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Schizencephaly with Agenesis of the Corpus Callosum in the Neonatal Period: A Case Report

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Authors' contributions

This work was carried out in collaboration among all authors. Authors OB and AD designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors OB and AD managed the analyses of the study. Author OB managed the literature searches. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Schizencephaly is a rare abnormality in supratentorial brain development, the etiopathogenesis of which is not yet clear. This disorder consists of the presence of a slit bordered with gray poly-microgyric substance, which extends from the subarachnoid space to the ventricles: the ventricle and the cortex communicate with each other. Here we report an infant with this condition; its clinical, radiological and prognostic aspects. This infant had unilateral open slit schizencephaly with agenesis of the corpus callosum.

Keywords: Schizencephaly; corpus callosum agenesis.

1. INTRODUCTION

Schizencephaly, from the Greek "skhizein" (fractionation, crack, division) and "cephalon" (head), is an abnormality of supra-tentorial cerebral development consisting of the presence of a slit bordered with gray poly-microgyric substance, s' extending from the subarachnoid space to the ventricles, thus making the ventricle and the cortex communicate. The

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etiopathogenesis of this malformation is still under discussion. Although this malformation was first described by Wilmarth in 1887, the term and first exhaustive anatomo-pathological descriptions were reported by Yakovlev and Wadsworth. This malformation can be uni- or bilateral with open or closed edges. The diagnostic strategy for schizencephalia in the ante- and postnatal period has been revolutionized by sectional imaging, essentially MRI, the only technique capable of providing a precise and complete lesion assessment. Here we describe a case of schizencephaly with agenesis of the corpus callosum at the national reference center for neonatology in Rabat.

2. CLINICAL CASE

It is a newborn baby of a 19 year old mother, primigravidaand primiparous, without personal or family history, in particular without concept of inbreeding or drug or toxic contribution. Syphilitic (VDRL/TPHA), rubella and toxoplasmosis serologies were negative. The prenatal ultrasound performed at 34 weeks which showed an increase in uterine height compared to gestational age, made it possible to suspect a fetal supratentorial encephalic malformation with hydramnios. The delivery was vaginal at 38 weeks, after a labor time of 13 hours, with no history of obstructed labor or fetal distress in utero. He was eventually admitted on the first day of life. Poor adaptation to ectopic life was found with an Apgar score equal to 8 points in the first minute; 5 points at the 5th minute and 8 points at the 10th minute after an oropharyngeal aspiration and a tactile stimulation. The birth weight was 3100 g (eutrophic) and the head circumference was 36 cm.

The clinical examination revealed a newborn with respiratory distress evaluated at 2/10 according to the Silverman score. Neurologically, he had a Glasgow score of 15, an abolition of primitive reflexesand axial hypotonia.

During his hospitalization, the newborn had two generalized tonic crises with chewing movements, complicated by a convulsive state.

A transfontanella ultrasound was performed on day 2 of life, which showed hydrocephalus with agenesis of the corpus callosum. It was supplemented by a cerebral CT finding of an open slit schizencephaly, agenesis of the corpus callosumand bi-ventricular dilation without sign of transependymal resorption (Fig. 1). The rest of the malformation report (transthoracic and abdominal ultrasound) was unremarkable. It should be noted that the search for cytomegalovirus by PCR was negative, as was rubella serology. Brain magnetic resonance imaging was not performed due to the critical condition of the patient. Unfortunately, our patient died on the 14th day of his life as a result of nosocomial pneumonia.

3. DISCUSSION

Schizencephaly is an extremely rare central nervous system malformation, with a reported prevalence at birth of 0.54-1.54 per 100,000 live births in the United States, European countries and Japan [1-3].

In terms of frequency, several studies have reported that unilateral schizencephaly is slightly more common than bilateral cleft [4]. In contrast, other studies have shown that bilateral schizencephaly is slightly more common or of a prevalence comparable to unilateral cleft [5]. We also distinguish open or cystic schizencephaly, which is more frequent according to most studies compared to the closed form [6-8]. Our patient had open unilateral schizencephaly.

Schizencephaly can be detected by antenatal ultrasound, directly if the slit is large and open, or indirectly by visualizing a ventricular dilation. Prenatal MRI is better suited than ultrasound for prenatal diagnosis of such anomalies, because it can detect abnormalities in brain cell migration and associated malformations such as corpus callosum agenesis, polymicrogyria, etc. This makes it possible to assess the prognosis of the disease and will subsequently help in the management of obstetric risks. Morally, the diagnosis of ventricular dilation is an abnormality frequently detected by prenatal ultrasound and must be supplemented by an MRI [9]. For our patient, the diagnosis was suspected by antenatal ultrasound performed at 34 weeks of gestation which objectified a fetal encephalic malformation above tentorial with hydramnios.

In the postnatal period, the clinical picture is not specific and the symptoms of schizencephaly are extremely variable. Denis et al reported that asymmetry in muscle tone is often the first clinical manifestation of the disease in the unilateral form, as is the case with our newborn baby who presented axial hypotonia with abolition of archaic reflexes from birth. Other series have found that hemiparesis is the most common presentation in this unilateral form and is associated with seizures in bilateral clefts.

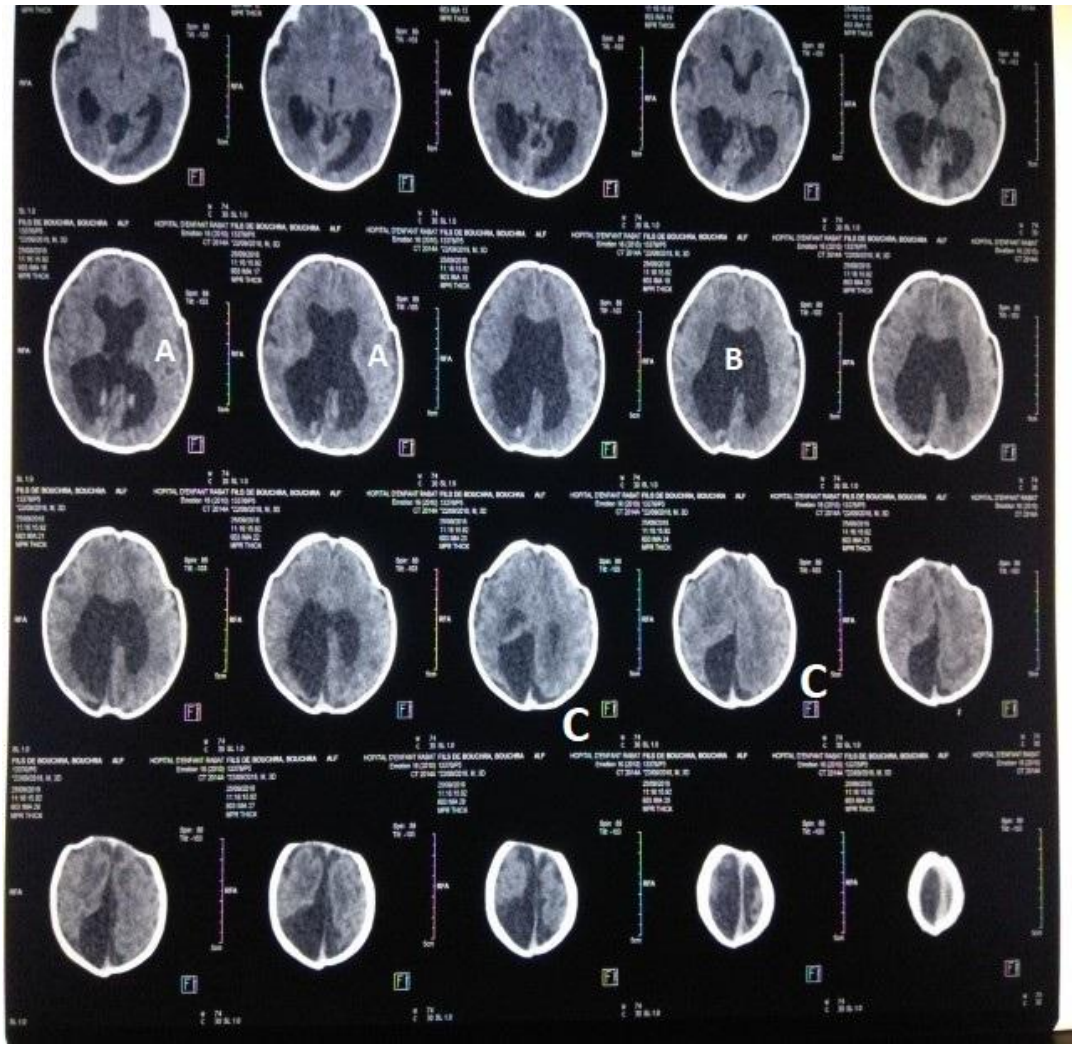

Fig. 1. Brain CT scan sections showing an agenesis of the corpus callosum (A), bi-ventricular dilation (B) and open schizencephaly (C)

In addition, neurological deficits and developmental delay were detected in most patients during the first year, especially in the bilateral clefts. A review analyzed a combined cohort of schizencephaly patients from 156 studies. The most remarkable finding is that neurocognitive and motor dysfunctions were present in respectively 77.5% and 90.3% of cases and that bilateral clefts, motor deficit, microcephaly and agenesis of the corpus callosum were strongly associated with this neurocognitive impairment [10].

Certain series have also shown that schizencephaly is the cause of certain cases of drug-resistant epileptic seizures. Our patient had agenesis of the corpus callosum and he presented from the first days of life an axial hypotonia with abolition of archaic reflexes; tonic seizures and a state of convulsive sickness. A clinical observation reported a case of schizoncéphalie with agenesis of asymptomatic corpus callosum of incidental discovery by cerebral scanner carried out in a polytraumatized male infant [11].

Sectional imaging (CT and MRI) plays a key role in the positive diagnosis and the lesion assessment.

Regarding the positive diagnosis: Open or cystic schizencephaly results in the presence of a uni-or bilateral fluid cavity extended from the cortical surface to the wall of the lateral ventricle

and surrounded by gray matter. Closed schizencephaly results in the identification of a linear signal of the gray matter, extending from the brain surface to the wall of the lateral ventricle. The demonstration of a localized dilation of the lateral ventricle, in the form of a dimple at the level of its lateral wall, constitutes a precious sign for the diagnosis of closed schizencephaly.

For the lesion assessment: In addition to schizencephaly, it is necessary to look for other abnormalities such as: areas of polymicrogyria; a sub ependymal heterotopia; Callous dysgenesis; Agenesis of the septum pellucidum.

The association of schizencephaly and Septo-optic dysplasia can be noted but it remains rare but known which can be linked to the primary defect leading to schizencephaly. Schizencephaly can also cause dysgenesis of the septum pellucidum or the optic nerve [12].

The severity of mental disorders and motor deficits is linked to the size and location of the clefts of schizencephaly. The presence of callous agenesis as seen in our newborn is a sign of poor prognosis [10].

The etiology of schizencephalia remains unclear. Two complementary pathogenic hypotheses are discussed: on the one hand, a defect in neuroblastic migration due to the intervention of an exogenous aggressive factor would occur during embryogenesis between the 12^{th} and 17^{th} weeks of pregnancy. This would be responsible for stopping the migration of future cortical neurons along the radiator fibers, or even their necrosis, leading after distortion to the constitution of a solution of continuity in the cortical mantle with communication between the lateral ventricle and spaces under arachnoid. Mechanically, it could be ischemia (especially in the area of the middle cerebral artery), fetal distress due to maternal trauma, fetal infection due to cytomegalovirus or even prenatal exposure to toxins such as cocaine or other alpha stimulants, or to carbon monoxide poisoning [13,14]. In addition, alongside this exogenous hypothesis linked to fetal aggression during gestation, several familial cases of schizencephaly linked to a mutation in the EMX2 gene have been published in the literature, supporting the involvement of a genetic mechanism, at least in part, in the pathogenesis of schizencephaly. This gene, located on chromosome 10q26, is thought to be involved in brain development. The mode of transmission is said to be autosomal recessive [15]. Genes such as LHX2, HESX1 and SOX2 have also been studied by Mellado and colleagues [16], although none has been mutated in a cohort of 97 patients. A study found that the young age of the mother, lack of antenatal care and alcohol consumption were all significantly associated with the risk of developing schizencephaly [9]. In our case, the genetic test was not requested.

As a general rule, the therapeutic management of these two types of schizencephaly is conservative and consists mainly of rehabilitation for motor deficits and mental retardation and the treatment of epilepsy. Surgical treatment is undertaken only in a few cases of hydrocephalus or concomitant intracranial hypertension [6].

Epilepsy attacks are often focal and difficult to treat. Surgery is often impossible to perform due to the central topography of the lesions and the presence of large epileptogenic zones [10].

4. CONCLUSION

In the light of this observation and the review of the literature it can be concluded that Schizencephaly remains a rare congenital cerebral malformation; the clinical presentation differs from one subject to another; sectional imaging is essential in the positive diagnosis and the lesion assessment and the severity of the disorders is essentially linked to the size; localization as well as other associated brain malformations.

CONSENT

As per international standard, parental written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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