ATYPICAL CASES OF A COMMON NEUROMUSCULAR DISORDER

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PATIENT I

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

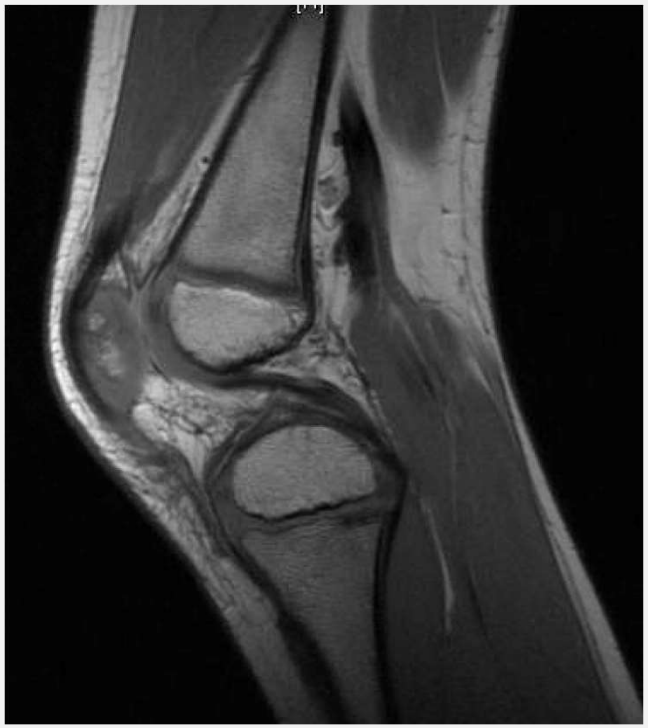
EXERCISE-INDUCED MUSCLE STIFFNESS

- 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

Total/free carnitine normal
Acylcarnitine profile normal
Plasma amino acids normal

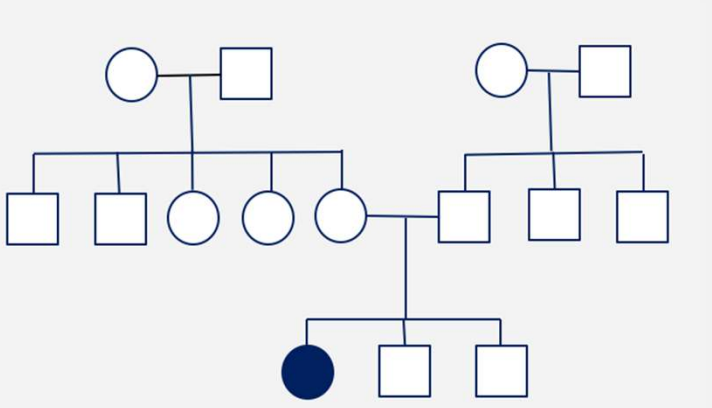


MRI knee

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

DYSTROPHIN

Patient	Dystrophin testing results
1	4 base pair deletion in exon 62: c.9204_9207delCAAA; p.Asn3068Lysfs*20
2	In-frame deletion exons 14-30
3	Single base pair insertion in codon 413 (exon 10)

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

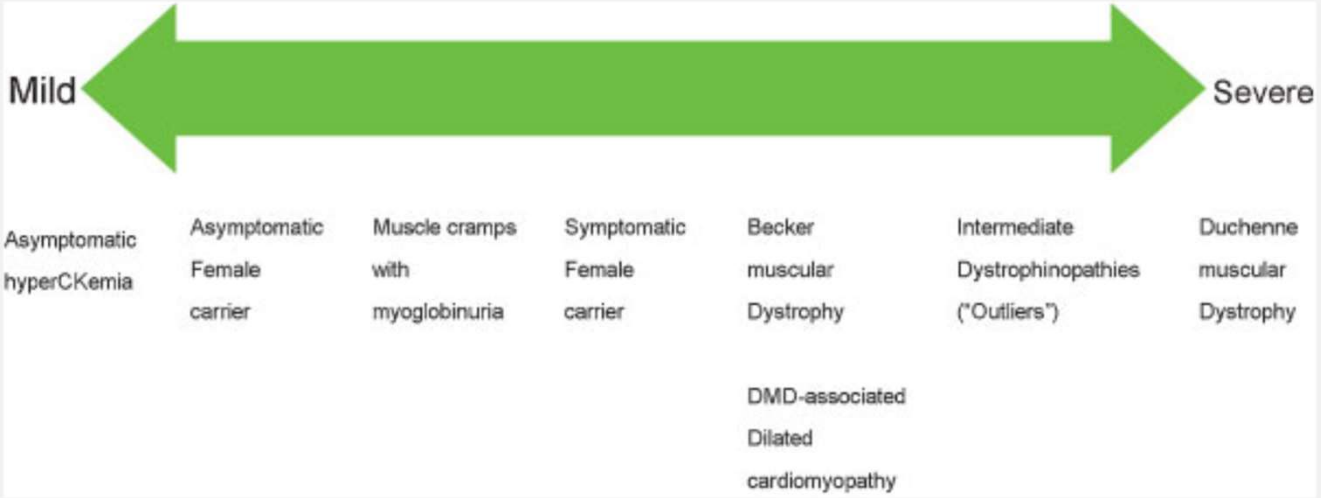
- 7 yo male:
  - Still having episodes of stiffness with exercise
  - Normal PFTs and echocardiogram
  - No weakness

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

TAKE HOME MESSAGE

Dystrophinopathies are a spectrum of disorders



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

THANK YOU

- **Sarada Sakamuri, MD**
- **Carolina Tesi Rocha, MD**

- Stanford Neuromuscular and Pediatric Neuromuscular Team:

John W. Day, MD, PhD	S. Charles Cho, MD	Les Dorfman, MD
Neelam Goyal, MD	Safwan Jaradeh, MD	Srikanth Muppidi, MD
Jacinda Sampson, MD	Yuen So, MD	Hannes Vogel, MD
Karolina Watson, NP	Jessica Guzman, RN	Carly Siskind, MS, LCGC
Michileen Oberst, LCSW	Bridgette Donahue, MPT	Richard Gee, MPT
Janis Kitsuwa-Lowe, OTR/L	Judy Henderson, CCC-SLP	Gayla Weng
Rika Yamasaki	Tim Fassler	Ewa Fratczak
Erum Jahan	Mauricio Rodriguez	MyMy Buu, MD

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