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A Cause of Severe Hypotonia in Infancy: Allan-Herndon-Dudley Syndrome

Sakir GENC, Ozlem YAYICI KOKEN, Sait ACIK, Senay HASPOLAT

Medical Faculty of Akdeniz University, Pediatric Neurology, Antalya, Turkiye

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INTRODUCTION

Allan-Herndon-Dudley syndrome (AHDS) is an X-linked recessive intellectual disability syndrome characterized by severely impaired intellectual and motor development, dysarthria, athetoid movements, and spastic paraplegia (1). The syndrome is caused by mutations in the *SLC16A2* (also, known as MCT8) gene. This gene encodes the brain transporter of thyroid hormones. As *SLC16A2* encodes the monocarboxylate transporter 8 (MCT8), a thyroid hormone transporter, patients with Allan-Herndon-Dudley syndrome present a specific altered thyroid hormone profile. But, there is a large phenotypic interfamilial and intrafamilial variability in these cases. The reported phenotypic features of the AHDS by HPO terms were added in Table-1 to show the involvement of multiple systems and a wide phenotypic spectrum.

OBJECTIVES

Here we present a boy with AHDS diagnosed with a novel pathogenic *SLC16A2* gene mutation with mild dysmorphic signs, global developmental delay, severe hypotonicity and, movement disorder (2).

PATIENT AND METHODS

A 1-year-old boy was referred to our clinic due to mild dysmorphic signs such as large ears, elongated face, global developmental delay, and severe neonatal and infantil hypotonicity. A severe axial and peripheral hypotonicity, increased patellar deep tendon reflexes and clonus, and positive Babinski sign were determined in his neurological examination. Dystonic posturing was realized in his right hand. He had a drop neck and he could not able to sit independently which indicates a delay in motor steps. Intermittent ataxia was observed in his upper extremities. Despite the normal serum levels of thyroid-stimulating hormone, free T3 had increased. The cranial MRI was reported as normal which was planned around 10 months old. Table-1 summarizes the clinical features of the disease by HPO terms (https://hpo.jax.org/app/browse/disease/ORPHA:59)

The *SLC16A2* gene (c.467_469 delTCT) hemizygous deletion was determined at c.467_469 in WES analysis. The detected variant was reported as pathogenic due to ACMG 2015 guideline. The family study is in progress.

CONCLUSIONS

We emphasize that diagnosis of ADHS, is a very rare condition and can not be distinguished by phenotypic features; but should be remembered in patients, especially if there is an abnormal thyroid test, severe neonatal-infantil hypotonicity, and motor and cognitive delay.

REFERENCES

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Table 1 summaries the HPO terms related with AHDS

HPO_TERM_ID	Categories of characteristics Signs	Frequency	Characteristic Signs	Reported case
HP:0001371	Connective tissue	o	Flexion contracture	+
HP:0008872	Digestive System	f	Feeding difficulties in infancy	+
HP:0002926	Endocrine	f	Abnormality of thyroid physiology	+
HP:0000639	Eye	o	Nystagmus	+
HP:0000028	Genitourinary system	o	Cryptorchidism	-
HP:0045082	Growth	f	Decreased body mass index	+
HP:0001531	Growth	f	Failure to thrive in infancy	+
HP:0004322	Growth	o	Short stature	+
HP:0001518	Growth	vr	Small for gestational age	+
HP:0002058	Head and neck	f	Myopathic facies	-
HP:0000275	Head and neck	f	Narrow face	-
HP:0000276	Head and neck	f	Long face	+
HP:0004488	Head and neck	vr	Macrocephaly at birth	-
HP:0008081	Limbs	f	Pes valgus	+
HP:0001763	Limbs	f	Pes planus	-
HP:0002509	Limbs	o	Limb hypertonia	+
HP:0011448	Limbs	o	Ankle clonus	+
HP:0008936	Musculature	vf	Axial hypotonia	+
HP:0003202	Musculature	f	Skeletal muscle atrophy	+
HP:0002421	Musculature	o	Poor head control	+
HP:0001319	Musculature	o	Neonatal hypotonia	+
HP:0003324	Musculature	o	Generalized muscle weakness	+
HP:0001249	Nervous System	vf	Intellectual disability	+
HP:0007256	Nervous System	f	Abnormal pyramidal sign	+
HP:0001251	Nervous System	f	Ataxia	+
HP:0001266	Nervous System	f	Choreoathetosis	-
HP:0001257	Nervous System	f	Spasticity	+
HP:0001347	Nervous System	f	Hyperreflexia	+
HP:0001332	Nervous System	f	Dystonia	+
HP:0031936	Nervous System	f	Delayed ability to walk	+
HP:0000750	Nervous System	f	Delayed speech and language development	+
HP:0012448	Nervous System	f	Delayed myelination	-
HP:0012444	Nervous System	f	Brain atrophy	-
HP:0001256	Nervous System	o	Intellectual disability	+
HP:0001250	Nervous System	o	Seizure	-
HP:0002510	Nervous System	o	Spastic tetraplegia	+
HP:0001348	Nervous System	o	Brisk reflexes	+
HP:0002071	Nervous System	o	Abnormality of extrapyramidal motor function	+
HP:0003487	Nervous System	o	Babinski sign	+
HP:0000252	Nervous System	o	Microcephaly	-
HP:0100660	Nervous System	vr	Dyskinesia	-
HP:0011451	Nervous System	vr	Primary microcephaly	-
HP:0001561	Prenatal and Birth	vr	Polyhydramnios	-
HP:0001558	Prenatal and Birth	o	Decreased fetal movement	-
HP:0001622	Prenatal and Birth	vr	Premature birth	-
HP:0000767	Skeletal system	f	Pectus excavatum	+
HP:0002751	Skeletal system	f	Kyphoscoliosis	+
HP:0006579	Skin, Hair, and Nails	o	Prolonged neonatal jaundice	-

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