Spinal muscular atrophy

Key facts

- Spinal muscular atrophy (SMA) is an autosomal recessive disorder, characterised by progressive muscle weakness due to the degeneration and loss of the anterior horn cells (the lower motor neurons) in the spinal cord and the brain stem nuclei.
- SMA affects around 1 in 25,000 individuals in the UK, with a carrier frequency of between 1 in 50 and 1 in 80.
- SMA is caused by an alteration in the *SMN1* gene on chromosome 5.
- DNA testing is now the preferred method of diagnosis for the condition.
- Once a diagnosis has been made, careful and ongoing assessments are required to establish the personal needs of the individual. This often includes assistance with feeding and ventilation, as well as mobility and physiotherapy support.

Clinical features

- SMA is characterised by progressive muscle weakness, causing the inability to sit or walk, as well as respiratory difficulties. Intelligence and brain development remain unaffected.
- The condition is extremely variable, and the onset of weakness ranges from before birth to early adulthood.
- Before the genetic basis of SMA was understood, the condition was classified into clinical subtypes (see below) based on the age of onset of symptoms.

Diagnosis

The five main subtypes of SMA are described in this section. This classification is still useful for both management and prognosis, and though it is now apparent that there is no clear delineation between them, the different subtypes form a continuum of disease symptoms, all of which are caused by genetic variants in the motor neuron 1 gene (*SMN1)*.

  - **SMA 0**: Prenatal onset of symptoms, usually fatal in the first six months of life.
  - **SMA I (Werdnig-Hoffman disease):** Onset before six months of age. Infants may present with a 'frog leg' posture due to muscle weakness and hypotonia. Facial weakness is minimal or absent. Life expectancy is normally less than 2 years.
  - **SMA II:** Onset between 6 and 18 months. More than 70% of affected individuals have a life expectancy over 25 years.
  - **SMA III (Kugelberg-Welander syndrome):** Onset in childhood after 12 months of age. Normal life expectancy.
  - **SMA IV:** Adult onset. Normal life expectancy.
- Other forms of SMA have been described and may not be associated with alterations in *SMN1*. For example, about 50% of babies with SMA 0 are affected due to variants in other genes.
- Other investigations, including creatine kinase levels, may be important if the diagnosis of SMA cannot be established by *SMN1* testing.

Genetic basis

- SMA is an inherited condition, caused by genetic alterations in the *SMN1* gene on chromosome 5; about 95% of individuals with SMA share a common genetic alteration.
- The condition is autosomal recessive, meaning that the affected individual has two altered copies of the *SMN1* gene.
- Both parents will usually be carriers for SMA, and healthy, because although they each have one altered copy of the gene, this has no adverse effect when the second copy of the gene is unaltered.
- Each child of two carriers has a 25% (one-in-four) chance of inheriting both gene alterations and developing SMA. In 2% of affected cases, individuals have one new ('de novo') genetic alteration, meaning that only one parent is a carrier. Recurrence risks in this situation are considerably lower.
- The genetic basis of SMA is complex, and alterations in a second gene, *SMN2*, which is adjacent to *SMN1*, are known to modify the phenotype. Referral to the local clinical genetics service is advised.

Genetic testing

Indications for genetic testing and genetic counselling include:

- confirmation of the diagnosis in an individual suspected of having SMA;
- siblings and relatives of affected children with symptoms suggestive of the condition;
- two individuals who are carriers contemplating a pregnancy, who may consider prenatal or pre-implantation genetic diagnosis. Prenatal diagnosis is usually possible by chorionic villus sampling (CVS) or amniocentesis. If a couple are considering prenatal diagnosis, referral should be made to the local clinical genetics service prior to a pregnancy. This ensures that appropriate advice and investigations are undertaken and confirm whether or not prenatal diagnosis is possible. All couples considering pre-implantation genetic diagnosis must be referred to their local clinical genetics service.
- to provide information about the genetic status of other relatives of someone with SMA through carrier testing; and
- presence of features suggestive of SMA on routine antenatal ultrasound scans, even when that pregnancy is not known to be at increased risk.

Clinical management

- SMA I is a life-limiting illness and appropriate management, including palliative care, should be given with full discussion and support from the parents. Prolonged survival may be achieved with ventilation, feeding and physiotherapy support.
- Individuals with other forms of SMA may require mobility assistance, physiotherapy, assistance with feeding and nocturnal ventilation.
- SMA is a condition where needs may change with time. Optimum care from a multidisciplinary team, with input of a number of healthcare professionals, may improve the quality of life of an individual with SMA.
- An individual with SMA and their family should actively engage with the process of individualising care. 'A Family Guide to the Consensus Statement for Standard of Care in Spinal Muscular Atrophy', published in 2007, is a useful booklet designed to help with this process.

Direction to further reading, guidelines and patient groups

- More information about SMA is available to read on the NHS website.

- Individuals can also register the condition with the National Congenital Anomaly and Rare Disease Registration Service.

Patient support groups:

- Spinal Muscular Atrophy UK support group
  - Tel: 01789 267520
  - Monday - Thursday: 9.00am - 3.30pm
  - Friday: 9.00am - 1.00pm
  - (Closed on public holidays)
- Muscular Dystrophy UK
  - Tel: 0800 652 6352

This information is intended for educational use and was current in May 2020. For clinical management, it is recommended that local guidelines and protocols are used.

Produced in collaboration with Birmingham Women's NHS Foundation Trust's Clinical Genetics department and Royal Cornwall Hospital NHS Trust's Clinical Genetics department.