

DIAGNOSTIC APPROACH TO THE ALTERATIONS OF THE CORPUS CALLOSUM: STATE OF THE ART

Abordaje diagnóstico de las alteraciones del cuerpo calloso: estado del arte

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Summary

Alterations of the corpus callosum have a general prevalence of 1/1,000 live births, and are found in 2-3% of children with developmental disabilities. These disabilities include agenesis, dysgenesis, hypoplasia and hyperplasia. Because these alterations are associated in a large percentage to different brain anomalies and syndromes, it is relevant to perform an adequate prenatal diagnostic approach. There are several key signs in the prenatal ultrasound that determine if there is any alteration in the corpus callosum. Magnetic resonance is indicated in cases of suspected anomalies in the prenatal ultrasound, and it can also evaluate more specifically if an additional cerebral anomaly is present. This is important because it allows to determine the neurological prognosis and to perform promptly interventions.

Resumen

Las alteraciones del cuerpo calloso tienen una prevalencia en general de 1 por 1.000 nacidos vivos, estas alteraciones se encuentran en un 2-3 % de los niños con discapacidad o alteraciones del neurodesarrollo. Dentro de estos trastornos se incluyen la agenesia, la disgenesia, la hipoplasia y la hiperplasia. Debido a que estas alteraciones se asocian en un gran porcentaje con diferentes anomalías cerebrales y síndromes es relevante realizar un adecuado abordaje diagnóstico prenatal. Existen varios signos clave en la ecografía prenatal que permiten determinar si existe alguna alteración en el cuerpo calloso. La resonancia magnética se indica en casos de sospecha de alguna alteración en la ecografía prenatal y permite evaluar de manera más específica si existe alguna anomalía cerebral adicional. Esto es importante para determinar el pronóstico neurológico y realizar intervenciones oportunas.

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Introduction

The corpus callosum (CC) is the main bundle of white matter fibers connecting the neocortical areas of the two hemispheres (1). CC alterations occur regularly in children who are evaluated for neurodevelopmental delay. There are a variety of conditions that disrupt early brain development, including metabolic and chromosomal disorders, as well as intrauterine exposure to teratogens and infection (2). Alterations in CC are frequently associated with other central nerve malformations or somatic abnormalities (3-5).

The CC defect may be complete or partial, depending on the stage at which it develops. The prevalence

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Key words (MeSH)

Corpus callosum Agenesis of corpus callosum Prenatal diagnosis Magnetic resonance

Palabras clave (DeCS)

Cuerpo calloso Agenesia del cuerpo calloso Diagnóstico prenatal Resonancia magnética of corpus callosum disorders in children with developmental disabilities is approximately 2-3 % (6) and the overall prevalence is 1 per 1,000 live births (7). Corpus callosum agenesis has an overall prevalence of 1 per 4,000 live births and 230-600 per 10,000 in children with neurodevelopmental disorders (8). The hypoplasia of CC is estimated at 1.8 per 10,000 live births (9). These alterations have a complex pathogenesis and there are genetic, infectious, vascular and toxic causes (10).

The clinical spectrum is very broad, there may be patients who are completely asymptomatic or with mild intellectual difficulties, such as problems in the functions of higher order language and social deficits apparent only in detailed psychometric tests (11, 12). However, there are patients with severe cognitive deficits; mental retardation is the most common (13). Many patients with corpus callosum agenesis have a diagnosis of attention deficit or autism spectrum disorder (14,15). There are different neurological signs and symptoms, such as spastic paresias, hypotonia, pyramidal syndromes, ocular anomalies and hearing disorders, some patients manifest with epilepsies (16). The symptoms are nonspecific and most are part of syndromic forms.

The purpose of the article is to review the embryology, anatomy, physiopathology of the corpus callosum, discuss the etiologies and classification of the pathologies of the corpus callosum and explain how to make a proper diagnostic approach to these alterations. Relevant signs are described that suggest that there is an alteration in the corpus callosum in prenatal ultrasound and the importance of magnetic resonance imaging (MRI) both prenatal and postnatal for this purpose.

1. Embryology and anatomy

CC develops between weeks 11 and 15 of gestation (17), this depends on different cellular and molecular mechanisms, which include the formation of a large glial population in the midline and the expression of specific molecules required to guide the axons of the corpus callosum when they cross the midline. The mechanism used by the axons of the corpus callosum, of the neurons in the neocortex, is to grow within the pathway formed by the pioneering axons derived from the neurons in the cortex of the cingulum (18) cavum septi pellucidi. The pericallic arteries, right and left, are seen superior to the corpus callosum, from anterior to posterior, are the face, knee, body and splenium (19). The body is subdivided into the isthmus and the anterior, middle and posterior segments (Figure 1).

2. Physiopathology

The corpus callosum comprises more than 190 million topographically organized axons, each forming homotopic or heterotopic connections between distant regions of the cerebral cortex. These connections participate in a series of cognitive functions that include language, abstract reasoning, and the integration of complex sensory information (20). This fiber tract facilitates the integration of motor and sensory information from both sides of the body, as well as higher cognition associated with executive function, social interaction, and language. The function of the CC is to distribute perceptual, motor, cognitive, learned, and voluntary information between the two hemispheres of the brain (21).

The size and composition of the fibers of the corpus callosum are in accordance with the topographic organization of the cortex. The anterior part of the CC contains the highest density of myelinized axons connecting the prefrontal cortex and higher order sensory areas.

The density of the fibers decreases from the front to the middle of the CC, this middle part contains axons that go towards the parietal and temporal lobes. The anterior segment of the midpart has connections to somatosensory, primary motor and secondary areas. The posterior middle segment contains thick axons that are involved in the transfer of information from the primary and secondary auditory areas. The density of the fibers increases again in the back of the corpus callosum, the splenium and connect with visual areas in the occipital lobe. The area between the body and the splenium is thin and known as the isthmus, which connects to motor fibers, somatosensory and primary auditory areas (22-28).

3. Classification of corpus callosum pathologies

Developmental disorders of the corpus callosum include agenesis or complete absence (Figure 2), partial dysgenesis or hypogenesis, hypoplasia, and hyperplasia (29). In partial dysgenesia, the corpus callosum is shorter in its anteroposterior length as a result of missing segments, primarily the splenium (Figure 3 a). In hypoplasia, the corpus callosum is normal in its anteroposterior length and all its segments are formed; however, there is a thinning of this (Figure 4 a). It is important to mention that in the majority of cases in which thinning occurs the cause is atrophy by cerebral hypoxia.

4. Etiology

Changes in the corpus callosum may be genetic, infectious (TORCH and Zika), vascular or toxic; genetic factors are the most common. Advanced maternal age, over 40 years, is associated with CC alterations in children with chromosomal disorders. They are observed in the context of chromosomal anomalies in 17.3 %, so-matic malformations (musculoskeletal in 33.5 %, cardiac in 27.6 %) and central nervous system (CNS) in 49.5 % (9). Monogenic causes are identified in 20-35 % of cases and associated with syndromes in 30 %-45 % of cases. In the vast majority of genetic syndromes is the agenesis of the corpus callosum and the most frequently associated symptoms are microcephaly, infantile spasms, progressive neuropathy, visual alterations, hearing and intellectual deficit (30).

There are cerebral anomalies in 21 to 93 % of the cases of agenesis of the corpus callosum (31), the most commonly associated are: alterations of the ventricular system, such as hydrocephalus, colpocephalus, disorders of cortical development with abnormal circumvolutions, interhemispheric cysts and lipomas and alterations of the posterior fossa, such as Dandy Walker malformation and cysts of the posterior fossa, Chiari II and III malformations, agenesis of the cerebellum vermis and rhomboencephalosinapsis (32,33). Craniofacial anomalies, congenital heart defects, limb alterations and growth restriction are found in 65 % of cases (34).

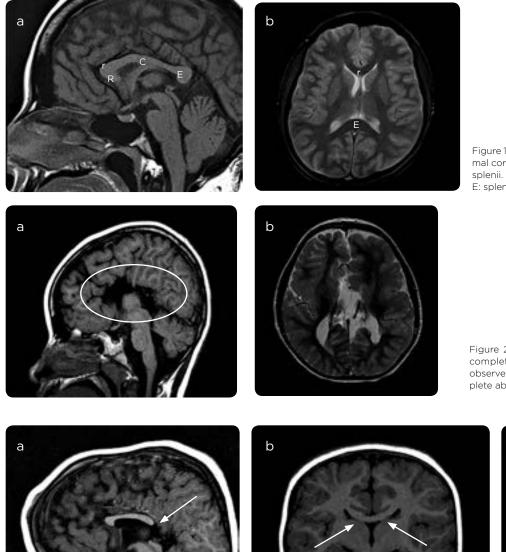
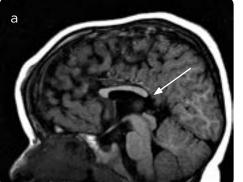
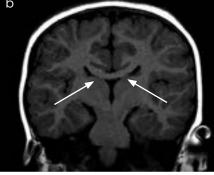


Figure 1. a) Sagittal MRI with T1 information. Normal corpus callosum. R: face, r: knee, C: body, E: splenii. b) Axial MRI with T2 information. r: knee, E: splenium.

Figure 2. a) Sagittal MRI, T1 sequence FLAIR: complete absence of the corpus callosum is observed. b) Axial MRI with T2 information: complete absence of the corpus callosum.





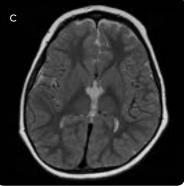
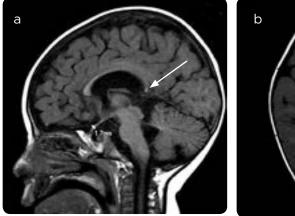


Figure 3. a) Sagittal MRI T1 sequence FLAIR: absence of splenium (arrow). b) Coronal MRI T2 sequence FLAIR: sign of "Viking helmet" (arrow). c) Axial MRI T2 sequence: colpocephaly (arrow).



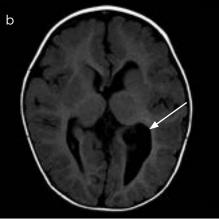


Figure 4. a) Sagittal MRI T1 sequence FLAIR: thinning of the corpus callosum, remnant of splenium (arrow). b) Axial MRI T2 sequence FLAIR: colpocephaly (arrow).

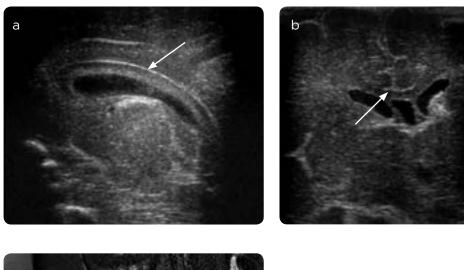


Figure 5. a) Transfontanellar ultrasound, sagittal, anterior fontanel: normal corpus callosum (arrow). b) Transfontanellar coronal ultrasound, anterior fontanel: normal corpus callosum (arrow).



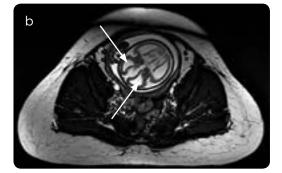


Figure 6. Sagittal pelvic MRI. Patient in pregnancy of 28 weeks of gestation. a) Sagittal acquisition with T2 information: absence of corpus callosum (*), ectasia of the lateral ventricles (arrows), diastasis of the interhemispheric space (-). b) Axial pelvic MR: colpocephaly (arrows).

5. Diagnosis

El The normal corpus callosum can be seen ultrasonographically in weeks 18 and 20 of gestation in a middle section of the brain. Its final formation is completed at 20 weeks, although it continues to grow during fetal life and the first two months after birth (Figure 5). During routine screening for fetal abnormalities from 20 to 22 weeks gestation, the two most important signs that the corpus callosum needs further evaluation to exclude an anomaly are: no visualization of cavum septi pellucidum and ventriculomegaly (lateral ventricles >10 mm) (35).

The direct ultrasound characteristics of the agenesis of the corpus callosum in the middle section are the complete absence of the corpus callosum and the cavum septi pellucidum. After the 25th week, additional findings include the absence of cingulate rotation and the radial matrix of the grooves. Indirect features are seen in the axial section, such as narrow and laterally displaced frontal horns, and slightly dilated occipital horns (colpocephaly [Figure 3 c, Figure 4 b, Figure 6 b]) (36). In the coronal section, in the sickle of the brain, a wide interhemispheric fissure can be seen that communicates with the third ventricle, the lateral ventricles are widely separated and oriented vertically (sign of the "Viking helmet" [figure 3 b]). The thalami are widely separated due to dilation of the third ventricle (37).

In partial dysgenesis or hypogenesis, the anteroposterior length is shorter, there is absence of any segment of the corpus callosum, this finding is observed in the middle section of the fetal brain. The ultrasound diagnosis of the thin or hypoplastic corpus callosum is established when the anteroposterior length of the corpus callosum is normal, but is thinned. Routine prenatal ultrasound has been and continues to be the main tool for early identification of such alterations (38).

Because ultrasound has some limitations for direct visualization of the corpus callosum and in some cases a certain diagnosis is not obtained, it is relevant to recognize the importance of prenatal MRI in these situations. The different planes provided by this imaging modality facilitate the direct visualization of the corpus callosum and provide an accurate diagnosis of its alterations, as well as making it possible to visualize with greater precision if there is any other associated cerebral anomaly.

This is particularly important for offering early counseling to parents, since additional brain abnormalities suggest broader neurodevelopmental disorders that are associated with further neurological impairment (39). Prenatal diagnosis of corpus callosum disorders is considered relevant as it may be associated with different CNS abnormalities (40,41). MRI is useful after the 20th week of gestation because in approximately 20 % of cases, apparently isolated, diagnosed by ultrasound, associated CNS abnormalities have been found in MRI (42) (Figure 6).

6. Discussion

Changes in the corpus callosum are abnormalities of the midline of the brain that can interrupt adequate cognitive progression (43). They have a relatively high prevalence in the general population and are associated with brain abnormalities of complex detection on second trimester ultrasound. Pre-determined axial planes do not provide enough information to make an accurate diagnosis (44). Changes in the corpus callosum are associated with genetic malformations and neurological disorders of varying severity (45).

There are specific key signs in the diagnosis made by prenatal ultrasound, which are evident in the axial and coronal sections. However, prenatal MRI is the most accurate imaging modality for evaluating fetal brain development. It identifies associated alterations not interpreted in another technique and allows an early diagnosis of congenital anomalies (46). MRI improves prognostic evaluation, since it allows the representation of associated anomalies, especially disorders of cortical development with abnormal circumvolutions, abnormalities of the ventricular system, malformations of the posterior fossa and intracranial cysts (47).

In a study that evaluated the agenesis of the corpus callosum by ultrasound and MRI, it was found that ultrasound suspected agenesis by indirect signs, while MRI made a diagnosis of the complete absence of the corpus callosum and, in addition, found additional neurological abnormalities, such as heterotopia, anomalies of the circumvolutions and asymmetry of the cerebral hemispheres (48-51).

7. Conclusion

The alterations of the corpus callosum have a very wide clinical spectrum, it is important to bear in mind that in most cases these alterations are associated with syndromes and present, with a high frequency, associated cerebral anomalies. There are several indirect signs that allow a diagnosis of these alterations in prenatal ultrasound. However, when this diagnosis is made difficult by certain limitations, it is necessary to perform a prenatal MRI, as it is a valuable complementary technique to diagnose with certainty and make a more accurate representation of the associated neurological abnormalities. A proper diagnosis of these alterations to improve the neurological prognosis of the patient.

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