A Case of Progressive Proximal Weakness in a Young Woman

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History of Present Illness

• Previously healthy 17 year old teenager first noticed symptoms of difficulty throwing the shot put in 8th grade (~4 years prior to presentation)

• Then about 3 years ago she notice it was becoming difficult for her to get up off the floor or out of low chairs.

• She also notes that her “legs would give out” and she would fall. It was often difficult getting up from these falls.

• As time progressed, she developed difficulty going up stairs and trouble raising her arms above her head to wash her hair.
History of Present Illness

• Over the years, her symptoms continued to worsen despite trying to work out and increase her physical activity to improve her strength.

• She reports no weakness in her hands

• Both side are equally affected.

• Pertinent Negatives:
  • No pain or cramping but sometime muscles feel “achy” with excessive use
  • No difficulty swallowing or speaking
  • No diplopia
  • No bowel or bladder dysfunction
  • No episodes of dark tea-colored urine
  • No episodic worsening
  • No numbness or tingling
  • No rash
Past Medical History

• Birth and Developmental History
  • Normal gestation and delivery.
  • She sat at 6 months, walked at 1 year, talked at 1 year.
  • When playing with others or doing sports at a young age, she was always top to middle of the pack

• Past Medical
  • None

• Past Surgical History
  • None

• Medications/Allergies
  • None
  • No supplements
  • She had not been on any long term medications. She had occasional antibiotics for various reasons throughout her life but none recently (prior to presentation).
Past Medical History

• Family History
  • Mom, Dad, and Brother (age 20) are healthy
  • MGM: thyroid issues
  • MGF: diabetes
  • PGM: breast and colon cancer
  • PGF: lung disease
  • No known muscle or nerve disease in any of her extended family members

• Social History
  • Lives with mother, father, and 20 year old brother
  • Junior in high school. Gets A’s and B’s with both regular and advanced classes. Some stress at school due to peer interactions and social group.
  • Likes playing piano and photography
  • Plans to attend college
  • No toxic exposures
  • No alcohol, tobacco, or illicit drug use
  • Has traveled throughout the US and once to Japan
Physical Exam

• Normal General Exam

• Cranial Nerves were all intact. Smile was normal and symmetric. There was no fatiguing with sustained upgaze


• Sensory: intact in all extremities

• Coordination: no ataxia on finger to nose; Heel-shin was limited by weakness

• Gait: Unable to rise from chair with out doing modified Gower’s. Waddling gait
Laboratory Data

- **CK**: 8919 U/L (initial), ~12,000 U/L (peak)
- **CMP**: elevated AST (194) and ALT (244)
- **CBC**: normal
- **TSH**: normal (1.03)
- **ESR**: normal (2)
- **CRP**: normal (0.11)
- **ANA, SSA, SSB, and myositis antibody panels** were normal
- **Emory University LGMD panel** was normal
EMG/NCS

- Normal NCS of the right leg
- EMG of select muscles of the right arm and leg showed evidence of an *irritable generalized myopathy*.
  - Fibrillations, positive sharp waves and complex repetitive discharge were seen in all proximal muscles
  - Myotonic discharges were seen in the deltoid muscle.
  - Myopathic motor units were seen in all proximal muscles examined.
Muscle Biopsy

- Biopsy of the left quadriceps showed an acute and chronic necrotizing myopathy. There were occasional small foci of inflammation and occasional vacuolar changes.
Muscle Biopsy

• Biopsy was sent to the University of Iowa for further analysis.
• Immunostaining with a variety of muscular dystrophy-associated proteins failed to suggest a specific diagnostic pattern.
• MHC class 1 staining was positive but in a multifocal pattern (not diffuse)

Meanwhile, the patient was empirically tried on oral prednisone (0.5mg/kg) without any significant improvement.
Diagnosis???
Immune Mediated Necrotizing Myopathy Associated with HMGCR Antibodies

• HMGCR IgG >200 (normal 0-19)
  • From ARUP Laboratories (Salt Lake City)
Immune Mediated Necrotizing Myopathy Associated with HMGCR Antibodies

• First described by Dr. Mammen
• In adults, often associated with prior statin use and/or HLA DRB1*11:01.
• Recently, Dr. Mammen’s group screen 440 juvenile myositis patients and found 5 (1.1%) were anti-HMGCR positive.
  • None of the Five were exposed to statins
  • The DRB1*07:01 allele was present in all 5
    • 4 patients with DRB1*07:01-DQA1*02:01
  • Characteristic findings in these patients included severe proximal weakness, distal weakness, high CK levels, muscle atrophy, joint contractures, and arthralgias.
• Partial response to immunosuppressive therapy
Immune Mediated Necrotizing Myopathy Associated with HMGCR Antibodies

• The patient was started on monthly IVIG (2g/kg divided over 2-5 days)
• Methotrexate 10mg weekly (0.1mg/kg weekly)
• She’s been making steady improvements in regards to her weakness.
  • Able to get up off the floor
  • Able to raise her arms above her head
  • Fewer falls
• CK is now ~800 U/L
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