Unexpected Outcomes In A Child with SMA type 1 (Pre-Spinraza treatment)

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Background

Spinal muscular atrophy is an autosomal recessive genetic disorder. Type I (Werdnig-Hoffman, acute) is the most severe form of SMA. Onset is noted at 0-3 months due to hypotonia and severe weakness, feeding difficulties and/or need for respiratory support. Type I SMA has historically been characterized as fatal, with lifespan reported as 1 or 2 years. With current improved care and respiratory support, many children are living much longer. Some children live up to age eight and are able to attend school with appropriate support and accommodations.

Children with SMA have a reduced number of anterior horn cells in the spinal cord, and there is progressive deterioration of the ones that are present, which leads to progressive loss of strength and function.

The genetic defect in SMA is the survival motor neuron (SMN) gene on chromosome 5q11.2-13. SMN codes for SMN protein, which maintains the anterior horn cells. In the absence of adequate SMN protein, the anterior horn cells die. Diagnosis can be confirmed by EMG, biopsy, or more commonly genetic testing. Upon muscle biopsy, noted are changes characteristic of diseases involving denervation and many atrophic fibers among groups of normal or hypertrophic fibers.

Common impairments and functional limitations in children with Type I SMA:

- significant weakness of the neck, spine and extremities
- proximal>distal weakness

* great risk for development of scoliosis
* risk of contracture formation due to persistent gravity-dependent positioning
* respiratory distress and use of compensatory “belly breathing” or paradoxical breathing
* decreased ability or inability to tolerate upright positioning due to oxygen desaturations and inability to manage secretions.

Purpose

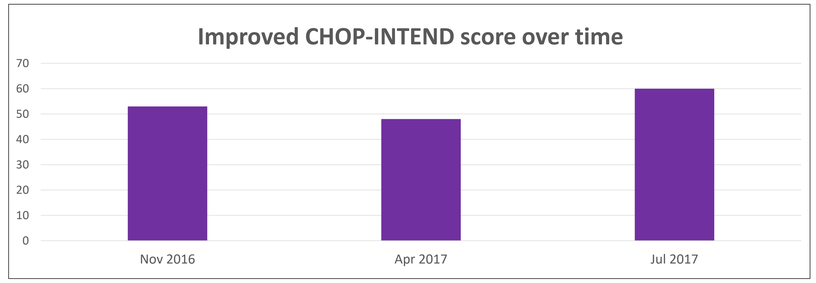
Physical therapy intervention focused on 24–hour positioning programs and maintenance of upright positioning is crucial for children with Type I SMA for maintenance of optimal spinal alignment, prevention of contractures and optimization of function.

Methods

Patient characteristics:

- 3 year old boy with SMA type 1
- 6/2014: Formally diagnosed at 7 months, significant weakness noted earlier
- 0 copies SMN 1, 3 copies of SMN 2 (mild type 1 SMA)
- 5/2015: initial PT equipment evaluation at Duke. Prior therapy services had focused mostly on stretching and supine positioning. Pt. continued with previous aquatic therapy, but transitioned land-based PT to Duke 1X/week with goals of progress towards upright activities and improved functional strength.
- 5/2015: functional mobility (19 months old): rolled supine to either side with mod-min A. Required max A to be supported in sitting-was able to maintain his head upright (with stacking) for 1-2 minutes before neck became fatigued. If head began to fall forwards, unable to right.
- 12/16: 2 week PICU admission due to acute respiratory failure; weakness s/p hospital stay.
- 7/14/2017: first Spinraza dose

Results



Functional skills attained prior to Spinraza initiation: independent rolling, independent head control, independent sitting (hands free), standing with KAFO’s at a posterior support independently, independent reaching and manipulation of toys, independent propulsion of manual wheelchair (Panthera Micro), independent maintenance of prone on extended elbows with head erect once placed, independent step taking with/forward propulsion of Kaye body weight support walker.

Conclusions/Clinical Relevance

What we know about the natural history of all types of SMA is likely to be changing. Disease modifying treatment with an antisense oligonucleotide (Spinraza) is now available for Spinal Muscular Atrophy (SMA), and gene therapy for SMA is also currently in clinical trials with exciting preliminary results reported. If Spinraza or gene therapy is administered in the newborn period, before cell death has occurred, the potential exists for children with SMA type 1 to sit, stand and/or walk. Physical therapy intervention has never been more critical for these children as we now will be focused on prevention of primary and secondary musculoskeletal impairments and improving function and participation more aggressively than ever before due to increased capacity for change. This patient demonstrated unexpected improvement before Spinraza and has continued to gain strength post-Spinraza administration.