CASE REPORT

Dravet syndrome: A case report

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SUMMARY

We report a rare case of Dravet syndrome in a 13-year-old boy who presented due to pleomorphic multi-drug resistant seizures. He was initially treated for generalized epilepsy after repetition of several febrile seizures in the first year of life. But, due to the resistance of seizures to one antiepileptic drug, additional drugs were added over time. Generalized seizures started at the age of 8 months as febrile seizures, repeating often at each febrile episode until the age of 5 when they became pleomorphic, and cognitive and motor function decline was noted. There was no relevant family history and no consanguinity. EEG showed severe epileptic discharge in both hemispheres and brain MRI revealed cortical atrophy. Consequently, the child was referred for genetic testing for Dravet syndrome which confirmed the diagnosis of a positive mutation on the SCN1A gene.

INTRODUCTION

Dravet syndrome (DS), formerly referred to as severe myoclonic epilepsy in infancy (SMEI), is classified as an epileptic encephalopathy characterized by prolonged seizures occurring within the first year of life. These seizures frequently manifest in conjunction with fever or illness and are often initially misidentified as febrile seizures. The accurate diagnosis of DS and subsequent follow-up care are usually postponed. At the onset, the electroencephalogram (EEG) appears normal, and neuroimaging does not indicate any structural abnormalities. Although early developmental milestones are typically met, signs of regression may emerge during the second year of life, often accompanied by convulsive status epilepticus, alternating hemiconvulsions, and myoclonic seizures. Genetic testing, which is now accessible, can confirm the diagnosis by identifying mutations in the SCN1A gene. Timely recognition and diagnosis of DS, along with the implementation of suitable anticonvulsants and a comprehensive treatment plan, may help alleviate the frequency of seizures and enhance long-term developmental outcomes.1 We report a case of a 13-year-old boy who presented with drug-resistant seizures and deteriorated neurological, cognitive, and behavioural status.

CASE PRESENTATION

A 13-year-old Albanian boy was referred to the Department of Neurology at the University Clinical Centre of Kosovo due to pleomorphic drug-resistant seizures, cognitive and motor function decline. Prenatal and postnatal history did not include any pathology. He started to walk at 18 months and say his first words between 12 and 15 months. His growth and development were going well at the beginning. He was diagnosed with epilepsy in the first year of life.

He had a febrile seizure at the age of 8 months old, during a viral gastroenteritis associated with high fever. At 13 months, he had the second febrile generalized seizure, as part of a viral infection and was treated accordingly. Eight months later, he had the third febrile seizure and was referred to the neurologist. At 15 months, due to a recurrence of seizures, he was prescribed an antiepileptic drug (AED), valproic acid, which he tolerated well. Six months later, he got a generalized seizure again. Since seizures persisted during febrile episodes, the second drug, clonazepam, was added. However, seizures continued during febrile episodes, despite compliance with therapy. Seizures were generalized and mostly occurred while the child was awake. At the age of 5 years, seizures occurred more frequently, almost on a monthly basis, and were no more febrile. They occurred during sleep too, and also in circumstances of sleep deprivation. The nature of the seizures varied too, from generalized tonic-clonic, alternating hemiconvulsions, myoclonic, and status epilepticus. Developmental delays started to appear. Different combinations of therapy were administered during these years, apart from the initial antiepileptic drugs, including phenobarbitone, levetiracetam, lamotrigine, phenytoin, rufinamid, synacthen, but with no full control over seizures.

At the age of 5, a decline in motor skills was noted, deteriorating from 7 to 13 years, with the child losing the ability to run, do sports, or any other moderate physical activity. Speech was also impaired, and occasionally ataxia was present. Cognitive decline was noted, including behavioural and psychological difficulties. Therefore, he dropped out of school, affecting his social life, too. When the recent general decline was noted, he was referred for genetic testing, and mutation of SCN1A gene was detected. As a result, stiripentol was added gradually, while other drugs were discontinued. Parental testing was recommended, as well as genetic counselling. Due to social, cognitive and behavioural status, the psychologist was involved in the care for an initial assessment and provision of professional service regularly. Electroencephalogram was performed regularly over the years and brain MRI, too. The next step for his further management includes vagal nerve stimulation.

This article was accepted: 03 September 2024
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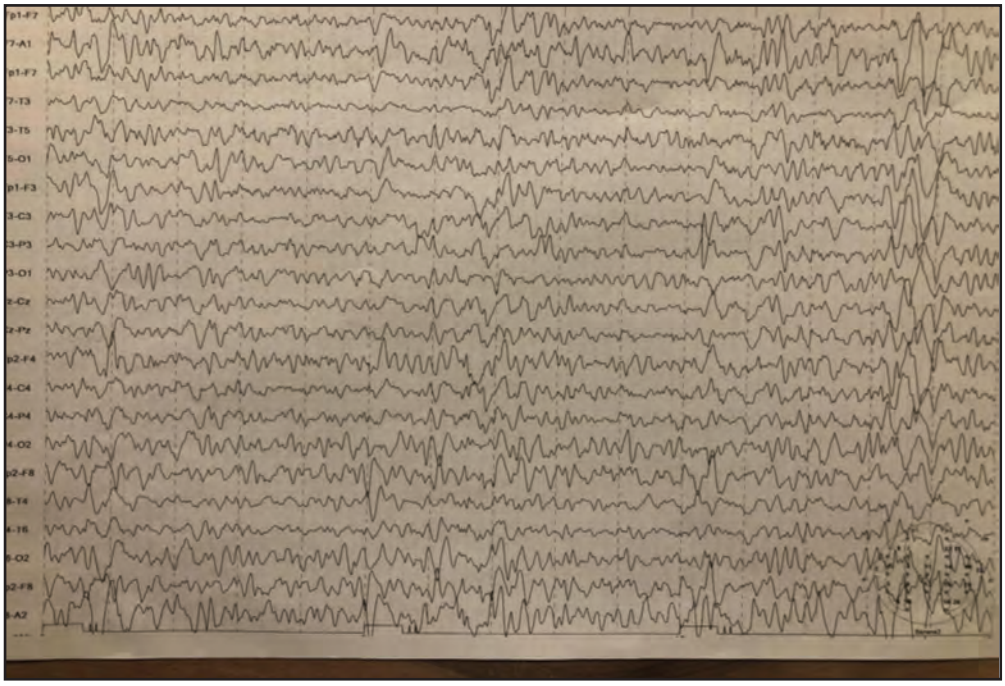

Fig. 1: EEG showing severe epileptic paroxysm activity in both hemispheres

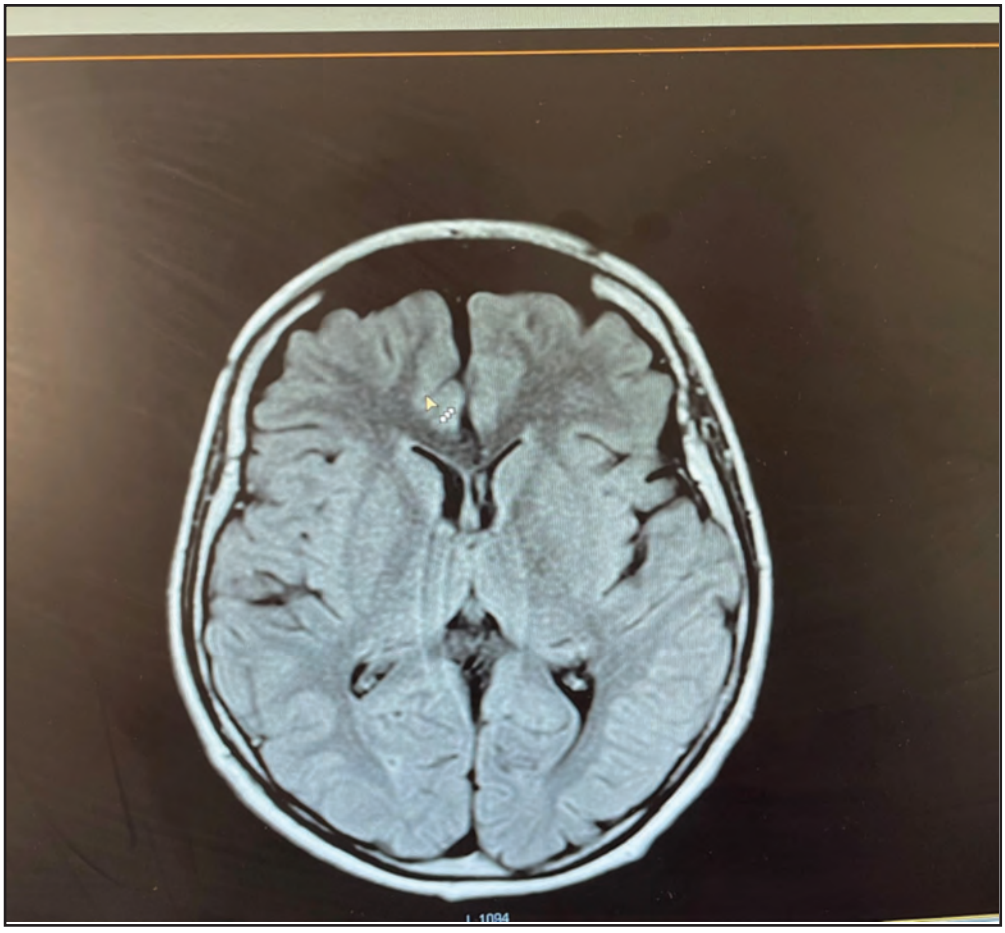

Fig. 2: Brain MRI showing cortical atrophy

DISCUSSION

DS evolves with age and after seizure onset during infancy, neurodevelopmental delays progress to severe neurological disability.[1] Patients develop an unsteady gait and general motor impairment, language delay, and behavioural disturbances such as attention-deficit/hyperactivity, autism traits, aggressiveness, irritability, and other social difficulties.[1,2] Although optimal treatment of seizures may improve outcomes, these neurodevelopment delays result from both, the genetic variant and the epilepsy.[2] These impairments cause poor quality of life and impact the long-term course.[3] First line treatments include valproate, clobazam, stiripentol, topiramate, and bromide whereas cannabidiol and fenfluramine were shown to be effective and become standard second-line drugs in Dravet syndrome.[4] Conventional antiepileptic drugs are usually insufficient for most patients as DS is highly drug-resistant and seizure freedom is rare. Stiripentol, cannabidiol, and fenfliramine have shown reductions in seizure frequency and are well tolerated.[5] Timing of introduction of these "add-on" treatments is subject to availability in different countries, patient features, and health professional's decision.6 Later therapeutic options include other ASM, ketogenic diet, and vagus nerve stimulation.[3] In any case, early diagnosis is important to avoid medications that exacerbate seizures, such as carbamazepine, oxcarbazepine, vigabatrine, lamotrigine, phenytoin.[7] Genetic testing should be conducted as early as possible in a previously healthy child presenting with refractary seizures, initially during febrile episodes, and neurodevelopmental decline over time.[8] It is important to emphasize that not all treatments, in particular the new ones, are available in all of the countries making it even more challenging optimal management of Dravet syndrome in such circumstances.[5] EEG are initially normal but after 2 years they reveal generalized spike-wave and polyspike activity with multifocal discharge, while imaging in normal or nonspecific, such as atrophy.[7]

In our case, the clinical manifestations were typical with generalized tonic clonic seizures in the first years of life, triggered by febrile episodes due to common childhood infections. Febrile seizures continued during the first two years despite antiepileptic drugs. Later on, additional seizure types appeared including alternating hemiconvulsiones, myoclonic, and status epilepticus. Seizures were highly resistant to multi-drug combinations. Between the age of 5 and 7 years, general deterioration was noted progressing to general neurological and cognitive decline over the years. EEG of our patient comprise severe epileptic discharge while brain MRI revealed nonspecific findings, such as cortical atrophy. These changes are in line with those described in the literature and provide a solid basis for considering Dravet syndrome in differential diagnosis and undertaking genetic testing for the same. This could lead to early diagnosis and targeted better management of seizures, as well as other comorbidities occurring during the course of the disease. However, it is important to mention that not all the treatment options are available in all the countries, as well as diagnostic possibilities for that matter, such as genetic testing, which poses a burden on the health professionals, as well as the families themselves. Millions of patients with suspected neurogenetic disorders around the world have no access to genetic testing.[7] Apart from that, multi-disciplinary approach to providing care for patients with Dravet syndrome is as equally important. Severe behavioural problems, which are common in patients with Dravet syndrome, should receive specific professional attention during clinical management.[9]

In our case, the clinical status of the patient worsened over time as described in the literature and he is now limited to basic motor functioning and significant general decline. As such, his social life has been highly affected too, by dropping out of school, as well as the life of his parents as the main caregivers, and the whole family in general. As suggested, one of the steps to help families of patients with Dravet syndrome, apart from the right diagnosis and appropriate treatment, is to address burden of the disease on the family and provide all the possible assistance to reduce that burden.[10]

ACKNOWLEDGEMENT

We would like to thank and acknowledge the contribution of everyone involved in completing this case report. Firstly, we thank sincerely the family for their consent and their contribution to our work. Then, we thank the whole staff at the Department of Neuropediatric and Department of Psychology for their ongoing support.

DECLARATION

The authors declare no conflict of interest.

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