Patient Case Study #1

Typical Presentation

HPI

45-year-old, right-handed, Caucasian male presents after having an abnormal EMG. Patient reports weakness in his legs for the last 2 to 3 years and atrophy in his thigh muscles. He denies muscle twitching, upper extremity weakness, back pain, sphincter dysfunction, or bulbar symptoms. He is a plumber and it has become progressively more difficult due to carrying heavy equipment and getting up from the ground. He does c/o SOB but this has preceded his muscle complaints by 5 years.

SocHx

He is married with a 12-year old son who is healthy. He is a plumber but currently on disability from his job due to SOB. No tobacco or drugs. Drinks ETOH occasionally.

FamHx

No known neuromuscular disorders. One brother and several half-brother/sisters are all healthy and without similar symptoms.

PMHx

- Chronically elevated LFTs, s/p liver biopsy x 2 reported as normal
- Elevated CPK 4 years ago treated with prednisone by a rheumatologist. No h/o muscle biopsy
- SOB – found to have an elevated hemi-diaphragm

Medications

Not available

Allergies

NKDA

Exam

- Gen: NAD, VSS, HEENT normal, Heart RRR without murmur, Pulm CTA, Extremities warm without edema
- MS: Alert & Oriented x 3, clear and fluent speech, normal affect
- CN: PERRLA, EOMI, Facial muscle strength and sensation are normal. Masseter and temporalis muscles are normal and without atrophy. Palate is midline with normal tongue size and strength without fasciculations
- Motor: UE 5/5 bilaterally

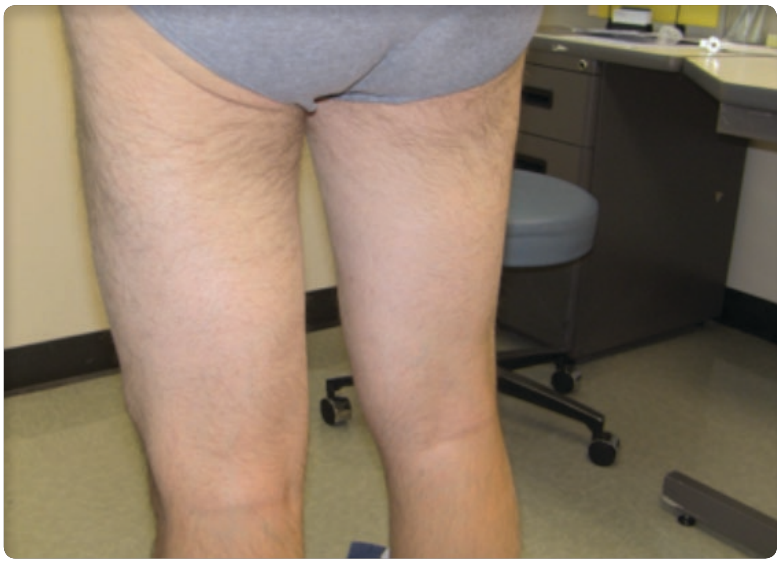
  LE hip flexor 3/5 bilaterally, hamstring 4/5 bilaterally, thigh adductors 4-/5 bilaterally, knee extensors/thigh abductors/ankle dorsiflexors/plantar flexors 5/5

  Atrophy of the posterior and medial thigh muscles bilaterally (figure 1)

  No fasciculations or hypertrophy were seen

  Normal muscle tone
- Sensory: Intact to all modalities in the UEs and LEs
- Coordination/Gait: No dysmetria in the UEs. No truncal ataxia. LE dysmetria testing was difficult to assess due to weakness. Gait is waddling and lordotic

Figure 1: Atrophy of the posterior and medial thigh muscles bilaterally



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Labs/Diagnostics

CBC, CMP, ESR, CRP, ANA profile, complement levels, Jo-1 antibody, TSH, vitamin B12 were all normal except for:

- AST 89 IU/L [normal <50]
- ALT 107 IU/L [normal <60]
- CPK 733 IU/L [normal <196]

Imaging

CXR showed a right-elevated hemidiaphragm.

EMG/NCV

Irritative myopathy with proximal myotonic discharges.

PFT

- Upright FVC 1.79 L [37% of predicted]
- Supine FVC 0.66 L [13% of predicted]

Genetic Analysis

Calpain-3 mutation was normal. GAA enzyme activity via DBS was 1.3 pmol/punch/hr [normal >10.0]. GAA sequencing showed compound heterozygote mutations with the common intronic mutation often seen in late-onset Pompe disease (LOPD) in 1 allele and a premature stop codon in the other allele.

Discussion

Classic presentation of LOPD

- Elevated LFTs due to muscle AST and ALT suggesting years of muscle damage
- Early respiratory muscle involvement with breathing difficulties due to diaphragm weakness especially in the supine position
- Proximal muscle involvement with hamstring and thigh adductor weakness

Respiratory involvement may be a subtle feature of LOPD

- Pulmonary evaluations can be negative except for the identification of restrictive lung disorder
- Neuromuscular respiratory weakness is a critical component of neurologist's awareness

Clinical pattern of proximal muscle weakness narrows the diagnosis of muscle diseases

- LGMD2A, which is the most common cause of autosomal recessive muscular dystrophy, has mutations of the Calpain-3 gene, which were normal in this patient
- Polymyositis and proximal myotonic myopathy (myotonic dystrophy type 2) present with myotonic discharges on EMG/NCV but do not include the other symptoms seen in late-onset Pompe disease

Findings critical to making the diagnosis of LOPD

- Pattern of lower extremity weakness predominant, especially in the thigh adductors and hamstrings
- Respiratory symptoms and signs, especially the reduction of the FVC in the supine position
- Respiratory symptoms may precede limb weakness
- Proximal muscle weakness with EMG findings of proximal myotonic discharge

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