PRENATAL SCHIZENCEPHALY DIAGNOSIS WITH PROGRESSIVE UNILATERAL TO BILATERAL EVOLUTION - CASE REPORT

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ABSTRACT

Schizencephaly is a rare congenital malformation of the central nervous system (CNS). Belonging to the group of CNS cell migration defects, it appears between the 2nd and 5th month of gestation, characterized by a gray dysmorphic substance outlining the slits in the cerebral cortex that extend medially from the subarachnoid space communicating with the ipsilateral cerebral ventricle.

This report is from a fetus that was referred with the diagnosis of ventriculomegaly and a morphological examination identified a rare pathology of the CNS, unilateral type II schizencephaly.

During monitoring it evolved to a bilateral form with progressive increase in the cleft, subarachnoid space, cerebral ventricle and identification of associated brain abnormalities. This evolution from unilateral to bilateral form is not described in the medical literature. You can assume that the diagnosis was very early and although the event had been bilateral, its manifestation took some time to become identified on ultrasound examination.

An etiology, associated anomalies, differential diagnosis and prognostics factors in schizencephaly will be addressed.

KEYWORDS: SCHIZENCEPHALY, DIAGNOSIS, PRENATAL CARE, ULTRASOUND, EVOLUTION, ETIOLOGY, PROGNOSTIC FACTORS

INTRODUCTION

Schizencephaly is a rare congenital malformation of the central nervous system (CNS), with a prevalence of 1.5: 100,000 live births [1,2]. It was first described in 1946 by Yakovlev and Wadworth when they defined schizencephaly as a congenital cleft in the brain mantle in a post-mortem study [3].

Belonging to the group of the cell migration defects of the CNS, it appears between the 2nd and 5th month of gestation, being characterized by a gray dysmorphic substance outlining the cracks in the cerebral cortex. These clefts extend medially from the subarachnoid space, communicating with the ipsilateral cerebral ventricle. The identification of the gray matter bordering the cleft is a pathognomonic characteristic of the lesion, differentiating it from severe porencephaly.

Unilateral schizencephaly is more frequent (60%) than the bilateral cleft and in 75-95% of cases the predominant anatomical location is in the frontal and parietal lobes [3-5] .

ETIOLOGY:

Most cases of schizencephaly are sporadic and unfamiliar, not having a recognized etiologic cause. Theories such as anomalous neuronal migration and obstruction of the middle cerebral artery as a result of an intrauterine inflammatory process have been suggested, as in the cytomegalovirus infection[3,4] .

The theory of abnormal early neuronal migration involves the pleating and fusion of the layers of the pia mater with the ependyma. Figure 1 illustrates coronal histological section at [10], 17 and 28 gestational weeks showing the pleating and fusion of the layers of the pia mater with the ependyma, and subsequent development of the cerebral cortex[5] .

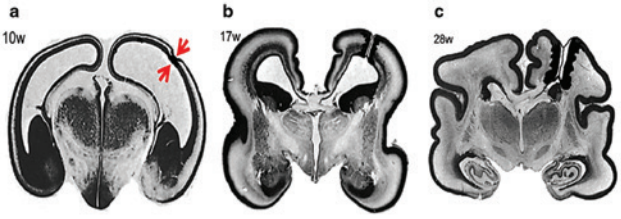

Figure 1. Illustrates the pleating and fusion of the pial and ependymal layers in the cerebral cortex at 10, 17 and 28 weeks of gestation [5].

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Figure 2 illustrates the changes in the cerebral cortex and their evolution during pregnancy. In the figure, the red square represents the focal damage of the entire thickness of the early cerebral cortex and subsequent destruction of the brain tissue. During the period of neuronal migration, around 28 weeks, regions of polymicrogyria are formed, seen at the edges of the schizencephaly cleft[5]

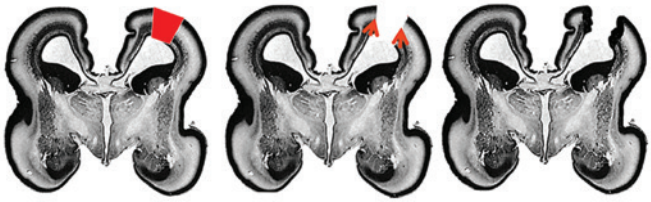

Figure 2. Illustrates the changes in the cerebral cortex and their evolution in the course of pregnancy [5].

On the other hand, if the event occurs after the sixth month of pregnancy, there is not neuronal migration that is sufficient enough to circumvent the existing lesion and therefore there is not enough organization to develop polymicrogyria.

Therefore, brain damage is produced by reabsorption of the injured tissue and, due to inadequate neuronal migration; there is an absence of gray matter at the edges of the lesions, resulting in the formation of porencephalic cysts, different from schizencephaly. On the other hand, the theory of vascular obstruction of the middle cerebral artery corroborates the fact that the majority of schizencephaly is seen in the region of the lateral sulcus of the brain, territory that is irrigated by the middle cerebral artery, including in the bilateral forms [3,4] .

Some authors point to certain genetic factors as etiology, such as mutations in the EMX2 gene that regulates the structural development of the forebrain. The mutation causes a lesion in the periventricular germinal matrix, impairing cell migration between the 6-7th week of pregnancy[4,6] .

Other genes such as EPG5 and COL4A1 causing vulnerability in the vascular wall are considered responsible for schizencephaly [7,8] .

Other related factors were age below 20 years, alcohol abuse, narcotic drugs, exposure to organic solvents, death of a twin, alloimmune thrombocytopenia, thrombophilia, congenital infections, maternal trauma and warfarin[8].

CLINICAL PRESENTATION:

Schizencephaly is divided into two clinical types: type I or closed lip, the cerebral cleft does not communicate with the ventricle turning prenatal diagnosis difficult. Griffiths PD performed a review with 11 fetuses and found type I (closed) schizencephaly in 45% of cases when using an magnetic resonance imaging (MRI) study [5] .

Type II or open lip schizencephaly, the cleft communicates with the ventricle being filled with fluid and with characteristics that can be described in prenatal care, occurring in 55-60% of cases[5]. The cleft margins are surrounded by dysplastic and heterotopic gray matter [1,8] .

Both types of schizencephaly can be unilateral or bilateral. The unilateral form is characterized by a markedly smoother course; may be asymptomatic or have epileptic seizures, mild motor defects and abnormal vision. The bilateral type is a severe and irreversible malformation of the CNS that manifests with seizures that are difficult to control, severe mental retardation, blindness and varying degrees of motor defects[8] .

There are no reports of schizencephaly diagnosed by ultrasound before 20 weeks of gestation. Howe et al evaluated 18 cases of prenatal schizencephaly and they all had a gestational age greater than 21 weeks of gestation[8] .

ASSOCIATED ANOMALIES:

The literature describes the association of schizencephaly with chromosomal abnormalities, genetic syndromes, congenital infections and death of monochorionic twinning. Other concomitant brain pathologies have been described as hydrocephalus (30% of cases and almost exclusively with type II), ventriculomegaly (85%), agenesis of the corpus callosum and septum pellucidum (40-70%), atrophy of the optic nerve (30%), arachnoid cyst and cerebellar malformations, cortical dysplasia, heterotopia, pachygyria, polymicrogyria, periventricular leukomalacia[1,8] .

Griffiths PD reported absent or interrupted septum pellucidum in 64% of fetuses with a tendency to be absent in fetuses with type II (open) schizencephaly[5].

DIFFERENTIAL DIAGNOSIS:

The differential diagnosis must be made with agenesis of the corpus callosum, hydrocephalus, holoprosencephaly, encephalocele, arachnoid cyst and porencephaly. The porencephalic lesion is a separate challenge, especially in type I, being differentiated from schizencephaly, on magnetic resonance, due to the absence of gray matter in the lesion outline.

CASE REPORT:

ARSC patient, 19 years old, white, regular cycle, natural conception, primiparous, date of the last menstruation unknown; no history of previous pathologies. She was referred to our service with a diagnosis of severe unilateral ventriculomegaly.

On December 31, 2019, the first ultrasound examination was performed on the pregnant woman, identifying a left unilateral cleft communicating the ventricular system to the subarachnoid space in the region of the parietal lobe - (figures 3). The diagnosis was unilateral type II schizencephaly. No other associated major structural anomaly was seen.

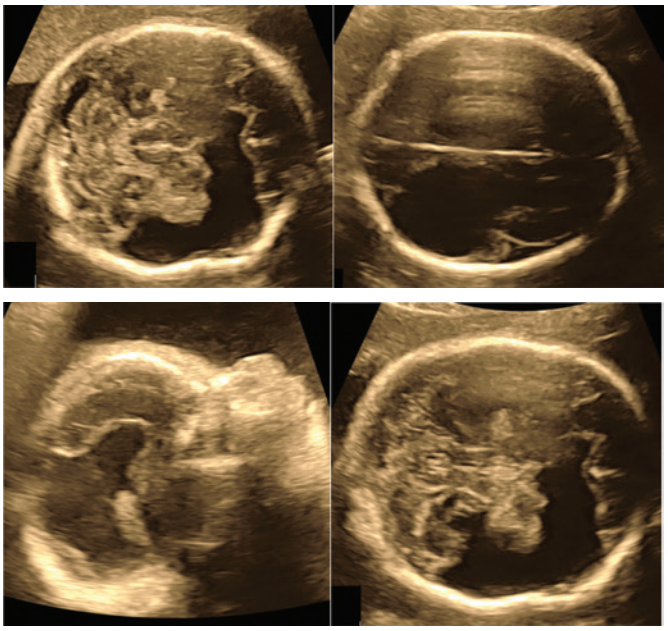

Figure 3. Ultrasound images show an anechoic area in the left parietal lobe region (unilateral type II schizencephaly).

On January 28, 2020, the second exam was performed, when an evolution from unilateral to bilateral was observed, communicating the ventricular systems to the subarachnoid spaces bilaterally - (figures 4). No other major associated structural anomaly was identified.

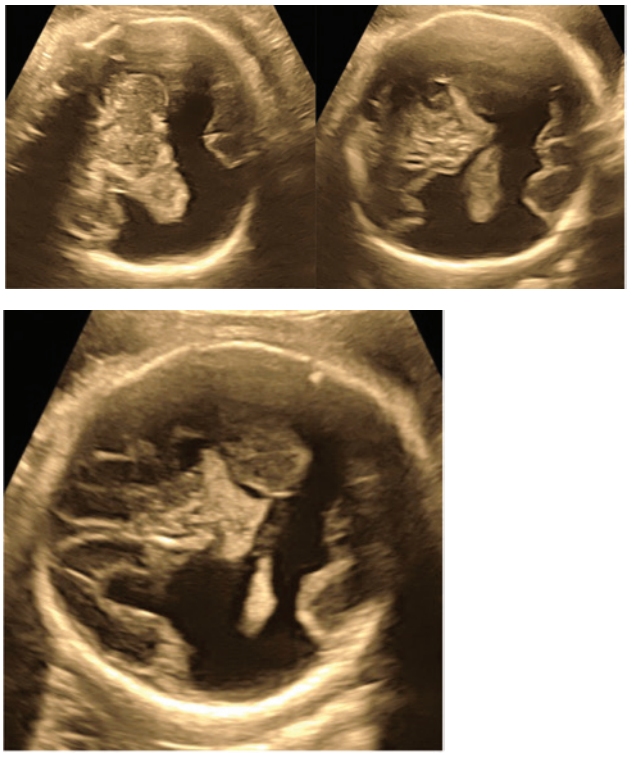

Figura 4. Ultrasound images show an anechoic area in the bilateral parietal lobe region (bilateral type II schizencephaly).

On February 14, 2020, a third ultrasound examination was carried out, in which an anechoic image was observed, communicating the right subarachnoid space to the right ventricle, an anechoic image of the same characteristics communicating the left subarachnoid space to the left ventricle and absence of cavum septum pellucidum, noting increased communications from the subarachnoid spaces to the ventricles. No other major structural anomalies associated.

On March 10, 2020, a fourth ultrasound examination was performed, which revealed a progressive increase in the subarachnoid space, in the cleft and in the cerebral ventricles and the absence of cavum septum pellucidum. Choroid plexus is seen floating in the ventricular cavity - (figures 5).

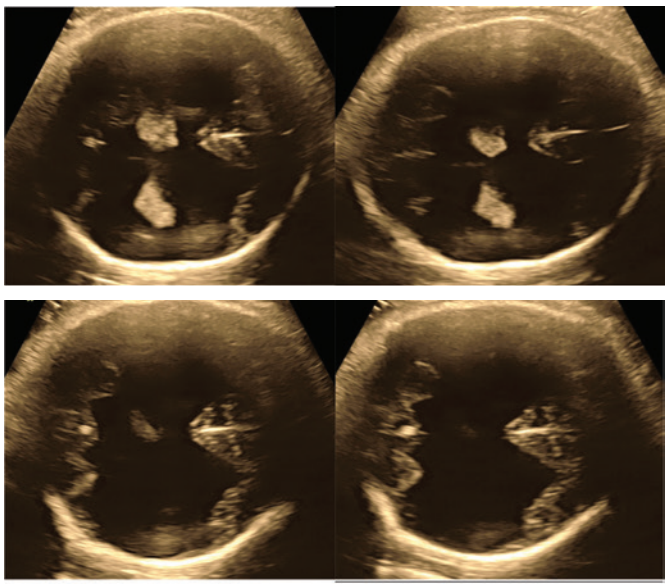

Figura 5. Ultrasound images show an anechoic area in the bilateral parietal lobe region (bilateral type II schizencephaly).

DISCUSSION:

Schizencephaly is usually associated with other CNS malformations, such as ventriculomegaly, polymicrogyria, pachygyria, heterotopia, lissencephaly, absence of cavum septum pellucidum, agenesis of the corpus callosum, hypoplasia of the optic nerve. Although the gold standard for the diagnosis of schizencephaly is the magnetic resonance imaging exam, there are rare cases described in the literature. The largest series was described by Nabavizadeh et al who studied 10 fetuses with intrauterine magnetic resonance and confirmed with a postnatal study, including eight bilateral cases. An interesting finding was the disagreement in the classification between prenatal and postnatal with 47% of schizencephaly type II (open) detected intrauterine that became type I (closed) in the postnatal period. They reported that about 26% of fetal polymicrogyries were not detected[10].

Another circumstantial evidence in this research by Nabavizadeh et al, is the finding of hemosiderin deposi-

tion and/or hemorrhage in the cleft and in the ventricles of the fetuses affected by schizencephaly in the magnetic resonance imaging exam. In addition, more than half of the fetuses presented microcephaly due to the destruction of the brain tissue. These findings corroborate with the theory that the main etiology for the cases of schizencephaly is due to bleeding and/or destruction of the brain matrix [10].

The clinical manifestations of schizencephaly include different levels of developmental delay, neuropsychomotor seizures and different degrees of abnormalities in vision and speech. Hunt et al studied 21 patients with schizencephaly (16 unilateral and 5 bilateral). Most patients with neurological deficits were detected before one year of age, especially in bilateral clefts. The main clinical presentation was hemiparesis in unilateral schizencephaly and seizures in the bilateral form.

About 81% of patients manifested generalized tonic-clonic epileptic seizure, with 38% of cases developing refractory epilepsy. Most patients developed motor, intellectual and language deficits, especially in bilateral schizencephaly [11].

This report is from a fetus who was referred with the diagnosis of ventriculomegaly and a morphological examination identified a rare pathology of the CNS, the unilateral type II schizencephaly. During monitoring, it evolved to a bilateral form with a progressive increase of the cleft, subarachnoid space, cerebral ventricle and identification of associated anomalies such as the absence of the cavum septum pellucidum and corpus callosum. This evolution from unilateral to bilateral form is not described in the medical literature.

It can be presumed that the diagnosis was very early and although the event had been bilateral, its manifestation took some time to become identified on ultrasound examination. The differential diagnosis is made to distinguish this disorder from holoprosencephaly, hydranencephaly and bilateral arachnoid cysts. Cases of schizencephaly type I and porencephaly most of the time can only be distinguished on the MRI exam in which the dysplastic and heterotopic gray matter bypasses the cystic lesion in type I schizencephaly.

In most cases an etiology will not be identified. The long-term prognosis will depend on the size and location of the lesion, whether unilateral or bilateral and if there are associated brain malformations. The newborn should be evaluated by a pediatric neurologist and follow-up with MRI is recommended. Therefore, an accurate prenatal diagnosis is important for adequate parental genetic reproductive counseling.

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