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

LGMD 2A (also known as Calpainopathy)
LGMD 2A is an autosomal recessive form of limb-girdle muscular dystrophy (LGMD). It is one of the most common forms of LGMD. The age of onset of muscle weakness is extremely variable; the most common being between 8 and 15 yrs, though it can range between 2 to 50 years.

What causes it?
LGMD 2A is caused by faults in the calpain 3 gene, which gives instructions to produce a protein important to the muscle fibres.

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 (Calpain 3 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 LGMD2A 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 can result in frequent falls, difficulty in running, climbing stairs and rising from the floor. As the condition progresses, people can have problems with walking.

Shoulder and arm weakness can lead to difficulties in raising the arms over the head and shoulder blade winging may be present (scapular winging). Some people complain of muscle pain, especially in the legs. Joint contractures (tightening) may be present and more frequently involve the ankles. Facial and neck muscles are not usually involved and therefore swallowing problems are unlikely.

Heart problems are not reported in this condition. Patients with LGMD2A are at risk of developing respiratory muscle weakness and experience breathing difficulties with the progression of the condition, but this is usually a very late complication.

What are the implications of the diagnosis?

Inheritance
LGMD2A is an autosomal recessive condition caused by a change in a gene. People affected with this condition have 2 faulty copies of the Calpain 3 gene; one inherited from each parent. This means that both parents must be carriers but remain healthy.

The exact frequency of Calpain 3 gene faults in the population is not known but it is a rare condition. Therefore, people with LGMD2A 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 LGMD2A will have inherited one faulty copy of the Calpain 3 gene and therefore will all be carriers but are unaffected.

Consequently, carrier testing is not generally available unless the risks are increased due to intrafamilial marriage.
Progression and complications
LGMD2A is quite a variable condition in terms of severity and the weakness is always progressive with
time although the rate of progression varies from person to person. The course of the condition can be
mild and wheelchair use may be required many years after onset.

Life expectancy is generally within a normal range because the heart and breathing muscles are
usually not affected. In later stages of the condition, breathing difficulties can occur but are usually
less severe than in other muscular dystrophies. These symptoms can include; poor sleep, nightmares,
tiredness or headaches after waking up in the morning, lack of appetite and falling asleep during the
day.

Treatment and management
So far there are no specific treatments for LGMD2A, 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 LGMD2A 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.

With progression of the muscle weakness, people with LGMD2A are at risk of developing breathing
difficulties. Therefore regular monitoring of respiratory function (FVC) is recommended. Sometimes
overnight studies are indicated (Pulse Oximetry).

Regular cardiac assessment is usually not required because there is no involvement of the heart
muscle in this condition.

Other relevant factsheets from the Muscular Dystrophy Campaign
The limb-girdle muscular dystrophies (LGMD)

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