TEXAS Health and Human Services | Texas Department of State Health Services

Newborn Screening ACT Sheet

Spinal Muscular Atrophy (SMA)

Exon 7 Deletion (Pathogenic Variant) in Survival Motor Neuron Gene (*SMN1*)

Condition Description: Spinal muscular atrophy (SMA) is an autosomal recessive neurodegenerative motor neuron disease caused by pathogenic changes in the Survival Motor Neuron 1 gene (SMN1) gene. Newborn screening (NBS) detects patients with homozygous deletions in SMN1, which represents ~95% of cases. SMA type I accounts for more than half of cases and presents at or shortly after birth with hypotonia, breathing and feeding difficulties. Disease severity is attenuated by the number of copies of a related gene, SMN2. Individuals with three or more copies of SMN2 present with later infantile (SMA type 2), childhood (SMA type 3) or adult-onset SMA. For infants identified via NBS with two or three copies of SMN2, rapid confirmation of genetic diagnosis, assessment and treatment initiation prior to six weeks of age is critical for optimal outcome. The most severe form (SMA type 0) is associated with larger deletion in Exon 7 or the entire gene.

Medical Emergency: You Should Take the Following IMMEDIATE Actions

- Contact family to inform them of the newborn screening result, ascertain clinical status, arrange immediate clinical evaluation, and provide them with basic information about SMA.
- Take a family history
- Telephone consultation and referral to a neurologist or neurogeneticist within 24 hours for comprehensive clinical evaluation, and initiation of treatment. Genetic counseling is strongly recommended.
- Take immediate steps to ensure rapid molecular (DNA) confirmation of the NBS result, including SMN1 and SMN2 gene dosage (copy number).
- Report findings to state newborn screening program.

Diagnostic Evaluation: Evaluation includes rapid molecular confirmation of *SMN1* mutations and *SMN2* copy number, and physical and neurological assessment by an experienced SMA specialist. Adeno-associated virus serotype 9 (AAV9) antibody titer is often obtained at initial visit for those considering gene therapy.

Clinical Considerations: Individuals with the infantile-onset forms of SMA can present with rapidly progressive symptoms at or shortly after birth. Symptoms can include hypotonia, weakness, trouble feeding or respiratory failure. Infants with three or more *SMN2* copies may not present until later childhood or even adulthood. The more severe forms of SMA are associated with high mortality unless diagnosed and treated promptly in the first weeks of life (intrathecal nusinersen or gene therapy, and possibly other emerging therapies). Standard-of-care recommendations include monitoring respiratory, developmental and nutritional status.

Additional Information:
Gene Reviews: https://www.ncbi.nlm.nih.gov/books/NBK1352
Genetics Home Reference: https://medlineplus.gov/genetics/condition/spinal-muscular-atrophy/
OMIM http://omim.org/entry/232300
Cure SMA: http://www.curesma.org/
Muscular Dystrophy Association (MDA) Care Center Network:
https://www.mda.org/care/mda-care-centers

Referral (local, state, regional and national):
Testing: https://medlineplus.gov/genetics/condition/spinal-muscular-atrophy/
Find Genetic Services: https://clinics.acmg.net

Baby's First Test:
http://www.babysfirsttest.org/newborn-screening/conditions