Spinal Muscular Atrophy, Type II

**Alternative Names**
- SMA2
- SMA II
- Muscular Atrophy, Spinal, Intermediate Type
- Muscular Atrophy, Spinal, Infantile Chronic Form

**WHO International Classification of Diseases**
Diseases of the nervous system

**OMIM Number**
253550

**Mode of Inheritance**
Autosomal recessive

**Gene Map Locus**
5q12.2-q13.3

**Description**
The spinal muscular atrophies represent a heterogeneous group of neuromuscular disorders with predominantly autosomal recessive inheritance, characterized by degeneration of the anterior horn cells in the spinal cord and, in some cases, of the motor nuclei in the brain stem, resulting in symmetrical muscle weakness and atrophy. The condition is clinically heterogeneous and has been divided into several subtypes according to age of onset and clinical severity.

Spinal muscular atrophy Type II has an intermediate form of severity between the infantile form of SMA type I and SMA III. SMA II, is characterized by onset usually between 3 and 15 months and survival beyond 4 years and usually until adolescence or later. Proximal muscle weakness is the cardinal feature as in other forms of spinal muscular atrophy.

**Molecular Genetics**
Linkage studies in families of spinal muscular atrophy patients found that 95% of all cases of spinal muscular atrophy were linked to the 5q13 region of chromosome 5. Two candidate genes within this region were first described: the survival motor neuron (SMN) gene and neuronal apoptosis inhibitory protein gene. Each of these genes was found to be present in at least two copies. Later, the p44 gene (a subunit of the basal transcription factor) was identified as a third candidate gene.

Recently, two candidate genes, namely SMN (survival motor neuron) and NAIP (neuronal apoptosis inhibitory protein), have been suggested as SMA-determining and SMA-modifying genes, respectively. The SMN gene has been found to be homozygously absent or interrupted in 98.6% of childhood SMAs and in at least some patients with the adult form. The frequency of homozygous deletion of the intact NAIP gene was found to be different in SMA type I and type II/III (45% versus 18%), thus leading to the suggestion that the severity of the disease may depend on the deletion of the NAIP gene.

**Epidemiology in the Arab World**

**Bahrain**
[See also: Kuwait > Haider et al., 2001]

**Kuwait**
Samilchuk et al. (1996) carried out deletion analysis of the SMN and NAIP genes in 11 cases of type I SMA and 4 cases of type II SMA. The patients were of Kuwaiti origin and represented all of the patients diagnosed in years 1995-1996 in Kuwait. They also analyzed samples from 41 healthy relatives of these patients and 44 control individuals of Arab origin. They found homozygous deletions of exons 7 and 8 of the SMN gene in all SMA patients studied. Exon 5 of the NAIP gene was homozygously absent in all type I SMA patients, but was retained in the type II patients.
Among relatives, they identified one mother with a homozygous deletion of NAIP. All of the control individuals had normal SMN and NAIP. Samilchuk et al. (1996) concluded that the incidence of NAIP deletion is much higher in the clinically more severe cases (type I SMA) than in the milder forms, and all of the type II SMA patients in their study had at least one copy of the intact NAIP gene.

Haider and Moosa (1997) investigated the presence of survival motor neuron gene and neuronal apoptosis inhibitory protein gene deletions in 17 Arab and 1 Indian families with spinal muscular atrophy (15 type I and 3 type II). In two patients with type II spinal muscular atrophy, only exons 7 and 8 of the survival motor neuron gene were deleted whereas exons 5 and 13 of the neuronal apoptosis inhibitory protein gene were present. In another patient with spinal muscular atrophy type II, exons 7 and 8 of the survival motor neuron gene and exon 5 of the neuronal apoptosis inhibitory protein gene were deleted. This latter patient also had the Pierre Robin syndrome. No deletion was detected in healthy siblings or the parents.

In 2001, Haider et al. assayed deletions in two candidate genes, the survival motor neuron (SMN) and neuronal apoptosis inhibitory protein (NAIP) genes, in 108 samples, of which 46 were from SMA patients, and 62 were from unaffected subjects. The SMA patients included 3 from Bahrain, 9 from South Africa, 2 from India, 5 from Oman, 1 from Saudi Arabia, and 26 from Kuwait. Type II SMA patients had onset before the age of 18 months and were able to sit but were unable to walk or stand without assistance. SMN gene exon 7 was deleted in all type II SMA patients while exon 8 was deleted in 19 of 21 type II patients. In 1 type II SMA patient, both centromeric and telomeric copies of SMN exon 8 were deleted. None of the 62 unaffected subjects had deletions in either the SMN or NAIP gene. The incidence of biallelic polymorphism in SMN gene exon 7 (BsmAI) was found to be 97%. The incidence of a second polymorphism in SMN gene exon 8 (presence of the sequence ATGGCCT) was 97%.

**Oman**

[See also: Kuwait > Haider et al., 2001]

**Saudi Arabia**

[See also: Kuwait > Haider et al., 2001]

**References**


**Contributors**

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