A case of SLC6A1 gene mutation with isolated, early-onset absence seizures and learning disability

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INTRODUCTION

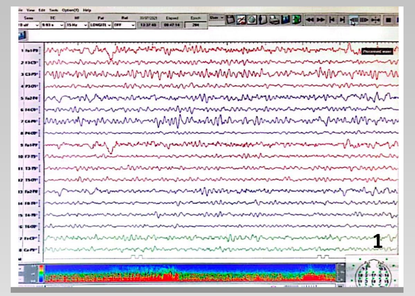
The SLC6A1 gene encodes one of the major gamma-aminobutyric acid (GABA) transporters (GAT-1) that reuptake GABA from the synaptic cleft. In SLC6A1 gene mutations, GAT-1 function is impaired and seizures with neurodevelopmental disorders occur by preventing the reuptake of the basic inhibitor GABA into the synaptic cleft. (1,2) The SLC6A1 neurodevelopmental disorder (SLC6A1-NDD) is characterised by various types of epilepsy (often myoclonic-atonic epilepsy), mild to severe developmental delay and/or intellectual disability, movement disorders, speech delay, hypotonia and psychiatric manifestations such as autism spectrum disorders and attention-deficit/hyperactivity disorder.(3) After developmental delay, seizures are one of the main symptoms of SLC6A1-NDD. They are described in more than 80% of patients. In the case series published up to this time, myoclonic-atonic seizures of the patients, which frequently started around the age of 2 years, were frequently emphasised.(4) Absence seizures are commonly reported, but usually in the context of miyoclonic-atonic epilepsy (MAE) and not as the only seizure type. In the study by Caputo et al, two patients have an absence seizure phenotype but not MAE.(5) This confirms previous reports that childhood-onset absence epilepsy is also part of the phenotypic spectrum of SLC6A1-NDDs.

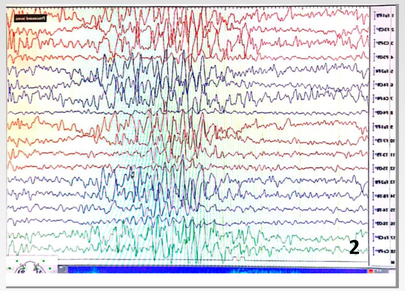
OBJECTIVES

In our case, we also describe the clinical and EEG data of a patient with mild cognitive impairment who had a typical absence epilepsy that was completely controlled by valproic acid.

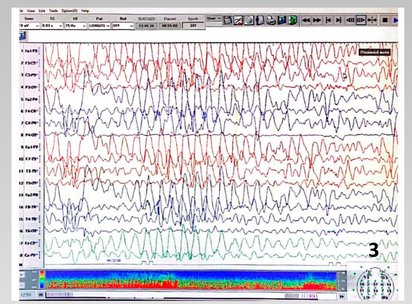
MATERIAL& METHODS

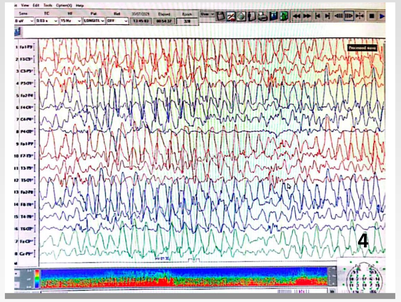
The 5,5-year-old girl was brought because of paroxysmal, short-term absence attacks which started at the age of 18 months, The patient's perinatal history was uneventful. History of gross and fine motor development was normal, but the speech of the patient began at the age of three. Physical examination and head circumference were normal. Absence seizures were observed to be triggered during hyperventilation. EEG showed 3-3,5 Hz spike-wave, regular generalised abnormalities and valproic acid was ordered with the diagnosis of early-onset childhood absence epilepsy. Absence seizures were controlled with valproic acid monotherapy.





Activated by hyperventilation (figure 1 to 4)





RESULTS

Brain MRI and detailed biochemical analysis were normal. GLUT-1 deficiency syndrome was excluded by performing lumbar puncture and *SLC2A1* Sanger sequencing. Due to early-onset absence seizures and poor school performance, a whole exome analysis was planned to determine the etiology, and a de novo, heterozygous, pathogenic variant c.919G>A; p.Gly307Arg was detected in the *SLC6A1* gene.

CONCLUSION

We would like to emphasize that *SLC6A1*-related neurodevelopmental disorder should be considered in the differential diagnosis of patients with isolated, early-onset absence seizures and mild cognitive retardation.

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