tibial muscular dystrophy

Tibial muscular dystrophy is a condition that affects the muscles at the front of the lower leg. The signs and symptoms of this condition typically appear after age 35. The first sign is usually weakness and wasting (atrophy) of a muscle in the lower leg called the tibialis anterior. This muscle helps control up-and-down movement of the foot. Weakness in the tibialis anterior muscle makes it difficult or impossible to walk on the heels, but it usually does not interfere significantly with regular walking.

Muscle weakness worsens very slowly in people with tibial muscular dystrophy. Ten to 20 years after the onset of symptoms, weakness may develop in muscles that help extend the toes (long-toe extensors). Weakness in these muscles makes it difficult to lift the toes while walking, a condition known as foot drop. Later in life, about one third of people with tibial muscular dystrophy experience mild to moderate difficulty with walking because of weakness in other leg muscles. However, most affected individuals remain able to walk throughout their lives.

A small percentage of people with tibial muscular dystrophy have a somewhat different pattern of signs and symptoms than those described above. Starting in childhood, these individuals may have generalized muscle weakness, weakness and atrophy of the thigh muscles (quadriceps) or other muscles in the legs, and weakness affecting muscles in the arms.

Frequency

Tibial muscular dystrophy is most common in Finland, where it is estimated to affect at least 10 per 100,000 people. This condition has also been found in people of Finnish descent living in other countries.

Additionally, tibial muscular dystrophy has been identified in several European families without Finnish ancestry.

Genetic Changes

Mutations in the *TTN* gene cause tibial muscular dystrophy. This gene provides instructions for making a protein called titin. Titin plays an important role in muscles the body uses for movement (skeletal muscles) and in heart (cardiac) muscle.

Within muscle cells, titin is an essential component of structures called sarcomeres. Sarcomeres are the basic units of muscle contraction; they are made of proteins that generate the mechanical force needed for muscles to contract. Titin has several functions within sarcomeres. One of its most important jobs is to provide structure,

flexibility, and stability to these cell structures. Titin also plays a role in chemical signaling and in assembling new sarcomeres.

Mutations in the *TTN* gene alter the structure and function of titin. Researchers suspect that these changes may disrupt titin's interactions with other proteins within sarcomeres. Mutations may also interfere with the protein's role in chemical signaling. The altered titin protein disrupts normal muscle contraction, which causes muscles to weaken and waste away over time. It is unclear why these effects are usually limited to muscles in the lower legs.

Inheritance Pattern

This condition is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder.

Other Names for This Condition

- tardive tibial muscular dystrophy
- TMD
- Udd distal myopathy
- Udd-Markesbery muscular dystrophy
- Udd myopathy

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Distal myopathy Markesbery-Griggs type
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1838244/

Other Diagnosis and Management Resources

- GeneReview: Udd Distal Myopathy
  https://www.ncbi.nlm.nih.gov/books/NBK1323

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: Lower Leg Muscles (image)
  https://medlineplus.gov/ency/imagepages/9887.htm
- Health Topic: Muscular Dystrophy
  https://medlineplus.gov/musculardystrophy.html

Additional NIH Resources

- National Institute of Neurological Disorders and Stroke: Foot Drop Information Page
  https://www.ninds.nih.gov/Disorders/All-Disorders/Foot-drop-Information-Page
- National Institute of Neurological Disorders and Stroke: Myopathy Information Page
  https://www.ninds.nih.gov/Disorders/All-Disorders/Myopathy-Information-Page

Educational Resources

- Disease InfoSearch: Distal Myopathy Markesbery-Griggs Type
  http://www.diseaseinfosearch.org/Distal+Myopathy+Markesbery-Griggs+Type/2304
- MalaCards: udd distal myopathy
  http://www.malacards.org/card/udd_distal_myopathy
- Neuromuscular Disease Center, Washington University
  http://neuromuscular.wustl.edu/musdist/distal.html#finnish
- Orphanet: Tibial muscular dystrophy
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=609

Patient Support and Advocacy Resources

- Muscular Dystrophy Association: Facts About Rare Muscular Dystrophies
  https://www.mda.org/sites/default/files/publications/Facts_RareMDs_P-214_0.pdf
- Muscular Dystrophy Canada
  http://www.muscle.ca/
- Muscular Dystrophy UK
  http://www.musculardystrophyuk.org/
- National Organization for Rare Disorders (NORD): Distal Myopathy
  https://rarediseases.org/rare-diseases/distal-myopathy/

GeneReviews

- Udd Distal Myopathy
  https://www.ncbi.nlm.nih.gov/books/NBK1323

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28udd%5BTIAB%5D%29+AND+%28myopathy%5BTIAB%5D%29%29+OR+%28tibial+muscular+dystrophy%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

OMIM

- TIBIAL MUSCULAR DYSTROPHY, TARDIVE
  http://omim.org/entry/600334

Sources for This Summary

- GeneReview: Udd Distal Myopathy
  https://www.ncbi.nlm.nih.gov/books/NBK1323
- Hackman JP, Vihola AK, Udd AB. The role of titin in muscular disorders. Ann Med. 2003;35(6): 434-41.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/14572168
- Hackman P, Marchand S, Sarparanta J, Vihola A, Pénisson-Besnier I, Eymard B, Pardal-Fernández JM, Hammouda el-H, Richard I, Illa I, Udd B. Truncating mutations in C-terminal titin may cause more severe tibial muscular dystrophy (TMD). Neuromuscul Disord. 2008 Dec;18(12):922-8. doi: 10.1016/j.nmd.2008.07.010. Epub 2008 Oct 22.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18948003
- Hackman P, Vihola A, Haravuori H, Marchand S, Sarparanta J, De Seze J, Labeit S, Witt C, Peltonen L, Richard I, Udd B. Tibial muscular dystrophy is a titinopathy caused by mutations in TTN, the gene encoding the giant skeletal-muscle protein titin. Am J Hum Genet. 2002 Sep;71(3): 492-500. Epub 2002 Jul 26.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12145747
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC379188/
- Pollazzon M, Suominen T, Penttilä S, Malandrini A, Carluccio MA, Mondelli M, Marozza A, Federico A, Renieri A, Hackman P, Dotti MT, Udd B. The first Italian family with tibial muscular dystrophy caused by a novel titin mutation. J Neurol. 2010 Apr;257(4):575-9. doi: 10.1007/s00415-009-5372-3. Epub 2009 Nov 13.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19911250
- Udd B, Haravuori H, Kalimo H, Partanen J, Pulkkinen L, Paetau A, Peltonen L, Somer H. Tibial muscular dystrophy--from clinical description to linkage on chromosome 2q31. Neuromuscul Disord. 1998 Jun;8(5):327-32.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/9673987

- Udd B, Partanen J, Halonen P, Falck B, Hakamies L, Heikkilä H, Ingo S, Kalimo H, Kääriäinen H, Laulumaa V, et al. Tibial muscular dystrophy. Late adult-onset distal myopathy in 66 Finnish patients. Arch Neurol. 1993 Jun;50(6):604-8.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/8503797
- Udd B. Distal myopathies. Handb Clin Neurol. 2007;86:215-41. doi: 10.1016/S0072-9752(07)86011-8.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18809003
- Van den Bergh PY, Bouquiaux O, Verellen C, Marchand S, Richard I, Hackman P, Udd B. Tibial muscular dystrophy in a Belgian family. Ann Neurol. 2003 Aug;54(2):248-51.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12891679
- de Seze J, Udd B, Haravuori H, Sablonnière B, Maurage CA, Hurtevent JF, Boutry N, Stojkovic T, Schraen S, Petit H, Vermersch P. The first European family with tibial muscular dystrophy outside the Finnish population. Neurology. 1998 Dec;51(6):1746-8.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/9855539

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