Muscular Dystrophy New Zealand

Nemaline Myopathy

Nemaline myopathy is a disorder that primarily affects skeletal muscles, which are muscles that the body uses for movement. People with nemaline myopathy have muscle weakness (myopathy) throughout the body, but it is typically most severe in the muscles of the face, neck, and limbs. This weakness can worsen over time. Nemaline myopathy has an estimated incidence of 1 in 50,000 individuals.

Varieties of Nemaline Myopathy

Nemaline myopathy is divided into six types. In order of decreasing severity, the types are:

- Severe congenital
- Amish
- Intermediate congenital
- Typical congenital
- Childhood-onset
- Adult-onset

The types are distinguished by the age when symptoms first appear and the severity of symptoms; however, there is considerable overlap among the various types. The severe congenital type is the most life-threatening. Most individuals with this type do not survive past early childhood due to respiratory failure. The Amish type solely affects the Old Order Amish population of Pennsylvania and is typically fatal in early childhood. The most common type of nemaline myopathy is the typical congenital type, which is characterized by muscle weakness and feeding problems beginning in infancy. Most of these individuals do not have severe breathing problems and can walk unassisted. People with the childhood-onset type usually develop muscle weakness in adolescence. The adult-onset type is the mildest of all the various types. People with this type usually develop muscle weakness between ages 20 and 50.

Features of Nemaline Myopathy

Affected individuals may have feeding and swallowing difficulties, foot deformities, abnormal curvature of the spine (scoliosis), and joint deformities (contractures). Most people with nemaline myopathy are able to walk, although some affected children may begin walking later than usual. As the condition progresses, some people may require wheelchair assistance. In severe cases, the muscles used for breathing are affected and life-threatening breathing difficulties can occur.

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Diagnosis of Nemaline Myopathy

Diagnosis is based on clinical findings and the observation of characteristic rod-shaped structures (nemaline bodies) on muscle biopsy stained with a special chemical stain called Gomori trichrome.

Management of Nemaline Myopathy

Nemaline myopathy is by a multidisciplinary team who treat the different symptoms that present. Cardiologists, respiratory physicians, nutritionists, physiotherapists, speech language therapists and occupational therapists may all be required at some stage. Make sure you ask for a referral if you think any of these specialists can help you with current symptoms or if things change. It is recommended that:

• Lower respiratory tract infections be treated aggressively
• An evaluation be performed at an early stage of the need for intermittent or permanent use of a mechanical ventilator to prevent insidious nocturnal hypoxia (low blood oxygen levels)
• Effort is put into assuring adequate caloric intake and appropriate nutritional status, this might include special feeding techniques and high-calorie formulas and foods, if indicated
• Standard treatment of gastroesophageal reflux, if present
• Referral to an orthopedist for management of scoliosis and joint contractures
• Physical therapy for maintenance/improvement of function and joint mobility Contractures are muscles or tendons that have remained too tight for too long, thus becoming shorter. Once they occur they cannot be stretched or exercised away.
• Speech therapy if dysarthria (slow or slurred speech) and/or hypernasal speech is present • Assessment of cardiac status because of the low risk of cardiomyopathy (heart disease)

AVOID neuromuscular blocking agents as although nemaline myopathy has not been definitively associated there may be a susceptibility to malignant hyperthermia - a reaction usually triggered by exposure to certain drugs used for general anesthesia.

Also avoid long periods of immobilization after illness or surgery as this can lead to increased muscle weakness.

Genetics of Nemaline Myopathy

Mutations in at least six genes can cause nemaline myopathy. These genes provide instructions for producing proteins that play important roles in skeletal muscles. Within skeletal muscle cells, these proteins are found in structures called sarcomeres. Sarcomeres are necessary for muscles to tense (contract). Many of the proteins associated with nemaline myopathy interact within the sarcomere to facilitate muscle contraction. When the skeletal muscle cells of people with nemaline myopathy are stained and viewed under a microscope, these cells usually appear abnormal. These abnormal muscle cells contain rod-like structures called nemaline bodies.

Mutations in any one of the six genes associated with nemaline myopathy lead to disorganization of the proteins found in the sarcomeres of skeletal muscles. The disorganized proteins cannot interact normally, which disrupts muscle contraction. Inefficient muscle contraction leads to muscle weakness and the other features of nemaline myopathy.

Inheritance of Nemaline Myopathy

The human genome consists of 23 paired chromosomes, which contain genes composed of DNA. 22 pairs of chromosomes are autosomes, meaning they are not involved in sex determination. The 23rd pair of chromosomes are the sex chromosomes, with males having one X and one Y chromosome, and females having two X chromosomes. Nemaline myopathy is usually inherited in an autosomal recessive pattern, which means that both copies of the abnormal gene must be present for the disease to develop fully. Thus, both parents must have the abnormal gene for their child to develop the disease. 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. Each child they have has a 25% chance of inheriting the disease.

Less often nemaline myopathy are inherited in an autosomal dominant fashion, which means that only one copy of the abnormal gene is needed to cause the disease. Children of an affected parent have a 50% chance of inheriting the condition.

Although, most cases result from new mutations in the gene and occur in people with no history of the disorder in their family.

Genetic counselling is available to families who have had a diagnosis of nemaline myopathy (as there are two different inheritance patterns it is important that the diagnosis is correct). This service provides information, helps families understand

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Inheritance patterns and what this means in their family, as well as enabling people to make more informed family-planning decisions.

Further support available

The MDA offers its members a fieldwork service as well as free counselling (conditions apply) and access to the MDA Support Network, which puts you in touch with others in a similar situation. Please contact your local branch or the National Office for more information on how to join. There is also more information and details available on the MDA website www.mda.org.nz

Useful websites

http://www.nemaline.org/ - this page is regularly updated and has links to others and information

http://www.buildingstrength.org/ - this page is dedicated to a cure and also has a care guide for families

Sourced from:
http://ghr.nlm.nih.gov/condition/nemaline-myopathy
http://www.ncbi.nlm.nih.gov/books/NBK1288/