SPINOCEREBELLAR ATAXIA TYPE 3 (SCA3)

Spinocerebellar ataxia type 3

Spinocerebellar ataxia type 3 (SCA3) is a type of inherited cerebellar ataxia. It is caused by a defect in a gene. This results in damage to certain parts of the brain, particularly the cerebellum (ie the co-ordination centre). SCA3 is also known as Machado Joseph Disease (MJD).

What are the symptoms?

SCA3 is a progressive cerebellar ataxia.

Most people experience the following symptoms; balance problems (ataxic gait), inco-ordination of hands, slurred speech (dysarthria), and some problems with blurred vision (due to problems with eye movements).

Other possible symptoms include problems with swallowing, stiffness, muscle spasms or a reduced ability to discriminate temperature. There are sometimes similarities between SCA3 and Parkinson's disease, such as rigidity and slowness in movements and resting tremors. Dystonia can also be experienced by people who have these Parkinson-like symptoms. These symptoms may respond to treatments given to people with Parkinson's disease. In SCA3 the nerves in the limbs are generally affected resulting in reduced feelings in hands and feet (peripheral neuropathy). Some people have problems with sleeping and some experience 'restless legs' syndrome. [Handbook of Ataxia Disorders. Ed. Klockgether, 2000; *The Lancet Neurology* 2004; 3:291-304]

Some people may experience mild memory problems or verbal fluency deficits in the later stages of the condition. [*Mov Disord* 2002; 17 (5):1004-10; *Arch Neurol* 2004; 61: 1757-60]
Symptoms and their severity vary between individuals.

What causes SCA3?

SCA3 is an inherited condition caused by a defect in the so-called SCA3 gene, located on the 14th chromosome. (Each person has 23 pairs of chromosomes). This gene is more extended than normal in people with SCA3.

All genes are made up of nucleotides that are held together in a chain. Each nucleotide is identified by a letter (A, T, C or G). The SCA3 gene is extended because of extra copies of a series of nucleotides identified by the letters C-A-G. In general, the more additional copies there are, the more severe the condition.

The SCA3 gene has instructions for the production of a protein called ataxin 3. The abnormally extended SCA3 gene results in the production of an extended ataxin 3 protein. Research is underway to understand what the function of the ataxin 3 protein is and what happens when it is extended. This information is important in order to develop treatments. Research using cells models of SCA3 has recently given promising results for a form of gene therapy (known as RNAi). [PNAS 2003; 100 (12): 7195-200.] More information in Ataxia UK's magazine.

How is SCA3 inherited?

SCA3 is inherited in an autosomal dominant way. For more information on inheritance see Ataxia UK's *'Ataxia: what's that'?'* leaflet.

When do symptoms start?

The age of onset varies greatly, from 10-70 years of age. In general, the later the onset of symptoms, the slower the progression. There are people in their seventies who have very mild symptoms. Generally people will need to use a wheelchair after a number of years.

Sometimes, SCA3 results in earlier age of onset and more severe symptoms as the gene is passed down the generations. This phenomenon is known as anticipation. The explanation for this phenomenon is the instability of the extended SCA3 gene, which gets longer as it passes from parent to child. The opposite can happen in rare cases ie later age of onset and less severe symptoms as the gene is passed down the generations. [Handbook of Ataxia Disorders. Ed. Klockgether, 2000]

How is SCA3 diagnosed?

A genetic test will confirm a diagnosis of SCA3. This involves taking a blood sample to detect the abnormal gene.

How common is SCA3?

There is no recent information on the prevalence of SCA3 in the UK. Ataxia UK is currently funding research to address this lack of knowledge. The first study published from this research estimates that the prevalence of all the dominant ataxias (of which SCA3 is one) in North East England is 1 in 12,500. [Ann Neurol. 2004 May; 55 (5):752-5].

Management of SCA3

As with other cerebellar ataxias, physiotherapy and speech therapy can be helpful. A visit by an occupational therapist will be useful in order to assess the need for items such as walking aids, or for adaptations to the home. A referral to a neuro-ophthalmologist may help if blurred vision is a problem. There are medications that can be taken for problems with sleeping, muscle spasms or Parkinsons-disease like symptoms.
It is important to see a neurologist, who will monitor the condition, on a regular basis.

This information leaflet was written by Ataxia UK in collaboration with Dr Giunti, Consultant Neurologist at National Hospital for Neurology and Neurosurgery, London.

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