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My46 Trait Profile

Limb girdle muscular dystrophy

Limb girdle muscular dystrophy are a group of muscle diseases characterized by progressive muscle weakness in the arms and legs. It can be caused by mutations in any one of many different genes.

Characteristics of Limb girdle muscular dystrophy

Limb Girdle Muscular Dystrophy (LGMD) is a term used to describe a group of muscle diseases with similar symptoms caused by a large number of different genes that make proteins important in muscle structure, function and repair. The common symptoms seen in most individuals with LGMD include muscle weakness and/or wasting starting at the hip and shoulder girdle muscles. Most LGMDs are progressive and the muscle weakness and wasting advances from the hips, upper thighs, upper arms and shoulders (proximal muscles) to the feet, lower legs, lower arms and hands (distal muscles) by late in the disease course. Usually in the LGMDs, there is no weakness of the muscles of the face. Individuals may receive a general diagnosis of LGMD, which describes their symptoms, but then further studies can be done to determine the subtype of LGMD. The subtype of LGMD will give patients more specific information about other risks (e.g. cardiac) or long-term prognosis.

Diagnosis/Testing

Initial testing in a person suspected to have LGMD often involves measuring an enzyme specifically found in muscles, Creatine Kinase (CK) or Creatine Phosphokinase (CPK). This enzyme is released in to the blood stream when muscles break down. Therefore, people with LGMD usually have elevated levels of CK in the blood.

A muscle biopsy may also be done to diagnose LGMD. A muscle biopsy is when a small piece of muscle is removed from a muscle showing weakness (such as the shoulder or hip muscles) and then studied to look for certain features common to muscular dystrophy (increased connective tissue/degenerating muscle fibers/replacement of muscle tissue by fat tissue). Further studies can be done to measure the presence and amount of certain muscle specific proteins that are known to cause the different subtypes of LGMD when absent or altered in the muscle tissue.

Genetic testing can also be done to try to find changes or mutations in the many genes known to cause LGMD. There are over 20 genes known to cause LGMD. Family history can be helpful to narrow down which genes to test by looking at the inheritance pattern in the family.

Management/Surveillance

The management of a family with LGMD is multidisciplinary and includes neurology, physical/occupational therapy, orthopedics, cardiology, pulmonology, and nutrition. It is recommended that individuals with LGMD be followed closely to monitor any orthopedic problems, cardiac symptoms, scoliosis, breathing problems, and nutrition in order to help maintain a healthy weight.

Individuals with LGMD can be at risk for increased muscle break down (rhabdomyolysis) with excessive exercise. Affected individuals should watch for urine the color of cola (myoglobinuria). If this happens, they should be taken to the emergency room for hydration to avoid kidney damage and/or sudden death. It is frequently recommended that anyone with a muscle disease avoid anesthetic agents due to the risk of malignant hyperthermia (dangerous increase in body temperature).

Mode of inheritance

The LGMDs can be inherited either in an autosomal dominant pattern (LGMD1s) or in an autosomal recessive pattern (LGMD2s). The LGMD1 and LGMD2 subtypes are further defined by a letter that corresponds to a specific gene (e.g. LGMD1C is an autosomal dominantly inherited LGMD caused by a mutation in the CAV3 gene, while LGMD2A is an autosomal recessively inherited LGMD caused by mutations in the CAPN3 gene).

For autosomal dominantly inherited LGMD1s, inheriting one mutation is enough for an individual to be affected and show signs of LGMD. The mutation can be inherited from an affected parent or it can occur brand new (de novo) in an affected child.

For recessively inherited LGMD2's, an individual has to inherit two mutations (i.e., one from each parent) to be affected with LGMD. If both parents are carriers of a mutation, they have a 1 in 4 (25%) chance with each pregnancy of having a child with LGMD.

Risk to family members

The risk to family members depends on whether or not the individual with LGMD1 subtype has a parent affected with LGMD. If a parent also has the condition, the risk of having a child with LGMD is 50% with each pregnancy. If a parent does not have the condition, the risk of other siblings being affected is very low.

Parents of a child with LGMD2 subtype are carriers of LGMD. If a sibling of a child with LGMD is unaffected, he/she has a 2 in 3 (66%) chance of being a carrier of LGMD.

If an individual with LGMD is the only person in their family affected (simplex case), it is very difficult to determine recurrence risks without genetic testing results.

Special considerations

None

Resources

Muscular Dystrophy Association (MDA)
http://mda.org/disease/limb-girdle-muscular-dystrophy/overview
Jain Foundation
http://www.jain-foundation.org
Genetics Home Reference: Limb-girdle muscular dystrophy
http://ghr.nlm.nih.gov/condition/limb-girdle-muscular-dystrophy

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Updated: mm/yyyy **Edited by:** Seema Jamal, MSc, LCGC