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A case of Dravet syndrome with focal cortical myoclonus

Xiaoqing Luo, Xiaolu Wang and Jun Jiang*

Abstract

Background: Dravet syndrome (DS) is a severe epileptic encephalopathy in children dominated by polymorphic seizures. Focal cortical myoclonus indicated on conventional electroencephalogram (EEG) was rarely observed in DS.

Case presentation: The child, boy, thirteen months old, suffered from clonic seizures during bathing at two months old. Later he suffered from recurrent afebrile or febrile generalized tonic–clonic seizures often developing into status epilepticus. A genetic analysis of the *SCN1A* gene revealed a de novo heterozygous frame shift mutation in exon 21(c.3836_c.3837del AT).His myoclonic jerks of unilateral arm occurred spontaneously in response to movement. A spike wave from right central-parietal cortex immediately preceded a left myoclonic muscle activity, while a spike wave from left immediately preceded a right myoclonic muscle activity. The onset of the detected spike preceded the onset of myoclonic muscle activity by 42 ms using jerk-locked back-averaging of electroencephalogram data. The focal cortical myoclonus was not noted when one year old.

Conclusions: Focal cortical myoclonus could be a form of seizures during the first year of life in DS, which may broaden the types of seizures of DS and may provide some diagnostic clues for DS.

Keywords: Dravet syndrome, Conventional electroencephalogram, Focal cortical myoclonus

Background

Dravet syndrome (DS) is a severe age-dependent epileptic encephalopathy dominated by febrile and afebrile seizures during the first year of life [1, 2]. The syndrome is characterized by intractable multiple types of epileptic seizures: hemi-clonic, generalized tonic clonic, atypical absence, focal impaired awareness, and myoclonic [3, 4]. Developmental delay, intellectual and motor deficits, autistic features and sleep impairment are noted during the second year of life and stabilizes later. Neuroimaging studies show nonspecific findings. The diagnosis of DS is given based on the clinical state and the genetic testing. It is identified that 80% of cases are associated with mutations of the *SCN1A* gene [4, 5]. Focal cortical myoclonus is a rare seizure pattern in DS. We firstly reported one infant diagnosed with DS with focal cortical myoclonus on conventional EEG when he was six months old, which might contribute to widen the clinical and neurophysiological spectra of DS.

Case presentation

The case, a thirteen-month-old-boy, was admitted to our hospital because of six times of partial seizures over three months when he was six months. He was born at 38 weeks after a trouble-free pregnancy and delivery without asphyxia from healthy and unrelated parents. Birth weight, length, and head circumference were normal. He had no familial history of any neuropsychiatric disease. His psychomotor development was initially compatible with his peers. His parents reported that his development was delayed later after seizure, with sitting at nine months and walking with support at eleven months. He

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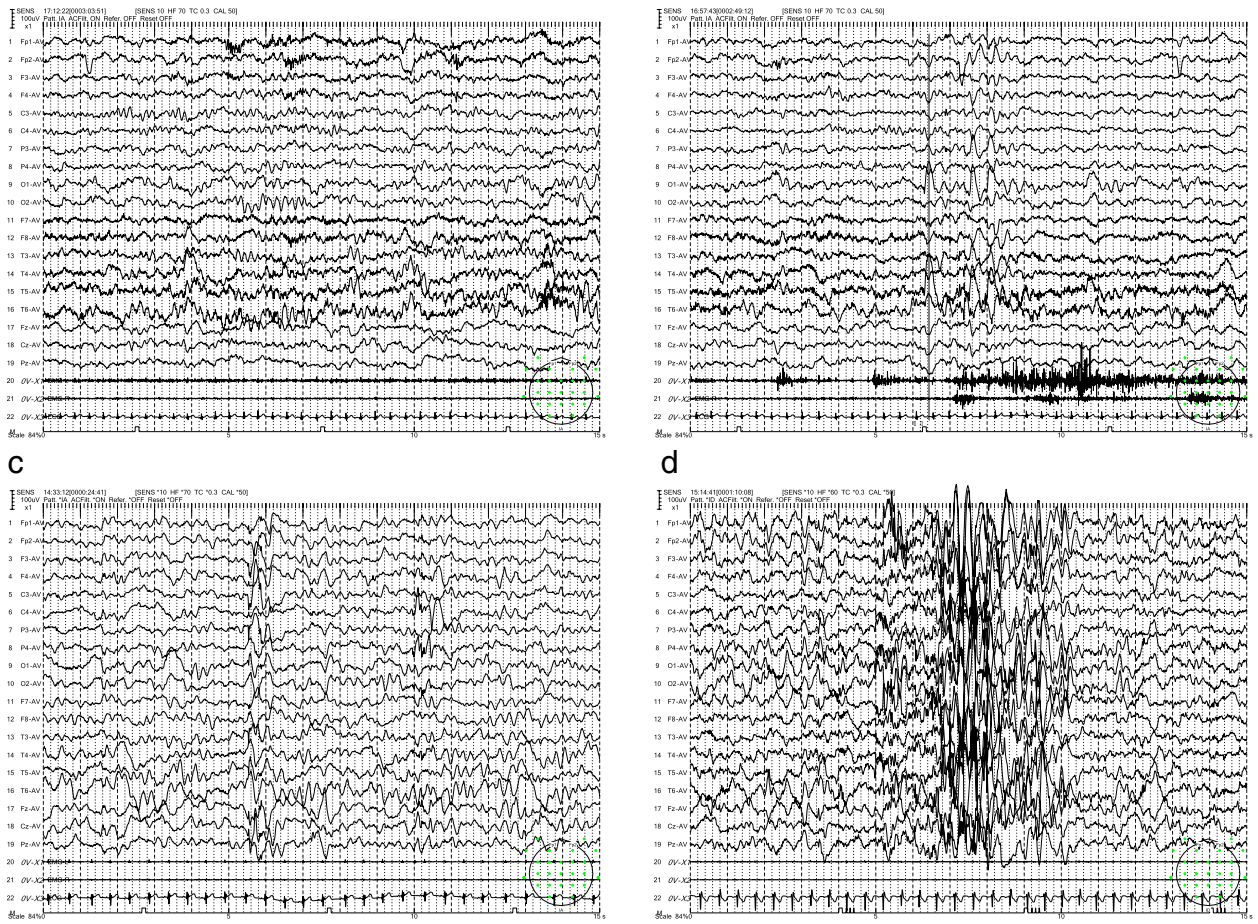

Fig. 1 Results displayed background activity and interictal data.**a**. EEG displayed background activity at six mouth old. **b**. EEG displayed interictal data during awake at six mouth old. **c**. EEG displayed interictal data during asleep at six months old.**d**. EEG displayed interictal data at 13 months old. Electromyogram: on both deltoid muscles. EEG: electroencephalogram

presented a prolonged hemi-convulsive seizure for a few minutes during the hot bath at the age of two months. He had six times of prolonged afebrile partial seizures from the ages of four to six months. A cerebral magnetic resonance image showed a slightly larger left lateral ventricle. The 24-h video monitoring EEG recordings revealed a normal background activity (Fig. 1a). But, during awake and sleep slightly multifocal low- high amplitude spike wave were mainly noted in the left Rolandic and occipital region (Fig. 1b-c). Seizures as described by parents were not detected during EEG recordings. However, a new seizure pattern without attention of the parents was noted by the EEG physician. His myoclonic jerks of unilateral arm occurred spontaneously, which was visible on the recorded electromyography (EMG) channels representing deltoid muscle. He presented involuntary jerks of the right arm more frequently than the left. The jerks always showed one time and sometimes showed rhythmic repetition and occasionally developed into nodding, which were in response to movement. A visible spike wave from right central-parietal cortex immediately preceded a left myoclonic muscle activity, while a visible spike wave from left central-parietal cortex immediately preceded a right myoclonic muscle activity, which was noted during sleep (Fig. 2A-C). The onset of the spike wave preceded the onset of myoclonic muscle activity by 42 ms through jerk-locked back-averaging of electroencephalogram data (Fig. 2D). These findings suggested that the boy had focal cortical myoclonus during the first year. He was given antiepileptic treatment of levetiracetam. The symptoms were not better and even worsen. Soon after, he suffered from recurrent febrile hemiclonic seizures that often

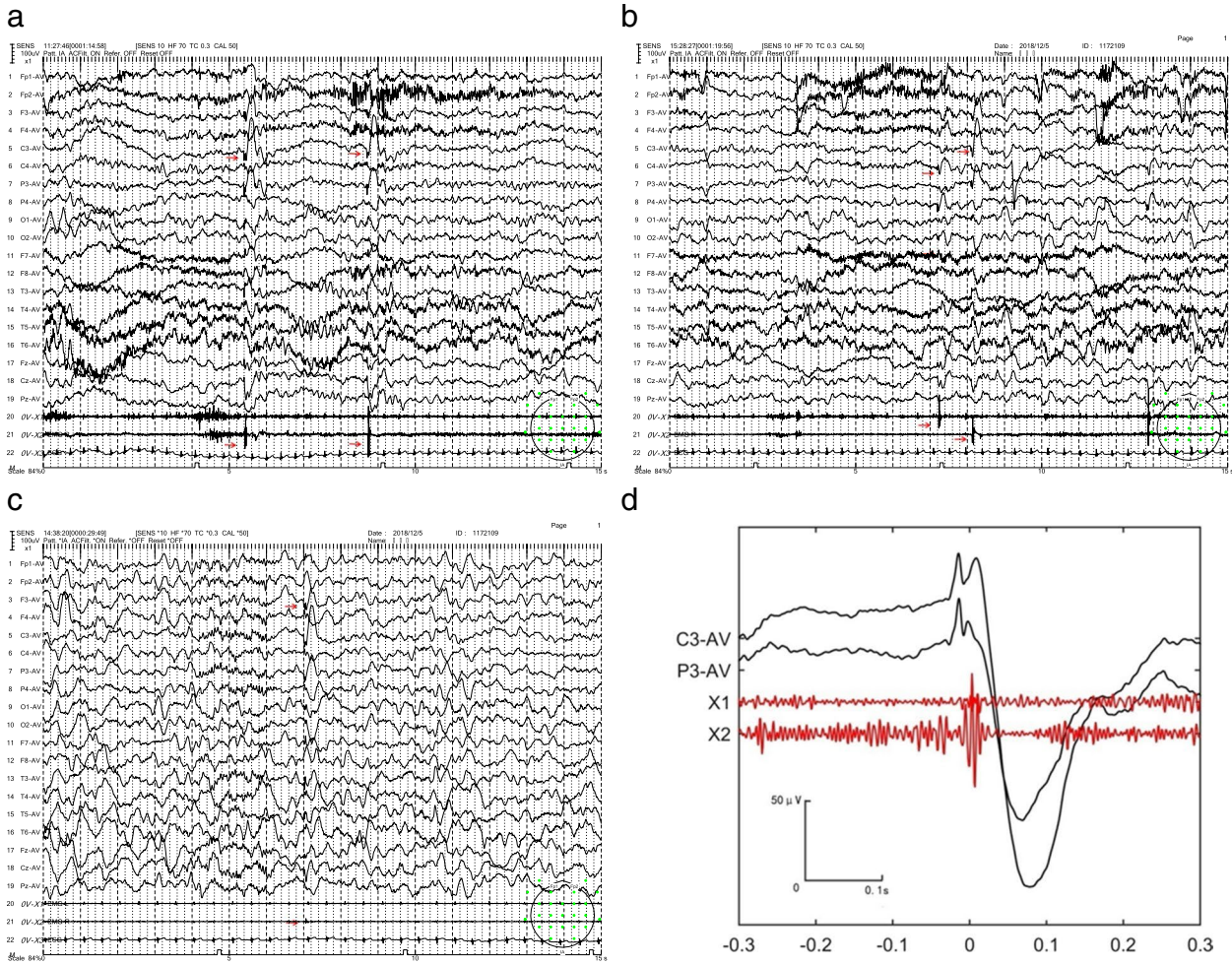

Fig. 2 Results displayed ictal EEG and back-averaging of of the ictal EEG data. **a** and **b**. A visible spike wave at left central-parietal cortex immediately preceded a right myoclonic muscle activity,while a visible spike wave at right central-parietal cortex immediately preceded a left myoclonic muscle activity. **c**. A visible spike wave at left central-parietal cortex immediately preceded a right myoclonic muscle activity during sleep. **d**. Jerk-locked averaging discloses a pre-myoclonic negative peak predominantly at the central-parietal electrode; this peak precedes the EMG onset by approximately 42 ms. Electromyogram: on both deltoid muscles. The red line represents the abnormal electrical activity in the brain and burst of EMG activity. EEG: electroencephalogram

developed into status epilepticus with fever or bathing. The longest febrile seizure lasted about five hours. A genetic analysis revealed a de novo heterozygous frame shift mutation in exon 21(c.3836_c.3837del AT) of the *SCN1A* gene.His was taken to the hospital again when he was thirteen months old. The boy underwent 24-h video monitoring EEG again. Focal myoclonic symptoms was not noted and the interictal EEG evolved into a generalized high-amplitude polyspike slow wave (Fig. 1d). Sodium valproate was added to treat the recurrent seizures. The total frequency of seizures was less following receiving leviteracetam at 41.6 mg/kg/day, sodium valproate at 16 mg/kg/day from 13 to 16 months old by the phone call following-up.

Discussion

We presented a unique case of DS with focal cortical myoclonus on conventional EEG. A visible spike wave from right central-parietal cortex immediately preceded a left myoclonic muscle activity, while a visible spike wave from left central-parietal cortex immediately preceded a right myoclonic muscle activity. The focal myoclonus was noted by physician when he was six months old, and was not noted when thirteen months old from a 24-h video monitoring EEG.

Myoclonic seizures with generalized or multiple spike-waves in DS have been reported to be isolated or grouped in brief bursts of two or three jerks [6, 7]. Focal myoclonus is muscle jerks resulting from epileptic discharges

in the cerebral cortex [8]. Kobayashi et al. reported a female children with DS with a segmental myoclonus without obvious spike-wave discharge on conventional EEG [9]. Conventional EEG of our case showed that a left myoclonic muscle activity originated from a spike wave form right central-parietal cortex, while a right myoclonic muscle activity originated from a spike wave form left central-parietal cortex.Our case further verified that focal cortical myoclonus was a seizure pattern of DS. The underlying mechanisms of focal cortical myoclonus in our case may be cortical hyperexcitability because of no obvious structural brain lesions. Other rare forms of seizure of DS with *SCN1A* mutation were reported such as photosensitive myoclonic absence seizures, intermittent photic stimulation-induced occipital seizures, musicogenic reflex seizures, and seizures triggered by perineal stimulation or diaper change [10–14]. Although the seizures of DS are intractable, the interictal EEG remains free of epileptic discharges during the first year of life [15]. The female case with DS with a focal myoclonus, provided by Kobayashi et al., began to present recurrent generalized tonic–clonic seizures at two months of age, and the interictal EEGs were not remarkable [9]. She presented erratic segmental myoclonus when was admitted at six months, but the disappearance time it was not mentioned [10]. Our case was also at the age of 2 months when beginning to experience a prolonged hemiconvulsive seizure, but interictal EEG was abnormal during the first year of life. Focal myoclonic of our case with was noted at the age of six months, and not noted at thirteen months old. The two cases suggested that focal cortical myoclonus usually appeared, and may disappear during the first year of life. The limitation of this case report is the small number of cases, so more DS cases are needed to fully grasp the characteristics of focal cortical myoclonus to provide some diagnostic clues for DS.

Conclusions

Focal cortical myoclonus could be a form of seizures during the first year of life in DS, which may broaden the types of seizures of DS and may provide some diagnostic clues for DS.

Abbreviations

DS: Dravet syndrome; EEG: Electroencephalogram; EMG: Electromyography.

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None

Authors' contributions

XQL participated in the research and manuscript writing. XLW participated in the design of the research and data analysis. JJ designed, supervised studies, interpreted results, and prepare the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets during and/or analysed during the current study available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This case report has been approved by the Wuhan Children's Hospital's Research Ethics Board (approval number is 2019013). Written informed consent was obtained from the parents for the publication of this case report as per the hospital guidelines.

Consent for publication

Parental written informed consent was obtained from the case.

Conflicts of interests

The authors (XiaoqingLuo, Xiaolu Wang and JunJiang) declare no competing interests.

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