

Type I Spinal Muscular Atrophy

Spinal muscular atrophy (SMA) is a lower motor neuron disease caused by mutations in the survival motor neuron gene (SMN). The most common mutation is a deletion in the SMN1 gene located on chromosome 5, which results in degeneration of anterior horn cells in the spinal cord and lower brainstem. The inheritance pattern is autosomal recessive. Symmetric flaccid paralysis and hypotonia are common clinical findings. A distinctive feature is that the extraocular muscles are spared. The disease is progressive, and patients may die of respiratory muscle failure. The diagnosis is confirmed with genetic testing by identifying the SMN1 mutation. Treatment consists of supportive therapy, and disease-modifying therapies such as nusinersen.



PLAY PICMONIC

Pathophysiology

Lower Motor Neuron Disease

[Below-ground Motor Neuron-guy](#)

Spinal Muscular Atrophy (SMA) is a lower motor neuron (LMN) disease. Since LMNs directly innervate muscles, degeneration of the anterior horn cells in the spinal cord and lower brainstem nuclei in SMA leads to weakness, hypotonia, and symmetric flaccid paralysis. The denervation of muscle fibers leads to muscle atrophy.

SMN1 Mutation

[Mutated SMN-SiMiaN with \(1\) Wand](#)

The most common cause of SMA is a mutation in the survival motor neuron 1 (SMN1) gene located on chromosome 5. SMN1 codes for a protein that plays an important role in motor neuron function and survival. Mutations in both copies of SMN1 leads to the degeneration of motor neurons located in the anterior horns.

Degeneration of Anterior Horn Cells

[Anteater-horn degenerating](#)

Mutation of SMN1 leads to degeneration of the anterior horn cells in the spinal cord and in the motor nuclei located in the lower brainstem, which leads to progressive muscle weakness and symmetric flaccid paralysis.

Autosomal Recessive

[Recessive-chocolate](#)

The inheritance pattern of this disease is autosomal recessive, with the most common mutation being the biallelic deletion of exon 7 in the SMN1 gene located on the long arm of chromosome 5.

Clinical Features

Symmetric Flaccid Paralysis

[Symmetric Limp Wheelchair](#)

SMA is classified according to the clinical presentation and age of onset. SMA type 1, or early-onset SMA, presents before six months of age and is characterized by severe symmetric flaccid paralysis. All other forms of SMA present with diffuse symmetric proximal muscle weakness with decreased or absent deep tendon reflexes. The lower extremities are more affected than the upper extremities.

Hypotonia

[Floppy Hippo-baby](#)

In infants with unexplained weakness or hypotonia, SMA should be suspected. Infants with hypotonia have decreased spontaneous activity, lie in a frog-like position with abducted hips when placed supine, and show no resistance to passive movements of the joints.

Bulbar Palsy

[Bulb Pause-nerve](#)

Degeneration of motor nuclei located in the lower brainstem leads to weakness of the bulbar muscles. This results in poor suck and poor swallow reflexes, tongue fasciculations, pooling of secretions, and a weak cry. Bulbar palsy puts infants at a higher risk for aspiration pneumonia.

Extraocular Muscle Sparing

[Eye Muscles Okay](#)

In SMA, motor nuclei from the upper brainstem are spared. Since upper cranial nerves are mostly unaffected, patients have normal eye movements.

Respiratory Failure

[Dead Lungs](#)

As SMA progresses, there is respiratory muscle weakness, which can lead to respiratory failure and death.

Diagnosis

Genetic Testing

[Jeans and Test-tubes](#)

In patients with suspected SMA, molecular testing targeting the SMN1 mutation can confirm the diagnosis.

Treatment

Supportive Therapy

[Supportive IV Bags](#)

Management of patients with SMA is based on supportive therapy. Patients require nutritional assistance and management of common gastrointestinal comorbidities such as gastroesophageal reflux and delayed gastric emptying. Physical therapy and orthopedic evaluation should be sought to identify and address complications such as scoliosis. Respiratory function should be monitored, and respiratory therapy is usually needed.

Nusinersen

[Nurse-zen](#)

There are now disease-modifying therapies that can slow the progression of the disease and improve quality of life. Some of these new agents act by targeting SMN2. The SMN2 gene transcribes mostly nonfunctional SMN protein with a small amount of functional protein. Generally, the more copies a patient has of SMN2, the milder the symptoms. Nusinersen is an antisense oligonucleotide that modifies the SMN2 splicing process, enhancing the transcription of functional SMN protein levels.