Glycogen Storage Disease, Type IXd

Alternative Names
GSD9D
GSD IXd
Muscle Phosphorylase Kinase Deficiency
Muscle Glycogenosis, X-Linked

Record Category
Disease phenotype

WHO-ICD
Endocrine, nutritional and metabolic diseases > Metabolic disorders

Incidence per 100,000 Live Births
Unknown

OMIM Number
300559

Mode of Inheritance
X-linked recessive

Gene Map Locus
Xq13.1

Description
Glycogen Storage Disease, Type IXd is a disorder characterized by exercise-induced muscle stiffness and pain as well as myoglobinuria. Affected individuals are intolerant to exercise and suffer from muscle weakness and atrophy. Biochemical studies of patients reveal elevated levels of serum creatine kinase while muscle biopsies exhibit increased subsarcolemmal vacuolar glycogen accumulation, mitochondrial paracrystalline inclusions and decreased muscle-specific phosphorylase kinase activity.

GSD9D is a rare condition with only a handful of cases reported thus far. Symptoms usually present in adolescence or adulthood and are induced by intense exercise. The disorder is relatively mild and has a good prognosis, with some patients remaining asymptomatic even till late adulthood.

Diagnosis is confirmed based on clinical findings, laboratory investigations of blood and urine, muscle biopsies and genetic testing of the PHKA1 gene. Patients may benefit from physical therapy and can work with a metabolic nutritionist to optimize blood glucose concentrations. They are also advised to refrain from vigorous exercise and certain medications that can cause rhabdomyolysis such as succinylcholine and statins.

Molecular Genetics
The disorder follows an X-linked recessive pattern of inheritance and is caused by mutations in the PHKA1 gene. This gene encodes the alpha subunit of the muscle-specific phosphorylase b kinase enzyme, which is involved in the glycogen catabolism pathway. Mutations in the PHKA1 gene create a non-functioning phosphorylase kinase enzyme and thus lead to the accumulation of glycogen in muscle cells. Around 7 PHKA1 mutations, including deletions and missense, nonsense and splice site variants, have been identified in Glycogen Storage Disease, type IXd.

Epidemiology in the Arab World
Saudi Arabia
Monies et al. (2017) illustrated the findings of 1000 diagnostic panels and exomes carried out at a next generation sequencing lab in Saudi Arabia. One male patient suffered from dystonic posturing of the upper limbs, spasticity of the lower limbs, failure to thrive, learning disability and leukoencephalopathy. He also reported a family history of this phenotype. Using whole exome sequencing, a homozygous mutation (c.1174C>T, p.R392X) was identified in exon 12 of the patient's PHKA1 gene, associated with Glycogen Storage Disease, type 9D. Given the atypical presentation of the patient, this case helped in the phenotypic expansion of the disorder.

References

Monies D, Abouelhoda M, AlSayed M, Alhassnan Z, Alotaibi M, Kayyali H, Al-Owain M, Shah A, Rahbeeni Z, Al-Muhaizea MA, Alzaidan HI, Cupler E, Bohlega S, Faqeih E, Faden M, Alyounes B, Jaroudi D, Goljan E, Elbardisy H, Akilan A, Albar R, Aldhalaan H, Gulab S, Chedrawi A, Al Saud BK, Kurdi W, Makhseed N, Alqasim T, El Khashab HY, Al-Mousa H, Alhashem A, Kanaan I, Algoufi T, Alsaleem K, Basha TA, Al-Murshedi F, Khan S, Al-Kindy A, Alnemer M, Al-Hajjar S, Alyamani S, Aldhekri H, Al-Mehaidib A, Arnaout R, Dabbagh O, Shagrani M, Broering D, Tulbah M, Alqassmi A, Almugbel M, AlQuaiz M, Alsaman A, Al-Thihli K, Sulaiman RA, Al-Dekhail W, Alsaegh A, Bashiri FA, Qari A, Alhomadi S, Alkuraya H, Alsebayel M, Hamad MH, Szonyi L, Abaalkhail F, Al-Mayouf SM, Almojalli H, Alqadi KS, Elsiesy H, Shuaib TM, Seidahmed MZ, Abosoudah I, Akleh H, AlGhonaium A, Alkharfy TM, Al Mutairi F, Eyaid W, Alshanbary A, Sheikh FR, Alsohaibani FI, Alsonbul A, Al Tala S, Balkhy S, Bassiouni R, Alenizi AS, Hussein MH, Hassan S, Khalil M, Tabarki B, Alshahwan S, Oshi A, Sabr Y, Alsaadoun S, Salih MA, Mohamed S, Sultana H, Tamim A, El-Haj M, Alshahrani S, Bubshait DK, Alfadhel M, Faquih T, El-Kalioby M, Subhani S, Shah Z, Moghrabi N, Meyer BF, Alkuraya FS. The landscape of genetic diseases in Saudi Arabia based on the first 1000 diagnostic panels and exomes. Hum Genet. 2017 Aug;136(8):921-939. PMID: 28600779.

Related CTGA Records

Phosphorylase Kinase, Muscle, Alpha-1 Subunit (OMIM 311870)

External Links

https://rarediseases.org/rare-diseases/glycogen-storage-disease-type-ix/

https://ghr.nlm.nih.gov/condition/glycogen-storage-disease-type-ix#

http://www.orpha.net/consor/cgi-bin/OC_Exp.php?lng=EN&Expert=715

http://www.agsdus.org/

Contributors

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19.09.2017