CLINICAL CASE

DIAGNÓSTICO PRENATAL DE ROMBOENCEFALOSINAPSIS: REPORTE DE CASO

RHOMBENCEPHALOSYNAPSIS: CASE REPORT

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RESUMEN

El vermis, una estructura ubicada en el cerebelo, es el área del encéfalo encargada de numerosas funciones cómo la coordinación del movimiento, la integración de la información sensorial y la postura[1], está conectado con estructuras importantes del sistema nervioso central [2] incluyendo al tálamo, hipotálamo, corteza cerebral, tronco encefálico y la médula espinal, esta unión es sumamente importante para la correcta ejecución de movimientos[3]. La romboencefalosinapsis, es una malformación congénita cerebelar de la cual se tienen muy pocos registros en la literatura médica, está caracterizada por la fusión de los hemisferios cerebelosos[4] con aplasia o hipoplasia del vermis en la línea media[5], la mayoría de los casos aparecen esporádicamente y se asocian a un trastorno qué afecta la regulación de las vías de desarrollo compartidas incluyendo al primordio cerebeloso y mutaciones de novo dominantes[6]

PALABRAS CLAVE: romboencefalosinapsis, vermis cerebeloso, diagnóstico prenatal, malformación congénita, estenosis, feto.

ABSTRACT

The vermis, a structure located on the cerebellum, it is the area of the encephalon in charge of a big number of activities such as movement coordination, integration of sensory information and posture, is connected to important structures of the central

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nervous system including the thalamus, hypothalamus, brain cortex, brainstem and spinal cord, this union is incredibly important for the correct execution of the human body movement. Rhombencephalosynapsis is a cerebral congenital malformation which has just a few registries on the medical literature, characterized by the fusion of both cerebral hemispheres due to aplasia or hypoplasia of the vermis on the midline, most cases appear sporadically and are associated to a disorder that involves the regulation of several development pathways including the cerebellar primordium and de novo mutations.

Keywords: Rhombencephalosynapsis, cerebellar vermis, prenatal diagnosis, congenital malformation, stenosis, fetus.

Introduction

At the beginning of gestation, the rhombencephalon (one of the primary vesicles) begins to differentiate through a process directed from the isthmic zone (isthmic organizer), located between the mesencephalon and the metencephalon, which guides the development of the cerebellum, midbrain, and brainstem. The origin of the cerebellum arises from the first rhombomere, leading to the synchronous development of the cerebellar hemispheres and vermis. From the branches of the tuberculum cerebelli (which has an inverted V shape), the cerebellar hemispheres develop laterally; meanwhile, the central part will differentiate into the vermis (which gradually folds and completes its ventral rotation). Finally, the perforation of Blake's pouch with the formation of the foramina of Magendie allows the vermis to locate itself very close to the brainstem, closing the fourth ventricle.

Rhombencephalosynapsis is a rare disease characterized by a malformation of the mesencephalon and rhombencephalon in which there is vermian agenesis with fusion of the cerebellar hemispheres located in the posterior fossa. The genetic basis is unknown, but it presents a wide range of clinical manifestations and neurological development alterations that make diagnosis a challenging process for healthcare professionals. Findings may be incidental or part of broad and complex syndromes, often associated with significant neurological impairment that drastically affects the patient's quality of life.

According to a study published in the medical journal Brain: A Journal of Neurology, rhombencephalosynapsis has been classified as mild (partial absence of the nodule, anterior and posterior vermis), moderate (absence of the posterior vermis with some anterior vermis and nodule present), severe (absence of both posterior and anterior vermis with some nodule present), and complete (absence of the entire vermis, including the nodule). They demonstrated that the severity of the condition correlates with tonsillar fusion and also with mesencephalic anomalies, including aqueductal stenosis and fusion of the midline tectum.

In medical literature, cases of rhombencephalosynapsis have been

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described in both adults and children, but prenatal cases are very rare, and thus reports are scarce. It is also important to differentiate it from Dandy-Walker malformation, which is believed to result from a broad lesion of the alar plate involving the dorsal fourth ventricle and rhombic lips after the anterior vermis has already formed. This condition presents similarities with rhombencephalosynapsis, but the latter features absence of the anterior vermis, posterior vermis deficiency, and fusion of the cerebellar hemispheres. Accurate identification and documentation are important due to the high morbidity and mortality associated with this condition.

Prenatal diagnosis of mesencephalic-rhombencephalic (MB-HB) malformations is primarily based on the size and abnormal shapes of the cerebellum and retrocerebellar space, particularly an open fourth ventricle, which is the most common indicator of MB-HB malformations. The fourth ventricle index is an ultrasound marker of severe fetal vermian dysgenesis/agenesis.

Clinical Description

A 19-year-old primigravida at 23 weeks and 6 days of gestation presented to a perinatology consultation for a detailed anatomical ultrasound. She had a previous ultrasound with no reported abnormalities. She reported having attended three prenatal check-ups and had not undergone testing for toxoplasma IgM or VDRL for syphilis. She admitted to occasional alcohol consumption.

Ultrasound revealed in the axial view of the posterior fossa a cerebellar transverse diameter below the 3rd percentile for the patient's corrected gestational age, with fusion of the cerebellar hemispheres, absence of the cerebellar vermis, and ventricular system abnormality caused by ventriculomegaly of 13 mm. Nasal bone agenesis was also noted in the sagittal view. The patient had no relevant genetic history.

Therapeutic Management

The patient was informed of all possible risks and complications associated with the ultrasound findings. After receiving this information, she decided to proceed with a voluntary termination of pregnancy.

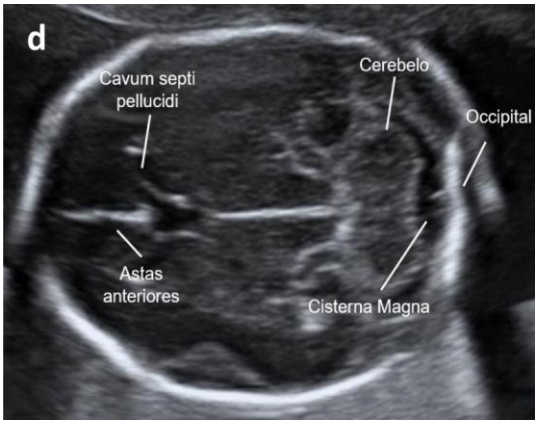
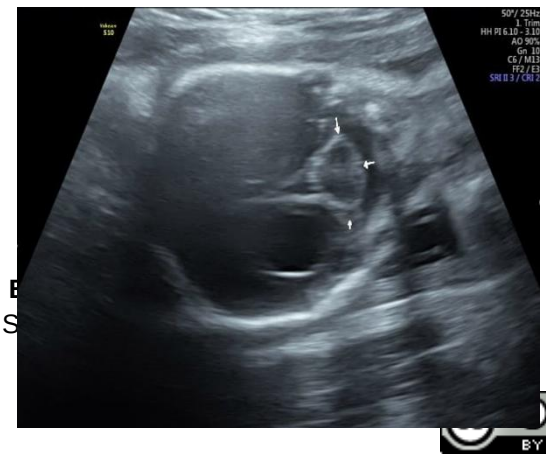


Figure 1. Reference image of cerebellum



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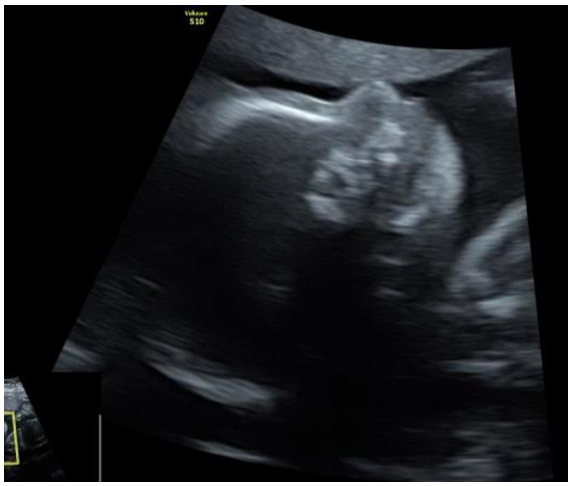

Figura 3. Agenesia del hueso nasal en ultrasonografía

DISCUSSION

Rhombencephalosynapsis (RES) is a condition characterized by aplasia or hypoplasia of the cerebellar vermis, causing fusion of the hemispheres at the midline. This is a rarely diagnosed pathology. In this case review, we encountered significant findings such as a reduced transverse cerebellar diameter on axial views, below the 3rd percentile, along with absence of the cerebellar vermis, fusion of the cerebellar hemispheres, and nasal bone agenesis. Based on these findings, there is a high probability of a genetic alteration in this case (Aldinger, Dempsey & Tully, 2018).

The genetic alterations involved in rhombencephalosynapsis are not entirely clear. To date, four microarray alterations have been documented in

Figure 2. Abnormal cerebellum, decreased diameter by ultrasonography
normal by ultrasonography16.

57 cases, and other cases have been associated with Gómez-López-Hernández syndrome (parietal alopecia, trigeminal anesthesia, and craniofacial dysmorphism) and the VACTERL-H syndrome (vertebral anomalies, anal atresia, cardiac defects, tracheoesophageal fistula, esophageal atresia, renal anomalies, and hydrocephalus). Associated brain anomalies and midline defects can also be present, including aqueductal stenosis, holoprosencephaly, corpus callosum dysgenesis, and septo-optic dysplasia. Extracranial anomalies may include segmentation and fusion defects of the spine, musculoskeletal anomalies, and cardiovascular and respiratory defects.

RES is often strongly associated with hydrocephalus and cerebellar hypoplasia but is frequently underdiagnosed as an underlying cause. As a result, **prenatal diagnosis is very rare**.

Rhombencephalosynapsis can be classified according to the degree of vermian agenesis and hemispheric fusion. This malformation may be related to signaling alterations at the level of the **isthmic organizer**.

Complete RES is defined by the total absence of the vermis. **Partial RES** is classified based on the missing part of the vermis and the corresponding region of hemispheric fusion as anterior, posterior, severe, or mixed.

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- **Anterior partial RES** is defined by the presence of remnants of vermian tissue, with varying degrees of hypoplasia.
- **Posterior partial RES** is defined by the presence of vermian tissue rostral to the primary fissure, with varying degrees of hypoplasia.
- **Severe partial RES** is defined by remnants of vermian tissue caudal to the fastigium (nodule), presenting a "thumb-like" projection on the floor of the fourth ventricle.
- **Mixed partial RES** is defined by the presence of both anterior and posterior vermian remnants, with fusion at the tubercle and central lobes.

Vermian agenesis can lead to various severe symptoms such as motor coordination deficits (ataxia), speech difficulties (dysarthria), balance problems, abnormal eye movements (nystagmus), motor developmental delay, and hypotonia.

CONCLUSIONS

During prenatal ultrasound monitoring, it is crucial that the professional conducting these evaluations considers the possibility of rare pathologies, one of the most relevant being rhombencephalosynapsis. Careful analysis of the brain and cerebellum, especially in cases where ventriculomegaly is suspected, should focus on evaluating the size and shape to rule out conditions that may compromise both fetal and maternal health.

For the diagnosis of RES, it is recommended to use **microarray studies** to support proper genetic counseling. Our patient chose not to undergo further complementary studies, such as prenatal-focused obstetric MRI or other invasive tests for accurate diagnosis.

Proper evaluation, well-trained personnel, and proficient equipment management lead to timely diagnosis, enabling appropriate counseling and care. This is essential for correctly addressing posterior fossa pathologies that may arise.

We present a case report within the context of a condition whose largest documented series includes 62 cases, highlighting the importance of including rhombencephalosynapsis as a potential **differential diagnosis** due to its very low frequency in prenatal diagnoses through ultrasound evaluation.

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