SEPN1-related myopathy

What is SEPN1-related myopathy?

SEPN1-related myopathy (including subtypes previously referred to as rigid spine congenital muscular dystrophy or RSMD1 and minicore myopathy) is caused by changes in the gene *SEPN1*, which is responsible for the production of a protein called selenoprotein N (SEPN1).

SEPN1-related myopathy, a subtype of congenital muscular dystrophy, has specific features including:

- the spine is 'rigid' or 'stiff' and can have an S-shaped curvature (scoliosis)
- muscle weakness is relatively mild compared to other forms of congenital muscular dystrophy and mainly involves the 'axial' muscles (muscles of the neck and trunk) and, to a lesser extent, the limbs
- respiratory insufficiency develops before adulthood with the need for night-time non-invasive ventilation typically evident while individuals remain ambulant.

What are the first signs?

Children with SEPN1-related myopathy often have hypotonia (low muscle tone, floppiness) at birth. They may have difficulty in achieving motor milestones such as head control, sitting unaided, crawling or walking.

Is SEPN1-related myopathy inherited?

Yes. The pattern of inheritance is known as 'autosomal recessive'. This means that both parents are carriers of the condition (although clinically unaffected) and the risk they have in each pregnancy, of passing the condition on to their children, is 25 percent, or one in four.

How is SEPN1-related myopathy diagnosed?

The diagnosis of SEPN1-related myopathy is usually suspected by examining an individual's symptoms and taking a detailed medical history. The specific diagnosis, however, is generally made by examining a small piece of muscle from a muscle biopsy.

Before doing a muscle biopsy, clinicians may also perform other tests. One of these tests may be a **blood test,** which measures the level of a muscle protein called creatine kinase (or CK). This enzyme is usually found in the muscles, however following muscle damage it can leak into the bloodstream.

Muscle ultrasound may also help to detect abnormalities in the muscle. This technique is very simple, similar to the ultrasound studies carried out in pregnancy and may provide further evidence of the involvement of the muscle.

Muscle magnetic resonance imaging (MRI), like muscle ultrasound, can assist in demonstrating patterns of muscle involvement which can be specific to particular muscle conditions.

A muscle biopsy involves removing a small piece of muscle, usually from the thigh. When the muscle is studied under the microscope, it is possible to look for changes, such

Version: 4

Published: December 2004

Updated: December 2014

Date of review: December 2015

Authors: MDC Research Department, in association with Dr Reghan Foley, Dr Stephanie Robb and Professor Francesco Muntoni, Dubowitz Neuromuscular Centre, Great Ormond Street Hospital, London

as variation in muscle fibre size and the replacement of some fibres by fat and fibrous tissue, which might indicate a muscular dystrophy.

Genetic tests looking for mutations in *SEPN1*, the gene responsible for SEPN1-related myopathy, are now available in the UK at a specific nationally-designated laboratory and can provide a definitive diagnosis. If you would like to have these genetic tests, speak to your neurologist about the nearest place to you and ask them to arrange a referral.

Pre-natal diagnosis may be possible in SEPN1-related myopathy. In families who have a child with SEPN1-related myopathy, in whom the genetic mutations have been identified and who decide to have another baby, it is possible to detect whether the baby has the same mutations early in the pregnancy.

Is there a treatment or cure?

At present, there is no cure for any form of congenital muscular dystrophy. There are ways, described below, to alleviate the symptoms of the condition and prevent complications. Research into the congenital muscular dystrophies, however, holds the promise of future experimental clinical trials in the not-too-distant future.

Can a child with SEPN1-related myopathy learn to walk?

The severity of this condition varies greatly from person to person. However, children with SEPN1-related myopathy invariably achieve the ability to walk, albeit at a delayed age. Most people with SEPN1-related myopathy maintain the ability to walk throughout life.

What other physical effects might SEPN1-related myopathy have on a child?

Most children with SEPN1-related myopathy develop a curvature of the spine (scoliosis) which needs to be carefully monitored.

People with SEPN1-related myopathy may also develop joint ‘contractures’ or ‘tightness’, meaning they may be unable to move the joints as freely as a healthy person. Physiotherapy can help to prevent or slow the progression of joint contractures, so a programme of exercises should be established with the help of a physiotherapist soon after diagnosis.

Is SEPN1-related myopathy progressive and is it life-limiting?

The condition is fairly stable. People who have SEPN1-related myopathy appear, at least initially, to gain strength as they age. However, while motor function remains relatively stable with only slowly progressive muscle weakness, the curvature of the spine (scoliosis) can progress rapidly. For this reason, it is important to carefully monitor the progression of the curvature of the spine in SEPN1-related myopathy and refer to a specialist spinal clinic as needed.

Because the muscles that assist breathing are affected, children with SEPN1-related myopathy experience breathing problems while sleeping at night. It is therefore essential to monitor lung function on a regular basis and to perform annual overnight ‘sleep studies’. Night-time breathing problems can cause children to feel tired during the day, have headaches on waking in the morning, have loss of appetite for breakfast and lose weight. A decrease in lung function can also result in frequent chest infections. If these signs are present, or if the level of oxygen recorded during an overnight sleep study is not

satisfactory, it is essential that children are referred to a respiratory clinician to initiate night-time non-invasive ventilation (NIV). NIV entails using a special facial or nasal mask attached to a small machine that pumps air into the lungs to maintain adequate ventilation.

Another frequent problem encountered by people with SEPN1-related myopathy is failure to gain weight normally. It is therefore essential to monitor weight (and height) to be sure that children with SEPN1-related myopathy receive enough food and energy. Some people with SEPN1-related myopathy may need to take nutritional supplements. Rarely, a small surgical procedure called a gastrostomy may be recommended, which entails inserting a tube directly into the stomach. Gastrostomy tube-feeding ensures an adequate level of nutrition is ingested, when sufficient calories cannot be consumed orally.

What help is available?

As mentioned above, physiotherapy can slow the progression of contractures, so an initial physiotherapy assessment at the time of the diagnosis should be followed by an exercise programme and regular check-ups. The main aim of physiotherapy is to keep the muscles as active as possible and to prevent or slow the progression of joint contractures. People with SEPN1-related myopathy are encouraged to remain as active as possible; swimming is a particularly good form of exercise.

Occupational therapists can also help by providing orthoses, such as splints, long leg callipers and a wheelchair as necessary.

If curvature of the spine (scoliosis) occurs, a spinal brace may help to improve posture and delay deterioration of the curvature, but surgical intervention (scoliosis surgery) may be needed in some cases.

Children and adults with SEPN1-related myopathy ideally should be followed regularly in a specialist neuromuscular clinic, with access to physiotherapy, orthotic, respiratory, orthopaedic, spinal and genetic specialists as needed.

Here for you

The friendly staff in the care and support team at the Muscular Dystrophy Campaign's London office are available on 0800 652 6352 or info@muscular-dystrophy.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.

Other related publications

This factsheet is to be used alongside the following publications:

- Congenital muscular dystrophies
- MDC1A (merosin-deficient congenital muscular dystrophy)
- Ullrich congenital muscular dystrophy
- Bethlem myopathy
- Carrier detection tests and pre-natal diagnosis of inherited neuromuscular conditions
- Inheritance and the muscular dystrophies
- Muscle biopsies
- Surgical correction of spinal deformity in muscular dystrophy and other neuromuscular disorders

Thank you for your support