Valley Children's HEALTHCARE

Central California
Pediatrics

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Specialty information for physicians who treat children and expectant mothers.

Understanding Spinal Muscular Atrophy

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Spinal muscular atrophy (SMA) is a life-threatening , progressive neuromuscular disorder caused by a mutation or deletion of the survival of motor neuron gene1 or SMN1. It mainly affects the anterior horn cells or motor neurons in the spinal cord. The mutation causes a decrease in the production of SMN protein, which is vital to the survival of motor neurons. Muscles used for ambulation, swallowing and respiration are affected early, and later almost all the muscles are involved. Ultimately, the patient loses the ability to move. Cognition is intact since the brain is not affected.

SMA is lethal in infancy. A less severe form of the disease will still result in disability and demand significant care from the patient's family. SMA affects one in 10,000-11,000 births and about one in 50 people are genetic carriers. SMA type I is the most common genetic cause of infant death. It also has the highest incidence but lower prevalence because a patient's lifespan is short.

SMA is transmitted through an autosomal recessive inheritance and is classified into four types, based on age of onset, severity of symptoms and survival.

What Are The Different Types of SMA?

In SMA type I, the symptoms are noted as early as birth to 6 months. Classic presentation is an awake, alert baby who is very floppy. They eventually develop respiratory distress and poor feeding habits. They do not develop the ability to sit. On examination, an outstanding feature is the presence of tongue fasciculation. This is an important finding that may differentiate hypotonia from other causes and SMA. The survival rate used to be 8% at 20 months. With the advent of therapy, this has likely changed.

In SMA type II, symptoms start between 6 months to 18 months. These children are unable to walk or stand without support. They eventually develop respiratory insufficiency and scoliosis. On examination, a common finding is a tremor-like movement of their fingers called polyminimyoclonus. These are seen when their hands are outstretched.

In type III SMA, symptom onset is observed after 18 months. The children are able to walk but eventually have progressive muscle weakness and will lose this ability around adulthood .

SMA type IV is adult onset. Weakness starts between 20 to 30 years of age. As with type III, they may lose ambulation.

SMA and Newborn Screening

IIt is important to recognize this disorder as early as possible, because the loss of motor neurons begin as early as intra utero and there is continued deterioration. Universal newborn screening is a great measure to ensure every child with SMA is diagnosed and treated early – timely intervention and early diagnosis can be lifesaving.

Valley Children's has been designated by the California Public Health Newborn Screening Program as one of seven service centers in the state, and the only one in the Central Valley. Since this designation, Valley Children's has screened newborns for SMA, and since June 2020, has

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diagnosed five patients through this program. All have received therapy within 3-5 weeks after diagnosis. So far, all are doing well and have shown progression in their milestones.

There has been significant medical breakthroughs in the past 4-5 years in SMA management. Before December 2016, there were no treatments for SMA. Now we have three therapeutic options.

SMA Treatment Options

Spinraza (nusinersen) is an antisense oligonucleotide, SMN2 splicing modifier, which was the first treatment to be approved by the FDA. It acts on the backup gene SMN2 to produce more SMN protein. It is approved in all patients with SMA regardless of age and type. It is given intrathecally with four loading doses, within the first two months, followed by a maintenance dose every four months.

In May 2019, Zolgensma, (onasemnogene abeparvovec) gene therapy was approved by the FDA. It is a single dose intravenous therapy that supplies the missing gene SMN1 in the form of a therapeutic transgene, that is packaged inside a virus. This virus is then injected intravenously. This results in the production of SMN protein which is critical in motor neuron preservation. It is approved for patients of all types under 2 years of age.

Evrysdi (Risdiplam) was approved for SMA in children over 2 months in August 2020. It is the first and only SMA medication that is given orally. Similar to Spinraza it acts on the backup gene SMN 2, to produce more SMN protein This is approved for all types of SMA that are 2 months or older.

All of these therapeutic options are available at Valley Children's.

The majority but not all patients may qualify for these treatments. About 95% of patients have a mutation on chromosome 5 q. 11. The rest without this mutation would not benefit from this treatment option, because the cause of their SMA is not SMN1 related.

It is critical that therapy is instituted as early as possible because SMA is an irreversible disease. A delay in diagnosis decreases the opportunity to provide maximal benefit from treatment. The destruction of motor neurons begins before or shortly after birth and for SMA type I, it is rapidly progressive.

Early treatment can result in the rescue of motor neurons, preventing disease progression, improve neuromuscular function, and most importantly increased survival and improved quality of life.

Medical Staff News

The following pediatric specialists recently joined Valley Children's:

Chief Residents
Chloe Kupelian, MD
Keenia Tappin, MD

Emergency Medicine
Brent Feudale, MD

Hospitalist
Irmeen Ashraf (Mercy San Juan)
Mitchell Platter, DO (Mercy San Juan)

Upcoming CME Opportunities

Pediatric Clinical Symposium: Multisystem Inflammatory Syndrome in Children - What you should know

Presented by Dr. Reshma Patel
Wednesday, August 25
12:15pm-1:15pm

Register for Valley Children's CME events through our CME Tracker, cmetracker.net/VCH

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