

Limb-girdle muscular dystrophy 2I (LGMD 2I)

LGMD 2I

LGMD 2I is an autosomal recessive form of limb-girdle muscular dystrophy (LGMD). It is one of the most common forms of LGMD, especially in Northern Europe. The age of onset of muscle weakness is extremely variable; the most common being between 10 and 20 years of age. It can also range between 2 to 40 years.

What causes it?

LGMD 2I is caused by faults in the Fukutin Related Protein gene (FKRP), which gives instructions to produce a protein important to the muscle fibres. Faults in the Fukutin Related Protein gene (FKRP) cause limb-girdle muscular dystrophy type 2I (LGMD2I), as well as a form of severe congenital muscular dystrophy (MDC1C).

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 diagnosis has to be confirmed by identifying the faulty gene (Fukutin Related Protein gene) which is done on a DNA sample from a blood test. This is often done following a clue from the muscle biopsy or examination.

What symptoms are common?

People with LGMD2I 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 and leg involvement is present before shoulder and arms. This 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). 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. Some people may complain of muscle pain and cramps, especially in the legs, even before the onset of muscle weakness.

Calf hypertrophy (large calves) and macroglossia (large tongue) can be present.

People with LGMD2I 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. Unlike congenital muscular dystrophy type 1C, learning difficulties and eye problems are not features of LGMD type 2I.

People with LGMD2I 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.

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 LGMD2I and these may occur before 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. As LGMD2I can involve the diaphragm, the first symptoms may be difficulty in breathing when lying flat.

What are the implications of the diagnosis?

Inheritance

LGMD2I is an autosomal recessive condition caused by changes in a gene. People affected with this condition have 2 faulty copies of the Fukutin Related Protein gene; one inherited from each parent. This means that both parents must be carriers but remain healthy.

The exact frequency of the Fukutin Related Protein gene faults in the population is not known but there is a particular fault which tends to recur relatively frequently, especially in the North European populations. Genetic carrier testing is available for this common fault, because the risk of meeting and having a child by a carrier of this common faulty gene is slightly increased. However we can not rule out that a person could carry a different fault in the same gene in which case, there is no genetic carrier testing available because the risk of meeting and having a child by such a carrier would be very unlikely.

To summarise, carrier testing is only available for the common fault for LGMD2I. Carrier testing of the whole gene is available only when the risks are increased due to intra-familial marriage.

Children of people affected with LGMD2I will have inherited one faulty copy of the Fukutin Related Protein gene and therefore will all be carriers but are unaffected.

Progression and complications

LGMD2I is quite a variable condition in terms of severity. The weakness is always progressive with time although the rate of progression varies from person to person. Some people may be only mildly affected, where as others may show a relatively rapid deterioration of weakness, resulting in loss of independent ambulation in early adulthood.

Life expectancy and quality of life depends upon the identification and treatment of the associated complications such as heart and breathing problems.

Treatment and management

So far there are no specific treatments for LGMD2I, 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 LGMD2I 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 LGMD2I are at risk of developing breathing difficulties. Therefore regular monitoring of respiratory function (FVC), in lying as well as sitting, is recommended in order to 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 LGMD2I in order to prevent serious chest infections.

Because of the risk of problems with the heart in LGMD2I, 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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