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Case report

Ring chromosome 20 syndrome – A rare chromosomal cause of refractory epilepsy in children

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ABSTRACT

Genetic disorders and chromosomal abnormalities have been shown to represent 2–3% of all cases of epilepsy. Ring chromosome 20 syndrome is a rare chromosomal abnormality and a rare cause of intractable epilepsy. Exact prevalence of ring chromosome 20 is not known. We report a case of a 10-year old boy who had had intractable epilepsy since 2 years of age. Birth history was insignificant and there was no obvious dysmorphism. His motor milestones were normal but cognition and speech were delayed. Electroencephalography showed progressive worsening from initial bi-frontal epileptiform activity to generalized discharges. Neuroimaging and metabolic work up was normal. Karyotype study showed ring chromosome 20. Diagnosis of ring chromosome 20 or r(20) syndrome was made. Ring chromosome 20 syndrome is a rare cause of refractory epilepsy A patient who present with intractable epilepsy with frontal epileptiform discharges, mental developmental delay, without dysmorphic features should be suspected of chromosomal abnormalities especially ring chromosome 20.

1. Case

A 10 year old boy, first by birth order, born of non-consanguineous marriage was referred for evaluation of refractory epilepsy. He had history of refractory seizures since 2 years of age. Perinatal history was insignificant. There was no family history of epilepsy or mental retardation. Child did not have obvious dysmorphic features. Seizures were hypo motor with staring and psychomotor arrest associated with drooling and unresponsiveness without much motor involvement, lasting for few minutes followed by postictal drowsiness and sleep. No drops or myoclonic jerks or tonic seizures were seen. Initially seizures used to occur only in awake state however with advancing age he started getting seizures in sleep state as well. Seizure frequency also increased from once in a month to 1 to 2 per week. Sometimes he used to get episodes of altered behavior or confusion with intermittent blinking of eyes and decreased responsiveness, lasting for few hours (atypical absence or non-convulsive status epilepticus – NCSE). His motor milestones were normal but, he showed significant delay in cognition and speech. His Developmental quotient at 10 years of age was 60% only.

Magnetic resonance imaging (MRI) of brain with 3 T resolution at 7 year of age did not reveal any obvious dysplasia or other abnormality. Electroencephalography (EEG) at 4 year of age (Fig. 1) showed bi-frontal spike-wave discharges. EEG gradually showed worsening over the years with generalized but predominantly bi frontal discharges with slow waves and spikes (Figs. 2 and 3). Metabolic work up including simultaneous blood and CSF sugar, tandom mass spectroscopy (TMS) for amino acids and carnitine profile and urine gas chromatography and mass spectroscopy (GCMS) for organic acids were normal.

His karyotype analysis of 100 metaphases showed ring shaped chromosome 20 (Fig. 4). Diagnosis of ring chromosome 20 or r(20) syndrome was made. Ring chromosome 20 syndrome is a rare cause of refractory epilepsy.

He was treated with multiple antiepileptics including valproate and clobazam. Topiramate and oxcarbamazepine in view of recurrent seizures. Despite of giving antiepileptic drugs in optimum dose for optimum period, his seizure frequency was not controlled. Hence he was labeled to have refractory epilepsy and started on classical ketogenic diet since last 6 months with only marginal response.

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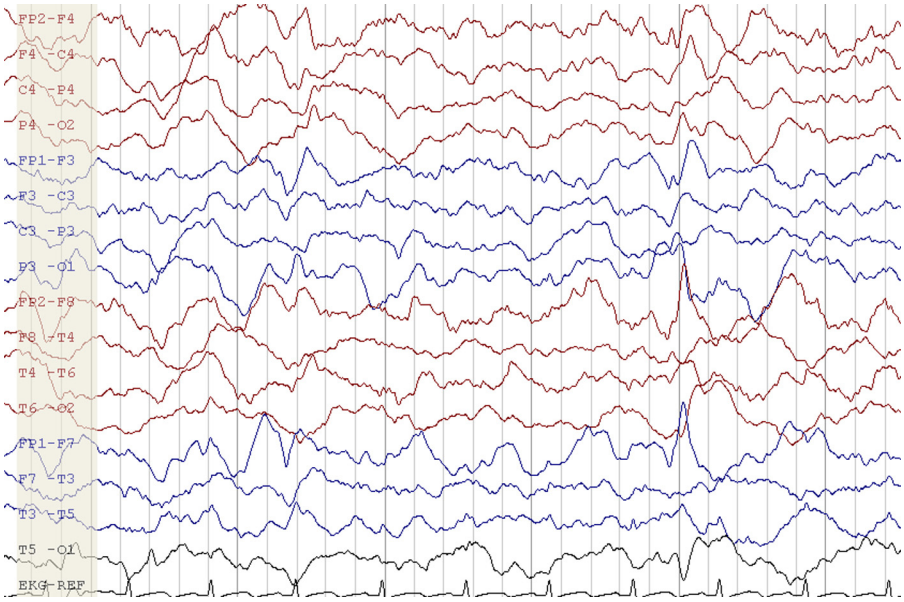

Fig. 1. EEG with bipolar longitudinal montage at 4 year of age with occasional Frontal discharges.

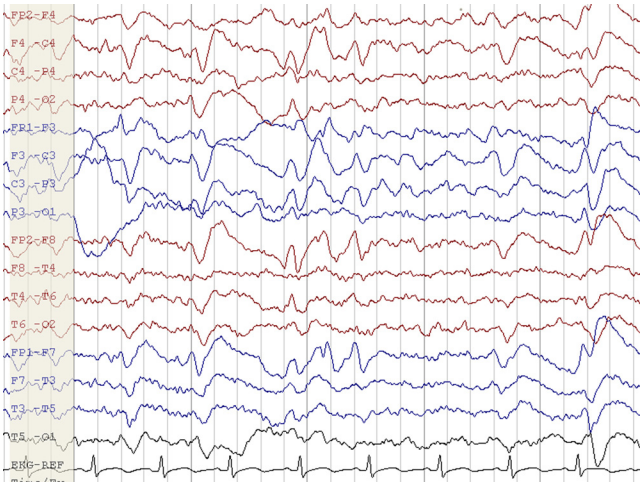

Fig. 2. EEG with bipolar longitudinal montage at 6 year of age – bi-frontal synchronous discharges.

2. Discussion

Ring chromosome 20 syndrome was 1st described in 1972 by Atkins et al. and by various other groups separately.[1] Exact prevalence of ring chromosome 20 is not known. Overall genetic and chromosomal abnormalities constitute 2–3% of all epilepsy cases. Epilepsy is often the first sign of ring 20 syndrome. Children with ring chromosome 20 syndrome do not show any dysmorphic features and usually have normal psychomotor development at onset of seizures.[1,2]

Seizures start at around 2–5 year of age and typically do have brief partial seizures initially and later may have generalized seizures with episodes of non-convulsive status epilepticus (NCSE) with prolonged confused states and clouding of consciousness. In present case, patient had seizure onset at 2 years of age, initially brief seizures and then progressed to refractory epilepsy, sometimes associated with status and NCSE. Nocturnal frontal lobe seizures have been described.[3] Gradually, there is cognitive decline as described in our case. No obvious dysmorphic features have been described.[1–3]

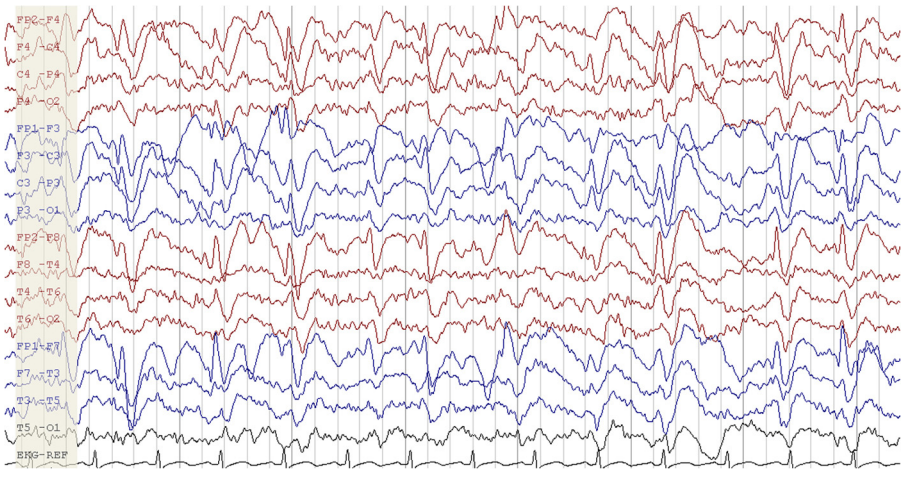

Fig. 3. EEG with bipolar longitudinal montage at 8 year of age – bi-frontal maximum generalized discharges.

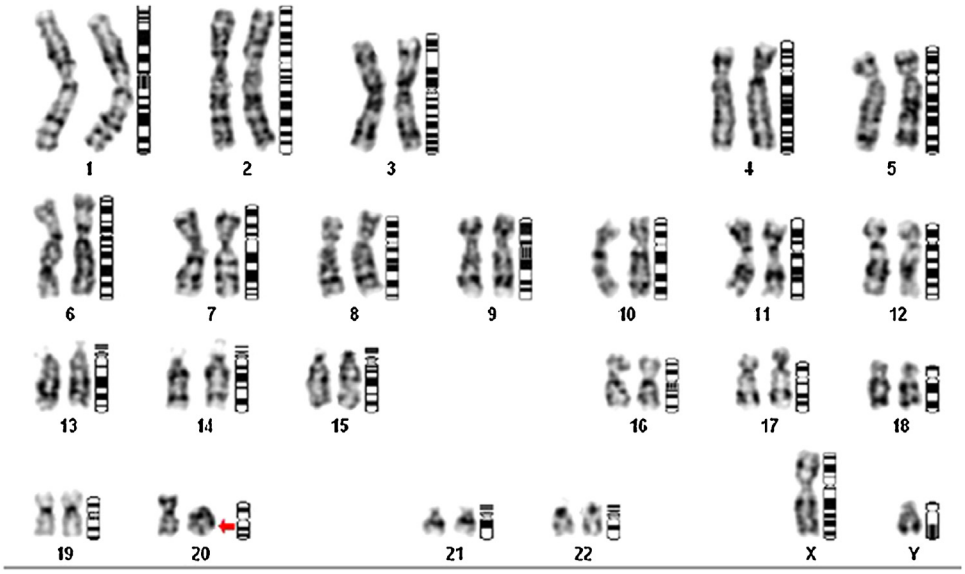

Fig. 4. Karyotyping showing ring chromosome 20 – red arrow. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Few authors have described possibility of relationship between percentage of mosaicism and clinical features, however, it has been also postulated that in addition some other factors must be the trigger of this peculiar type of epilepsy.[3,4] It is a sporadic condition with no risk of recurrence.[3]

EEG described in ring 20 chromosome condition is generalized 2–3 Hz high amplitude rhythmic slow delta with superimposed spike or sharp waves of bi-frontal maximum.[2–5] Index case also showed bi-frontal synchronous discharges at the presentation and later generalized but bi-frontal predominant discharges. Characteristically, these are less spiky as compared to slow spike wave discharges of Lannox Gestaut syndrome (LGS).[2–5] Also tonic seizures and drops characteristic of LGS were not seen in our case. MRI imaging of brain is usually normal, although few cases with cortical dysplasia or focal atrophy has been described.[5] Neuroimaging findings were unremarkable in our case.

It is postulated that, loss of telomeric material at both ends of chromosome 20, causes refractory epilepsy. The genes postulated for the epilepsy like KCNQ2 and CHRNA4 – both located on telomeric regions.[6] Biraben et al. studied F-dopa-PET in ring chromosome 20 syndrome and found that there is reduced uptake of dopa in putamen and caudate and postulated that it causes impaired seizure interruption and refractory epilepsy.[7]

Ring 20 syndrome is refractory to antiepileptic medications. Only one case of seizure control by antiepileptic medications has been reported.[8] There are no specific antiepileptic drugs recommended but occasional good results have been obtained with a combination of valproate and lamotrigine.[2,3,5] There is no role of resective surgery.[3,8] There is a case report of focal cortical resection done in a case ring 20 syndrome with no seizure control.[3] Vagal nerve stimulation for the refractory epilepsy with ring 20 syndrome has showed partial response.[9]

To summarize, it is important to evaluate patients with refractory epilepsy to rule out genetic causes like ring 20 syndrome. Genetic cause should be suspected in patients with refractory epilepsy and normal MRI brain. Ring 20 chromosome is a rare genetic cause for refractory epilepsy.

Authors' contribution

Dr. Umesh Kalane – data collection, literature search and writing the case, Dr. Chaitanya Datar – literature search and writing the manuscript, Dr. Shilpa Kalane – final editing and writing the manuscript.

Conflicts of interest

The authors have none to declare.

Source of funding

None.

Ethical

Informed consents were taken from parents of patients prior to this work.

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