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Doose Syndrome

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Abstract

A 7 year old male child presented with recurrent forward falls, with a non-healing forehead wound. The falls were associated with brief period of unresponsiveness and eye blinking. Such episodes were 15-20 in number per day. Earlier treatment with carbamazepine only increased the number of falls. Imaging and electroencephalographic findings were suggestive of Doose Syndrome. He was started on divalproex sodium, topiramate and ketogenic diet.

Keywords: Doose Syndrome; Divalproex; Ketogenic Diet

Introduction

Childhood epilepsy syndromes are many. Sometimes we come across cases which are puzzling, do not fit into any particular category and require lot of time and patience to identify and to get a therapeutic response even after appropriate treatment is initiated. Doose Syndrome (DS) is one such condition. DS is also termed as myoclonic-atonic (or myoclonic-astatic epilepsy) epilepsy because of the characteristic initial myoclonic component followed by a fall. It is a rare early-onset generalized idiopathic epilepsy syndrome of childhood. The myoclonus manifests as large-amplitude symmetric jerks of the arms, legs, neck, and shoulders that may result in a head drop and upper limb flexion or abduction. This is followed by loss of muscle tone and a fall. Besides myoclonic-atonic events, other seizure types can also occur, including absence, tonic-clonic, and tonic as well as myoclonic or nonconvulsive status epilepticus.

The syndrome was first described by Dr Hermann Doose in 1978 [1]. It commonly presents between 18 months and 5 years of age, with a peak at age 3 years. The EEG demonstrates recurrent paroxysms of generalized spike or polyspike and wave, typically without clinical correlate and with a satisfactory background, although parasagittal theta frequency slowing is a characteristic as well. Though the condition is mostly idiopathic, a case of myoclonic-astatic epilepsy syndrome secondary to oxcarbazepine treatment was described by Ewen *et al.* in a child with Sturge-Weber syndrome [2].

We are herewith presenting a case of DS because of its rarity and because it could not be identified for nearly 2½ years even though seen by several clinicians. It is also interesting to see that there was worsening when treated with inappropriate medication. The dietary modification also had given reasonably good result in the index case.

Case Details

Master SR, a 7 years old male child, presented to the Neurology Department of our Hospital with a history of recurrent forward falls. He was the first product of non consanguineous parentage, with normal birth history and was vaccinated for age appropriately. His milestones of development were normal.

The falls were associated with brief unresponsiveness and with repetitive eye blinking. The actual fall was preceded by a brief myoclonic jerk. They were noticed first at the age of 5 yrs with a frequency of 15-20 episodes per month. Over the next two years the frequency increased too many per day. The falls produced repeated forehead injuries on left side (Video 1 and Video 2) (Figure 1). There was no history of tonic-clonic movements of limbs, bladder or bowel incontinence or spasms. He was on medication with Carbamazepine 100 mg per day without any response. On the other hand the falls increased in frequency after starting the medication to the present frequency of 15-20 per day.

Figure 1: Child with left frontal non-healing wound due to repeated falls.

His examination in the outpatient department revealed normal head circumference, normal intelligence without any focal neurological deficit. There was a non healing ulcer over the left side of the forehead due to repeated falls. He was evaluated with electroencephalogram (EEG). During the 30-minute EEG recording, there were episodes of brief unresponsiveness with myoclonic jerk and forward fall. At times there were recurrent eye blinking noticed while recording the EEG. The corresponding EEG showed recurrent paroxysms of generalized spike or polyspike and wave discharges against a normal background activity (Figure 2,3 and 4). His neuro- imaging (cranial magnetic resonance imaging) and other routine work up were normal.

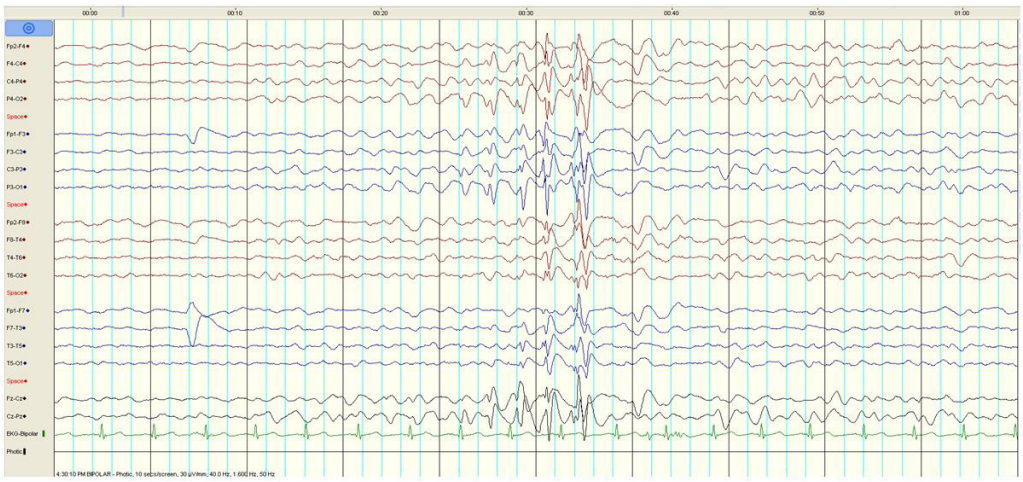

Figure 2: Generalized 4-Hz spike and wave discharges

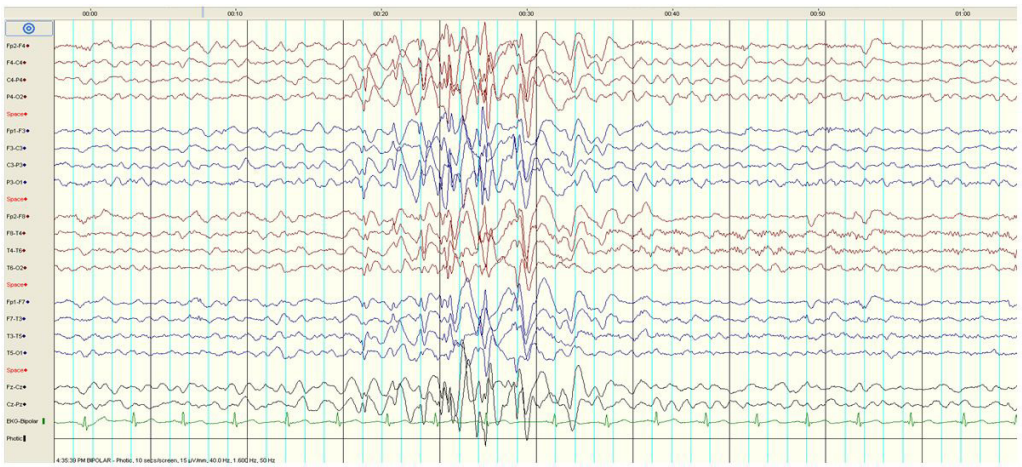

Figure 3: Generalized spike/ polyspike and wave activity against 6-7 frequency background activity

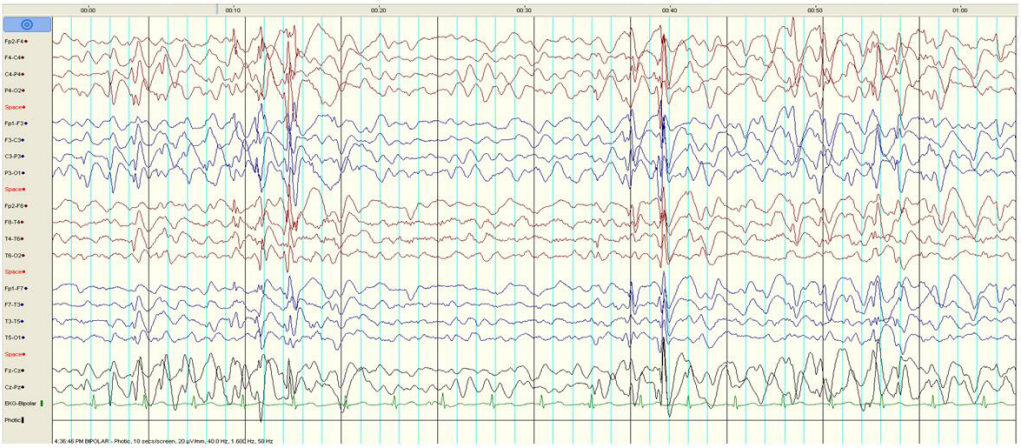

Figure 4: Generalized spike/ polyspike and wave activity against 6-7 frequency background activity

The child was started on divalproex sodium 250 mg twice daily along with ketogenic diet (KD). There was an initial response in the form of reduction in the number of falls. When he was reviewed 2 months later the falls continued. The dose of divalproex was escalated and a second line drug was chosen in the form of topiramate. When last seen one month after introduction of topiramate the child was better with significantly less number of falls and the forehead wound was healing. The parents were still hesitant to send him to school, and they would not allow him to walk alone (without a family member holding his hand) even in their house for fear of fall. A cloth is tied around his head, to prevent further injuries to the forehead.

Discussion

This case describes typical presentation of a male child with recurrent falls secondary to myoclonic jerks and loss of postural tone. The events are correlated with typical electrographic changes and forehead injury.

The myoclonic events are associated with bursts of 2 Hz to 4 Hz spike and polyspike epileptiform activity. Nonconvulsive status epilepticus may occur, resembling an epileptic encephalopathy. "Status of minor seizures" is described as a specific finding in 36% of DS patients in which the child is stuporous, drools and aphasic, and which can continue for many days[3]. The KD and its variants have been particularly helpful in some patients with nearly 50% reduction in the frequency of seizures [4]. The KD is reported to have nearly 100% effect on clinical seizures and on electrical activity in DS in some reports [5]. Topiramate is a good drug for refractory atonic seizures and can be continued for a long period in many patients [6,7]. Though levetiracetam is a good antiepileptic drug for myoclonic seizures, it can exacerbate seizures paradoxically [8]. Carbamazepine and phenytoin should not be given in myoclonic epilepsies as they can aggravate the myoclonus. Protective measures (such as wearing a helmet) may be needed because of the atonic falls. In refractory cases parenteral administration of adrenocorticotropic hormone (ACTH) had given relief in some patients. But this treatment or oral steroids cannot be prescribed for long term because of their side effects.

DS needs to be differentiated from childhood febrile seizures, Lennox-Gastaut syndrome (LGS), progressive myoclonic epilepsy, severe infantile myoclonic epilepsy (Dravet syndrome). LGS patients may have some focal seizures also besides the atonic seizures and the EEG background activity is abnormal while in DS the EEG background activity is normal and there are no focal seizures.

De novo overlapping 3p25.3 microdeletion was described as the causative mutation in DS, but further studies are necessary for confirmation [9].

Long-term remission occurs in the some patients, although the majority of them tend to develop intractable epilepsy with intellectual impairment. The intellectual deficit could partly be secondary to missing school because of the falls.

Appendix

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