GLUT-1 Deficiency Syndrome; HSP Mimic: A Case Report

A 33-year-old farmer presented with a history of gradually progressive stiffness in both lower limbs and toe walking for 4 years. He also gave a history of episodes of unconsciousness along with turning of the head to one side, clonic tonic movements of all four limbs, and frothing, lasting for 2–3 min for the last 4 years. There was no history of any sensory symptoms, abnormal movements, or bladder and bowel involvement. There was a history of delayed milestones of development in that he started walking at the age of 3 years and speaking at the age of 5 years. There was no family history of similar illness in parents or siblings. There was no history of any sensory, bowel, or bladder symptoms. He had no history of consumption of Lathyrus sativus or exposure to toxins. There was no history of similar illness in parents or siblings. He had a son aged 3 years whose milestones of development were normal.

Clinical examination revealed normal head circumference, and Mini Mental Scale Examination (MMSE) was 21/30. Cranial nerves were normal. There was modified Ashworth scale grade 3 spasticity in both lower limbs and grade 1+ spasticity in both upper limbs. Power was grade 5/5 in both upper limbs and grade 4+/5 in both lower limbs. Deep tendon jerks were exaggerated in both lower limbs and both plantar responses were extensors. Sensory examination was normal and there were no cerebellar signs. Gait was spastic with toe walking. In view of the history of delayed milestones, epilepsy, and spasticity, a clinical diagnosis of complicated HSP (hereditary spastic paraplegia) was made.

Routine hemogram, vitamin B12 levels, renal and liver function tests, HIV (human immune deficiency virus), VDRL (venereal disease research laboratory), nerve conduction studies, and electroencephalogram were normal. MRI (magnetic resonance imaging) brain and spinal cord were also normal. There were no white matter changes.

CSF (cerebrospinal fluid) examination revealed normal proteins and cells, and sugar was 11 mg% with a corresponding blood sugar of 128 mg%. In view of low CSF sugar, the possibility of glutamine transporter-1 deficiency syndrome (GLUT-1 DS) was kept and whole genome sequencing was done. It revealed pathogenic heterozygous *SLC2A1* mutation at exon 8 c.988C>T, p. Arg330Ter variant on chromosome 1 suggestive of GLUT-1 DS with autosomal dominant inheritance pattern.

The patient was diagnosed as a case of GLUT-1 DS and advised ketogenic diet along with levetiracetam for epilepsy. The patient is under follow-up for the last one year and his seizures are controlled and spasticity in his lower limbs has reduced (modified Ashworth scale grade 2). Genetic screening of family members could not be done due to financial constraints.

HSP is an inherited disorder. Complicated HSP can present with seizures, ataxia, peripheral neuropathy, intellectual disability, and extrapyramidal movement disorders. Essentially the diagnosis is after the exclusion of other causes (most of which are treatable) which can present with epilepsy and myelopathy-like infections (HIV, human T-cell lymphotropic viruses type 1 (HTLV-1), neurosyphilis, and tuberculosis), demyelinating disorders like multiple sclerosis, certain inherited metabolic defects like *MTHFR* (methylenetetrahydrofolate reductase) gene mutation, and vitamin E and B12 deficiency. Genetic analysis is confirmatory for the diagnosis of HSP, which reveals a mutation in the SPG gene (spastic paraplegia gene).

GLUT-1 DS is a rare neuro-metabolic disorder due to a mutation in the SCL2A1 gene on chromosome-1 which encodes for glucose transporter type 1; a membrane protein responsible for the transport of glucose across the blood-brain barrier to astrocytes.[1] The classical type is early onset (less than 2 years) with microcephaly, epilepsy (mainly childhood absence, myoclonic–astatic), and mental and motor retardation. The non-classical type includes late-onset paroxysmal exertion-induced dyskinesia (also known previously as dystonia 18 and dystonia 9; now considered part of the Glut1-DS spectrum), epilepsy, episodic choreo-athetosis, and spasticity.[2,3] Clinically it may be difficult to distinguish complicated HSP from GLUT-1 DS as both share many similar clinical features like spasticity, movement disorder, and epilepsy. Examination of the CSF is important to differentiate the two clinical entities.[4] The low blood sugar level in CSF is suggestive of GLUT-1 DS.

This case highlights the importance of doing a CSF examination in all cases of complicated HSP to rule out GLUT-1 DS, which is potentially a treatable disorder. A ketogenic diet may improve symptoms of GLUT-1 DS and may even reverse the symptoms if started early.[5]

Patient's consent

Obtained for publishing reports and videos online

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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Submitted: 29-Nov-2022 **Revised:** 13-Jan-2023 **Accepted:** 20-Jan-2023
Published: 13-Mar-2023

DOI: 10.4103/aian.aian_955_22