Muscular Dystrophy UK

Fighting muscle-wasting conditions

Nemaline myopathy

Overview

Nemaline, or rod, myopathies are a group of conditions which fall under the umbrella of congenital myopathies. They are characterised by rod-like structures in the muscle cells, and clinical features such as muscle weakness, breathing problems, and feeding problems. There are six sub-groups which are defined according to age of onset and severity.

Around one in 50,000 individuals are estimated to be affected, and these include both males and females. In the majority of cases (90 percent) the condition becomes apparent at birth or early childhood, although in very rare cases, it does not become apparent until adulthood. There is currently no effective treatment or cure to halt the progression, but management of the condition is very important and includes physiotherapy, and where necessary the use of ventilation and/or a feeding tube.

Symptoms

There are six sub-groups of nemaline myopathy, which are defined based on age of onset and severity of condition, although there is a high degree of overlap between the conditions. There does not seem to be a correlation between severity of the condition and the gene which has the mutation. Although heart problems are not common in people with a rod myopathy, it is important that cardiac function is regularly monitored.

The progression of these conditions is variable, and some may progress more quickly than others. Generally it is accepted that the earlier the onset, the more severe the condition. For children who live beyond the early years, only some will lose the ability to walk. Respiratory function is thought to improve over time, with the most severe problems occurring earlier in life.

Severe congenital form

- Onset at birth
- Severe floppiness and muscle weakness

- Little spontaneous movement
- Difficulties with sucking and swallowing
- Severe breathing problems
- Death usually occurs early

Amish nemaline myopathy

- Onset at birth
- Floppiness/hypotonia
- Contractures/tightening of joints
- Breathing problems
- Death usually within two years of life

Intermediate congenital form

- Onset at birth
- Severity in between severe and mild forms
- Early development of contractures/tightening of joints
- Delayed motor milestones
- Independent breathing at birth
- Use of ventilatory support and/or wheelchair by 11 years

Typical (mild) congenital form

- Onset between birth to one year
- Floppiness/hypotonia
- Weakness in muscles closest to trunk, and sometimes spreading to more distal muscles
- Feeding difficulties
- Some respiratory weakness, but less severe than other forms

Childhood-onset

- Onset between 8 and 15 years
- Early motor development normal
- Symmetrical weakness of ankle, including foot drop
- Slowly progressive weakness with eventual involvement of all ankle movement
- Motor development normal

Adult-onset

- Onset between 20 to 50 years
- Generalised weakness with rapid progression
- Muscle pain

- Sometimes severe neck weakness
- Usually no previous family history

Causes

In the majority of cases, a rod myopathy is inherited, although there are sometimes sporadic cases where there are no other family members affected. There have been mutations identified in five different genes, which cause rod myopathies. The protein products of all of these genes are involved in muscle tone and contraction.

ACTA1 – This gene produces a protein called α- actin. Mutations in this gene account for around 15 to 25 percent of cases. Errors in this gene are inherited in an autosomal dominant or autosomal recessive pattern.

NEM2 – The product of this gene is a protein called nebulin. It is thought that mutations in this gene are a common cause of nemaline myopathy but definite statistics are unavailable. Mutations in this gene are inherited in an autosomal recessive pattern.

TPM3 – The product of this gene is a protein called α- Tropomyosin 3. Mutations in this gene account for only two to three percent of affected individuals, and are inherited in an autosomal dominant or autosomal recessive pattern.

TPM2 – This gene encodes a protein called β-Tropomyosin. Only very few individuals have been identified with errors in this gene. Inheritance is in an autosomal dominant pattern.

TNNT1 – This gene produces a protein called Troponin 1. Errors in this gene have only been identified in a population of Old Order Amish individuals. Inheritance is in an autosomal recessive pattern.

Diagnosis

Generally, diagnosis is made through a muscle biopsy, however this can also be done through molecular testing, prenatal diagnosis and carrier testing.

Muscle biopsy – Generally, diagnosis is made through a muscle biopsy. A sample of muscle is taken, and examined under a microscope. This is done in one of two ways: either a small piece of muscle is taken under general anaesthetic or a needle biopsy is performed to remove a small sample. Muscle from people affected by nemaline myopathy has a distinctive pattern with thin thread- or rod-like structures in the muscle cells. It is important to note that these structures are also seen in other, unrelated conditions. For this reason, the muscle sample must be considered along with the physical signs and/or molecular tests, in order for a diagnosis of nemaline myopathy to be made. See our factsheet on muscle biopsies.

Molecular testing – In families where the mutation is known to occur in the gene for α- actin, molecular testing is available. This involves taking a blood sample and analysing the DNA for the presence of a mutation. The gene is 'read' from end to end, and this sequence is compared to a normal α- actin sequence. This process can take several weeks to complete. Once this error has

been identified in one family member, it is possible to use this sequence to diagnose other family members.

Prenatal diagnosis – Prenatal diagnosis is available for families where the mutation has been identified as being in the gene for α- actin, and the precise nature of the mutation established. The technique is described in the section 'Molecular testing', but there are two ways to obtain samples for testing:

- Amniocentesis is traditionally performed at 15 to 17 weeks into the pregnancy. Using ultrasound to visualise, a needle is inserted through the abdominal wall, and a sample of the fluid surrounding the baby (amniotic fluid) is taken.
- Chorionic villus sampling (CVS) is carried out at 10 to 11 weeks. This involves taking a sample of tissue from the placenta. Results are available earlier using this technique than amniocentesis, but the rate of spontaneous abortion is slightly higher.

Carrier testing – As with prenatal diagnosis, carrier testing is currently only available for families where a mutation in the α- actin has been identified and characterized.

Treatment

There is currently no effective treatment to halt the progression of the nemaline myopathies, but management of the condition is very important for prolonging life.

Night-time ventilation – Breathing problems are common with the nemaline myopathies, and thus respiratory function should be regularly monitored. A decrease in oxygen intake can lead to, among other things, headaches, breathlessness, poor appetite and disturbed sleep. Night-time ventilation involves the use of a face mask attached to a small machine, which assists in breathing. This aids the muscles that control breathing, and allows a greater intake of oxygen. Night-time ventilation may be beneficial to people with a rod body myopathy, but this should be discussed fully with a consultant to determine whether it is appropriate.

Feeding tube (or gastrostomy) – This is a tube that goes into the stomach through the stomach wall and enables a person to be given food and fluids by passing them directly into the stomach via the tube. People with a myopathy may have problems with swallowing, which can lead to choking and inhalation of food. This can result in chest infections. A feeding tube prevents this from happening. There are a number of different types of feeding tube that are available, and these are fitted by a short surgical procedure. See our factsheet on Gastrostomy.

Physiotherapy – The primary aim of an individual with a neuromuscular condition is to increase or at least maintain function and mobility. Physiotherapy can assist in doing this, and it can also maintain breathing capacity, delay the onset of curvature of the spine (scoliosis), and help prevent the development of contractures. It is important that the physiotherapist involved is familiar with the treatment of people with neuromuscular conditions.

Exercise – There is debate over whether people with neuromuscular conditions should undertake strenuous physical exercise. Some say that putting additional strain on already weakened muscles will cause additional harm, while others believe the exercise may increase muscle strength. Insufficient evidence exists to support either, but it is believed that moderate non-weight bearing exercise such as swimming, walking or pedalling may be the best solution. This sort of aerobic exercise helps to maintain a healthy cardiovascular system and a steady weight. It is however important that this is discussed fully with a clinician.

Antibiotics – Chest infections are common with the nemaline myopathies and complications with breathing can lead to a variety of other problems, including lethargy, headaches, and poor appetite. Antibiotics are used to treat chest infections. There are a variety of antibiotics available, and a GP will be able to advise on the most suitable. If there is a tendency towards chest infections, it is worth considering pneumovax (prevenar in children under two years) and the flu vaccine.

Currently there is no cure for the nemaline myopathies. However, much research is currently being conducted into the myopathies, including the rod body myopathies. Although there is no effective treatment to halt the progression, there are a couple of different ways in which to manage the symptoms of the nemaline myopathies, as outlined above.

Researchers worldwide are exploring many avenues in an attempt to develop more effective treatments and, it is hoped, a cure. The research department at Muscular Dystrophy UK regularly monitors research advances in the congenital myopathies, and sends updates to members when significant scientific advances occur.

Other things to consider

Anaesthetics – It has now been recognised that the use of both local and general anaesthetics in people with neuromuscular conditions can cause a variety of different problems. Although anaesthetics are generally well-tolerated by people with a nemaline myopathy, owing to the nature of the anaesthetic drugs used, problems can include dysfunction of the heart and relaxation of the muscles around the lungs, causing problems with breathing. Generally if a patient is properly assessed and monitored, the risks associated with anaesthetic use are low, but it is very important that the medical professionals involved are fully aware of the muscle condition.

Medical alert card – It is very important that health professionals are aware of your condition, should you require treatment. There are often issues they will have to consider. Many companies are able to provide a Medic Alert Card, which can be carried to advise of any medical condition. These come in the form of bracelets, pendants, etc and carry essential information. Please contact the Care and Support team for details of companies that produce alert cards.

Pregnancy – Pregnancy and delivery are generally well-tolerated in mothers with nemaline myopathy. It is, however, important to monitor breathing and heart function, and consideration should be given to any muscle weakness of contractures, which may complicate the delivery.

Disclaimer

If you have feedback about this factsheet or want to request references, please email info@musculardystrophyuk.org.

Here for you

The friendly staff in the care and support team at the Muscular Dystrophy UK's London office are available on 0800 652 6352 or info@musculardystrophyuk.org.

Version: 02 / Date published: 1 August 2008 / Original author: MDC Research Department, in association with Dr Ros Quinlivan, Consultant Paediatrician / Updated: 1 April 2008 / Updated by: / Date of review: 1 November 2011