2016 AANP Diagnostic Slide Session Case #7:
An unusual case of progressive muscle weakness in an adult woman

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Nothing to disclose.
Clinical history

- 78 y/o woman with 10 years of progressive lower extremity weakness causing difficulty with ambulation requiring use of a cane or walker and eventually a wheelchair.

- Also had progressive weakness in her arms more recently over the last couple years.

- Serum CK level has never been elevated.

- Evaluated multiple times during disease course with reportedly normal serum CK levels and EMG and nerve conduction studies.

- Failed trials of prednisone, mycophenolate, azathioprine, and pyridostigmine.

- Current physical exam shows symmetrical weakness in proximal>distal muscles.

- Kyphotic posture and antalgic gait.

- Repeat EMG shows myopathic motor units without muscle membrane instability in multiple muscle groups consistent with a myopathic process.

- Muscle biopsy from the biceps was performed.
H&E on frozen section
Gomori trichrome
NADH stain
NADH stain
ATPase stain at pH 9.2
ATPase stain at pH 9.2
PAS stain
PAS stain
Toluidine blue stain of Epon-embedded section
electron microscopy
electron microscopy
electron microscopy
So what’s the diagnosis?
ATPase stain at pH 9.2
immunostain for slow myosin
immunostain for slow myosin
immunostain for slow myosin
immunostain for slow myosin
Final diagnosis:

Biceps, biopsy: Myosin storage (hyaline body) myopathy. Recommend cardiac evaluation and assessment for MYH7 gene mutation.
Myosin storage myopathy

- Is a congenital myopathy characterized by subsarcolemmal inclusions in type 1 skeletal muscle fibers composed of slow myosin.
- Previously was identified as hyaline body myopathy.
- Patients have variable age of onset ranging from childhood to middle age and typically suffer from progressive proximal weakness and respiratory insufficiency but do not usually have cardiac disease.
- Has been linked to mutations within the MYH7 gene that encodes the slow/beta-cardiac myosin heavy chain.
Myosin Storage Myopathy Associated with a Heterozygous Missense Mutation in MYH7

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MYH7 mutations and human disease spectrum

- Mutations in MYH7 in patients with myosin storage myopathy cluster within the C-terminal rod domain and have been found to disrupt normal myosin filament assembly and stability.

- Mutations in MYH7 are also known to cause hypertrophic cardiomyopathy (present in 45% of cases) but instead cluster within globular head domain and have been shown to disrupt ATPase activity or actin binding.

- Mutations in MYH7 are also known to cause Laing distal myopathy and cluster in the C-terminal rod domain similar to myosin storage myopathy.

- Genotype-phenotype relationship of MYH7 mutant disease:
  Mutations in exons 1-25 = hypertrophic cardiomyopathy
  Mutations in exons 32-36 = Laing distal myopathy
  Mutations in exons 37-39 = myosin storage myopathy
Myosin storage myopathy is a congenital myopathy characterized by subsarcolemmal inclusions in type 1 skeletal muscle fibers composed of slow myosin.

Autosomal dominant disease with variable clinical presentation due to mutations within the MYH7 gene that cluster within the C-terminal rod domain.

Cardiac assessment is recommended in these patients as some cases are accompanied by hypertrophic cardiomyopathy.
References


Questions???