ATYPICAL CASES OF A COMMON NEUROMUSCULAR DISORDER

Jenna Klotz, MD

Pediatric Neuromuscular Fellow
Division of Neuromuscular Medicine
Department of Neurology
Stanford University
HYPERTONIC INFANT

• Birth history:
  • Born at 39 3/7 weeks
  • Delivery complicated by late decels, nuchal cord and meconium
  • Apgars 7, 8
  • Exam: Low tone, incomplete Moro, partial grasp, absent suck
  • Cord VBG: 6.87/75.4/15/-19

• NICU course:
  • Therapeutic hypothermia x 72 hours
  • EEG: excessive sharp waves, no seizures
  • MRI brain: normal
  • Stayed in NICU until 11 days old for feeding
  • Exam at discharge: Increased appendicular tone

• Labs:
  • Lactic acid: 9.1 → 2.3
  • Ammonia: 54 → 44
  • CK: > 16,000 → 4851
HYPERTONIC INFANT

- Evaluated in neuromuscular clinic at 3 months
- Exam: Increased muscle bulk with firm consistency, increased tone, hyperreflexia
- CK 7467

- EMG/NCS:
  - Normal NCS upper and lower extremities
- EMG:
  - No abnormal spontaneous activity
  - Myopathic units, full early recruitment in biceps, TA and paraspinals
PATIENT 2
6 YO MALE WITH EXERCISE-INDUCED MUSCLE STIFFNESS

- 6 yo male presenting with episodic muscle stiffness triggered by exercise
  - 1st noticed at age 3 y
  - After playing soccer for 10-15 minutes, he would run stiff-legged
  - After playing with legos for a long time, reported arm pain and stiffness
  - Episodes resolve with rest

- No history of myoglobinuria
- No association with fasting, temperature, illnesses
- Episode witnessed by orthopedics team in clinic:
  - Walking with knees locked in extension
  - Muscles did not appear tense
  - Examiner gradually able to passively flex leg at knee
EXERCISE-INDUCED MUSCLE STIFFNESS

- Past medical history: Simple febrile seizure
- Developmental history: Normal
- Family history: Febrile seizures in father and several paternal uncles
- Exam: Normal
  - No myotonia
  - Negative Trousseau’s maneuver
  - Floor to stand 1.8 seconds, no Gower’s sign
  - 10 m run: 3.2 seconds

Labs:
- Lactic acid 1.2
- Ammonia 37
- Pyruvic acid 0.7
- CK 6915

MRI knee
PATIENT 3
6 YO FEMALE WITH LIMB-GIRDLE WEAKNESS

- Normal pregnancy and early development, walked at 14 months
- Preschool: Not as active as other children, not able to run or jump as well
- At age 6: Trouble with stairs and standing up from the ground, fatigue with short distances
6 YO F WITH LIMB-GIRDLE WEAKNESS

- Exam:
  - CN normal, no macroglossia
  - Increased bulk and fibrotic consistency of calf muscles
  - Neck flexion, hip flexion, extension, abduction and ankle dorsiflexion weakness
  - DTR 2+
  - Unable to perform a squat or heel walk
  - + Gower’s sign

- ESR 19
- CK > 12,000 → 5835
THOUGHTS?
GENETIC TESTING RESULTS
<table>
<thead>
<tr>
<th>Patient</th>
<th>Dystrophin testing results</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>4 base pair deletion in exon 62: c.9204_9207delCAAA; p.Asn3068Lysfs*20</td>
</tr>
<tr>
<td>2</td>
<td>In-frame deletion exons 14-30</td>
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<tr>
<td>3</td>
<td>Single base pair insertion in codon 413 (exon 10)</td>
</tr>
</tbody>
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## DYSTROPHINOPATHY

### CLASSIC
- Duchenne Muscular Dystrophy
  - CK > 10x normal
  - Complete/near complete absence of dystrophin
  - Symptom onset < 5 yo
  - Non-ambulatory by 13 yo

- Becker Muscular Dystrophy
  - CK > 5x normal
  - Later onset, non-ambulatory > 16 yo

### ATYPICAL PRESENTATIONS
- Dilated cardiomyopathy
- Asymptomatic hyperCKemia
- Muscle cramps with myoglobinuria
- Intellectual disability without muscle disease
- Symptomatic females
PATIENT FOLLOW UP

PATIENT 1
- 3 yo male
  - Receptive/expressive language delay
  - Mild cognitive, gross motor and fine motor delays
  - Calf pseudohypertrophy
  - Tight heel cords
  - DTR 2+

PATIENT 2
- 7 yo male:
  - Still having episodes of stiffness with exercise
  - Normal PFTs and echocardiogram
  - No weakness

PATIENT 3
- 17 yo female:
  - On weekend dosing of prednisone
  - Still ambulatory, + waddling gait
  - Asymmetric proximal > distal, right > left weakness
  - Mother negative for mutation in dystrophin
Dystrophinopathies are a spectrum of disorders

Brandesma JF and Darras BT. Dystrophinopathies. Semin Neurol 2015;35:369-384
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REFERENCES

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• Liewluck T et al., Dystrophinopathy mimicking metabolic myopathies. Neuromuscular Disorders, 2015;653-657.
• Magri F et al., Genotype and phenotype characterization in a large dystrophinopathic cohort with extended follow up. J Neurol.2011;258:1610-1623.