Chapter 15

Spinal Muscular Atrophy

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A three-year-old with spinal muscular atrophy presents for intrathecal administration of nusinersen (Spinraza).

What Is Spinal Muscular Atrophy?

Spinal muscular atrophy (SMA) is a motor weakness disease caused by a mutation in the survival motor neuron (SMN) gene on chromosome 5. In over 95% of cases, the defect is a homozygous deletion of exon 7 resulting in a lack of SMN protein. The SMN protein is essential for normal functioning of the motor neuron, including the neuromuscular junction. The protein is involved in transport of mRNA along axons and local RNA processing. This deletion leads to loss of anterior horn cells of the spinal cord despite the presence of normal numbers of motor neurons. Its incidence is approximately 1 in 6,000–10,000 live births, and it is inherited in an autosomal recessive fashion. Sensation is generally intact. This disorder is heterogeneous in clinical presentation and has therefore been subcategorized for prognostic utility. Muscle weakness affects most major muscle groups as well as the intercostal muscles, but the diaphragm is spared.

What Are the Different Types of SMA?

SMA type 1 (Werdnig–Hoffmann) has onset at birth or shortly thereafter. Without ventilatory support, 90% of these infants will succumb to respiratory failure before 1 year of age, and none will survive to two years. Noninvasive artificial ventilation (e.g., CPAP) may lead to survival past five years of age, and invasive ventilation via tracheostomy may increase lifespan into adulthood.

Often, the infant has no spontaneous movements of extremities except tremor of the fingers and tongue fasciculations. Intercostal muscles are so weak that diaphragmatic breathing is required.

SMA type 2 (juvenile spinal muscular atrophy) usually presents between 6–18 months of age. While infants are weak, motor milestones such as sitting unassisted are often achieved but walking is never achieved. In less severe cases, spirometry may be unaffected. If untreated, about 70% will reach adulthood, but modern medical care improves the situation considerably.

SMA type 3 (Wohlfart–Kugelberg–Welander syndrome) usually presents after two years of age with abnormal gait. Most of these children will eventually be able to walk, and survival into adulthood is not unusual.

Electromyography shows denervation with fibrillation potentials and muscle biopsy often shows neurogenic atrophy, but diagnosis of SMA is confirmed by genetic testing for the SMN mutation.

What Is Nusinersen (Spinraza)?

Nusinersen is an SMN2-directed antisense oligonucleotide indicated for the treatment of SMA in pediatric and adult patients. Nusinersen binds to a specific sequence in the intron downstream of exon 7 of the SMN2 transcript. The administration of antisense oligonucleotides should increase production of full length SMN2 proteins. Treatment begins with four loading doses. The first three loading doses should be administered at 14-day intervals. The fourth loading dose is given 30 days after the third. Patients will then receive maintenance doses every four months. Patients with SMA who require lumbar puncture and administration of nusinersen will often need sedation or general anesthesia for immobility due to the high cost of the drug and the risk of failed administration.

What Are the Important Anesthetic Considerations in Patients with SMA?

The anesthetic considerations posing the most risk to SMA patients are related to possible difficult

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intubation (from atrophy of the masseter muscle and ankylosis of the mandibular joint) and postoperative respiratory failure caused by global motor weakness. For minimally invasive procedures, such as the one described above, a facemask or supraglottic airway is sufficient. Infants with SMA Type I usually need postoperative respiratory support, while SMA Type II and III may not, depending upon their individual clinical condition. SMA patients tend to exhibit increased sensitivity to and prolonged effect of nondepolarizing neuromuscular blockers. Succinylcholine is usually avoided because of possible exaggerated release of potassium. Preoperative pulmonary evaluation and consultation are recommended.

How Will You Induce and Maintain Anesthesia for This Procedure?

There are no contraindications to the use of inhalational or intravenous anesthetic agents in patients with SMA. In our practice, most children with SMA receive inhalational anesthesia by facemask or tracheostomy followed by IV catheter insertion. Some practitioners prefer insertion of a supraglottic airway during the lumbar puncture procedure in the lateral position. Opioids and other respiratory depressant agents are avoided.

Suggested Reading

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