Clinical Case Report

Three siblings with multiform seizures: An unusual presentation of Doose syndrome

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ABSTRACT

Doose syndrome, or epilepsy with myoclonic–atonic seizures, is a rare electroclinical syndrome. It is important to distinguish it from related epilepsy syndromes such as Lennox Gestaut syndrome and Dravet syndrome. We report the occurrence of this disorder in three siblings born of a non-consanguineous marriage.

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INTRODUCTION

The syndrome of myoclonic–astatic epilepsy or 'epilepsy with myoclonic–atonic seizures', also called Doose syndrome (DS), has a characteristic and dramatic clinical presentation. Forty years after the description of this entity by Herman Doose in 51 children, the clinical and electrographic features of DS are well characterized.[1] Even though it accounts for 1%–2% of all epilepsies, the diagnosis is often missed and differentiation from other epileptic syndromes such as Dravet syndrome, Lennox Gestaut syndrome (LGS), progressive myoclonic epilepsy and Landau Kleffner syndrome (LKS) is important.[2] Genetic factors are an important determinant with clinical seizures or subclinical electroencephalographic (EEG) abnormalities being reported in family members in 40%–80% of cases. We report the occurrence of DS in three siblings with late onset myoclonic jerks in their father.

THE CASES

Three siblings aged 5, 6 and 7 years were brought to the neurology outpatient of our hospital with a history of similar types of epileptic seizures with onset around the age of 4–5 years.

The children were born of a non-consanguineous marriage and had normal antenatal, perinatal and developmental histories as well as normal for age scholastic performances. By the time they were between 4 and 5 years of age, their parents noticed brief jerky movements affecting both upper and lower limbs, individually and at times simultaneously. These increased in frequency and severity and over 2–3 months became a daily occurrence. By this time, they also started having episodes of abrupt loss of contact with their surroundings with prolonged staring (3–5 minutes) and few eye blinks. At times, they also had abnormal behaviour with irrelevant talking and aggression. By the age of 5 years, all of them fell frequently. The falls were at times secondary to a sudden jerky movement throwing them forward while at other times they slumped to the ground usually preceded by a jerky movement. There were no recognizable precipitating factors such as a hot bath, cold, sleep or sleep deprivation, fever, infection, bright lights or noise for any of the seizure types.

The patients were seen by a neurologist and treated with 20 mg/kg of sodium valproate which led to a 20%–30% reduction in seizures. The children continued to have normal cognitive abilities in the inter-ictal period. However, decreased attention and hyperactivity set in about 1–2 years into the illness. Poor social behaviour and interaction with peers at school was also reported.

Their father, 37 years of age, revealed that he had been having brief jerky movements of the upper limbs for the past 2 years. No other family members were affected.

On examination, the children had a normal head size, and no neurocutaneous markers. Two of the siblings were hyperactive while all three had decreased attention. Subtle autistic features were also observed. Cranial nerves, motor, sensory and cerebellar examinations were unremarkable. The rest of the general and systemic examination was normal.

An EEG was done on each child after sedation. The findings were similar in all three with generalized spike and wave discharges on a slow background. Brain imaging was normal. All the children were treated with oral sodium valproate 20 mg/kg and oral levetiracetam 20 mg/kg. Telephonic follow-up after 6 months revealed that the children had infrequent seizures.

DISCUSSION

DS is a form of childhood epilepsy where the patient has classical myoclonic–astatic or myoclonic–atonic seizure along with other seizure types such as absence, complex partial and generalized tonic–clonic seizures. However, this syndrome is distinct from related syndromes such as LGS, Dravet syndrome and LKS in that the affected individuals have a normal or only a mildly affected cognition and normal development.[2]

The classical seizure type in DS is a myoclonic atonic seizure where the patient suddenly drops to the ground but the falls may be difficult to distinguish from those precipitated by severe myoclonic jerks. These falls are usually time-locked to a generalized spike and wave or poly spike and wave discharges in the EEG.[3] Myoclonic, tonic–clonic, absence and complex partial seizures can occur concurrently. Our patients had all seizure types with the exception of generalized tonic–clonic seizures.

EEG findings in DS can vary from normal to marked slowing and generalized spike wave discharges. Subclinical EEG abnormalities and abnormal responses to hyperventilation and photic stimulation may be found in family members without overt seizures. In our patients, generalized sharp and slow wave discharges were found uniformly while patterns such as central theta were not evident. All the EEGs were done after sedation and the background frequencies were slow without any K complexes or sleep spindles.[3]

The unusual aspect was the occurrence of clinically definite DS in three siblings of non-consanguineous parents. Neuronal

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sodium channel 1 (SCN1),[4] possible links to GEFS+ syndrome and a few other genes are implicated in this syndrome with polygenetic and multifactorial inheritance being favoured for its aetiopathogenesis.[1]

Treatment of DS is not very successful. Polytherapy is often needed with valproate, levetiracetam, topiramate and lamotrigene being the commonly used drugs.[5] Ketogenic diet and immunotherapy with adrenocorticotropic hormone (ACTH) and steroids have also been found to be effective in some patients.[6]

Conclusion

DS is a distinct clinical syndrome which can have a familial presentation but clustering of cases is uncommon. The recognition of this entity and its distinction from related electroclinical syndromes can sometimes be challenging.

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