

Case Report

Hereditary myoclonus dystonia - rare entity diagnosed in younger children: report of a sporadic case with atypical features

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ABSTRACT

Hereditary myoclonus dystonia is a rare movement disorder characterized with combination of myoclonic jerks with mild to moderate dystonia. Mostly caused due to changes in SGCE gene. Author report case of a 3 years old girl with atypical features of lower limb onset, mild dystonia, upper limb and neck myoclonic jerks and younger onset. She was detected to have pathogenic variant of SGCE gene. A diagnosis of myoclonus dystonia should be considered at an early age also like in our case so that treatment is initiated early for better results and improved quality of life and development.

keywords: Atypical onset, Myoclonus-dystonia, SGCE gene

INTRODUCTION

Hereditary myoclonus dystonia is a rare movement disorder with jerky movements and dystonia usually involving upper limbs, neck, trunk and lower limbs. Sometimes myoclonus can be generalized. SGCE is a ubiquitous membrane protein which is part of the dystrophin-associated glycoprotein complex in brain and is widely expressed in the cerebellum.¹ Dysfunctional cerebello-thalamic pathways is critical in the pathogenesis of myoclonus-dystonia. Apart from cerebello thalamic pathway dysfunction abnormality in globus pallidus and cortical neuronal activity has also been implicated.

In a genetic mouse model of SGCE deficiency, impaired striatal plasticity was found thus increasing the excitability of these neurons by augmenting the motor threshold. An Adenosine A2 Receptor (A2AR) antagonist was found to restore normal plasticity in this model thus promising new treatment options. Myoclonus dystonia patients tend to develop cortical plasticity more as compared to other dystonic disorders.² Sometimes

psychiatric co-morbidities are also seen in these patients like anxiety, depression, panic attacks obsessive-compulsive disorders, and personality disorders. Mostly cases of myoclonus dystonia have autosomal dominant pattern of inheritance and result from a mutated SGCE gene (also known as DYT11). Even if a child inherits a faulty SGCE gene, they may not manifest myoclonus dystonia as this SGCE gene may undergo maternal imprinting. Sporadic cases have also been reported of this entity. Usual age of presentation is in first or second decade.³ Youngest case reported till now from India is in a 4 years boy, here we report it in a 3 years girl child.⁴ In mostly cases myoclonus responds to consumption of alcohol. About 30-50% cases of myoclonus dystonia syndromes are due to variant in SGCE gene, but few cases with variants in RELN,⁵ ANO3,⁶ TOR1A,⁷ and the locus for DYT158 have also been reported with similar features.^{5,6} Neuroimaging of these patients is normal. Sometimes the symptoms respond to single or a combination of different agents like levetiracetam, clonazepam, tetrabenzene.⁷ Palliative deep brain stimulation has shown some efficacy in management of disabling symptoms.³

CASE REPORT

3 years girl child presented at our neurology clinic with difficulty in walking since 2 years of age, frequent falls while walking and daily multiple jerky movements of upper limb and neck since 2 years of age. Born of a nonconsanguineous marriage, full term vaginal delivery with uneventful neonatal period, she achieved all the developmental milestones as per age till 2 years of age. Family history for any kind of movement disorder was negative. (pedigree chart shown in figure 1) Thereafter mother noticed abnormal gait of the child which was wide based with slight circumduction with difficulty in walking and frequent falls. This was progressive in nature. She had multiple jerky movements of right upper limb with neck which increased with voluntary actions (eating, playing, writing) and were absent during sleep. There was progressive increase in frequency of these jerky movements. There was no history of cognitive decline, hearing, vision problems. She also had occasional night leg cramping with stiffness. Higher mental function was normal, right lower limb had slightly increased tone with brisk deep tendon reflexes and withdrawal plantar. Gait was slightly dystonic. Tone of upper limbs and neck muscles was normal. All cranial nerves were intact and power of facial muscles was normal. Initially a provisional diagnosis of progressive myoclonic epilepsy and neuronal ceroid lipofuscinosis was kept and child was investigated. younger sibling is asymptomatic. MRI brain showed asymmetry of bilateral lateral ventricles with right more prominent than left (s/o normal variant). Nerve conduction studies were normal. Arterial lactate was normal. Child had a pathogenic variant of SGCE gene (exon 6) on genetic testing and was diagnosed with hereditary myoclonus dystonia. She was started on levetiracetam, trihexyphenidyl and clonazepam. She is still under follow up. Till last visit her myoclonic jerks have decreased in frequency and mild dystonia is persisting. Videos of patient's limb dystonia and myoclonus was recorded after consent. (Supplementary material).

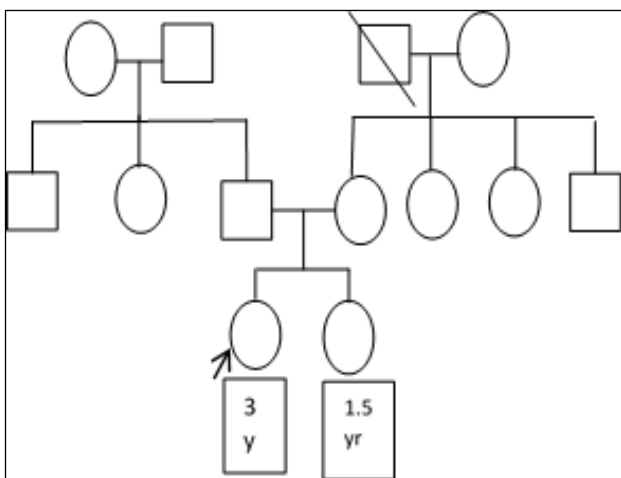


Figure 1: Pedigree chart showing index case.

DISCUSSION

Myoclonus dystonia typically presents as rest or action myoclonus and is sometimes associated with mild to moderate dystonia.⁸ The symptoms generally predominate in the upper body. Involvement of Lower limbs have been reported in 25% of cases and is usually seen in girls.⁸ This case had initial dystonic onset of lower limbs followed by myoclonic jerks of upper body. Puneet et al had reported lower limb onset myoclonus in 2 sisters of a family.⁴ Though psychiatric disturbances are commonly reported in patients with SGCE-DYT mutations but our patient did not have any such problems.^{4,8} Cognitive impairment is generally not seen in these patients but a case of intellectual disability has been reported in a 21 years female with a splice variant of SGCE gene.⁶ This patient did not have any cognitive decline and achieved all developmental milestones normally. This patient was detected to have a SGCE mutant gene variant. There was negative family history of any movement disorder. Her younger sibling is asymptomatic till now. Parents and sibling have denied genetic testing. 50% cases with SGCE variant have typical clinical features but our patient presented with atypical features like onset with lower limb dystonia and younger age. Rarely MDS causes serious disabilities. Severity of symptoms and rate of progression is largely unpredictable in this disease. Children diagnosed at an early age may have progression of symptoms with previously unaffected body parts involved. These patients need close follow up to watch for development of new behavioural abnormalities into later childhood and adolescence. Antiepileptic levetiracetam can achieve symptomatic improvement may be achieved with leverateracetam, raise quality of life can be improved in some patients.

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