Muscular Dystrophy UK

Fighting muscle-wasting conditions

GNE myopathy (GNEM)

Overview

GNEM is a distal myopathy; a very rare, genetic condition that causes gradual progressive muscle weakness

It is also known as hereditary inclusion body myopathy (HIBM), quadriceps-sparing myopathy (QSM), distal myopathy with rimmed vacuoles (DMRV), Nonaka myopathy or hereditary inclusion body myopathy type 2.

How rare is it?

It is a very rare condition. The worldwide prevalence of GNE myopathy is estimated to be one person in a million.

Symptoms

GNEM leads to weakness and wasting of muscles in the legs and arms.

The first symptoms normally occur in young adults (usually in their 20s or 30s). It is also possible to have an earlier or later onset of the condition, but that is rare. Initial signs of GNEM can include foot drop, which may lead to frequent tripping and difficulty in climbing stairs. Foot drop is dropping of the forefoot because of muscle weakness.

The severity and rate of progression are highly variable, even within families where more than one person is affected. The condition can worsen over time. As the condition progresses, it may lead to weakness in the upper leg muscles, leading to difficulty in climbing stairs or rising from a chair.

A person with GNEM may also eventually experience weakness in their hands and shoulder muscles. Quadriceps muscles, however, typically remain unaffected, even in late stages. People with GNEM generally experience increased disability and loss of ability to walk in later life.

The condition doesn't usually affect the heart or respiratory muscles, or speech and swallowing.

Causes

GNEM is caused by mutations (a mutation is a mistake in a gene that leads to a disorder or condition) in the GNE gene, which contains the instructions to make an enzyme called glucosamine (UDP-N-acetyl)-2-epimerase/N-acetylmannosamine kinase.

This has a key role in the production of sialic acid in the body. Sialic acid is a sugar that gets incorporated into several molecules important for cell function, including proteins and lipids. The gene may also have other roles important for muscle contraction. (Studies are currently underway.)

People with GNEM have a deficiency of sialic acid in the muscle cells. Researchers don't understand fully how this leads to muscle weakness, but it could be that insufficient sialic acid affects the function of certain proteins in the muscle.

How is it inherited?

GNEM is inherited in a 'recessive' manner, which means that both copies of the GNE gene have to be mutated for someone to have the condition. If only one copy of the gene is mutated, that person is a carrier and will not have symptoms. When two carriers have a child together, there is a:

- 25 percent chance that the child will have inherited both mutated copies of the GNE gene and will develop GNEM
- 50 percent chance that the child will inherit only one mutated copy and thus be a carrier
- 25 percent chance that the child will inherit two healthy copies, so will neither have the condition nor be a carrier.

For more information on inheritance, please read our Inheritance and genetics factsheet.

How will my children be affected?

Children of a person with a diagnosis of GNEM are likely to have one mutated copy of the GNE gene and thus be carriers. This means they won't have GNE myopathy or any signs of muscle weakness. Carrier genetic testing is available to confirm the presence or absence of GNE mutations in your children. This could be advisable if you and your partner are close relatives. You can get a referral for genetic counselling through your GP.

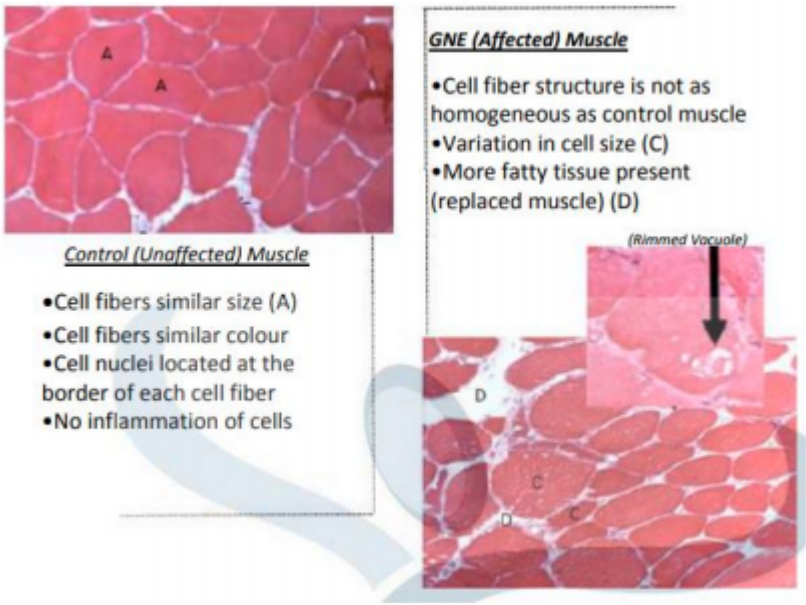
For more information, see our Genetic counselling and family planning factsheets.

Diagnosis

There are certain signs and symptoms that may prompt clinicians to suspect a diagnosis of GNEM: a characteristic gait (type of walk), or weakness in certain muscles only, for example.

A muscle biopsy will help in the diagnosis. It involves taking a small sample of muscle and studying its structure under the microscope (read our Muscle biopsies factsheet for more information).

Muscle affected by GNEM has a characteristic appearance under the microscope; there are circular structures called 'rimmed vacuoles' inside the muscle cells.



Your consultant may wish to carry out magnetic resonance imaging (MRI) on the leg muscles to see which muscles are affected and to what extent. If the pattern of muscle involvement on MRI is typical for GNEM, this can be helpful in recognising the condition earlier, and therefore requesting gene testing earlier. The MRI scan is non-invasive and painless, and is becoming more widely used to test for various muscle disorders.

A genetic test is essential to confirm a diagnosis of GNEM. This involves having a small sample of blood taken and sent off to a diagnostic laboratory. There, they will extract DNA from the blood and test it for the presence of mutations in GNE. For more information, please read our Diagnostic tests factsheet.

Treatment

Currently, there is no approved treatment for GNEM. Several researchers are working on developing therapies aiming to increase sialic acid levels in the muscle.

Others are investigating potential therapies that correct the mutated GNE gene. If you want to know more about this research or take part in clinical studies, you can join the GNEM registry at www.gne-registry.org.

Current management of the condition aims to improve quality of life through physiotherapy, assistive devices for walking (for example, ankle or foot orthoses), pain management (if needed) and social and emotional support. It's recommended that people with GNE myopathy, who use a wheelchair on a daily basis, have the seasonal annual flu and the five-yearly pneumococcal jab.

What is the prognosis?

The condition progresses slowly, but this varies between individuals. Many people with GNEM will need to use a wheelchair in later life; for some, this may be seven to 10 years after the onset of symptoms, for others this may be 20 or more years.

Maintaining a healthy lifestyle and having physiotherapy or hydrotherapy (with caution to avoid over exercising, muscle aches and tiredness) might help to delay the need for a wheelchair. But a wheelchair may eventually be useful in maintaining your independence and help to reduce fatigue.

Disclaimer

While every reasonable effort is made to ensure that the information in this document is complete, correct and up-to-date, this cannotbe guaranteed and Muscular Dystrophy UK shall not be liable whatsoever for any damages incurred as a result of its use. MuscularDystrophy UK does not necessarily endorse the services provided by the organisations listed in our factsheets.

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: 01 / Date published: 1 June 2018 / Original author: Dr Oksana Pogoryelova / Updated: 1 January 1970 / Updated by: / Date of review: 1 January 1970