Sarcoglycanopathies: LGMD2C, LGMD2D, LGMD2E and LGMD2F

[“LGMD – limb girdle muscular dystrophy”]

What are LGMD2C (γ-sarcoglycan deficiency); LGMD2D (α-sarcoglycan deficiency); LGMD2E (β-sarcoglycan deficiency); and LGMD2F (δ-sarcoglycan deficiency)?

These conditions are also known as sarcoglycanopathies. LGMD2C, 2D, 2E and 2F are autosomal recessive forms of limb-girdle muscular dystrophy (LGMD). The age of onset of muscle weakness is variable but most commonly happens in childhood, but can also occur in early adulthood. These forms of LGMD were previously called ‘autosomal recessive muscular dystrophy on childhood’.

What causes these conditions?

Sarcoglycanopathies are a group of limb girdle muscular dystrophies (LGMD) caused by faults in one of the four genes which give instructions to produce four proteins (sarcoglycans) important to the muscle fibres. Each type of sarcoglycanopathy is genetically different but people have similar symptoms.

How is it diagnosed?

The diagnosis can be suspected by findings on a muscle biopsy or when a doctor experienced in muscular dystrophy examines you. A serum creatine kinase (CK) blood test may also show raised levels which indicate a problem in the muscles.

The muscle biopsy usually shows a deficiency of the involved proteins and can be helpful to identify the specific gene responsible of the symptoms.

The diagnosis has to be confirmed by identifying the mutated gene (γ-SG, α-SG, β-SG, δ-SG gene) which is done on a DNA sample from a blood test.

Sarcoglycan genes are large genes and sometimes genetic analysis of all four genes is necessary, so testing is very lengthy and results may not be available for many months.
Is there a treatment or a cure?
To date there are no specific treatments for sarcoglycanopathies, however careful management of the symptoms of the condition can improve a person’s quality of life.

Keeping mobile is important for all people affected by muscular dystrophy. There are no guidelines about the type or intensity of activities however it is recommended that any exercise undertaken is done within your limitations and ensuring you remain comfortable. Extreme tiredness, muscle pain and cramps during or after activities can mean that you have pushed yourself too hard and therefore those activities should be avoided. Swimming is a good activity because it promotes movement of all muscles without increased strain.

Joint contractures (tightening) can occur in sarcoglycanopathies and therefore regular physiotherapy is recommended. This can be carried out by a physiotherapist or people can be taught to do this by themselves in their own home. These types of exercise can include the stretching of all joints, in particular the ankles, knees and elbows. If ankle contractures impair mobility, referral for an orthopaedic opinion may be indicated. Orthoses (splints) are sometimes worn day or night to enhance good positioning of the ankle joints. In the case of severe contractures, minor surgical procedures may be necessary.

People with sarcoglycanopathies are at risk of developing breathing difficulties. Therefore regular monitoring of respiratory function (forced vital capacity – FVC) is recommended for identifying any problems early on and treat them if necessary. Sometimes overnight studies are indicated (pulse oximetry) and people may benefit from treatment with assisted ventilation at night.

All people affected by sarcoglycanopathies should have the pneumovax vaccination and annual flu immunisation to prevent serious chest infections.

Because of the risk of problems with the heart in sarcoglycanopathies, regular heart checks are required and these should include an electrocardiogram (ECG) and echocardiogram. Many treatments are available and these will be discussed with you by a cardiologist.

What is the prognosis?
People with sarcoglycanopathies often have initial symptoms of weakness and wasting (loss of muscle bulk) in the hip, thigh and shoulder muscles. This weakness is usually even on both sides of the body. Leg weakness can result in frequent falls, toe-walking or in a particular ‘waddling gait’ (swaying from side to side). This can also cause people to have hyperlordosis (arched back) and scoliosis (curved spine). People can have difficulty in running, climbing stairs and rising from the floor. As the condition progresses, mobility may become increasingly difficult.
Shoulder and arm weakness can lead to difficulties in raising the arms above the head and in lifting objects, and shoulder blade winging may be present (scapular winging). Some people may complain of muscle pain and cramps, especially in the legs. Calf hypertrophy (large calves) and macroglossia (large tongue) can be present. People with sarcoglycanopathies can develop joint contractures (tightening), most frequently involving the ankles.

Facial and neck muscles are not usually involved and therefore swallowing problems are unlikely.

People with sarcoglycanopathies are at risk of heart and breathing problems. These problems can occur even when weakness is mild, however, as the condition progresses, heart and breathing involvement tend to increase.

Heart involvement is more frequent in people affected by LGMD2E (β-sarcoglycanopathy), while LGMD2D is rarely associated with heart problems.

People with heart problems can experience symptoms of breathlessness and tiredness. However, some people can have heart problems even when they do not show symptoms.

Breathing problems are common in sarcoglycanopathies, but this is usually after losing the ability to walk (loss of ambulation). The first symptoms of breathing involvement can include poor sleep, nightmares, tiredness or headaches after waking up in the morning, lack of appetite and falling asleep during the day.

Sarcoglycanopathies are variable conditions in terms of severity. The weakness is always progressive with time although the rate of progression varies from person to person. Many people show a relatively rapid deterioration of weakness, resulting in loss of ambulation in early adulthood. Consequently, wheelchair use may be required with progression of the condition. LGMD2D is usually milder than LGMD2E and 2C.

Life expectancy is into adulthood and depends upon the identification and treatment of the associated involvement of the heart and the breathing muscles.

We’re here for you at the point of diagnosis and at every stage thereafter, and can:

- give you accurate and up-to-date information about your or your child’s muscle-wasting condition, and let you know of progress in research
- give you tips and advice about day-to-day life, written by people who know exactly what it’s like to live with a muscle-wasting condition
- put you in touch with other families living with the same muscle-wasting condition, who can tell you about their experiences
This factsheet is under review, due for updating later in 2017. If you have any queries, please contact us.

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The clinical neuromuscular team at the Institute of Genetic Medicine, Newcastle upon Tyne, incorporating the National Specialised Commissioning Team service for the limb girdle muscular dystrophies. Clinical neuromuscular team at Newcastle upon Tyne: Professor K.M.D. Bushby MD FRCP, Professor of Neuromuscular Genetics; Professor V. Straub MD, Professor of Neuromuscular Genetics; Professor H. Lochmuller MD, Professor of Experimental Myology; Dr M. Eagle, Consultant Physiotherapist; Dr M. Guglielmi, Senior Research Associate, Honorary Consultant Geneticist; L. Hastings, Neuromuscular Nurse Specialist; A. Sarkozy, Specialty Doctor in Neuromuscular Genetics.

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 from 8.30am to 6pm Monday to Friday to offer free information and emotional support.

If they can’t help you, they are more than happy to signpost you to specialist services close to you, or to other people who can help.

www.musculardystrophyuk.org

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