Case Report

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Treatment of schizencephaly: A brief review and case study

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Introduction: Schizencephaly is a rare disease. It is a poorly understood pathology. The clinical signs are variable and the diagnosis is made by elimination. The treatment is varied with poor results. Corticosteroids are not commonly used medications.

Case Presentation: The observation concerns a 5-month-old child, born with a motor deficit in the right hemibody. His parents had an unremarkable medical history. After brain imaging for epileptic seizures, the child is referred for neurosurgery 5 months later. The diagnosis of schizencephaly was mentioned. Antiepileptic treatment associated with corticosteroid therapy for two weeks was started. Motor physiotherapy began at the same time. At 6 months after start of treatment, the evolution was satisfactory marked by a clear improvement in the motor deficit and a complete cessation of seizures.

Conclusions: Due to its rarity, the diagnosis of schizencephaly is made by elimination. Brain MRI is the best radiological examination. Corticosteroid therapy combined with physiotherapy can have an impact on good progress. Treatment should be early.

Keywords: *schizencephaly; epilepsy; hemiparesis; malformation; pediatric neurosurgery*

Introduction

Schizencephaly is a rare congenital disorder of cerebral cortical development [1]. Due to insufficient knowledge of this condition, several definitions had been proposed. The most recent which seems to be the synthesis of the previous definitions is from Naidich et al [2]. It includes a trans-mantle column of dysplastic gray matter extending from the ependyma to the pia mater without a cleft containing CSF [2]. A recently discovered condition, schizencephaly was first described at the end of the 19th century [3]. The term was first introduced by Yakovlev and Wadsworth 1946 [4] to designate a malformative lesion due to a deviation from normal development and not secondary to destruction of the mature cortex as in porencephaly. The prevalence of this disease is estimated at approximately 1.5 per 100,000 babies born alive, according to estimates from a review of four million births in California [5]. According to Howe et al. a combined live birth and stillbirth rate of 1.48 per 100,000 was found in a population of over 2.5 million in the United Kingdom [6]. Its etiology is still subject to debate. Treatment is symptomatic with poor results. Corticosteroids are not commonly used in the treatment of schizencephaly. The objective was to report the first case of type 3 in our practice treated effectively with corticosteroids and physiotherapy. We do not have statistical data on this pathology on a hospital level, much less on a national scale.

Case Presentation

This concerns a 5-month-old child brought for consultation by his parents for a motor deficit of the right hemibody associated with seizures. Coming from a monogamous marriage without any notion of consanguinity, the child was born to a housewife mother and a soldier with no particular medical history. The pregnancy monitoring diary did not note anything particular apart from high blood pressure for the mother who responded favorably to the drug treatment. Second child of the siblings, the first of which is a two-year-old boy living in apparently good health, the child since his vaginal birth has presented functional impotence of his right hemibody. A few weeks later, he was seen by a pediatric surgeon who recommended an opinion with rehabilitation sessions. Without improvement, the evolution was marked at the age of 4 months by the occurrence of partial tonic-clonic epileptic seizures affecting the right upper limb and secondary generalized over the entire body. Faced with this painting, the child was taken to the pediatrician. After clinical evaluation, a brain computed tomography (CT) scan was performed at the age of 4 months and the patient was referred for neurosurgery consultation. Received one month later (because of the delay in obtaining the appointment), the clinical examination found a patient in good general condition, responsive and conscious. The pupils were equal in size, reactive and concentric. There was a motor

deficit rated at 1/5 in the right upper limb and 0/5 in the right lower limb. The rest of the exam was unremarkable. The brain CT performed revealed the presence on the left side of the brain a fronto-parietal cleft causing the left lateral ventricle to communicate with the ipsilateral pericerebral space through a dehiscence of the brain parenchyma ***(Figure 1)***.

The absence of the septum pellucidum was also noted. This combination suggests type 3 Schizencephaly. The brain MRI requested was not carried out due to financial accessibility, availability (because it is done in a private hospital) and the difficulty of carrying out (the examination is carried out under anesthetic sedation in patients less than 1 year old). Electrophysiological examinations were not carried out because they are not available. At the end of a concern meeting, a treatment based on valproic acid 10 mg/kg divided into one dose every 12 hours per day for a period of 6 months was proposed by the neuropediatrician; under his directive and also on the instructions of the physiotherapist, corticosteroid therapy based on methylprednisolone 0.5 mg/kg only in the morning was implemented for two weeks. The child continued his motor rehabilitation of his right half body. This treatment was started in the child at 5 months old. At 6 months of evolution when the child was 11 months old, we noted a recovery of the motor deficit. This was 5/5 in the right upper limb and 4/5 in the right lower limb with remission of seizures under antiepileptic treatment. The child did not present any delay in psychomotor development.

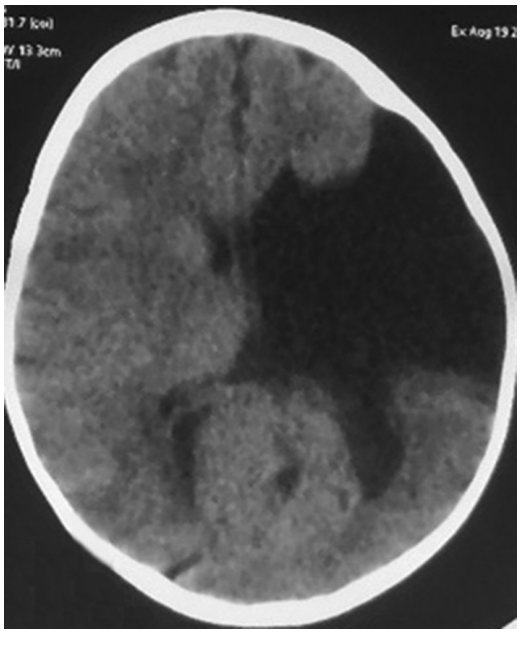


Figure 1. The cleft of the brain tissue of the hypodense density of the left fronto-parietal area, which communicates with the left lateral ventricle. Nonenhanced CT

Discussion

Etiology and risk factors

Many etiologies have been mentioned for the occurrence of schizencephaly. Work between 2010 [7] and 2013 [8] had aroused interest in genetic anomalies even if the first reports by Merello et al. in 2008 linking schizencephaly to mutations in the EMX2 gene have not been confirmed [9]. The majority of cases of schizencephaly are sporadic and not familial, and in most cases no cause is found [10]. Schizencephaly is thought to be due to "a defect in growth and differentiation of a circumscribed part of the brain wall" [11]. According to Griffiths, this disease would have its origins in the first trimester of pregnancy, more precisely the first 2 months after conception [12]. The theory of pinning of the ependyma and the pia mater, refined by Naidich [2], which are anatomically very close during the first trimester is not shared by Griffiths who finds it difficult to explain the banks largely open openings and loss of volume frequently present in schizencephaly (type 3) [12]. Further evidence against the pinning theory is the consistent presence of abnormal cortex lining the clefts, which indicates an etiological factor in the second trimester: "...Coincidental polymicrogyria suggests that the timing is between the fourth and the sixth month [12]. Chen states that the primary etiology is due to "in utero vascular insufficiency" [13]; this vascular etiology was found in the work of Nabavizadeh et al. [14]. There is now clinical, morphological and experimental evidence in favor of a destructive origin of these lesions" [11]. Among the risk factors recognized for the occurrence of schizencephaly, transplacental infections by cytomegalovirus [11] and recently by Zika virus [15] have been well documented. No notion of genital infection was found in the patient's mother. Our observation would relate to a sporadic case of schizencephaly.

Clinical aspects

The clinical presentation of schizencephaly is very variable. In their 10-year study in Thailand, the authors found that the most common clinical features of schizencephaly were motor disability, developmental disorders and epilepsy [16]. Some authors claim that gravity is closely linked to the size of the cleft [17]. According to Denis et al. children with unilateral schizencephaly present hemiparesis and mild mental retardation [17]. Maurine et al. [1] had reported the existence of a correlation between clinic and imaging. They found that patients with closed-cleft schizencephaly were more likely to have mild to moderate clinical signs than those with open clefts. That children with unilateral schizencephaly more frequently presented a mild or moderate course than those with bilateral lesions. Single lobe involvement accounted for 88% of those with mild results and 53% of those with moderate results [1]. We do not share these statements in the sense that the case reported in our observation presented type 3 schizencephaly (open cleft), but did not have the severe neurological form. Apart from hemiparesis which was regressive and comitiality improved under treatment, the child had no other signs (delay in psychomotor development, axial hypotonia, and microcephalus). However, the lesion was located between the frontal

and parietal lobes. Perhaps the unilateral attack had something to do with it.

Diagnostic aspects

The diagnosis of schizencephaly is raised by neuroradiology. The absence of a consensual definition meant that this diagnosis was established by elimination when made in early childhood. The ideal is to make the diagnosis during the antenatal period. Magnetic resonance imaging (MRI) is the best of choice. In utero magnetic resonance imaging (iuMRI) is now used for prenatal detection of brain abnormalities, including schizencephaly [4]. In the United Kingdom, less than half of cases of schizencephaly were detected prenatally [6]. As this examination is difficult to access in our context, we relied on brain CT-scan to make the diagnosis. This examination is a good tool for uncovering the cleft, its location and its extent. It made it possible to detect the absence of the septum pellucidum in our patient. According to Maurine et al. found it in 45% of patients in their study [1]. The absence of septum pellucidum is associated with "open cleft" schizencephaly (type3) [12]. The reasons for the association of schizencephaly with the absence of the septum pellucidum are not yet known with certainty [12]. Although MRI is essential for diagnosis of schizencephaly [18]; also, it can highlight the abnormal existence of ventricular diverticulum which hinder the free circulation of cerebrospinal fluid [19]. A high-performance brain CT scan can be an important means of clarifying confusion, as was the case in our observation. The stereoelectroencephalography (SEEG) can be used to identify seizure foci in patients whose clinical symptoms do not correspond to imaging results and/or routine electroencephalogram (EEG) results [20].

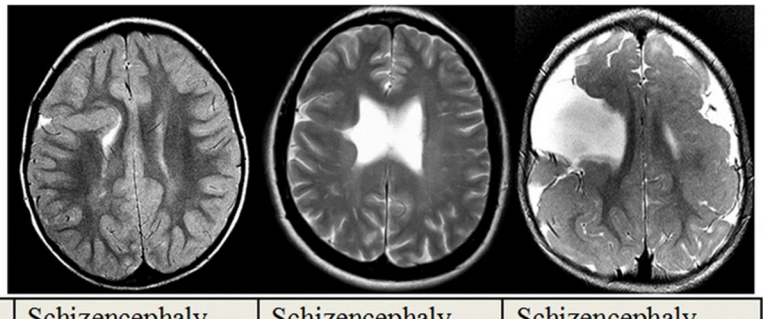
Classification

Griffiths P.D. in his work on schizencephaly proposed a classification which takes into account all the definitions of the anomaly reported in the literature [12]. This classification is recorded in ***Table 1***.

Therapeutic aspect

Treatment is symptomatic. There is no cure for the disease. Short-term corticosteroid therapy was used in our study because of its anti-inflammatory effect. According to Becker et al. corticosteroids have been used for the treatment of patients with epilepsy for more than 6 decades, based on the hypothesis of inflammation in the genesis and/or promotion of epilepsy [21]. We have not had any document relating to the use of corticosteroids in the treatment of schizencephaly. In the event of an epileptic seizure, antiepileptic treatment may be administered depending on the patient's weight and the type of seizure. In the event of partial seizures, carbamazepine should be preferred. For other forms of seizures, all other antiepileptic drugs can be used at the minimum effective and tolerated dose. When monotherapy is not effective, a combination of antiepileptic drugs can be used. In our observation, valproic acid had been used successfully. For refractory

Table 1. Classification of schizencephaly according to P.D. Griffiths [12]



Nomenclature used in this article	Schizencephaly (type 1)	Schizencephaly (type 2)	Schizencephaly (type 3)
Nomenclature if a cleft is required for the diagnosis of schizencephaly	Trans-mantle heterotopion	Closed lip schizencephaly	Open lip schizencephaly
Nomenclature if a cleft is NOT required for the diagnosis of schizencephaly	Closed lip schizencephaly	Open lip schizencephaly	Open lip schizencephaly

epilepsy, high-dose steroids may be administered before possible surgical treatment [18]. In cases of drug resistance, which concerns a third of patients, epilepsy surgery can be offered. This can be the resection either of the schizencephalic cleft alone, or of the cleft and the surrounding epileptogenic tissue, or of temporal or fronto-temporal lobectomy. Also, surgery may consist of the removal of abnormal intraventricular diverticulum which can lead to intracranial hypertension [19]. This surgery is done endoscopically. In case of failure, we will convert to open surgery. Preventive treatment of epilepsy is not permitted. Functional rehabilitation is necessary to hope for recovery from the motor deficit. In our patient, over a period of 6 months after start of treatment, recovery was good. We cannot say with certainty whether this therapeutic effectiveness is due to rehabilitation or corticosteroid therapy or to the combined effect of the two methods.

Prognostic aspects

The prognosis is variable and depends on the extension of the cleft, its extent and the association with other craniocerebral malformations. Children with a severe motor deficit associated or not with drug-resistant epilepsy will present a very poor outcome. Open lip clefts were associated with poor seizure control, and a larger cleft was related to a younger age at seizure onset [22].

Conclusions

Schizencephaly is a rare congenital pathology that is most often diagnosed in the second instance. Brain neuroimaging is essential for the diagnosis of this disease. Corticosteroid therapy can be included in symptomatic treatment. Multidisciplinary care must begin as early as possible in order to hope for a favorable outcome.

Disclosure

Ethical Considerations

Compliance with ethical guidelines: Ethical considerations, anonymity and patient modesty were respected.

Informed consent

We obtained parental consent for the use of the child's medical data.

Conflict of interest

No conflict of interest.

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