glycogen storage disease type VII

Glycogen storage disease type VII (GSDVII) is an inherited disorder caused by an inability to break down a complex sugar called glycogen in muscle cells. A lack of glycogen breakdown interferes with the function of muscle cells.

There are four types of GSDVII. They are differentiated by their signs and symptoms and the age at which symptoms first appear.

The classical form of GSDVII is the most common form. Its features usually appear in childhood. This form is characterized by muscle pain and cramps, often following moderate exercise; strenuous exercise can lead to nausea and vomiting. During exercise, muscle tissue can be abnormally broken down, releasing a protein called myoglobin. This protein is processed by the kidneys and released in the urine (myoglobinuria). If untreated, myoglobinuria can damage the kidneys and lead to kidney failure. Some people with the classical form of GSDVII develop high levels of a waste product called uric acid in the blood (hyperuricemia) because the damaged kidneys are unable to remove uric acid effectively. Affected individuals may also have elevated levels of a molecule called bilirubin in the blood that can cause yellowing of the skin and whites of the eyes (jaundice). Individuals with classical GSDVII often have elevated levels of an enzyme called creatine kinase in their blood. This finding is a common indicator of muscle disease.

Infants with the severe infantile form of GSDVII have low muscle tone (hypotonia) at birth, which leads to muscle weakness (myopathy) that worsens over time. Affected infants have a weakened and enlarged heart (cardiomyopathy) and difficulty breathing normally. Individuals with this form of GSDVII usually do not survive past their first year of life.

In the late-onset form of GSDVII, myopathy is typically the only feature. The muscle weakness appears in adulthood, although some individuals have difficulty with sustained exercise starting in childhood. The weakness generally affects the muscles closest to the center of the body (proximal muscles).

The hemolytic form of GSDVII is characterized by hemolytic anemia, in which red blood cells are broken down (undergo hemolysis) prematurely, causing a shortage of red blood cells (anemia). People with the hemolytic form of GSDVII do not experience any signs or symptoms of muscle pain or weakness related to the disorder.

Frequency

GSDVII is thought to be a rare condition; more than 100 cases have been described in the scientific literature.

Genetic Changes

Mutations in the *PFKM* gene cause GSDVII. This gene provides instructions for making one piece (the PFKM subunit) of an enzyme called phosphofructokinase, which plays a role in the breakdown of glycogen. The phosphofructokinase enzyme is made up of four subunits and is found in a variety of tissues. Different combinations of subunits are found in different tissues. In muscles used for movement (skeletal muscles), the phosphofructokinase enzyme is composed solely of PFKM subunits.

In skeletal muscle, the cells' main source of energy is stored as glycogen. Glycogen can be broken down rapidly into the simple sugar glucose when energy is needed, for instance to maintain normal blood sugar levels between meals or for energy during exercise. Phosphofructokinase is involved in the sequence of events that breaks down glycogen to provide energy to muscle cells.

PFKM gene mutations result in the production of PFKM subunits that have little or no function. As a result, no functional phosphofructokinase is formed in skeletal muscles, and glycogen cannot be completely broken down. Partially broken down glycogen then builds up in muscle cells. Muscles that do not have access to glycogen as an energy source become weakened and cramped following moderate strain, such as exercise, and in some cases, begin to break down. In other tissues, other subunits that make up the phosphofructokinase enzyme likely compensate for the lack of PFKM subunits, and the enzyme is able to retain some function. This compensation may help explain why other tissues are not affected by *PFKM* gene mutations. It is unclear why some individuals with GSDVII are affected with more severe forms of the disorder than others.

Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- glycogenosis 7
- GSD VII
- GSD7
- muscle phosphofructokinase deficiency
- PFKM deficiency
- phosphofructokinase deficiency
- Tarui disease

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Glycogen storage disease, type VII
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0017926/

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Muscle Cramps
  https://medlineplus.gov/ency/article/003193.htm
- Encyclopedia: Weakness
  https://medlineplus.gov/ency/article/003174.htm
- Health Topic: Carbohydrate Metabolism Disorders
  https://medlineplus.gov/carbohydratemetabolismdisorders.html
- Health Topic: Muscle Disorders
  https://medlineplus.gov/muscledisorders.html

Genetic and Rare Diseases Information Center

- Glycogen storage disease type 7
  https://rarediseases.info.nih.gov/diseases/5686/glycogen-storage-disease-type-7

Educational Resources

- American College of Rheumatology: Metabolic Myopathies
  http://www.rheumatology.org/I-Am-A/Patient-Caregiver/Diseases-Conditions/Metabolic-Myopathies
- Children's Hospital of Pittsburgh: Glycogen Storage Diseases
  http://www.chp.edu/our-services/transplant/liver/education/liver-disease-states/glycogen-storage-diseases
- Cincinnati Children's Hospital: Glycogen Storage Disease (GSD)
  https://www.cincinnatichildrens.org/health/g/gsd
- Disease InfoSearch: Phosphofructokinase Deficiency
  http://www.diseaseinfosearch.org/Phosphofructokinase+Deficiency/5727
- Duke Children's Hospital & Health Center
  http://www.dukechildrens.org/services/medical_genetics/glycogen_storage_disease_types/#GSD_VII
- Johns Hopkins Medicine: Glycogen Storage Disease
  http://www.hopkinsmedicine.org/healthlibrary/conditions/adult/liver_biliary_and_pancreatic_disorders/glycogen_storage_disease_134,227/
- MalaCards: glycogen storage disease due to muscle phosphofructokinase deficiency
  http://www.malacards.org/card/glycogen_storage_disease_due_to_muscle_phosphofructokinase_deficiency
- Merck Manual Consumer Version: Disorders of Carbohydrate Metabolism
  http://www.merckmanuals.com/home/children-s-health-issues/hereditary-metabolic-disorders/disorders-of-carbohydrate-metabolism
- Muscular Dystrophy Association: Facts About Metabolic Diseases of Muscle
  https://www.mda.org/sites/default/files/publications/Facts_Metabolics_P-207.pdf
- Orphanet: Glycogen storage disease due to muscle phosphofructokinase deficiency
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=371
- Washington University, St. Louis: Neuromuscular Disease Center
  http://neuromuscular.wustl.edu/msys/glycogen.html#pfk

Patient Support and Advocacy Resources

- Association for Glycogen Storage Disease
  http://www.agsdus.org/type-vii.php
- CLIMB: Children Living with Inherited Metabolic Diseases (UK)
  http://www.climb.org.uk/

- Contact a Family (UK): Glycogen Storage Diseases
  http://www.cafamily.org.uk/medical-information/conditions/g/glycogen-storage-diseases/
- National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/glycogen-storage-disease-type-vii/
- The Association for Glycogen Storage Disease (UK)
  http://www.agsd.org.uk/tabid/1139/default.aspx
- The Children's Fund for Glycogen Storage Disease Research
  http://www.curegsd.org/portal/#.Uw4IeoWmCUo

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?term=%22glycogen+storage+disease+type+VII%22+%5BDISEASE%5D+OR+%22Tarui+disease%22+%5BDISEASE%5D+OR+%22phosphofructokinase+deficiency%22+%5BDISEASE%5D+OR+NCT01461304+%5BID-NUMBER%5D+OR+NCT02057731+%5BID-NUMBER%5D

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28glycogen+storage+disease+type+VII%5BTIAB%5D%29+OR+%28Tarui+disease%5BTIAB%5D%29+OR+%28GSD+type+VII%5BTIAB%5D%29+OR+%28phosphofructokinase+deficiency%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

OMIM

- GLYCOGEN STORAGE DISEASE VII
  http://omim.org/entry/232800

Sources for This Summary

- Brüser A, Kirchberger J, Schöneberg T. Altered allosteric regulation of muscle 6-phosphofructokinase causes Tarui disease. Biochem Biophys Res Commun. 2012 Oct 12;427(1): 133-7. doi: 10.1016/j.bbrc.2012.09.024. Epub 2012 Sep 17. Erratum in: Biochem Biophys Res Commun. 2013 Feb 8;431(2):367.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/22995305
- Di Mauro S. Muscle glycogenoses: an overview. Acta Myol. 2007 Jul;26(1):35-41. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17915567
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2949320/

- Musumeci O, Bruno C, Mongini T, Rodolico C, Aguennouz M, Barca E, Amati A, Cassandrini D, Serlenga L, Vita G, Toscano A. Clinical features and new molecular findings in muscle phosphofructokinase deficiency (GSD type VII). Neuromuscul Disord. 2012 Apr;22(4):325-30. doi: 10.1016/j.nmd.2011.10.022. Epub 2011 Nov 30.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/22133655
- Toscano A, Musumeci O. Tarui disease and distal glycogenoses: clinical and genetic update. Acta Myol. 2007 Oct;26(2):105-7. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18421897
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2949577/
- Vives-Corrons JL, Koralkova P, Grau JM, Mañú Pereira Mdel M, Van Wijk R. First description of phosphofructokinase deficiency in spain: identification of a novel homozygous missense mutation in the PFKM gene. Front Physiol. 2013 Dec 30;4:393. doi: 10.3389/fphys.2013.00393. eCollection 2013.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/24427140
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3875906/

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