Case of proximal weakness in an elderly man

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INTRODUCTION

- 65 years old man with past medical history of diabetes type 2 and dyslipidemia
- Recent exacerbation of progressive symptoms of proximal weakness in arms and legs
- The exact onset of his symptoms was unclear
- Difficulty raising arms above the head and difficulty getting out of the chair
- Particularly bothered by myalgias and exertional muscle cramps
- Review of systems noticeable for muscle atrophy
  - No rashes or joint pain
  - No back pain or bladder dysfunction
  - No diplopia, ptosis, or bulbar abnormalities
Review of medications revealed:

- Atorvastatin for 4 years
- While on that agent his CK was 4,000 range
- Agent was stopped and CK reduced, but still mildly elevated in the range of 300s
- No clinical improvement was noted in his symptoms despite discontinuation of atorvastatin
RESULTS

**Pertinent elements of his Neurological exam:**

- Strong neck extensors, but neck flexors (4/5)
- Atrophy of the proximal muscles of both arms

**Strength in the arms (B/L):**

- Deltoids (3/5), Biceps (4-/5), Triceps (4/5), ECR and FCR (5/5), APB (5/5), and Ulnar intrinsics (5/5)

**Strength in the legs (B/L):**

- Iliopsoas, (4+/5), and very minimal weakness of the Gluteus maximus bilaterally (5-/5). Remaining legs muscles were strong

**Deep tendon reflexes, sensation and cranial nerve examination otherwise normal**
Initial Neuromuscular Impressions

- Possible cholesterol-lowering agent myopathy
- Possible inflammatory myopathy
- Possible metabolic myopathy

**Follow up plan**

- Electrophysiological studies
- Muscle biopsy
Electrophysiological Impression

Study was interpreted as showing:

- Evidence of clear myopathic motor units and spontaneous activity in proximal arm and leg muscles
- Evidence of probable generalized peripheral neuropathy affecting motor and sensory axons
Differential Diagnosis

- Inflammatory myopathies
  - Polymyositis
  - Inclusion body myositis
- Metabolic myopathies
- Muscular dystrophies
- Neuromuscular junction disorder
MUSCLE BIOPSY
Muscle Biopsy Results

Histopathology of muscle biopsy was interpreted as showing:

- Moderately severe muscle atrophy with mixed myopathic and neurogenic changes
- Myophosphorylase activity was not detected by immunohistochemical stains
- No evidence of inflammation or vasculitis
Discussion

- **McArdle’s Disease:**
- **Background**
  - In 1951, McArdle described 1st case in a 30 year-old man who experienced pain, weakness and stiffness after exercise.
  - In 1959, myophosphorylase was discovered and was found to be absent in individuals with McArdle’s disease.
Genetics

- Autosomal recessive disorder
- Rare cases of autosomal dominant inheritance
- Sporadic non-familial cases have been reported
- Mutations of the *PYGM* gene located on chromosomes 11q 13, are usually nonsense or missense
Pathophysiology

- Myophosphorylase catalyzes the removal of 1,4-glucosyl residues from the glycogen molecule, liberating glucose 1-phosphate.
- Consequently, the individual is unable to release glucose from glycogen storage in muscle.
- Symptoms in patients are most likely caused by the pattern of fuel utilization of exercising muscle.
Epidemiology

- 1-2 per 100,000 population
- Only a few hundred cases have been reported
- Probably under-diagnosed because of the mild symptoms in many patients
- Male > Female
- Typically presents in the second to third decade of life as limited exercise tolerance
- Late-onset (>60y) form is very rarely reported
Clinical Presentation

- **McArdle’s disease.**
  - Exercise intolerance with myalgias
  - Early fatigue
  - Muscle stiffness
  - Cramping
  - Symptoms relieved by rest
  - Second wind phenomenon
On Exam

- Classic and late-onset McArdle’s disease
  - Proximal muscle weakness
  - Fixed limb weakness
  - Muscle atrophy
Diagnosis

**Labs**
- Elevated serum CK levels at rest
- No rise of venous lactate after ischemic forearm exercise test usually seen as (flat venous lactate level)

**Electrophysiology**
- EMG – Abnormal spontaneous activity (fibrillation potentials, positive sharp waves) and myopathic motor unit action potentials

**Genetics**
- Analysis of DNA gene test for mutation in leukocytes

**Biopsy**
- Subsarcolemmal vacuoles with deposits of glycogen on (PAS) and Masson trichrome stains
- Total lack of myophosphorylase activity
Management

**DIET**

- Attempt to bypass the metabolic block by providing glucose or fructose
- High-protein diet may be beneficial
- Vitamin B-6

**TAKE ADVANTAGE OF SECOND WIND PHENOMENON**
CONCLUSION

McArdle’s disease

- Late onset is very rare, only few cases has been reported in literature
- Clinical picture may be nonspecific and highly variable
- Elderly patients with proximal myopathy should consider McArdle’s disease in the differential
- As in my case with onset in 7th decade