

Sarcoglycanopathies: LGMD2C, LGMD2D, LGMD2E and LGMD2F

LGMD2C (γ -sarcoglycan deficiency); LGMD2D (α -sarcoglycan deficiency); LGMD2E (β -sarcoglycan deficiency); LGMD2F (δ -sarcoglycan deficiency) 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 is in childhood. Onset can also occur in early adulthood. These forms of LGMD were previously called “autosomal recessive muscular dystrophy on childhood”.

What causes it?

Sarcoglycanopathies are a group of limb-girdle muscular dystrophies (LGMD) caused by faults in one of the 4 genes which give instructions to produce 4 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 faulty gene (α -SG-, β -SG, γ -SG-, δ -SG gene) which is done on a DNA sample from a blood test.

Because sarcoglycan genes are large genes and sometimes genetic analysis of all 4 genes is necessary, testing is very lengthy and results may not be available for many months.

What symptoms are common?

People with Sarcoglycanopathy 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 walking with “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 becomes increasingly more difficult.

Shoulder and arm weakness can lead to difficulties in raising the arms over 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) and more frequently they involve the ankles.

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

People with sarcoglycanopathy 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 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.

What are the implications of the diagnosis?

Inheritance

Sarcoglycanopathies are autosomal recessive conditions caused by changes in a gene. People affected with these conditions have 2 faulty copies of one of sarcoglycan genes, one inherited from each parent. This means that both parents must be carriers but remain healthy.

The exact frequency of sarcoglycan gene faults in the population is not known but they are rare conditions. Therefore, people with Sarcoglycanopathy rarely have affected children (for the risk of meeting and having a child by a carrier of the same faulty gene will be very unlikely unless you have a partner to whom you are related). Children of people affected with sarcoglycanopathy will have inherited one faulty copy of one of the sarcoglycan genes and therefore will all be carriers but are unaffected.

Consequently, carrier testing is not generally available unless the risks are increased due to intra-familial marriage.

Progression and complications

Sarcoglycanopathies are quite 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 usually is 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.

Treatment and management

So far there are no specific treatments for sarcoglycanopathies, however managing the symptoms of the condition improves a person's quality of life.

Keeping mobile is important for all people affected with muscular dystrophy. There are not any guidelines about the type or intensity of activities however it is recommended that any exercise undertaken is done within a person's limitation and remains comfortable. Extreme tiredness, muscle pain and cramps during or after activities can mean that a person has pushed himself too hard and therefore 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 exercises 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 (FVC) is recommended in order to prematurely identify any problems and treat them if necessary. Sometimes overnight studies are indicated (Pulse Oximetry) and people may benefit from treatment with assisted ventilation at night.

Pneumovax vaccination and annual flu immunisation should be performed in people affected by sarcoglycanopathies in order 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 ECG and Echocardiogram. Many treatments are available and these will be discussed with you by a cardiologist if necessary.

Other relevant factsheets from the Muscular Dystrophy Campaign

The Limb Girdle Muscular Dystrophies (LGMD)

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