Muscular Dystrophy New Zealand

SMA with respiratory distress (SMARD1)/Distal SMA Type 1 (DSMA1)

What is SMARD1?

Spinal muscular atrophy with respiratory distress Type 1 (SMARD1), also known as distal spinal muscular atrophy Type 1 (DSMA1) or distal hereditary motor neuropathy Type 6 (dHMN6 or HMN6) is an inherited condition that causes muscle weakness and respiratory failure typically beginning in infancy. It is caused by a genetic defect in the IGHMBP2 gene not by a deficiency of SMN protein which is the cause of spinal muscular atrophy (SMA). The subsequent loss of the motor neurons in both conditions is what causes the similarity in presentations. SMARD1 most closely resembles SMA Type 1 the more severe type of SMA. The main difference is the early onset respiratory difficulties babies with SMARD1 experience along with the muscle weakness.

Features of SMARD1

Early features of this condition are difficult and noisy breathing, especially when inhaling; a weak cry; problems feeding; and recurrent episodes of pneumonia. Uterine growth retardation and poor foetal movement have been observed in severe cases. Typically between the ages of 6 weeks and 6 months, infants with this condition will experience a sudden inability to breathe due to paralysis of the muscle that separates the abdomen from the chest cavity (the diaphragm). Normally, the diaphragm contracts and moves downward during inhalation to allow the lungs to expand. With diaphragm paralysis, affected individuals require life-long support with a machine to help them breathe (mechanical ventilation). Rarely, children with SMARD1 develop signs or symptoms of the disorder later in childhood.

Soon after respiratory failure occurs, individuals with SMARD1 develop severe muscle weakness in their distal muscles. (These are the muscles farther from the center of the body, such as muscles in the hands and feet). The muscles affected are those which enable walking, crawling, arm and hand movement, head and neck movement and swallowing. Children with SMARD are usually unable to walk. The weakness soon spreads to all muscles; however, within 2 years, the muscle weakness typically stops getting worse. Some individuals may retain a low level of muscle function, while others lose all ability to move their muscles.

Some affected children develop an abnormal side-to-side and back-to-front curvature of the spine (scoliosis and kyphosis, often called kyphoscoliosis when they occur together). After approximately the first year of life, individuals with SMARD1 may lose their deep tendon reflexes, such as the reflex being tested when a doctor taps the knee with a hammer.

Other features of SMARD1 can include reduced pain sensitivity, excessive sweating (hyperhidrosis), loss of bladder and bowel control, and an irregular heartbeat (arrhythmia).

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How is SMARD1 caused?

Mutations in the IGHMBP2 gene on chromosome 11q13.3 encoding the immunoglobulin micro-binding protein 2 causes SMARD1. IGHMBP2 gene mutations lead to the production of a protein with reduced ability to aid in DNA replication and the production of RNA and proteins. These problems particularly affect alpha-motor neurons, which are specialized cells in the brainstem and spinal cord that control muscle movements. Although the mechanism is unknown, altered IGHMBP2 proteins contribute to the damage of these neurons and their death over time. The cumulative death of alpha-motor neurons leads to breathing problems and progressive muscle weakness in children with SMARD1.

Research suggests that the amount of functional protein that is produced from the mutated IGHMBP2 gene may play a role in the severity of SMARD1. Individuals who have some functional protein are more likely to develop signs and symptoms later in childhood and retain a greater level of muscle function.

Diagnosis of SMARD1

Foot deformities and a weak cry can sometimes be early symptoms of SMARD1/DSMA1 although it is usually diagnosed within the first year of life when the child develops severe respiratory distress and presents as a medical emergency.

If SMARD1 is suspected, a blood sample will be taken for genetic testing to help confirm the diagnosis. Further tests, such as an electromyogram (EMG) or muscle biopsy, may be considered if there is uncertainty about the diagnosis.

Management of SMARD1

There is no known cure to SMARD1, and care is primarily supportive. Patients require respiratory support. The child may also undergo additional immunisations and be offered antibiotics to prevent respiratory infections. Maintaining a healthy weight is also important. Patients are at risk of undernutrition and weight loss because of the increased energy spent for breathing. Physical and occupational therapy for the child can be very effective in maintaining muscle strength.

Once a child with SMARD1 starts to show symptoms of respiratory failure, they will require mechanical ventilation to be able to breathe which may include non-invasive ventilation or tracheal intubation. The child's parents and medical team will need to discuss openly which possible medical interventions are in the best interest of the child. This should assist in developing a plan for the child's care, including care in a medical crisis. They may decide to focus on palliative care services or more invasive medical management involving a tracheostomy followed by long term ventilation.

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Inheritance

This condition is inherited in an autosomal recessive pattern. This means that both copies of the abnormal gene must be defective for the disease to develop fully. In this situation each parent is a carrier of one defective gene. Each child they have has a 25% chance of inheriting the disease.

Genetic counseling is available to families who have had a diagnosis of SMARD1. This service provides information, helps families understand inheritance patterns and what this means in their family, as well as enabling people to make more informed family-planning decisions. You can access this via your GP, self-refer or an MDA Fieldworker can assist you.

Useful websites:

www.fsma.org

www.spinalmuscularatrophy.info

www.smasupportuk.org.uk/smard

Support

The MDA Fieldworkers are available for support. They have in-depth knowledge of a range of neuromuscular conditions, and will have a better understanding of your needs and challenges. Have a chat over the phone or they can come to you for a kanohi ki te kanohi/face-to-face visit. They may have some real practical suggestions that have worked for others to offer as well. This service is offered free of charge to MDA members and is funded through donations and grants. Contact your local MDA Branch to be put in contact with your fieldworker.

The MDA Support Network allows people with similar circumstances or challenges to come together to share their experiences and provide each other with emotional and moral support in addition to practical advice and information. By bringing together people with common experiences, support networks can provide an invaluable addition to medical care. The MDA of New Zealand Support Network currently has over 700 members throughout New Zealand who want to be in touch with others livings with neuromuscular conditions. Please see the MDA website www.mda.org.nz for contact details and more information that you might find relevant for you and your whanau.

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Information in this fact sheet was sourced from:

http://www.mda.org/disease/spinal-muscular-atrophy/types-of
https://en.wikipedia.org/wiki/Distal_spinal_muscular_atrophy_type_1
http://www.ncbi.nlm.nih.gov/books/NBK1352/
http://www.ncbi.nlm.nih.gov/gtr/conditions/C1858517/
http://www.smasupportuk.org.uk/smard.

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