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Case Report

Rare Case of Allan-Herndon-Dudley-Syndrome with Delayed Motor Mile Stones and Diffuse Encephalopathy in an Indian Child

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Abstract

The Allan-Herndon-Dudley Syndrome (AHDS) is a rare X-linked inherited disorder of the central nervous system (X-linked mental retardation) that leads to severe intellectual developmental delays and motor disturbances. This condition, which only affects male infants, causes developmental disruption even before birth. The syndrome, first described in 1944 by William Allan, Florence C. Dudley, and C. Nash Herndon, is a result of impaired formation of two thyroid hormone transporters. This leads to the inability of nerve cells, which depend on thyroid hormones, to absorb them. Affected children exhibit early muscle weakness (myasthenia) and underdeveloped musculature. Later, joint deformities and contractures may occur, leading to additional impairment of mobility, as well as muscle cramps and involuntary movements of the arms and legs. Most individuals with AHDS are unable to walk independently. They also suffer from severe intellectual disorders, often to the extent that they are unable to speak. This is an case report of an rare case in an 14 month old Indian child with a new variant of SLC16A2 (c.997del (p.Gly334AlafsTer9) gene defect variant.

Introduction

Allan-Herndon-Dudley syndrome (AHDS) is a rare X-linked inherited disorder of the central nervous system (X-linked mental retardation) that leads to severe intellectual developmental delays and motor disturbances. This condition, which affects only male infants, causes developmental disruption even before birth. First described in 1944 by William Allan, Florence C. Dudley, and C. Nash Herndon, the syndrome is a result of impaired formation of two thyroid hormone transporters. This leads to the inability of nerve cells, which depend on thyroid hormones, to absorb them. Affected children exhibit early muscle weakness (myasthenia) and underdeveloped musculature. Later, joint deformities and contractures may occur, further impairing mobility, along with muscle cramps and involuntary movements of the arms and legs. Most individuals with AHDS are unable to walk independently. Additionally, affected individuals suffer from severe intellectual impairments, often to the extent that they are unable to speak. After muscle injuries, skeletal muscle stem cells are activated. These cells divide and replace damaged muscle cells, allowing the muscle to heal. Healthy muscle stem cells increase the production of two thyroid hormone

transporters, MCT8 and OATP1C1, after injuries. In AHDS, a mutation in the SLC16A2 gene causes a defect in MCT8. MCT8 facilitates the uptake of thyroid hormones in muscle and nerve cells. In AHDS, active thyroid hormone T3 is lacking in muscles and the brain. Elevated T3 levels (High-T3 syndrome) are present in laboratory tests, while TSH and FT4 levels are normal. The disease is inherited in an X-linked recessive manner. Women, who have two X chromosomes in each cell, can pass on the disease but typically do not develop it themselves due to the low probability of both X chromosomes carrying a mutated SLC16A2 gene. Men, with only one X chromosome, manifest the disease if a mutation occurs.

Currently, there is no established therapy for AHDS, but clinical trials are ongoing. TRIAC (Triiodothyroacetate, a non-classical thyroid hormone normally produced in the body) is theoretically beneficial, but early clinical studies did not show significant improvement in children, possibly due to late initiation or inadequate dosage. However, a case in 2014 reported significant improvement in intellectual development and mobility with early TRIAC therapy in infancy. A recent study demonstrated the effectiveness and safety of TRIAC therapy.

Case Report

Clinical Diagnosis / Symptoms / History

a) Patient born of a non-consanguineous marriage, showed delayed motor milestones, afebrile fits, poor neck holding, and inability to sit. Lab results indicated elevated ammonia.

b) MRI revealed severe brain changes with enlarged extra-axial spaces, suggesting a metabolic or mitochondrial disorder. Suspected conditions include developmental epileptic encephalopathy, glutaric aciduria, neurometabolic disorder, or mitochondrial disorder.

DNA Test Report

- MedGenome Labs Ltd. Bengaluru, India.
- DNA TEST REPORT - MEDGENOME LABS.
- Gender: Male Sample Type: Blood.
- Date of Birth / Age: 14 months.
- Date of Sample Collection: 8th July 2025.
- Date of Report: 2nd September 2025.
- Test Requested: Whole Exome Sequencing.

Results

Likely Pathogenic Variant Detected Snv(S)/Indels

- Gene# (Transcript) Location Variant Zygosity Disease (OMIM) Inheritance Classification$
- SLC16A2 (+)
- (ENST00000587091.6) Exon 3 c.997del
- (p.Gly334AlafsTer9) Hemizygous Allan-Herndon-Dudley syndrome
- X-linked Pathogenic (OMIM#300523)
- (PVS1,PM2)
- COPY NUMBER VARIANTS CNV(s)
- No significant CNVs detected for the reported symptoms.

Variant Interpretation and Clinical Correlation

Variant (Slc16a2 Gene): A hemizygous single base pair deletion in exon 3 of the SLC16A2 gene was found, resulting in a frameshift and premature truncation of the protein. The variant is damaging and not commonly reported in databases. The reference region is conserved across mammals.

OMIM Phenotype: Allan-Herndon-Dudley syndrome (OMIM#300523) is caused by mutations in the SLC16A2 gene (OMIM*300095). This disorder is characterized by severely impaired intellectual development, dysarthria, athetoid movements, muscle hypoplasia, and spastic paraplegia. Based on the evidence, the SLC16A2 variation is classified as a likely pathogenic variant and should be correlated with clinical symptoms.

Additional variant(s) are listed in the Appendix Table. No other significant variants were detected. Genetic test results are reported following ACMG recommendations. Incidental findings are reported with patient consent.

All samples are processed at MedGenome labs in Bengaluru, India, MedGenome Labs Ltd is located at Sy. Nos. 94/1C and 94/2, Tower 1, Ground Floor, Veerasandra Village, Attibele Hobli, ElectronicCity Phase-1, Electronics City, Bangalore, Bangalore South, Karnataka, India, 560100, MedGenome Inc is located at 348 Hatch Dr, Foster City, CA 94404, United States.

a) Sequencing Metrics: Average sequencing depth: 245x

b) Average on-target percentage: 86.77%

c) Percentage of target base pairs covered at 0x, 5x, and 20x: 0.11%, 99.75%, 98.84%

d) Total data generated: 9.16 Gb

e) Total reads aligned: 99.99%

f) Reads that passed alignment: 87.15%

g) Data Q30: 98.67%

Variant Classification

Pathogenic: Disease-causing variant in a gene that explains the patient's symptoms.

Likely Pathogenic: Variant very likely to contribute to disease development, but additional evidence is needed.

Variant of Uncertain Significance: Variant difficult to classify as pathogenic or benign, further testing may be required.

Transcript Reporting

i. Clinical reporting generally uses the canonical transcript (MANE Select) for reporting clinically relevant variants.

ii. Variants on incomplete or nonsense-mediated decay transcripts will not be reported.

In-Silico Predictions

i. Predictions are based on Variant Effect Predictor (v104) and MutationTaster2 using various databases and tools.

Disease Databases

i. Annotation includes ClinVar, OMIM, HGMD, LOVD, DECIPHER, and SwissVar.

MRI of the Brain

Clinical Findings

a) Severe involutional changes observed with enlargement of bifrontal extra

b) Axial spaces and bilateral sulcal areas.

c) Gliosis present in bilateral periventricular region extending to subcortical regions.

d) Normal grey/white matter differentiation in cerebral hemispheres.

e) Basal ganglia, thalamus, internal and external capsules show normal appearance.

f) No intra- or extra-axial collections detected.

g) Main venous sinuses are patent.

h) Major cerebral arteries show normal caliber and course with preserved signal void.

i) Optic chiasm, optic nerves, pituitary gland, and stalk appear normal.

j) Cerebellar hemispheres, vermis, peduncles, and brainstem show no abnormal intensities.

k) Cerebellopontine angles and internal auditory canal exhibit normal MRI features.

l) Severe involutional changes with enlargement of bifrontal extra-axial spaces, possibly indicative of a metabolic/mitochondrial disorder. Clinical correlation recommended.

EEG Results

Induced Sleep Study Findings

i. Patient sedated with Phenergan syrup for sleep recording.

ii. EEG showed low amplitude background with delta waves (3 Hz/sec) and drug-induced fast activity.

iii. Symmetry was normal.

iv. No sleep spindles, k-complexes, spikes, sharp waves, or spike wave complexes observed.

Photic Stimulation

i. Normal response.

Conclusion

i. Diffuse encephalopathy noted.

Special Chemistry Report

SPECIMEN: SERUM

TEST(s)

T-3, Total

RESULT (s) UNITS

REFERENCE RANGE

197.64 ng/dL

113 - 189

T-4, (Thyroxin)

TSH

2.9 ug/dL

6.2 - 10.3

1.189 pIU/mL

0.7 - 4.2

Discussion

Allan-Herndon-Dudley syndrome (AHDS) is a rare, X-linked inherited syndrome that leads to severe intellectual and motor impairments (1-14). It is caused by mutations in the SLC16A2 gene, which result in a disruption of the thyroid hormone transporter MCT8 (1-14). Symptoms include developmental delays, intellectual disability, muscle hypotonia, spasticity, and movement disorders such as dystonia and chorea (2,3-11,14). As it is an X-linked recessive syndrome, it mainly affects males, while females are often carriers and may show no or mild symptoms. The syndrome is caused by a genetic mutation in the SLC16A2 gene. This gene encodes for the Monocarboxylate Transporter 8 (MCT8), which is important for the transport of thyroid hormones into cells. The defect leads to thyroid hormones not being able to reach the target cells, especially brain cells, properly, resulting in a neurological disorder. The syndrome is inherited in an X-linked recessive manner. Males are significantly more affected than females. In females, a mutation may be present on one of the X chromosomes without clinical symptoms. They are

then considered carriers of the gene. Future research should focus on one-time gene therapy approaches to cure the disease. These genetic attempts are too date in childhood shoes. Further research efforts must evaluate prenatal gene therapeutical treatment approaches to treat the foetus by intrauterine application to diminish early brain disturbances in the foetus [1-14].

Acknowledgement

None.

Conflict of Interest

None.

References

1. Bruschi F, Vaia Y, Antonello CE, Spada M, Porta F, et al. (2025) Altered Dopamine Metabolism and Response to Treatment with Levodopa/Carbidopa in MCT8 Deficiency. Mov Disord.
2. Karlsson JOG (2025) Rationale behind the European Thyroid Association 2024 Guideline to treat the Allan-Herndon-Dudley syndrome with tiratricol? Eur Thyroid J 14(5): ETJ250153.
3. Dubinski I, Debor B, Petrova S, Schiergens KA, Weigand H, et al. (2025) MCT8 Deficiency in Infancy: Opportunities for Early Diagnosis and Screening. Int J Neonatal Screen 11(3): 66.
4. Olivieri A, Vigone MC, Salerno M, Persani L (2025) Is It Time to Expand Newborn Screening for Congenital Hypothyroidism to Other Rare Thyroid Diseases? Int J Neonatal Screen 11(3): 65.
5. Laaraje A, Radi A, Ait Hmadouch S, Abilkassem R (2025) Novel MCT8 mutation: diagnostic value of T3/T4 ratio. J Pediatr Endocrinol Metab.
6. Ge Y, Dou T, Nguyen TU, Yadav GP, Wensel TG, et al. (2025) Structural insights into brain thyroid hormone transport via MCT8 and OATP1C1. Cell 188(20):5576-5588.
7. Lamb YN (2025) Tiratricol: First Approval. Drugs 85(8): 1059-1065.
8. Sonntag N, Schreiner F, Schweizer U, Braun D (2025) Pathogenic MCT8V235L creates a steric clash that is alleviated by a compensating mutation of MCT8F285A. Eur Thyroid J 14(3): e250009.
9. Ludwik KA, Küchler J, Sebinger D, Opitz R, Kühnen P, et al. (2025) Generation of two human induced pluripotent stem cell lines from Allan-Herndon-Dudley syndrome (AHDS) patients with SLC16A2:G401R or SLC16A2: H192R mutation. Stem Cell Res 86: 103725.
10. Lin P, Liu H, Lou J, Lyu G, Li Y, et al. (2025) Novel SLC16A2 Frameshift Mutation as a Cause of Allan-Herndon-Dudley Syndrome and its Implications for Carrier Screening. Pharmgenomics Pers Med 18: 85-94.
11. Ludwik KA, Opitz R, Jyrch S, Megges M, Kühnen P, et al. (2025) Correction of the Allan-Herndon-Dudley syndrome-causing SLC16A2 mutation G401R in a patient derived hiPSC line. Stem Cell Res 85: 103698.
12. Groeneweg S, van Geest FS, Martín M, Dias M, Frazer J, et al. (2025) Mapping variants in thyroid hormone transporter MCT8 to disease severity by genomic, phenotypic, functional, structural and deep learning integration. Nat Commun 16(1): 2479.
13. Joo EY, Yoo MJ, Lee JE, Kim SJ (2025) Diagnostic challenges of Allan-Herndon-Dudley syndrome: a case of hypothyroidism and developmental delay. Ann Pediatr Endocrinol Metab 30(1): 45-47.
14. Çelik N, Demir K, Dibeklioğlu SE, Dündar BN, Hatipoğlu N, et al. (2024) Clinical and genetic characteristics of patients with monocarboxylate transporter-8 deficiency: a multicentre retrospective study. Eur J Pediatr 184(1): 92.