Published on *My46* (https://www.my46.org) 10/16/2021

My46 Trait Profile

Charcot Marie Tooth disease

Other Names: Hereditary motor and sensory neuropathy, Charcot Marie Tooth Hereditary Neuropathy

Charcot Marie Tooth disease includes all inherited peripheral neuropathies. These are conditions that can be passed on from generation to generation that cause problems with the nerves that go from the spine to the feet and hands. Main features include foot drop (difficulty pulling the foot towards the head) and hand weakness.

Characteristics of Charcot Marie Tooth disease

Charcot Marie Tooth (CMT) causes weakness and loss in sensation beginning at the toes and going towards the head. This condition does get worse over time, but symptoms do not usually go above the knees or elbows. CMT causes difficulty walking; without bracing, an affected person needs to pick up the leg from the hip in order to avoid scraping his/her toes across the ground or tripping up steps. People with CMT often have difficulty with balance. They tend to trip with or without falls, sprain their ankles more frequently than others, be thought of as “clumsy” and have difficulty with fine motor tasks such as buttoning a shirt or opening a jar. Other features sometimes seen in CMT include abnormal curving of the spine (scoliosis), hearing loss, and difficulty talking/singing due to the vocal cords not moving well. CMT does not affect intelligence.

Diagnosis/Testing

A person must have an abnormal nerve conduction study (NCS) that shows problems in the nerves to the hands/feet. The NCS sends an electrical pulse down the nerve and then measures the speed and the strength of the signal. If the signal is slow, but relatively strong, there is a problem with the insulation around the nerve – the myelin sheath. If the signal travels quickly but the strength is reduced, there is a problem with the nerve body itself – the axon.

Changes or mutations in over 70 genes have been found to cause CMT. However, the majority of people who have a known genetic type have a mutation in one of four genes: PMP22 (an extra copy (duplication) causes CMT1A), GJB1 (mutations in this gene cause CMT1X), MPZ (mutations in this gene cause CMT1B) or MFN2 (mutations in this gene cause CMT2A).

PMP22 duplications: People with CMT1A have uniformly slowed NCS.

GJB1: NCS show somewhat slowed NCS, with men having slower speeds than women. This gene is located on the X-chromosome (see inheritance pattern explained below). Males have more severe symptoms than women in the family with the same mutation.

MPZ: There are two major groups within CMT1B: early onset, severe CMT with very slow NCS, and later onset, more mild symptoms with NCS showing reduced strength and near-normal speeds.

MFN2: About 90% of people with CMT2A have early onset, severe CMT and need a wheelchair full time by 20 years of age. NCS show normal speeds (when a signal can be found), but with very low strengths.

Outside of these types of CMT, finding the genetic cause can be very difficult. It is best to work with a doctor and/or genetic counselor familiar with CMT to guide genetic testing.

Management/Surveillance

Management of CMT often includes physical and occupational therapies, proper bracing and sometimes orthopedic

surgery. Proper bracing, allowing the foot to be held in a neutral position (i.e., where the foot is straight when it hits the floor) is one of the best ways to protect the joints, prevent ankle rolling and hold the ankle in a stretched position. Most people with CMT will need AFOs (orthotics which go from the foot to the ankle) at some point in their lives to control the foot drop. Usually orthopedic surgery is only used if the foot cannot be moved into a neutral position by hand.

Mode of inheritance

CMT may be inherited in one of three patterns of inheritance: autosomal dominant, autosomal recessive, and X-linked recessive.

Autosomal dominant inheritance:

CMT is most often inherited in an autosomal dominant pattern. This means inheriting one mutation is enough for an individual to be affected and who signs of CMT. The mutation can be inherited from an affected parent or it can occur brand new (de novo) in an affected child.

Autosomal recessive inheritance:

Autosomal recessive means that an individual has to inherit two mutations (i.e., one from each parent) to be affected. If both parents are carriers of a mutation they have a 1 in 4 (25%) chance with each pregnancy of having a child with the condition.

X-linked recessive inheritance:

The gene mutations causing this type of inheritance are found on the X chromosome. An X-linked recessive pattern means that in females, both copies of a gene (i.e., one on each X chromosome) must have a change or mutation, whereas in males, only one copy of a gene must have a mutation to be affected. A female with a mutation in one copy of a gene on the X chromosome is said to be a “carrier” for an X-linked condition, and is typically not affected.

Risk to family members

The risk to family members depends on the pattern of inheritance.

Autosomal dominant inheritance:

The risk to family members depends on whether or not the individual with CMT has a parent affected with CMT. If a parent also has CMT, the risk of having a child with CMT is 50% with each pregnancy. If a parent does not have CMT, the risk of other siblings being affected is very low.

Autosomal recessive inheritance:

Parents of a child with CMT are carriers of CMT. If a sibling of a child with CMT is unaffected, he/she has a 2 in 3 (66%) chance of being a carrier of CMT.

X-linked recessive inheritance:

If a father is affected with CMT, his daughters will be carriers of CMT and his sons will be unaffected. If a mother is a carrier of CMT, each daughter has a 1 in 2 chance (i.e., 50%) of being a carrier and each son has a 1 in 2 chance (i.e., 50%) of being affected with CMT.

Special considerations

None

Resources

Charcot-Marie-Tooth Association
http://www.cmtausa.org
Genetics Home Reference: Charcot Marie Tooth disease
http://ghr.nlm.nih.gov/condition/charcot-marie-tooth-disease

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Created: 08/2013 **Created by:** Carly Siskind, MS, CGC
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