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A Drug-Susceptible Focal Cortical Dysplasia: Radio-Clinical Reasoning: Case Report

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Abstract **Case Report**

Focal Cortical Dysplasia (FCD) is a limited abnormality in the cyto-architectural development of the cerebral cortical plate. It is characterized by great anatomopathological, clinical, electroencephalographic, radiological heterogeneity and by its pharmaco-resistance. Our observation concerns a 12-year-old girl, in whom the DCF was revealed by epilepsy initially focal and infrequent then rapidly generalized and increasing frequency. Brain MRI showed a typical aspect of FCD isolated and localized to the left parietal lobe. After the initial failure of valproate, epileptic seizures were controlled by Carbamezepine lasted for ten years. Through this observation, we will describe the clinical and radiological elements associated with drug-susceptible epilepsy FCD.

Keywords: Focal cortical dysplasia – drug-susceptible epilepsy.

INTRODUCTION

Focal cortical dysplasia (FCD) is a limited abnormality of the cyto-architectural development of the cerebral cortical plate. It is characterized by great anatomopathological, clinical, electroencephalographic and radiological heterogeneity, as well as by pharmaco-resistance. In this article, we describe the clinical and radiological features associated with this phamaco-sensitive FCD.

PATIENT AND OBSERVATION

BI, aged 12, is the 2nd of 3 siblings. She was undergoing consultation for epilepsy. She was born to non-consanguineous parents, with a well-monitored pregnancy carried to term without incident, and a medicalized vaginal delivery. The neonatal period was uneventful. There was no epilepsy or neuropathy in the family. The patient had no history of head trauma, toxic intake, febrile convulsions or infectious or non-infectious neurological pathology. Her story began 2 months ago with the sudden onset of a convulsive seizure on awakening in the morning, in a context of apyrexia. The seizure began with a deviation of the left commissure, then generalized to the whole body in the form of a tonic-clonic seizure with revulsion of the eyes, loss of consciousness for 15 minutes, followed by a 2-minute post-critical coma. After regaining consciousness, the patient retained paresis of the right upper limb for 5 minutes. She was taken to a health center, put on magnesium and referred to a pediatric consultation. Clinical examination was normal, except for a divergent strabismus of the right eye. Electroencephalography of wakefulness and sleep under chloral and awakening with intermittent light stimulation was performed. It showed a normal background rhythm, a symmetrical tracing, a few brief slow puffs predominantly on the left and sleep without hypnic figures. Cerebral CT was interpreted as normal (fig. 1). The patient was put on treatment (sodium valproate) and seen regularly in consultation. Six years later, the patient had another convulsive seizure in the morning on awakening, under the same conditions as the first, then at a rate of 1 seizure every month, then every week, then several times a day, despite readjustment of treatment. This prompted hospitalization and a brain MRI scan, which led to the diagnosis (fig. 2). Cerebral MRI showed thickening of the left parietal cortical mantle, an irregular appearance of the white matter/gray matter junction and a V-shaped hypersignal of the adjacent white matter in T2 joining the lateral ventricle. The white matter is not hypoplastic. There is no dilatation or cisterno-venricular anomaly, and medial structures are in place. No subtentorial abnormalities. This suggests a diagnosis of

type 2 cortical dysplasia or Taylor's focal cortical dysplasia. The lesion is also visible on cerebral CT (fig. 1).

After initial failure with sodium valproate 30mg/Kg/d for 1 month, the seizures were gradually and perfectly controlled after 3 weeks with Carbamezepine 200 mg taken 2 times a day. Today, the patient is 21 years old and has a normal family, social and academic life. She is still on Carbamezepine, and has had no side effects.

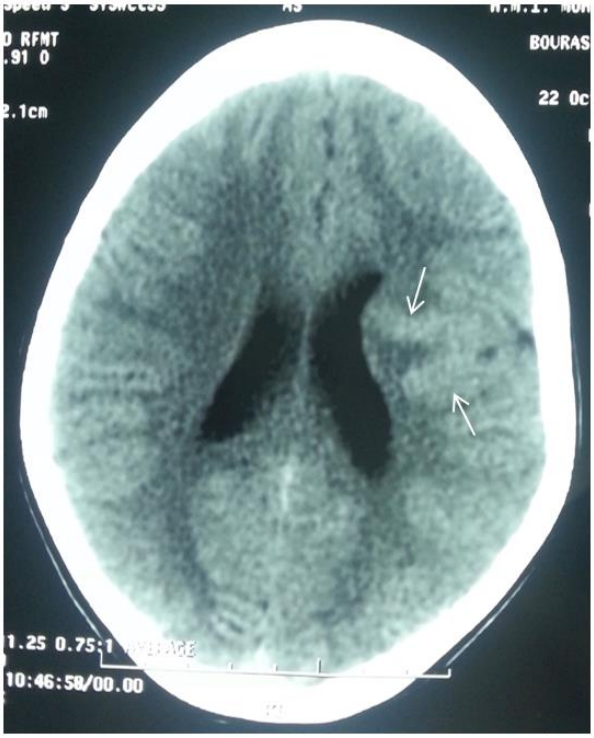

Figure 1: Cerebral CT: axial section showing two left parietal hyperdensities describing a 'V' (arrows) extending into the adjacent white matter up to the ventricular rim

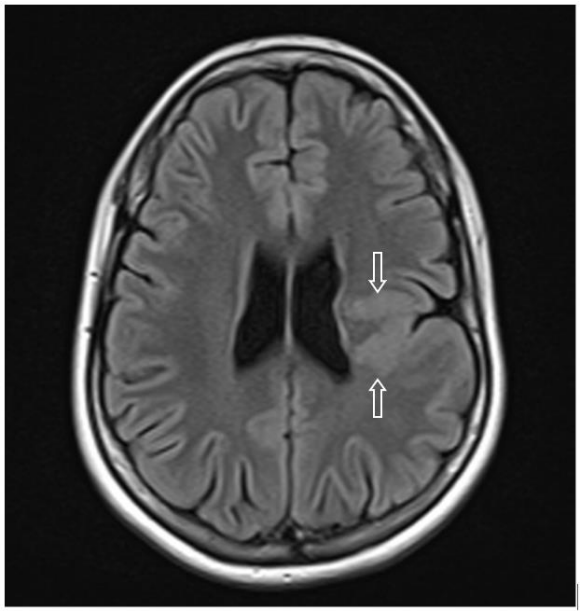

Figure 2: Cerebral MRI: axial section in T2 Flair-weighted sequence showing focal thickening of the left parietal cerebral cortex with hypersignal and white matter (arrows) extending from the white matter-gray matter junction to the ventricle

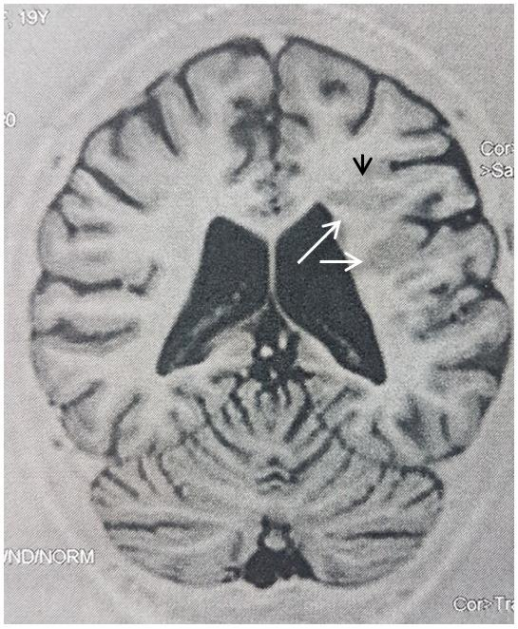

Figure 3: Cerebral MRI: T1-weighted coronal slice showing the same lesion in inverted signal (white arrows). White-gray matter junction with blurred boundaries (black arrow)

DISCUSSION

Focal cortical dysplasia (FCD) is currently defined neuropathologically as a limited abnormality in the cytoarchitectural development of the cortical plate [10], although rare cases of multifocal FCD have been described [11], usually with conservation of the gyral pattern [1, 12]. They are responsible for epilepsy that is usually drug-resistant. DCF was individualized by Taylor in 1971, with a characteristic anatomopathological presentation [1]. Macroscopically, it associates a thickening of the cortical mantle with imprecise boundaries with the white matter, and microscopically, disorders of cortical architecture affecting the entire cortical layer, with giant neurons and ballooning glial cells [1]. In fact, the dysplastic lesion may be visible to the naked eye and disrupt normal gyration, or microscopic and undetectable by conventional radiological techniques. Subsequent studies have shown that FCDs can present a wide variety of histological forms, ranging from simple changes in cortical architecture without ballooning cells (type 1) to severe forms (type 2) such as that described by Taylor and which bears his name [2]. In 2011, the International League Against Epilepsy (ILAE) established an international classification of FCD into types (type 1, 2 and 3) and subtypes based on their clinico-pathological characteristics, with the aim of facilitating medical and surgical therapeutic decisions [14]. According to this classification, type 1 includes isolated abnormalities of radial cortical striation (subtype 1a), tangential cortical striation (subtype 1b) and mixed striation (subtype 1c). Type 2, on the other hand, corresponds to the isolated presence of dysmorphic cortical cells (subtype 2a) associated with ballooned cells (subtype 2b). The latter is thought to be the consequence of early disorders of intrauterine development, during the period of neuronal and glial proliferation [4]. Type 3 corresponds to a cortical striaion anomaly adjacent to hippocampal sclerosis (subtype 3a), a glial tumor or glioneuroma (subtype 3b), a vascular malformation (subtype 3c), a lesion acquired early in life such as trauma, ischemia or encephalitis.... (subtype 3d). This classification was revised in 2018 to also take into account genetic characteristics, thanks to new data in the literature [13].

The radiological component is not included in this classification, as these different forms of DCF are indistinguishable on imaging [3]. In the majority of cases, no etiological factor is found [5]. Currently, two etiopathogenic frameworks can be distinguished: on the one hand, familial cortical malformations for which genetic causes have been found, and on the other, sporadic cases for which environmental factors occurring during the first half of gestation are incriminated, in particular infectious, toxic or ischemic factors [6]. FCDs, which account for 16% of cortical developmental malformations [5], are a frequent etiology of surgical partial epilepsy, found in 6% of cases [7].

The clinical presentation is extremely variable, depending on the age of onset of epilepsy [15], the size of the lesion [16, 2] and its location [15]. Indeed, the age of onset of epilepsy is inversely correlated with the frequency and severity of epileptic seizures [18]. In contrast to patients with early-onset epilepsy, those with late-onset epilepsy often had FCD localized to the temporal region, which was associated with a better postoperative course of epilepsy [19]. It results in partial epileptic seizures, which may later become generalized, as in our patient's case. The type of epilepsy depends on the age of the child. In infants, it may take the form of infantile spasm, with the possibility of focal components, whereas in older children, epilepsy tends to present as

focal seizures, the semiology of which depends on the location of the FCD [15].

Moderate to severe mental retardation may be associated with FCD [20]. Determining the role played by pathology, age of onset or type of epilepsy in the onset of mental retardation is difficult. In one series, 60-70% of patients with type II FCD had a below-average Intelligence Quotient (IQ) [20]. In one study, mental retardation was more frequent in patients with type II FCD than in those with type I [20], especially as the epilepsy began in childhood [15]. In another study, the authors observed an increase in cognitive deficit in type I FCD [17]. Our patient showed no cognitive deficit, most likely due to an attenuated histology (type I FCD) or the rapid control of his epilepsy.

MRI demonstrates a broad convolution, with cortical thickening, effacement of the cortex-white matter junction and a T2 hyperintense, T1 hypointense signal from the underlying white matter extending into the lateral ventricle [5]. In neonates and during the first years of life, the white matter adjacent to the FCD may show a T1-hyperintense and T2-hypointense signal. The cortical areas most frequently affected are around the central fissure, and the frontal and temporal cortex [2].

The MRI appearance of FCD is similar to that seen in the cortical tubers of tuberous sclerosis of Bourneville (TSB) [8]. The discovery of FCD should therefore prompt a search for stigmata of TBS. FCD extending to a cerebral lobe (particularly frontal) can be difficult to differentiate from quadra-megalencephaly. The identification of cortical or subcortical calcifications is probably an argument in favor of quadra-megalencephaly or TSB, since calcifications are exceptional in DCFTs observed outside TSB [9].

Somatic mosaic mutations of genes that encode proteins in the PI3K-AKTmTOR pathway, which also includes the tuberous sclerosis associated genes TSC1 and TSC2, have been implicated in FCD type II in a substantial subset of patients. mproved knowledge of the genetic causes of FCD offers promising new avenues for personalized treatment. FCD II results from mutations in genes in the MTOR pathway, a key regulator of cell growth, proliferation, survival, autophagy, transcription, and protein synthesis. MTOR inhibitors like everolimus are currently used as an adjunctive treatment option for epilepsy in TSC patients. It is a matter of debate whether an early suppression of abnormal mTOR signal with mTOR inhibitors before seizure onset might be an effective antiepileptogenic and disease-modifying strategy in infants with TSC [21].

FCD is characterized by the frequency of drug-resistant epilepsy. However, our patient's epileptic seizures, although initially unresponsive to Sodium Valproate, were controlled by Carbamezepine. Consequently, we did not need to resort to surgery. At present, after around 10 years, our patient is well integrated socially and pursuing her higher education. The late age of onset of the epilepsy, the favorable, early and long-lasting response to a single antiepileptic, and the isolated and localized appearance of the FCD on CT (absence of calcification) and MRI, obviate the need for an anatomopathological study and allow us to say that this is most probably a type 1 FCD.

New surgical approaches such as stereotactic surgery and laser interstitial therapy (LTT) have been applied to MCD related epilepsy with promising results [22–24]. LTT is associated with a decreased length of procedure time, shorter hospital stay, and lower rates of complications when compared to open surgery [24, 25].

CONCLUSION

This observation highlights the important role of brain imaging in epileptic pathology in children. A FCD with no adjacent brain lesions and a favorable response to anti-epileptic therapy should be the first to suggest a type 1 FCD.

Conflicts of Interest

The authors declare no conflicts of interest.

Authors' Contributions

All authors have read and approved the final version of the manuscript.

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