SLC2A1 mutations associated Glucose Transport Type 1 Deficiency Syndrome: A Single Center Case Series

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INTRODUCTION

Glucose transporter type 1 deficiency syndrome (GLUT1-DS) is usually due to the mutations of SLC2A1 gene and inherited in an autosomal dominant (AD) pattern with 90 percent de novo mutation. The phenotypic spectrum includes classic type (early-onset) which is characterized by refractory infantile epilepsy, developmental delay, acquired microcephaly and complex movement disorders. Non-classic phenotypes includes paroxysmal exercise-induced dyskinesia and epilepsy, paroxysmal choreoathetosis with spasticity, atypical absence or myoclonic astatic epilepsy and paroxysmal nonepileptic findings. The complex movement disorder, may occur in any combination and may be continuous, paroxysmal or continual with fluctuations in severity influenced by fasting or infectious stress condition.

OBJECTIVES

The aim of this study is to draw attention to the clinical and genetic features of patients with GLUT1-DS in Eastern Mediterranean Region of Turkey by determining the clinical and genetic features of GLUT1 deficiency syndrome cases in our center.

MATERIALS & METHODS

The clinical and genetic findings of four consecutive patients with SLCA1 related GLUT-1DS were reviewed, retrospectively.

RESULTS

The age at diagnosis was 2.5-9.5 years. First and second case admitted with paroxysmal ataxia and dystonia without seizure as non-classical phenotype. The third case was admitted with refractory absence seizures as non-classical phenotype. However the fourth patient admitted with febrile seizures and continued with afebrile seizures. His SCN1A-B gene and genetic panel for epileptic encephalopathy did not revealed any mutations. SLC2A1 gene mutation was detected after the exercise-induced dyskinesia was observed on follow-up. Therefore forth case were classified as non-classical phenotype with epilepsy. Generalized epileptic abnormality was detected in the EEG's of three patients. However forth case with multiple seizures had normal EEG. All of the patients had global developmental delay and put on ketogenic diet.

NO	NAME	AGE	APPLICATION SYMPTOM	ONSET AGE OF SYMPTOMS	APPLICATION AGE	NEUROLOGİC EXAMINATION	AGE OF DİAGNOSİS	GENETIC ANALYSES	GENETIC RESULTS	EEG	BRAIN MRI	AEI	KETOGENİC DIET	DEVELOPMENTAL DELAY
1	S.M.	12 years-old	Paroxysmal ataxia	3 years-old	9 years-old	Normal, Exercise-Induced Ataxia	9 years-old	SLC2A1 Gene	*SLC2A1 GENE: NM_006516.3 c.483g>t (p.q161h) (p.gln161his) heterozygous mutation (a novel, de novo mutation)*	Jeneralized epileptic activity	Normal	Levetiracetam + clonazepam	Yes	Global
2	E.U.	4 years-old	Dystonia on the left foot	1 years-old	1 years-old	Normal, Exercise-Induced Dystonia	2 year 6 months old	SLC2A1 Gene	*SLC2A1 GENE: NM_006516.3 c.458g>a (p.r153h) (p.arg153 his) heterozygous mutation (AD)*	First one was normal, Following EEGs: Jeneralized epileptic activities	Normal	Sodium Valporate + clonazepam	Not effective/ paitent non-compliance	Global
3	H.A.	6 years-old	Absence type seizures and developmental delay	5 years-old	5 years-old	MMR, Wide-based gait	5 years-old	SLC2A1 Gene	*SLC2A1 GENE: NM_006516.3 c.539t>a (p.m180k) (p.met180lys) heterozygous (a novel, de novo mutation)*	Jeneralized epileptic activity	Millimetric nodular lesion in the pineal gland	Ethosuximide + sodium valproate + clonazepam	Yes	Global
4	Y.Ç.	6 years-old	Febrile/afebrile seizures	1 years-old	4 years-old	Wide-based ataxic gait	6 years-old	SLC2A1 Gene	*SLC2A1 GENE: NM_00616.4 c.989_1005dup17bp (p.l336efs*10) (p.leu336glufster10) heterozygous mutation (AD)*	Normal	Normal	Levetiracetam	Yes	Global

CONCLUSION

The phenotypic spectrum designated as non-classic Glut1-DS has expanded over the past few years as more affected individuals have been identified. Paroxysmal non-epileptic manifestations that have been reported include intermittent ataxia, choreoathetosis, dystonia and alternating hemiplegia. Several disorders including paroxysmal choreoathetosis with spasticity (dystonia 9), paroxysmal exercise-induced dyskinesia and epilepsy (dystonia 18), atypical childhood absence epilepsy and myoclonic astatic epilepsy are now known to be caused by GLUT1-DS. Some findings may show overlap with those seen in classic Glut1-DS. All patients in our case series were in the non-classic phenotype and 3 of them diagnosed due to exercise-induced movement disorder and two of them had *de novo* mutation. Children with unexplained epileptic seizures, developmental delay and complex movement disorders with or without combination should be examined for GLUT1-DS.

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