Transitions in Care in DMD

Patient #2: Successful Transition in Process

16 y/o Male

Case contributor and commentary:
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Case provided by M. Eileen McCormick with commentary and discussion provided by Meghan Harper-Shankie

Pediatric Care

Early life

Symptoms:

» Patient Initially presented with elevation in transaminases

Initial workup by pediatrician:

» Patient was referred to gastroenterology

Background:

» One great-great maternal uncle diagnosed with "muscular dystrophy (MD)" passed at 36 years old
» Two maternal uncles diagnosed with "MD" passed at 18 and 21 years of age, respectively
» Mother is an asymptomatic carrier who follows up annually with cardiology

Age 4

Pediatrician workup:

» Referred patient to the neuromuscular team

Neuromuscular team workup:

» Ordered genetic testing

Findings:

» Genetic testing revealed a point mutation/splice site mutation [transversion of G>C] in the *DMD gene*
» From age 4 on, patient received managed care continuously in an MDA Care Center

Commentary: It is recommended that transition planning include a plan for continuity of healthcare with pediatric providers (primary care and specialists) until adult care is established.[1] Multidisciplinary care should continue throughout adult life.[2]

Age 5 - 6

Treatment:

» Steroid treatment initiated (0.75mg/kg /d prednisone)

Age 8

Neuromuscular team workup:

» Skeletal muscle biopsy showed an absence of dystrophin, confirming a Duchenne muscular dystrophy (DMD) diagnosis rather than the less severe Becker muscular dystrophy (BMD)

Age 13

Treatment:

» Steroid treatment changed from prednisone to deflazacort (daily 0.9 mg/kg) when the drug received FDA approval

Transitions in Care

Age 14 - 16

Ambulation status

» Patient continued to ambulate and bear weight

Musculoskeletal status:

» No significant scoliosis
» X-rays revealed a Cobb angle of 13%, but no visible curvature in the clinical exam

Cardiac status:

» Patient exhibited mild dilated cardiomyopathy but remained asymptomatic clinically
» Ejection fraction (EF) is 52% on stable doses of carvedilol and lisinopril

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Commentary: Children with DMD are commonly treated early with an ACE inhibitor (lisinopril) and/or beta blocker (carvedilol).[4] When used in combination, these appear to lead to initial improvement of left ventricular function. The 2014 NHLBI working group recommended use of ACE inhibitors or Angiotensin II receptor blockers (ARBs) by the age of 10 years in boys with DMD.[5]

Age
14 - 16

Respiratory symptoms:

- Pulmonary function tests: forced vital capacity 70% predicted, FEV1 34% predicted, FEV1/FVC 44% predicted
- Sleep study did not demonstrate significant obstructive sleep apnea (OSA)

Commentary: It is recommended that children with DMD receive baseline pulmonary function testing before beginning full-time wheelchair use (usually age ~9-10 years).[4] Twice-yearly evaluation by a pediatric pulmonologist is indicated after wheelchair use begins, reduction in vital capacity below 80% predicted or age 12 years.[6]

TIMELINE AND DOSING

Initial discussion
- Discuss use of steroids with family

Began steroid regimen
- Before substantial physical decline
- After discussion of side-effects
- After nutrition consultation

Recommended starting dose
- Prednisone or prednisolone 0.75 mg/kg per day

OR
- Deflazacort 0.9 mg/kg per day

Dosing changes

If side-effects unmanaged or intolerable
- Reduce steroids by 25-33%
- Reassess in 1 month

If functional decline
- Increase steroids to target dose per weight on the basis of starting dose
- Reassess in 2-3 months

Use in non-ambulatory stage
- Continue steroid use but reduce dose as necessary to manage side-effects
- Older steroid-native patients might benefit from initiation of a steroid regimen

CAUTIONS

Adrenal insufficiency
- Patient and family education
- Educate on signs, symptoms, and management of adrenal crisis
- Prescribe intramuscular hydrocortisone for administration at home
- 50 mg for children aged <2 years old
- 100 mg for children aged >2 years old and adults
- Stress dosing for patients taking > 12 mg/m^2 per day of prednisone/deflazacort daily
- Might be required in the case of severe illness, major trauma, or surgery
- Administer hydrocortisone at 50-100 mg/m^2 per day

Do not stop steroids abruptly
- Implement PJ Nicholoff steroid-tapering protocol
- Decrease dose by 20-25% every 2 weeks
- Once physiological dose is achieved (3 mg/m^2 per day of prednisone or deflazacort) switch to hydrocortisone 12 mg/m^2 per day divided into three equal doses
- Continue to wean dose by 20-25% every week until dose of 2.5 mg hydrocortisone every other day is acheieved
- After 2 weeks of dosing every other day, discontinue hydrocortisone
- Periodically check morning CRH-stimulated or ACTH-stimulated cortisole concentration until HPA axis is normal
- Continue stress dosage until HPA axis is recovered (might take 12 months or longer)

Figure adapted from reference #3.

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Side effect of chronic steroid use:

» Adrenal insufficiency
» Severe bone health decline
» Delayed puberty and short stature

Endocrine complications:

» Adrenal insufficiency

→ **Treatment:**

» Patient was treated according to the PJ Nicholoff Steroid Protocol for Duchenne and Becker Muscular Dystrophy and Adrenal Suppression[7]

Orthopedic complications:

» Age 14: Patient developed osteoporosis. Bone scan revealed a total Z score of -3.7.
» Age 15: Patient experienced a fall, leading to a buckle fracture of the left tibia and a wrist fracture.

→ **Treatment:**

» Bone health assessments by endocrinology

→ **Results:**

» Patient prescribed supplemental vitamin D3

Nutritional Status:

» Patient was diagnosed with failure to thrive, and was followed closely by a dietitian
» No oral motor dysfunction, choking, or coughing

→ **Treatment:**

» Patient was placed on a high calorie, high protein diet
» Patient was prescribed cyproheptadine to boost appetite

→ **Results:**

» Patient gained 3 pounds in 4 months

Loss of functional milestones during transition:

» Less endurance, however remains ambulatory for short durations
» Loss of independent transfers for toileting
» Strength: 4- distally, 3+ proximally. Low muscle tone (hypotonia)
» Ambulation: Gait reveals lumbar lordotic, toe stance; Six Minute Walk Test: 910 feet or 277.37 meters; North Star Ambulatory Assessment: 17 out of 34; Brooke Upper Extremity: 1

	GROWTH	PUBERTY
ASSESSMENT	Assess **every 6 months** until completion of puberty and attainment of final height	Assess **every 6 months** starting by age 9 years; use Tanner staging
SIGNS/SYMPTOMS	**Impaired growth** Any of the following: • Downward crossing of height percentile • Height velocity of <4 cm per year • Height <3rd percentile	**Delayed puberty** Testicular volume <4 cm^3 at age 14 years or older
	REFER TO ENDOCRINOLOGIST	
RECOMMENDED	• Assessment of bone age with left-hand x-ray • Thyroid function tests • Celiac panel • Growth factors • Comprehensive metabolic panel • Complete blood count	**Laboratory assays:** • Luteinizing hormone • Follicle-stimulating hormone • Testosterone • Treatment for confirmed hypogonadism: • Initiate testosterone replacement at low dose and gradually increase over time • Recommended for age ≥14 years; can be considered from aged 12 years
TO BE CONSIDERED	Growth hormone stimulation testing	Assessment of bone age with left-hand x-ray

Assessments and interventions for impaired growth and delayed puberty in patients with DMD. Adapted from reference #3.

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Age 14 - 16

Social environmental factors:

- Patient's parent died unexpectedly during early transition. Patient remains in counseling
- Patient received support from local and national programs such as Make a Wish Foundation and MDA Summer Camp

Clinical trial engagement:

- Patient did not qualify for targeted therapy trial
- Family is also unable to travel to a distant study site, making participation in upcoming trials unlikely

Issues of noncompliance:

- None

Age 16

Important milestones:

- Patient remains ambulatory
- Patient is experiencing decreased endurance and fear of falling, and is aware of his limitations

Activities of daily living:

- Patient requires some assistance with activities of daily living but continues to be functional for self-grooming. Patient does require transfer assist for toileting, etc.
- Patient is in the 10th grade and is a high-functioning student. He is working with family and care team to prepare for college (location, curriculum, etc.)

Commentary: It is recommended that education planning meetings should start when a person with DMD is around 13 years old and occur at least annually.[1] The focus should be on the student's needs and goals, assessment of personal strengths and interests, and assessment of physical challenges in the school environment. However, not all people with DMD seek education beyond high school, and the aims of transition planning toward adult roles need to be considered for each individual.[9]

Insurance:

- Patient is a minor covered by Medicaid
- Patient's mother is working with a financial planner to address future financial needs

Decision-making:

- Patient is beginning to make informed decisions regarding healthcare, education, therapies, and socialization, with mentoring from a parent

Commentary: The move from family-centered to patient-centered interactions is recommended when an individual shows an interest and ability to self-advocate and begins to participate in discussions about their care and needs.[1,10,11] A young person with DMD, their medical team, and their caregivers should engage in developmentally appropriate discussions at least once a year about long-term care goals. Time alone with at least one provider should begin in early adolescence. The MDA Roadmap to Independence[12] offers guidance about health-related concepts in the later stages of DMD.

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