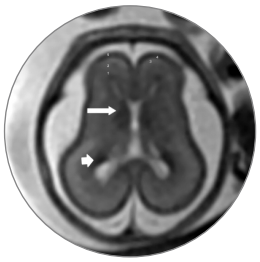

Ganglionic Eminence: Anatomy and Pathology in Fetal MRI

Eminencia ganglionar: Anatomía y patología en resonancia magnética fetal

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Summary

We present two cases of fetal MRI where anomalies of the ganglionic eminences (GE) are detected, one case in a single pregnancy and another in a twin gestation with only one of the affected fetuses. Alterations in the ganglionic eminences are rare entities, with very few published cases, both by MRI and fetal ultrasound, which are usually associated with severe neurological alterations. The MR findings of the pathology of the GE in these two cases are described. These findings were not visible on the previous ultrasound.

Resumen

Se presentan dos casos de resonancia magnética (RM) fetal en los que se detectan anomalías de las eminencias ganglionares (EG): un caso en una gestación única y otro en una gestación gemelar con solo uno de los fetos afectado. Las alteraciones en las eminencias ganglionares son entidades poco frecuentes, con muy pocos casos publicados, tanto por RM como por ecografía fetal, que suelen asociarse con alteraciones neurológicas graves. Se describen los hallazgos por RM de la patología de las EG en estos dos casos, no visibles en la ecografía previa.

Introduction

Ganglionic eminences (GE) are transient, proliferative, embryonic structures of the ventral telencephalon, which are located on the lateral wall of the frontal horns of the lateral ventricles with slight extension into the temporal horns (1). The GEs contain the neuronal precursors of the basal ganglia and amygdalae, and provide interneurons that migrate tangentially toward the cortex, via γ-aminobutyric acid (GABA) as the main neurotransmitter (2).

Fetal magnetic resonance imaging (MRI) allows the identification of these structures, as well as their pathology -which is classified, according to radiological findings, into cavitated or prominent GAs-. Despite being very rare entities, it is necessary to become familiar with their prenatal diagnosis.

Description of the cases

Patient 1. 35-year-old woman with a history of five pregnancies and no pregnancies at term. The miscarriages were: one caused by trisomy 21; one, complex cerebral malformation; two, in the first trimester and one, biochemical. Ultrasonography was performed at 20 weeks and 1 day, showing cerebellar hypoplasia and partial agenesis of the corpus callosum. Genetic study with normal conventional and molecular karyotype (array-CGH).

Fetal MRI was performed at the gestational age of 20 weeks and 5 days, with the finding of prominent GE in the germinal matrix, with bilateral and symmetrical cavitations and C-shaped morphology, without evidence of bleeding. No intermediate neuronal layer was identified between the germinal matrix and the immature outer cortex, but a prominent germinal matrix was identified. Horizontalization and thickening of the superior cerebellar peduncles with "molar" type malformation was observed. These findings were not visible on ultrasound. Other associated findings were: partial agenesis of the corpus callosum (absence of knee, splenium and rostrum), marked hypoplasia of both cerebellar hemispheres and to a lesser extent of the vermis; increased subarachnoid space and mild colpocephaly, prominent cavum septum pellucidum, small cyst of the velum interpositum and thickening of the nuchal fold, visible on ultrasound. The rest of the study was normal (Figure 1). The patient decided to voluntarily terminate the pregnancy without consent for necropsy.

Patient 2. 32-year-old woman, primigestation of 26 weeks with bicurial and biamniotic gestation. Ultrasound was performed at 25 weeks and 1 day with a finding of partial agenesis of the corpus callosum with absence of splenium in one of the fetuses. A fetal MRI was performed at gestational age of 26 weeks and 1 day. Prominent bilateral periventricular GE and heterotopias associated with altered cortical development were observed, with lissencephaly (poorly developed cysplasias of Sylvius, without signs of opercularization) and partial agenesis of the corpus callosum with absence of the splenium. The only altered pattern in fetal biometry was the fronto-occipital diameter ($p < 3$) (Figure 2). The other fetus showed no alterations.

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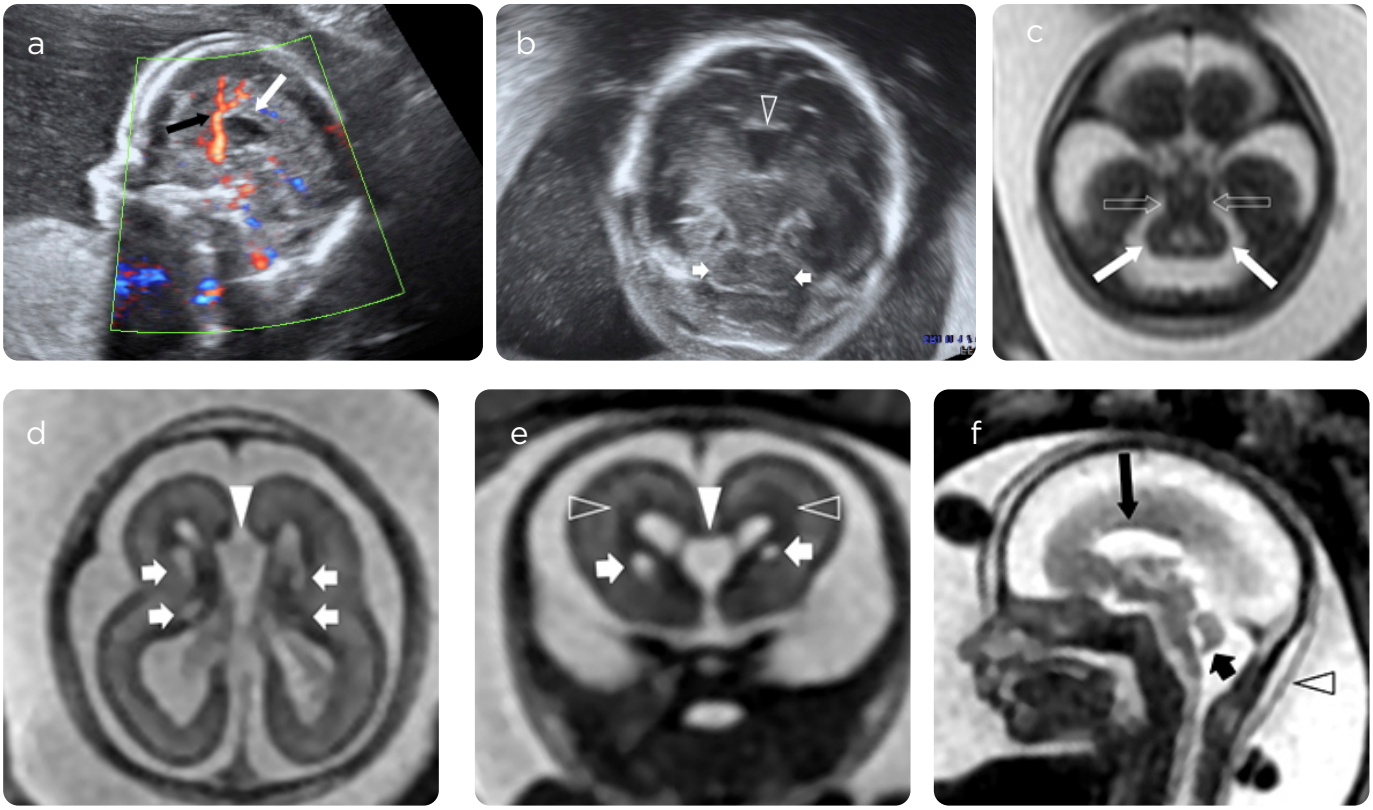

Figure 1. Bilateral cavitations in ganglionic eminences. Fetal ultrasound. Gestational age 20 weeks and 1 day. a) Neurosonography with mid-sagittal plane. The trunk of the corpus callosum is identified (solid long white arrow) with absence of the knee and splenium. The pericallosal arteries have a cranial direction without describing the typical semicircle around the corpus callosum (solid long black arrow). b) Axial plane neurosonography with hypoplasia of the cerebellar hemispheres (solid white arrows). Cerebellar transverse diameter 15.8 mm. Area of the cerebellar hemisphere 40 cm2 and of the left cerebellar hemisphere 41 cm2. Prominent cavum septi pellucidi (empty white arrowhead). Fetal MRI. Gestational age 20 weeks and 5 days. c) Axial FIESTA sequence. d) Axial e) Coronal f) Sagital SS FSE sequences with T2 information. Marked hypoplasia of both cerebellar hemispheres (solid long white arrows) and to a lesser extent of the vermis (solid short black arrow). Horizontalization and thickening of the superior cerebellar peduncles with molar-like malformation image (empty long white arrows). Prominent cavum septi pellucidi (solid white arrowhead). Microcephaly with prominent ganglionic eminences in the germinal matrix showing bilateral and symmetrical cavitations with C-shaped morphology without indentation (short solid white arrows). No intermediate neuromas layer is identified between the very prominent ventricular zone neuron layer (empty white arrowheads) and the immature outer cortex, future banded heterotopias with microlisencephaly. Nuchal fold thickening of 4.5 mm (empty black arrowhead). Dysgenesis of the corpus callosum visualizing the trunk of the corpus callosum (long solid black arrow) with absence of its knee and splenium.

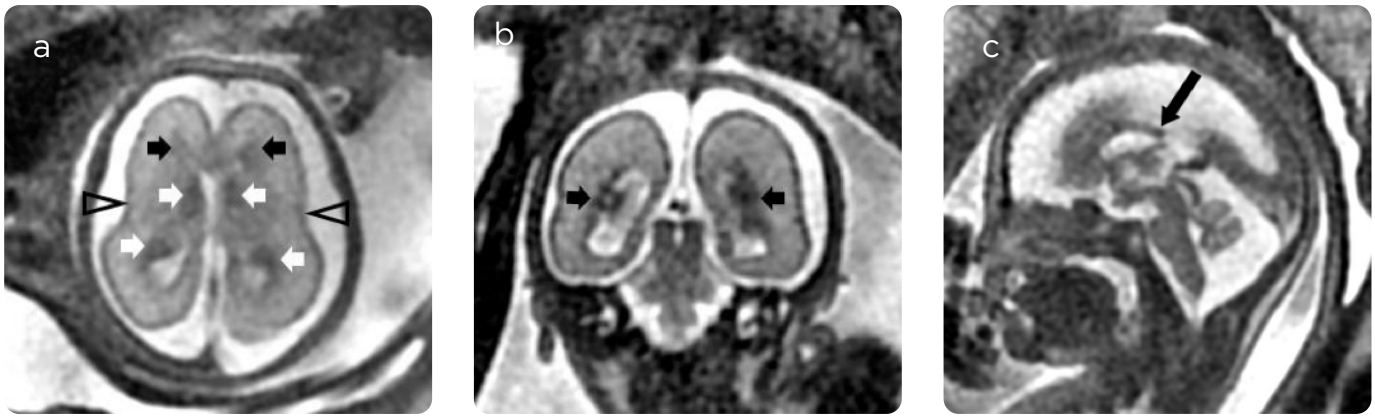

Figure 2. Enlargement of the ganglionic eminences. Bi-chorionic and biamniotic gestation of 26 weeks and 1 day. Pathological fetus: a) axial b) coronal and c) Sagittal SS and FSE sequences with T2 information. Prominent bilateral ganglionic eminences (short solid white arrows) and prominent layer of periventricular neurons that have not migrated forming subependymal heterotopias marking the walls of the lateral ventricles (short solid black arrows). Dysgenesis of the corpus callosum whose length is 19.1 mm with absence of the splenium (long solid black arrow). Scarce opercularization of the fissures of Sylvius (empty black arrowheads), the cortical surface is smooth with absence of Rolando's sulcus. She has a cerebral fronto-occipital diameter of 63.3 mm suggesting microlisencephaly. The cerebellum (not shown) is normal with a transverse cerebellar diameter of 29.8 mm.

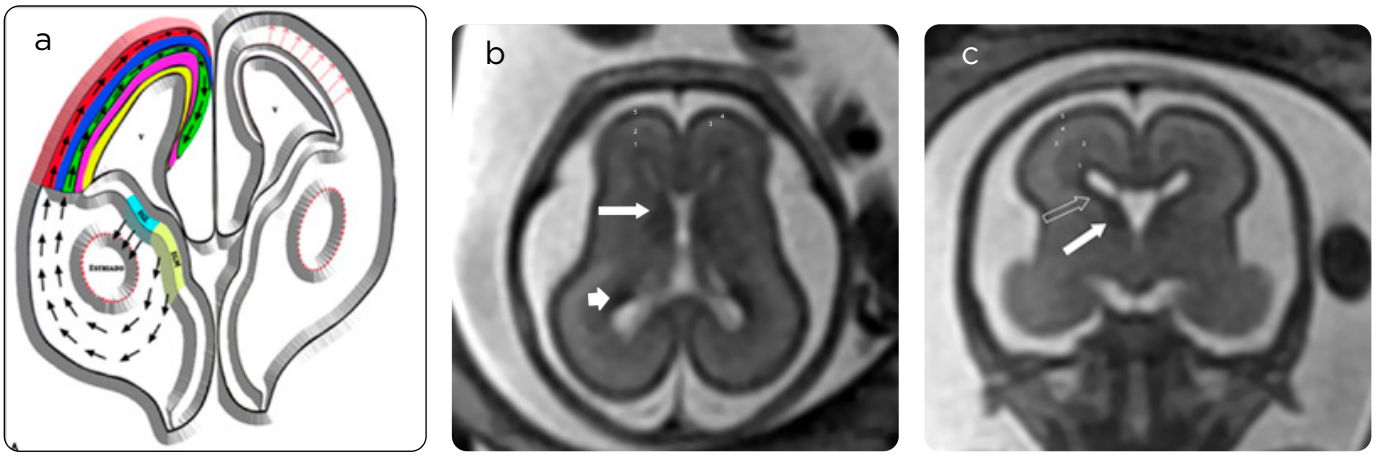

Figure 3. Normal anatomy and neuronal migration. Gestational age 22 weeks and 3 days. a) Schematic of neuronal migration: LGE: Lateral Ganglionic Eminence. MGE: Medial Ganglionic Eminence, V: Ventricles. Immature outer cortex. Subcortical white matter. Zone of intermediate neurons. Periventricular white matter. Ventricular neuronal zone. → Tangential migration ⇢ Radial migration. b) Axial SS FSE T2. c) Coronal SS FSE T2. The five layers of this phase of neuronal migration are visualized: (1) neurons of the ventricular zone, (2) periventricular white matter, (3) layer of intermediate neurons, (4) subcortical white matter and (5) immature outer cortex. Medial ganglionic eminences (solid long white arrows), lateral ganglionic eminences (empty long white arrows) and caudal ganglionic eminences (solid short white arrows) are identified.

Discussion

The cerebral cortex constitutes the most complex region of the mammalian brain and from it emanate most of the functions that differentiate us as human beings. Traditionally, cortical neurons have been divided into:

- 1. Projection neurons (excitatory, glutaminergic).
- 2. Interneurons (inhibitory, GABAergic) (3).

Projection neurons originate in the proliferative zone of the ventricular/subventricular dorsopallium and follow a radial migratory pathway (4). Thirty-five percent of the interneurons that migrate tangentially to the cortical plate originate from the GE (derived from the subpallium) (5).

Radial migration occurs between weeks 12 and 16 and ends at approximately week 24. It begins in the periventricular germinal zone and ends at the pial surface, with 6 successive layers (6). Tangential migration persists longer, ending after week 24 (7).

The GE is a proliferative and transient embryonic structure of the ventral telencephalon (subpallium) (3), which is located on the lateral wall of the frontal horn and to a lesser extent of the temporal horn of the lateral ventricles (1). The subpallium can be divided into three proliferative zones: medial ganglionic eminence (MGE), lateral ganglionic eminence (LGE) and caudal ganglionic eminence (CGE), depending on anatomical and genetic characteristics (8). The LGE produces olfactory bulb interneurons and projection neurons of the striatal nucleus, the LGE and CGE produce mainly cortical interneurons (9). Whereas MGE cells migrate laterally and extend through the cortex, most CGE cells migrate inferiorly toward the more caudal end of the telencephalon (8) (Figure 3). The volume of the CGE increases with gestational age, peaks at 18-22 weeks and decreases significantly around 30 weeks (10). It persists longer than other proliferative areas and is usually gone by birth (11).

Recently, there has been increasing interest in the origin and fate of interneurons, as certain neurological and psychiatric pathologies - schizophrenia, autism, bipolar disorders and severe epileptic encephalopathies, such as that associated with the ARX gene - have been linked to a decrease in GABAergic interneurons.

Riggini et al. studied by MRI eight cases of GE anomaly (excluding hemorrhage), of which three had prominent GE and 5 cavitations in that location (10, 11). The cavitations were symmetrical and bilateral with an image similar to an "inverted open C" (11). In all their cases they observed lissencephaly with partial agenesis or severe hypoplasia of the corpus callosum, similar to the cases described in this article. Other findings were: hypoplasia and rotation of the vermis, hypoplasia of cerebellar hemispheres, ventriculomegaly, increased subarachnoid space and "molar" type malformation, present in our first case. As in this study, alterations in the GE were not visible by ultrasound.

Increased size of the GE may or may not be associated with cavitations and, conversely, cavitations may or may not be accompanied by increased size of the GE. Hemorrhages in GE are irregular and high signal lesions in T1-weighted sequences, which is key to distinguish them from cavitations (10). It is believed that an ischemic process is responsible for the formation of these cavitations and that lissencephaly is caused by impaired neuronal migration (assuming that the cavitations act as a barrier to prevent proper neuronal migration) (11). This supports the idea that cavitations in GE are part of complex malformations involving alterations in neuronal migration.

In 2019, John Wiley published the first two cases of GE cavitations visualized by prenatal ultrasound (1). So far, there is no record of other publications describing this pathology by MRI.

Conclusions

GE abnormalities represent an infrequent finding that is usually associated with severe neurological abnormalities. It is important to be familiar with the fetal MR radiological findings of this pathology,

in order to facilitate its diagnosis and help in fetal management and prognosis.

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