is observed between weeks 23 and 28 of pregnancy, more evident in sequences with T1 information (37). An MRI shows three layers from the cerebral surface to the interior (4). The cortical mantle has a low intensity, with T2 information and its intensity is bright with T1 information. After week 29, it is difficult to limit it in sequences with T1 information; the white matter has an intermediate to high signal with T2 information and has low intensity with T1 information. It must not be interpreted as pathological during the 20th week of pregnancy (189; and the germinal matrix which has an involution towards the 34th week of pregnancy, only persisting in the caudothalamic groove up to post-natal life, is visualized as a band which covers the lateral ventricles, with low intensity with T2 information and high intensity with T1 information, due to its high cellularity (3) (figure 2).
- **Neuronal myelination:** It starts in the fifth week of pregnancy, and concludes in post-natal life. It is performed by the reduction in water content, an increase in the concentration of lipids, proliferation and maturation of olygodentrocytes precursors (38). It occurs from caudal to rostral, dorsal to ventral, and central to peripheral; and the high-intensity white matter with T1 information must be observed, as well as low-intensity white matter with T2 information (18,39) (table 2).
- **Corpus callosum:** The embryology of the corpus callosum is still controversial in scientific literature. Some investigations have proven that the body forms first, growing bi-directionally towards the knee and the spleen (40). Despite this, the lamina rostralis of the fetal rostrum is present before the development of the knee and the spleen (41). This structure is visible from week 20 of pregnancy. It is formed by the reduction in water content, an increase in the concentration of lipids, proliferation and maturation of olygodentrocytes precursors (38). It occurs from caudal to rostral, dorsal to ventral, and central to peripheral; and the high-intensity white matter with T1 information must be observed, as well as low-intensity white matter with T2 information (42-44).
The measurements of the cerebellum are useful in the evaluation of its normal development in relation to the pregnancy (45,46). The cisterna magna must not be larger than 10 mm.

**Ventricular system and subarachnoid space**

The lateral ventricles in the fetus must have a maximum diameter of 100 mm, with smooth margins without nodular areas, which suggest heterotopy or tuberous nodes (3-47). Ventricular atria greater than 12 mm and the progression of the ventriculomegaly are related to a poor neurological prognosis (48,49). The subarachnoid space is gradually reduced during the end of the third trimester, as the volume of the fetal brain increases; however, it is still prominent in the parietal-occipital region (50,51).

**Table 2. Pattern of myelinization by MRI in the brains of normal fetuses**

<table>
<thead>
<tr>
<th>Changes of intensity in the signal with T1 information</th>
<th>Week</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dorsal portion of the bridge and the brain stem (sensory tracts)</td>
<td>23</td>
</tr>
<tr>
<td>Middle brain</td>
<td>31</td>
</tr>
<tr>
<td>Posterior limb of the internal capsule</td>
<td>32</td>
</tr>
<tr>
<td>Optic radiations</td>
<td>35</td>
</tr>
<tr>
<td>Subcortical white matter (central area)</td>
<td>35</td>
</tr>
<tr>
<td>Corona radiata</td>
<td>36</td>
</tr>
</tbody>
</table>

Source: adapted from Girard N, et al. (37).

Figure 1. Fetuses of 25 (a), 26 (b), and 30 (c) weeks with normal brains. Para-sagittal images weighted with T2 information, which show the progress in the sulcation of the fissure of Silvio (arrow), which is visualized in neuropathological specimens starting from week 14 of pregnancy. Note the continuous closure and its operculization.

Figure 2. 30-week old fetus. Coronary image weighted with T2 at the level of the third ventricle (3v). A low-intensity germinal matrix (short arrow) can be seen under the frontal masts, the white matter with intermediate intensity (double arrow) and the low intensity cortical mantle (long arrow).

Figure 3. 30-week old fetus. Medial sagittal image with T2 information (BTFE). The corpus callosum is shown (arrows), as a low intensity inter-hemispheric band under the circumvolution of the cingulum. The developing cerebellar vermis can be visualized in the posterior fossa (v), as well as the fourth ventricle (4v).
Figure 4. Bilateral schizencephaly. 36-week-old fetus. Axial and coronal images (BTFE) weighted with T2 information which show clefts in both cerebral hemispheres, from the cortical mantle to the lateral ventricles, associated with grey matter heterotopy (arrow) and absence of septum pellucidum (*).

Figure 5. Corpus callosum agenesis. 35-week-old fetus. Medial-sagittal, coronal and axial images with T2 information. They show an absence of corpus callosum (black arrow), frontal maxes of the lateral ventricles with vertical orientation and parallel between each other (white arrows), radial arrangement of the convolutions, colpocephaly (*) and normal posterior fossa.

Figure 6. Hemorrhage of the germinal matrix and encephalomalacy. Axial image with T1 information and STIR coronal. Focus of high intensity in T1, in the left periventricular region (arrow), associated with an important reduction of the cerebral parenchymatous width and severe hydrocephaly.
Clinical utility

• Alterations of the cortical development: These include agyria, lissencephaly, polymicrogyria, grey matter heterotopy, schizencephaly, etc. Lissencephaly appears as a smooth brain, lacking the expected grooves for the pregnancy. Polymicrogyria is characterized by multiple abnormal retractions in the cerebral cortex, and its association with ventriculomegaly leads to the suspicion of the possibility of a genetic component, a metabolic alteration or congenital infection (52). In schizencephaly, one can see trans-cerebral grooves, from the ventricles to the cerebral cortex, which is usually dysplastic (53) (figure 4).

• Corpus callosum anomalies: The fetal MRI has shown a greater detection of the alterations of the corpus callosum and of associated anomalies, when compared with the ultrasound (53,54). These include agenesis, hypogenesis, dysgenesis, and hypoplasia (52). The rate of identification of additional findings in case of corpus callosum agenesis by fetal MRI is as high as 93%, which has implications both for the current pregnancy as well as for future pregnancies (55-57) (figure 5).

• Destructive encephalic lesions: This group covers ischemic and hemorrhagic lesions, laminar necrosis, periventricular leukomalacia, porencephaly, cystic encephalomalacia, hemiatrophy, hydrenencephaly, etc. (4,35).

• The lesions to the fetal CNS before week 20 of pregnancy produce necrosis without gliosis, when a porencephalic cavity with an intensity with a similar signal as LCR. Astrocytic proliferation starts to occur after week 26 of the pregnancy, which is manifested as a septated cavitation of irregular walls. Before week 34, the periventricular white matter is more susceptible to ischemic lesions. In ulterior periods, the subcortical white matter and the cortical mantle are most sensitive to anoxia (58). The focal or diffuse ischemic lesions are appreciated as high-intensity with T2 information.

• Hemorrhage is detected as areas of low intensity in sequences with T2 information and high intensity with T1 information; however, the signal varies depending on the stage of bleeding. This is better characterized in sequences with T2*GRE information (4,18,52) (figure 6). High intensity lesions have been described in the literature (53,58) in sequences with T1 information related to laminar necrosis, which signal intensity can be a product of the degradation of proteins. In some forms of periventricular leukomalacia one can see high-intensity images with T1 information and low intensity images in sequences with T2 information, attributable to microcalcification deposits, similar to those seen in the newborn baby.

• Arachnoid and neuroepithelial cysts: Arachnoid cysts are extra-axial collections of cerebrospinal fluid (CSF), which are formed inside the layers of arachnoids. In The MRI, they are isointense to the CSF. Those which have an inter-hemispheric locations are associated with corpus callosum dysgenesis. The most frequently observed neuroepithelial cyst in the fetus and in the newborn baby is the choroid plexus cyst (35) (figure 7).

• Cystic alterations of the posterior fossa and Chiari malformation: These alterations occur between the sixth and eighth weeks of pregnancy. The MRI helps evaluate the position of the tentorium and the morphology of the vermis (53), confirming the presence of cystic lesions and when performing an adequate differential diagnosis between Dandy-Walker, mega-cisterna magna and arachnoid cysts (figures 8 and 9).

Figure 7. Arachnoid cyst. 26-week old fetus. Coronary images (STIR) and sagittal images (BFFE) with T2 information, and axial T1 information. There is an interhemispheric extra-axial cavity, with a signal intensity similar to CSF. It deforms the left frontal lobe.
Figure 8. Dandy-Walker variant. 37-week old fetus. Sagittal (BBFE) and axial images (BTFE SENSE) with T2 information. Dilatation of the fourth ventricle which fills the posterior fossa is seen, extending to the cisterna magna, with hypoplasia of the vermis (v) and small cerebellar hemispheres (*).

Figure 9. Mega-cisterna magna. 30-week old fetus. Sagittal and axial images (BTFE) with T2 information which show a wide cisterna magna, with a posterior fossa and vermis with a normal morphology.

Figure 10. Chiari II malformation. 28-week old fetus. Coronary images (SSh), sagittal images (SSh), and axial images (BTFE) with T2 information. There is a herniation of the brain stem and the cerebellum through the foramen magnum (*), with hydrocephalia (arrow head), thoracolumbar myelomeningocele (arrow) and scoliosis.
The Chiari II malformation is included in the anomalies of the dorsal induction. These occur between the fourth and fifth weeks of pregnancy, and they are the product of the failure of the fusion of the neural tube, the cranium, and the backbone. These also include anencephaly, the brain/myelomeningocele, flow development disorders, anterior dysraphisms, among others (1). In the case of fetuses with Chiari II malformation, the fetal MRI is used to characterize the seriousness of the herniation of the rhombencephalon towards the cervical sub-arachnoid space, of the myelomeningocele, and the morphology of the vermis (59).

The literature shows a certain incongruity in the value of the fetal MRI in the contribution of additional information in cases of spinal dysraphism (60). However, it is useful in the evaluation of the anatomy of the backbone when the fetus has the posterior dorsal, and during the search for associated cerebral anomalies (61,62) (figures 10-12).

Conclusions

The MRI is a diagnostic modality performed as an additional technique when there is a suspicion of fetal alterations due to prenatal ultrasound. The MRI is mainly used to confirm and characterize alterations of the fetal CNS. Some of its advantages include the identification of additional anomalies which are hidden by the ultrasound. These findings are very important during surgical treatment and the prognosis of the fetus.

References


