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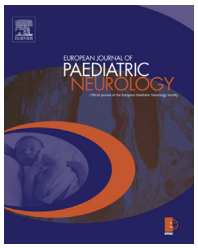

Case Study

Myoclonus in childhood-onset neurogenetic disorders: The importance of early identification and treatment

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ABSTRACT

Background: In clinical practice, myoclonus in childhood-onset neurogenetic disorders frequently remains unrecognized, because it is often overshadowed by other neurological features. Since treatment can lead to significant functional improvement, accurate phenotyping is essential. To demonstrate the importance of early identification and treatment, we report on four patients with various childhood-onset neurogenetic disorders suffering from myoclonus.

Methods: We evaluated four patients with established childhood-onset neurogenetic disorders and involuntary jerky movements, who visited our young-onset movement disorder outpatient clinic.

Results: We present the clinical data of four patients (aged 8–21 years) with childhood-onset neurogenetic disorders, including ataxia-telangiectasia, Coffin-Lowry syndrome and epileptic encephalopathy due to *SCN1A* mutations. All four suffered from jerky movements that hampered normal daily activities and that had gone unrecognized for several years. The presence of multifocal myoclonus was confirmed by polymyography. In all patients, treatment resulted in marked improvement of both myoclonus and overall functioning.

Conclusion: These cases highlight the relevance of actively searching for myoclonus in childhood-onset neurogenetic disorders, even when a molecular diagnosis has already been established. To further improve the awareness and recognition of myoclonus in

Abbreviations: AT, ataxia-telangiectasia; CLS, Coffin-Lowry syndrome; CM, cortical myoclonus; DS, Dravet syndrome; EEG, electroencephalography; EMG, electromyography; SEP, somatosensory evoked potentials; SIDEs, stimulus-induced drop episodes; SM, subcortical myoclonus.

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children, we provide a list of childhood-onset neurogenetic disorders with myoclonus as important associated feature.

1. Introduction

Myoclonus is defined as sudden, brief, shock-like involuntary movements caused by muscular contractions (positive myoclonus) or interruptions of tonic muscle activity (negative myoclonus).[1] A widely used approach is classification according to the anatomic origin, with the most common forms being CM (cortical myoclonus) and SM (subcortical myoclonus) (Table 1).[1]

Myoclonus in children and adolescents frequently remains unrecognized. However, it is an important feature in many childhood-onset conditions, especially in neurogenetic disorders (Supplemental Table), and identification is important because it is treatable. To illustrate this, we report on four patients with various childhood-onset neurogenetic disorders suffering from myoclonus, as confirmed by simultaneous electroencephalography/electromyography (EEG/EMG) recordings. Although myoclonus was not the main symptom in these patients, it had significant impact on their daily functioning. Treatment with clonazepam was effective in all patients.

2. Case study

2.1. *Cases 1 and 2*

Patient 1 and 2 are homozygote twin brothers, 21-years-old, with Dravet syndrome (DS) due to a C.3637C > T(p.Arg1213Stop) mutation of the *SCN1A* gene. They were referred to our young-onset movement disorders outpatient clinic because of involuntary jerky hand movements.

Since the age of 4 months both patients had suffered from intractable generalized tonic-clonic seizures, atypical absences and tonic seizures. During childhood, they had developmental delays with behavioral problems and autistic features. Their parents reported that the involuntary jerks had been present since birth and progressed during the last few years, limiting normal daily activities. Unexplained sudden falls had occurred since adolescence, with accidents and insecure gait.

Neurological examination showed continuous multifocal stimulus-sensitive myoclonic jerks, most pronounced in their hands and faces, with exacerbation on action (Video 1A). EEG/EMG findings were supportive of CM: myoclonic jerks with burst duration of 30–60 ms and occasionally also negative myoclonus. Back-averaging and coherence analysis showed no cortical potential or increased coherence, most likely because not enough segments were available for analysis. Somatosensory evoked potentials (SEP) studies showed no giant potentials, possibly due to valproate use (Ikeda et al, Supplemental references). We classified the jerks as CM, with negative myoclonus leading to falls.

Supplementary video related to this article can be found at http://dx.doi.org/10.1016/j.ejpn.2015.07.003.

As treatment with valproate and levetiracetam had not been beneficial, we initiated treatment with clonazepam (3 × 2 mg daily). This led to marked improvement of positive and negative myoclonus in both patients (Video 1B).

Supplementary video related to this article can be found at http://dx.doi.org/10.1016/j.ejpn.2015.07.003.

2.2. *Case 3*

A 20-year old patient with ataxia-telangiectasia (AT) visited the outpatient clinic because of involuntary jerky movements and a tremulous voice. Disease onset was at the age of 3 years with a gait disorder and delayed motor and language development. One year later, a cerebellar syndrome was reported with dysarthria, gait and limb ataxia. Sequential EMGs demonstrated progressive axonal sensorimotor polyneuropathy. The involuntary movements had been reported since he was 7 years old, with significant impact on his daily functioning.

Neurological examination showed limb ataxia, ocular apraxia, nystagmus, bilateral ptosis, dystonia of the fingers, areflexia, distal weakness and sensory loss. There was a marked cerebellar dysarthria and an irregular tremulous voice. Spontaneous multifocal myoclonic jerks were observed, mostly in both arms, worsening on action, without stimulus-sensitivity (Video 2). EEG/EMG demonstrated myoclonic jerks with burst duration of 30–80 ms, suggestive of CM. Back-averaging and coherence analysis showed no cortical correlate or increased coherence. SEP studies showed no potentials, due to the polyneuropathy. We classified the myoclonus as possibly cortical.

Supplementary video related to this article can be found at http://dx.doi.org/10.1016/j.ejpn.2015.07.003.

The patient was treated with clonazepam (2 × 0.5 mg daily), leading to a significant decrease in myoclonic jerks. The patient regained several fine motor skills such as eating without help and the ability to use his mobile phone. In addition, reduced voice tremor resulted in enhanced intelligibility. His overall functioning improved significantly.