Drug-resistant Focal Epilepsy due to Focal Cortical Dysplasia: A Case Report

Alam MS¹, Haroon K²

Abstract:
Focal cortical dysplasias (FCDs) belong to the large spectrum of malformations of cortical development (MCDs) and represent the most common structural brain lesion in children with drug-resistant focal epilepsies submitted to surgical treatment. It is responsible for nearly half of intractable epilepsy cases in children and adults, and at the same time it is characterized by quite good treatment outcome. We describe a case where a young girl had been suffering from intractable epilepsy and was on two medicines. She was operated upon and was relieved of her symptoms. Her histopathological examination revealed focal cortical dysplasia. We have to keep in mind that FCD can present as low grade glioma and treat it carefully.

Keywords: epilepsy surgery, focal cortical dysplasia, malformation of cortical development, balloon cell, intractable seizure

Abbreviations: FCD- Focal cortical dysplasia; MCD-malformations of cortical development; MRI- magnetic resonance imaging


Introduction:
Focal cortical dysplasias (FCDs) belong to the large spectrum of malformations of cortical development (MCDs) and represent the most common structural brain lesion in children with drug-resistant focal epilepsies submitted to surgical treatment. It is responsible for nearly half of intractable epilepsy cases in children and adults, and at the same time it is characterized by quite good treatment outcome. As many as a quarter of patients with epilepsy may harbor cortical dysplasia as the cause of their disease. Cortical dysplasia was present in up to 26% of a series of surgically treated cases of pediatric epilepsy. Cortical dysplasia is the most common substrate found in patients undergoing epilepsy neurosurgery younger than age 18 years, and the third most frequent lesion identified in adult epilepsy surgery patients.

Focal cortical dysplasia results from an early disturbance in the migration and final architecture of immature cortical neurons. Cortical dysplasia is a malformative lesion that occurs during neocortical development. The spectrum of derangements in neuronal proliferation, migration, differentiation, and programmed cell death can cause abnormalities in cortical architecture, leading to cortical dysplasia. Cortical dysplasia may be focal or diffuse and can cause intractable epilepsy, developmental delay, or focal neurological deficits.

Numerous classifications of these complex structural abnormalities have been proposed (for example Kuzniecky et al., 1991; Palmini et al., 1994; Barkovich et al., 1996). However, it is widely recognized that none are satisfactory. Cortical dysplasia, cortical malformation, neuronal migration disorder, and cortical dysgenesis all are appropriate terms in the correct setting.

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FCD 1a was defined as a blurred transition between different cortical layers. FCD 1b was diagnosed if the laminar disorganization was more prominent and occurred together with cytoarchitectural abnormalities such as immature neurons (a population of neurons with a large nucleus and a thin rim of cytoplasm) and/or giant neurons. Dysplastic tissue with the additional occurrence of dysmorphic neurons was classified as FCD 2a, and dysplastic tissue with additional balloon cells as FCD 2b.

A proposed underlying mechanism for neuronal hyperexcitability in FCD is the enhanced expression of glutamatergic receptors in dysplastic neurons, for example the Nmethyl-D-aspartate (NMDA) receptor subunits NR1-1a, 1b, 2a, 2b, NR2A/B, NR2B, and the a-Amino-3-hydroxy-5methyl-4-isoxazolepropionic acid (AMPA) receptor subunits GluR1 and GluR2/3.

Fauser et al had described hippocampal sclerosis with FCD as dual pathology. In their series most patient benefitted from surgery. Only ten percent patient did not get any benefit from surgery. The term ‘dual pathology’ describes the coincidence of extrahippocampal temporal lesions and Ammon’s horn sclerosis.

Surgical procedures resective surgery—that is, lobectomy, lesionectomy or corticectomy, or multiple subpial transections of the eloquent ictal area—was the major surgical approach. The aim of surgery was the complete removal of the lesion and the ictal zone.

Outcome of surgery was analysed by Fauser et al in 2008. They observed that older age at the time of epilepsy surgery, occurrence of secondarily generalised seizures and a multilobar extent of the dysplasia were the most important factors which significantly increased the risk of not becoming seizure free postoperatively. Successful epilepsy outcome was also related to duration of epilepsy, epilepsy surgery without the need for invasive EEG recordings and completeness of resection. In contrast, age at epilepsy onset, histological subtype and location (temporal or extratemporal) were not significant prognostic factors for postoperative epilepsy outcome.

EEG is an investigation of choice in FCD. Ictal and interictal paroxysmal, low-voltage, fast activity are

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<th>Classification of FCD</th>
<th>Palmini and Lüders</th>
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<td>FCD 1A: Isolated architectural abnormalities of the cortex</td>
<td>Mild cortical dysplasia: Ectopically placed neurones in or adjacent to layer 1 or microscopic neuronal heterotopia outside layer 1</td>
<td>Architectural dysplasia: Abnormal cortical lamination and ectopic neurones in white matter</td>
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<td>FCD 1B: Architectural abnormalities plus giant or immature, but not dysmorphic neurones</td>
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<td>Cytoarchitectural dysplasia: Giant neurofilament-enriched neurones and altered cortical lamination</td>
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<td>FCD 2A: Architectural abnormalities with dysmorphic neurones but without balloon cells</td>
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<td>Taylor-type dysplasia: Giant dysmorphic neurones and balloon cells with laminar disruption</td>
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<tr>
<td>FCD 2B: Architectural abnormalities with dysmorphic neurones and balloon cells</td>
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typically seen in intracranial recordings of FCD, and the presence of paroxysmal fast and slow repetitive spikes are, in turn, predictive of the ictal zone\textsuperscript{12}. Other patterns associated with seizure onset in these patients include spike and wave activity, burst of polyspikes, and delta brush\textsuperscript{12}.

With advent of 1.5T MRI, it was evident that FCD was more common in patients with intractable epilepsy than previously thought. Newer imaging shows MCD to be radiographically heterogeneous, with distinct signal characteristics, extent, and location\textsuperscript{16}. Typically, FCDs do not enhance with gadolinium. About 40% of patients with FCD type I and approximately 10% in type II have a normal brain MRI. Thus, a normal brain MRI in a patient with intractable epilepsy does not rule out FCD. Magnetic resonance imaging findings favoring FCD rather than a tumor include cortical gray matter thickening and a transmantle sign\textsuperscript{16}.

**Case report:**

A seventeen years old non-hypertensive nondiabetic girl was admitted to the Department of Neurosurgery, with the complaints of generalized convulsion. Her convulsion had precede by an aura, started from the left side of the body, deviation of the eyes to the left and persisted for few minutes. She was unresponsive for some time following the seizure. She was taking two anti-epileptic drugs in adequate dose and duration. But still she was having seizure. Her MRI shows a non-contrast enhancing lesion in the right parietal region which was hyperintense in the T2WI (figure 1). It was diagnosed as low grade glioma. It was localized, without any invasion of surrounding brain. She underwent parietal craniotomy and total removal of tumour. The tumour was soft, suckable, without any capsule but surrounded by a gliotic brain. Gross total removal of tumour was done. The patient recovered without any incidence. She was kept on a single antiepileptic medicine. Histopathological examination of the tumour tissue revealed focal cortical dysplasia (figure 2). Following her surgery she had no seizures. She was followed up to one year and no further occurrences of seizure had occurred. Her follow up MRI was also satisfactory.

![Fig.-1: T2WI axial section shows a hyperdense lesion at the right parietal region](image1)

![Fig.-2: Histopathological photomicrograph in H&E staining](image2)

**Discussion:**

In 1971, Taylor et al., described ‘An unusual microscopic abnormality has been identified in the lobectomy specimens removed surgically from the brains of 10 epileptic patients’\textsuperscript{17}. After that many pathologists had investigated it, they have correlated it with MRI findings. Now a days, surgery has become the main treatment option for FCD.

Surgery for epilepsy can provide relief in a majority of these patients. Resection of the focal dysplastic cortex to histopathologically clear margins may improve outcomes\textsuperscript{3}. According to Rowland et. al., regardless of etiology, the detectability and resectability of
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functional and structural abnormalities related to FCD appear to be the most critical determinants of seizure freedom. They showed that milder semiology, a temporal lobe location, and factors that facilitate the detection of dysplastic lesions, including positive MRI findings and histological FCD Type II, leading to complete resection of the lesion, were significantly associated with a seizure-free outcome.

Surgical outcome was best in the type 2B group and worst in the type 1B group. According to Willard et al, seventy percent of patients with drug-resistant epilepsy and MRI features of FCD attain a favorable seizure outcome after resective surgery. In their study, Kral et al found that, excellent seizure relief (class I) was obtained in 72% of the patients, and in 93% of children and adolescents.

Kracek et al suggested the following distinctive imaging characteristics of the pathological subtypes of cortical dysplasia: Increased cortical thickness, Lobar hypoplasia and atrophy are typical of FCD type I, Blurring of the gray-white matter junction, Gray matter signal abnormalities (in FLAIR and T2 weighted) and White matter signal abnormalities (in FLAIR, T2 weighted, and T1 weighted). The incidence of focal FLAIR signal increase in the 2B group (with balloon cells) was higher than in non-2B CD patients. Our patient had FCD2B.

Long-term outcome in a cohort of patients with FCD remains stable after the first postoperative year up to the last follow-up in 80% of patients; late seizure relapse was seen in 12%, and late seizure freedom in 8% of patients. This is study on a large cohort and it proves that surgery is a very good option for seizure control.

Conclusion:
Focal cortical dysplasia is not very uncommon. It is a cause of drug resistance epilepsy. It is often diagnosed by MRI examination and followed by surgical removal of tumor. Patients become seizure free or they require less medication, surgical treatment is a very good option for relieving the patient of intractable seizure.

References:


