Transitions in Care in SMA

Case contributor and commentary:
John Brandsema, MD
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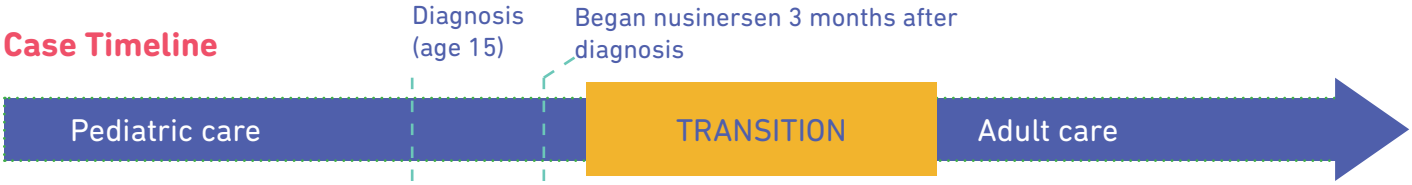
Patient #1: Transition planning following adolescent diagnosis

15-year-old-male

Case Timeline



Early life

The patient's family recalled preclinical symptoms during his early life.

- Different running ability to others since school age
- A fine tremor in hands for a few years and fatigue/hand cramping with prolonged writing
- No other functional impairments for many years

Age

14 **As the patient began his growth spurt, he began having issues with tripping and falling that slowly progressed over time.**

Symptoms

- Difficulty with stairs and rising from the ground
- Difficulty getting out of a car
- Needed rest breaks on longer walks
- Tended to trip over obstacles with intermittent falls, but no significant injuries
- Became fatigued when raising arms for a long time, such as when shampooing

Management

- Received 4 months of physical therapy, with only slight progress

Review of health status

Mental health status

- Anxiety
- Mild autism spectrum disorder

Musculoskeletal status

- No significant muscle pain or cramping
- No muscle stiffness

Cardiac status

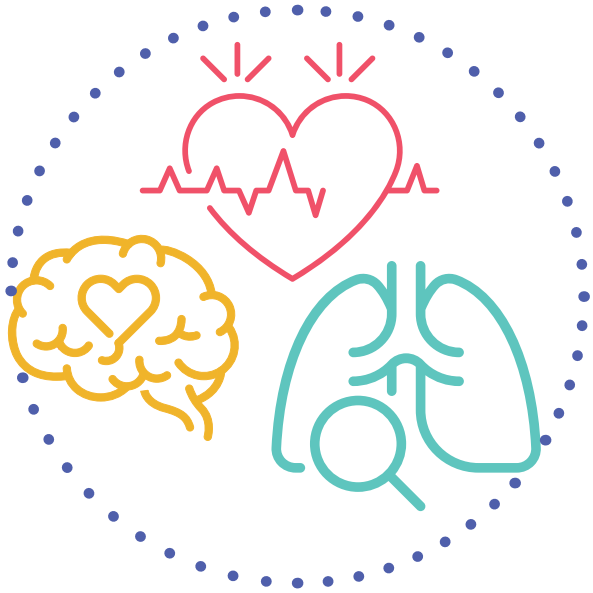
- No chest pain or palpitations

Respiratory status

- No dyspnea
- Slept well with rare snoring
- Recovered normally from respiratory illnesses
- No swallowing or speech concerns

Kidney status

- No episodes of cola-colored urine



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Age 15

The patient was presented to the neurology clinic for the first time.

Telemedicine physical examination

- Reduced bulk and weakness (proximal more than distal and legs more than arms), mildly asymmetric and of mild severity
- No scoliosis or scapular winging
- No fasciculations of the tongue
- Polyminimyoclonus tremor with hands outstretched

Diagnosis via genetic testing

- Type 3 SMA
  (0 copies of *SMN1*, 4 copies of *SMN2*)

Classification of SMA subtypes

- Spinal muscular atrophy (SMA) is a motor neuron disorder caused by low levels of SMN protein characterized by progressive weakness, muscle atrophy, and loss of physical function[1]
- SMA is caused by mutations in the survival motor neuron one gene, *SMN1*, with retention of one or more copies of the *SMN2* gene, which produces a fraction of the *SMN* gene message produced by *SMN1*
- *SMN2* copy number inversely correlates with clinical severity, although exceptions to this rule occur
- SMA affects all ages and was previously classified based on age at symptom onset and maximum function achieved:
  - Type 1: Infants with onset in the first 6 months, unable to sit unsupported, 2 *SMN2* copies
  - Type 2: Children with onset between 6-18 months, able to sit independently, 3 *SMN2* copies
  - Type 3: Childhood symptom onset after 18 months, can walk independently, 3-4 *SMN2* copies
  - Type 4: Adult onset SMA after 18 years, can walk independently, 4 or more *SMN2* copies
- In the era of disease-modifying therapies and newborn screening programs, newer classifications based on genotype, age at starting treatment, and current functional status are emerging[2]

Physical and occupational therapy (PT/OT)

- Continued PT and added OT
- Nighttime dynamic splinting for ankle contracture

Respiratory care

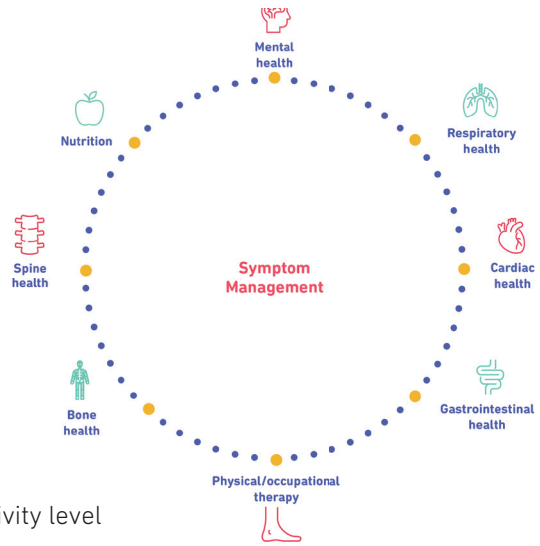
- Implemented pulmonary function test surveillance -> baseline normal for age

Spine health

- Clinical examination and x-ray used to diagnose lumbar hyperlordosis, with no scoliosis
- Plan for reassessment every 1-2 years

Bone health

- Vitamin D level checked and found to be low -> supplementation added



Nutrition

- Noted to be overweight -> Nutrition reviewed for balance between diet and activity level

Genetic testing

- Parents identified as SMA carriers -> Aunt of childbearing age decided to be tested before conceiving
- Microarray performed to understand the autistic features, which were not consistent with SMA -> no cause identified

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Supportive treatment

Medical Management

» Added enteral albuterol

Outcome

» Improvement in stamina noted
» Some mild tolerable increase in hand tremor
» No change in anxiety

Disease-modifying treatment

The goal for future treatment was to slow decline and achieve stabilization, or improvement, in motor function.

Reviewed options of nusinersen and risdiplam:

» Nusinersen concerns: Intrathecal injections, access to treatment given habitus
» Risdiplam concerns: Potential fertility impact -> discussed sperm banking

Nusinersen preferred due to:

» Concern for needing to remember a daily medication
» Potential difficulty transporting risdiplam suspension while camping

Nusinersen treatment was started 3 months after diagnosis. Outcomes of the nusinersen treatment were measured with commonly used functional assessments.

» Expanded Hammersmith Functional Motor Scale = 60 at 5 months after nusinersen initiation (previous 59)
» 6 minute walk test increased by 25 meters to 475 meters
» Revised upper limb module (RULM) stable at 37 bilaterally
» Family and patient noticed improved stamina and ability to walk longer distances before resting

The changing needs and growing independence of the patient during adolescence led to a number of lifestyle modifications.

Individualized education plan (IEP) for school

» Increased access to computer versus handwriting
» Extra time for tests
» Grading not based on population norms in physical education class

Continued to be active in nature hike activities with peers

» Implemented intermittent breaks
» Experienced rare falls
» Camping supplies were carried by others

Took steps to manage anxiety around initial diagnosis

» Required several visits to review cause of SMA, expected natural history, and treatment opportunities

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Important considerations for transition in care from pediatric to adult care neurologist

Role of the clinician

- Encourage independence in teenage patients in the following areas:
  - Reporting symptoms
  - Reviewing medications
  - Knowing the specialists involved in care
- Gradually increase the focus on the patient (vs. the caregiver) over serial visits
- Prepare the patient for transition of care by:
  - Discussing differences in nusinersen administration between sites
  - Weaning amount of sedation in preparation for goal of unsedated procedures

Timing and location

- Authorization for alternate dosing site will be pursued at time of care transition (~18 years of age)
- For patients who are planning to attend college out of state, considerations include:
  - Developing an emergency plan
  - Considering a scooter for longer distances
  - Determining optimal site of administration - new care team vs. returning for doses
  - Determining follow-up frequency, which may be influenced by insurance authorization

Key learning points

- A growth spurt in puberty can exacerbate subtle underlying weakness
- Adolescents are beginning to develop independence and self-identity and need to be actively involved in treatment decisions when developmentally appropriate
- Multiple discussions may sometimes be required before making a non-urgent treatment decision

References

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2. Tizzano EF, Finkel RS. Spinal muscular atrophy: A changing phenotype beyond the clinical trials. Neuromuscular Disorders. 2017;27(10):883-889. doi:10.1016/j.nmd.2017.05.011