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Spinal Muscular Atrophy (SMA) is a group of relatively common diseases, transmitted by autosomal recessive inheritance and characterized by loss of motor function and muscle atrophy due to degeneration of anterior horn cells in the spinal cord. Progressive myoclonic epilepsy (PME) is characterized by myoclonic and generalized seizures with progressive neurological deterioration. The association between SMA and PME has not yet been fully understood.

Keywords: Atrophy; epilepsy; myoclonic; muscular; progressive; spinal.

Introduction

Spinal muscular atrophies (SMAs) are a group of relatively common diseases, transmitted by autosomal recessive inheritance and characterized by loss of motor function and muscle atrophy due to degeneration of anterior horn cells in the spinal cord. SMA with progressive myoclonic epilepsy (PME) is characterized by combination of motor neuron disease and PME, sometimes associated with other features including sensorineural hearing loss (SNHL), action tremor, cognitive dysfunction as well as cerebral and cerebellar atrophy, and may be due to ASAH1 gene mutations.

Case Report

A 17-year-old male patient presented at clinic with bilateral symmetrical lower and upper limb weakness. Onset of disease had begun early in second decade of his life, and parallel to motor degeneration, he had developed intermittent, irregular jerking of upper limbs at 15 years old. Frequency was 5 to 10 times a day, and it was non-progressive. There was no finding of other seizure types. Familial history was negative for neuromuscular disorders or epilepsy. Neurological examination showed diffuse muscle atrophy and weakness involving proximal upper and lower extremities. There was no ataxia, and neuropsychological study showed no cognitive impairment that might suggest PME syndrome. There was no deafness, diplopia, dysarthria or dysphagia. Brain and spinal cord magnetic resonance imaging (MRI) did not show any structural lesions. Serum creatine kinase (CK) levels were normal. Electroencephalography (EEG) revealed irregular, generalized spike-and-wave and polyspike-and-wave complexes at 3–3.5 cycles/s. Paroxysmal activity was increased by hyperventilation, and was not significantly modified during sleep. Electromyography...
(EMG) indicated fasciculations, impaired recruitment with increased firing rate of motor units, and polyphasic, high-amplitude, long-duration potentials. Motor and sensory conduction velocities were within normal values. Lower motor neuron degeneration was identified. SMN1 gene deletion was observed in genetic analysis. Unfortunately, acid ceramidase and ceramide levels were not evaluated, as the necessary facilities were not available. In order to obtain seizure control, valproate (500 mg twice a day) was initiated. Seizure episodes were reduced in frequency and intensity.

Discussion

SMAs are a group of disorders defined by degeneration of anterior horn cells in the spinal cord and motor nuclei in lower brainstem. SMA Type I, also known as infantile spinal muscular atrophy or Werdnig-Hoffmann disease, is the most common and severe type of SMA. It typically presents in neonatal period. SMA Type II (intermediate form) presents before 18 months of age, whereas SMA Type III (Kugelberg-Welander disease) typically presents with signs of weakness at or after 1 year of age and progresses to a chronic course. Adult onset of SMA (Type IV) usually presents in second or third decade of life but is otherwise similar to SMA Type III.[2] The gene responsible is the survival motor neuron (SMN1) gene located on chromosome 5q and homozygous mutations or deletions of this gene are found in more than 90% of SMA patients. Even though a copy of the SMN gene located centromerically (SMN2) is not affected, its protein production is inadequate to prevent the disease, though it might affect severity. The number of copies of SMN2 gene has been associated with variable disease severity of SMA.[3] Different forms of SMAs have been recognized. Some patients may also have atypical clinical features (e.g. oculomotor palsy, myoclonic epilepsy, nerve deafness, olivoponto-cerebellar atrophy, ataxia, dysphagia, dysartria, multiple arthrogryposis, etc.)

In the last few years, experts have particularly focused attention on the so-called “SMA plus” phenotypes and have suggested clinical and genetic heterogeneity.[3] PME is a heterogeneous group of epilepsies characterized by myoclonic and generalized seizures with progressive neurological deterioration due to metabolic defects or degenerative diseases.[3,4] Described in the present report is case of late onset form, SMA Type III. However, there was no cognitive decline or ataxia even several years after onset of myoclonus to suggest a PME syndrome. Most authors have reported combination of SMA and PME, in contrast to present case. They have postulated that SMA with PME could be a rare form of PME where myoclonic epilepsy arises later in the course of the disease.[5] It has only been a few years since diagnosing SMA and myoclonic epilepsy. Literature regarding cases of SMA with PME describes myoclonic epilepsy starting within few years after the development of muscle weakness (with or without other features such as cognitive decline).[5] It will be necessary to follow the present patient on long-term basis for development of signs of PME.

References

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