

CASE REPORTS

Focal Cortical Dysplasia as Cause of Refractory Epilepsy- A Case Report

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Abstract:

Focal Cortical Dysplasia (FCD) is one of the most common causes of refractory epilepsy in children as well as adult where malformed cortical development occurs resulting from abnormal neuronal migration due to both genetic and acquired factors. Herein, a 22-year-old male presented with recurrent secondary generalized tonic seizure with aura since childhood. Despite adequate anti-epileptic medications with good compliance the seizure was uncontrolled. As a cause, Type II FCD was diagnosed by specific neuroimaging findings supported by EEG abnormalities. Till now in refractory epilepsy FCD is rarely diagnosed but there remains a good hope of cure by surgical intervention.

Key Words: Focal Cortical Dysplasia, Refractory Epilepsy

Introduction:

Focal Cortical Dysplasia (FCD) is a neuronal migration disorder resulting malformed cortical development¹. The current definition of FCD comprises presumed developmental abnormality of cortical plate, abnormal cytoarchitecture, preservation of gyral pattern, restricted in extent and manifesting with clinical seizure². Both genetic and acquired factors are responsible in pathogenesis of FCD. Genetic factors involve both somatic (TSC2) and germline (DEPDC5 and NPRL3) mutation but familial cases are exceptionally reported. Recently genetic abnormality has been found in mTOR pathway³. Some authors also suggested TSC1, characteristics for tuberous sclerosis, is also involved as FCD may constitute a form of tuberous sclerosis without extracerebral manifestation^{4, 5}. Proteins of Wnt and Notch signaling pathway, responsible for normal neuronal migration, are also found to be involved⁶. Several experimental study indicates that irradiation and methylazoxymethanol

may cause DNA damage resulting FCD⁷. FCD was first detected in 1971 by Taylor and colleagues. Since then several classifications were proposed – from Taylor et al. in 1971 to Palmini classification made by Blumcke in 2011¹. According to revised 2011 ILAE classification FCD is of three types by their neuropathological feature. FCD Type I refers to isolated lesions, which present either as radial (FCD Type Ia) or tangential (FCD Type Ib) dyslamination of the cortex, that may be identified in one or multiple lobes of the brain, FCD Type II is an isolated lesion characterized by cortical dyslamination and dysmorphic neurons without (Type IIa) or with balloon cells (Type IIb), FCD Type III describes FCD that occurs in combination with hippocampal sclerosis (FCD Type IIIa), with glioneuronal tumors (FCD Type IIIb), adjacent to vascular malformations (FCD Type IIIc) or in association with lesions acquired in early life, such as a previous ischemic injury (FCD Type IIId)³. Epilepsy is the core manifestation of FCD which is usually drug resistant sometimes associated with

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mental retardation. Usually no significant neurological deficit occurs despite large area of cortical involvement by a lesion. Symptoms appear at any age but FCD type II manifest earlier onset comparing to type I^{8, 9}. FCD type I is related to temporal lobe seizure^{10, 11} and in FCD type II multilobar lesions are found often with extratemporal location and mainly in frontal lobe^{9, 12}. Neuroimaging and EEG recording are two mainstay of lab-diagnostic procedures. The characteristic MRI findings are cortical thickening, blurring of white matter–gray matter junction, altered signal from white matter with or without the penetration through cortex (transmantle sign), altered signal from gray matter, abnormal sulcal or gyral pattern and segmental and/or lobar hypoplasia/atrophy^{1, 13, 14}. The presence of focal epileptiform discharge is the most characteristic feature of the scalp EEG³. As Epilepsy in FCD is usually medically intractable surgical intervention appears to be next therapeutic procedure¹.

Case report

The patient, a 22-year-old right handed Bangladeshi male, is the only issue of nonconsanguineous healthy parents and presented with recurrent generalized seizure since 10 years of age. The seizure was sudden in onset, generalized tonic in nature followed by versive neck movement towards the left with history of frequent fall. During seizure he also had protrusion of eyeball, occasional drooling of saliva, bladder incontinence, tongue biting and frequent injury to different body parts due to fall. The episodes were stereotyped, occurring in both awake and sleep, persisting for about 3-5 minute with post ictal confusion, amnesia and drowsiness for about 1-2 hours. On query, patient also gave history of stereotyped aura in the form of rotatory movement of visual field for about 5 minute before the episodes.

He had no history of asphyxia or trauma during birth and neonatal infection or convulsion. Pregnancy period of his mother was also uneventful. His milestone of development was normal with good school performance. But he discontinued due to repeated attacks and injury in school. He had no headache, focal weakness,

speech and visual disturbance, disorder of balance, involuntary movement, any positive sensory phenomenon except visual aura with normal intelligence, cognition and memory.

Initially seizure frequency was 5-6 episodes in a month without medication. Then Sodium Valproate was added and dose was increased gradually to 1400 mg/day with a frequency 2-3 episodes per month.

But due to weight gain and extreme tiredness dose was reduced gradually to 1000 mg/day and Carbamazepine was added. With Sodium Valproate 1000mg/day and Carbamazepine 800 mg/day frequency of seizure was 1-2 episodes/month with good compliance. He was no significant family history of illness. He was immunized as per EPI schedule.

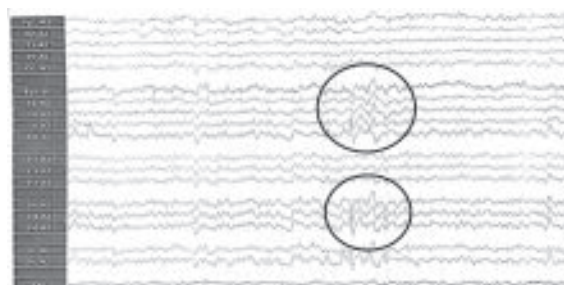


Fig.-1

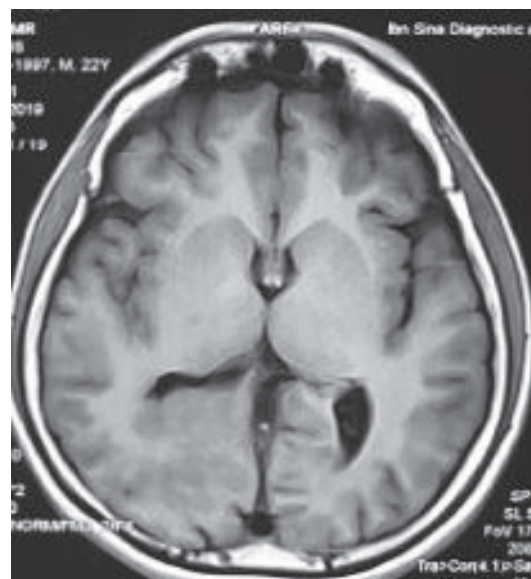


Fig.-2

General examination was normal with no abnormal cutaneous manifestation. Higher cerebral functions including speech and all cranial nerves including fundus were normal. Muscle power of upper and lower limbs both proximally and distally was MRC grade 5. All tendon and superficial reflexes including planter response were normal. All modalities of sensations were intact and there was no sign of cerebellar dysfunction.

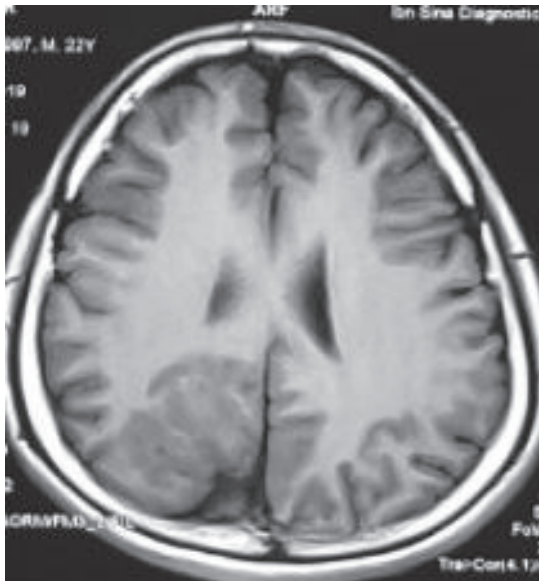


Fig.-3



Fig.-4

Investigations revealed normal CBC, renal function, liver function, S. Electrolytes including Calcium and Magnesium. About five years ago MRI of brain and EEG were done but patient lost the document. But according to party the reports were normal. So, we decided to do MRI of brain (Epilepsy protocol) and 3 hours video assisted EEG. Neuroimaging showed FCD in right parieto-occipital region and EEG showed focal spikes and slow waves in right temporo-parieto-occipital region with secondary generalization. Then Neurosurgical consultation was taken for surgical intervention but patient denied to do the surgery.

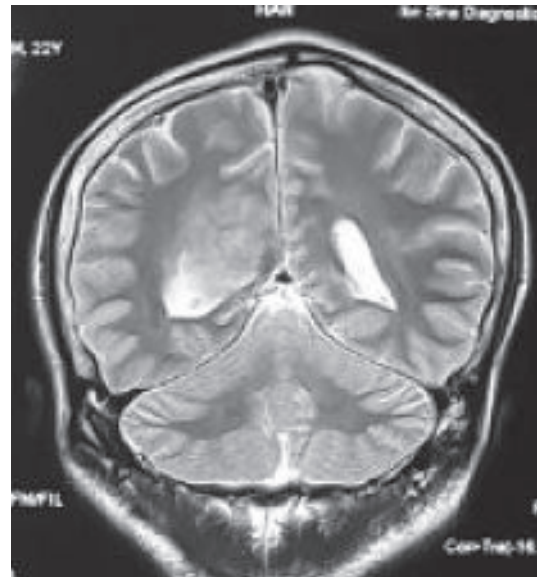


Fig.-5

Discussion:

FCD is considered to be the most common cause of medically refractory epilepsy in children and second or third common cause of medically intractable epilepsy in adults¹. Wide variation of seizure types can occur in FCD like focal, focal onset with secondary generalization, atypical absence, atonic, tonic, tonic-clonic, epileptic spasm, generalized or focal status epilepticus. Onset of seizure occurs usually in childhood and seizure type may change over time³. Seizure type in our patient was focal onset with secondary generalization.

Regarding EEG background may be normal or may show focal slowing. In epileptic spasm background

may show widespread slowing or hypsarrhythmia. Interictal EEG may be normal or may show focal spikes and waves or polyspikes³. In our patient there was focal spikes and slow waves in right temporo-parieto-occipital region (Fig: 1) with secondary generalization.

MRI of brain if abnormal may differentiate between Type I and Type II FCD. In Type I FCD lobar hypoplasia (mainly temporal lobe is involved along with hippocampal atrophy), blurring of Gray Matter/White Matter (GM/WM) junction (less prominent than Type II), abnormal gyral pattern, subcortical white matter T2 hyperintensity or T1 hypointensity are found. In Type II FCD there are cortical thickening, marked blurring of GM/WM junction, white matter T1 hypointensity and T2 hyperintensity which may extend towards ventricle (Transmantle sign). Transmantle sign is very specific for Type II FCD and here extra temporal involvement is more common¹. In our patient MRI of brain is suggestive of Type II FCD as evidenced by cortical thickening (Fig: A, broad arrow), marked blurring of GM/WM junction (Fig: 2, narrow arrow), white matter T1 hypointensity (Fig: 3) and T2 hyperintensity (Fig: 4) in subcortical white matter, Transmantle sign (Fig: 5) in right parieto-occipital region.

Seizure is invariably medically intractable. Our patient also experienced 1-2 episodes per month despite use of maximum tolerable dose of Sodium Valproate and Carbamazepine. So, surgical resection appeared to be next preferable therapeutic intervention. In this case Type II FCD (75%) has better seizure-free outcome than Type I FCD (20%-43%)². Complete resection of cortical abnormality is crucial for seizure-free outcome but removal of cortical rather than white matter component is critical. In case of subtotal resection seizure relapse in 30% cases only within 6 months of surgery^{13, 14}. So, expert neurosurgical approach is mandatory with variety of neuroimaging and EEG guidance to determine the specific focus.

Conclusion:

FCD is considered to be one of most common causes of medically intractable epilepsy not only in children but also in adult. But it is rarely diagnosed in spite of advancement in neuroimaging and EEG.

In case of intractable epilepsy despite normal conventional MRI of brain and EEG we should perform, if possible, advanced neuroimaging technique (3T MRI, DTI, fMRI, FDG-PET) and increased number of electrodes in EEG to detect FCD as there is a good hope of cure by surgical intervention. Also further studies of epileptogenesis in FCD may help to develop new pharmacological era.

Conflict of interests:

The authors declare that they have no conflict of interest.

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