

## Atypical Presentation

### HPI

62-year-old female presents to the neuromuscular clinic for evaluation of difficulty walking distances or up stairs. Over the last 10 to 15 years, she has had progressive weakness of the legs, with muscle wasting in the thigh muscles over the last 5 years. She admits to cramps in the legs which worsen with mild exercise, but denies having any fasciculations, sensory symptoms, or autonomic symptoms. She has had drooping of her eyelids since her teenage years which required surgical correction 10 years prior.

### SocHx

She is divorced with 3 children. She ceased tobacco use 30 years ago, drinks 1 to 2 ETOH drinks per day. She denies illicit drug use. Her occupation was a school teacher, and she has been retired for 10 years.

### FamHx

No family history of similar symptoms, but her daughter (age 43) has noticed some difficulty in her gait. However, she has not been formally evaluated.

### PMHx

- Asthma
- Hypothyroidism
- Depression
- s/p tonsillectomy, hysterectomy, blepharoplasty

### Medications

Synthroid 150 mcg/day, Fosamax 70 mg/week, fluoxetine 20 mg/day, Advair inhaler, and MVI.

### Allergies

NKDA

### Exam

- **Gen:** NAD, VSS, unremarkable with no skin changes, organomegaly, or joint abnormalities
- **MS:** Alert & Oriented x 3, speech is mildly dysarthric, normal affect
- **CN:** PERRLA, EOMI, marked bilateral ptosis with evidence of surgical repair. Facial muscle strength and sensation are normal. Masseter and temporalis muscles are normal without atrophy. Palate is midline but tongue is atrophic and weak bilaterally without fasciculations (figure 1)
- **Motor:** UE 5/5 bilaterally both proximally and distally  
LE hip flexor 3/5 bilaterally, hamstring 4+/5 bilaterally, knee extensors 4+/5, ankle dorsiflexors/plantar flexors 5/5  
Atrophy of the quadriceps muscles bilaterally  
No fasciculations or hypertrophy were seen  
Normal muscle tone without hypertrophy
- **Sensory:** Intact to all modalities in the UEs and LEs
- **Reflexes:** Biceps, triceps, brachioradialis, quadriceps, and ankle reflexes are 1+. Babinski and Hoffman signs are absent
- **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: Palate is midline but tongue is atrophic and weak bilaterally without fasciculations



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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:

- CPK 324 IU/L [normal <196]

### Imaging

Brain MRI without contrast was normal.

### EMG/NCV

Reported as normal.

### PFT

Upright FVC was 61% predicted for age and gender, supine FVC was 47% of predicted.

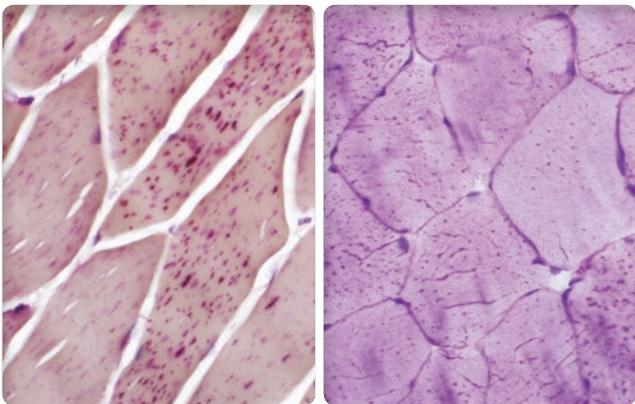
### Genetic Analysis

Repeat analysis in the PABP2 gene for oculopharyngeal muscular dystrophy showed normal numbers of repeats.

### Pathologic studies

Right biceps muscle biopsy revealed a vacuolar myopathy with PAS staining associated with some vacuoles. Ultrastructural analysis showed subsarcolemmal vacuoles and membrane-bound material consistent with glycogen (figure 2).

Figure 2: Right bicep muscle biopsy micrograph & EM



**References:** 1. Montagnese F, Barca E, Musumeci O, et al. Clinical and molecular aspects of 30 patients with late-onset Pompe disease (LOPD): unusual features and response to treatment. *J Neurol*. 2015;262(4):968-978. 2. Panosyan FB, Fitzpatrick MF, Bolton CF. Late onset Pompe disease mimicking rigid spine syndrome. *Can J Neurol Sci*. 2014;41(2):286-289. 3. Hobson-Webb LD, Jones HN, Kishnani PS. Oropharyngeal dysphagia may occur in late-onset Pompe disease, implicating bulbar muscle involvement. *Neuromuscular Dis*. 2013;23(4):319-323. 4. Laforet P, Doppler V, Caillaud C, et al. Rigid spine syndrome revealing late-onset Pompe disease. *Neuromuscular Dis*. 2010;20(2):128-130. 5. Hanisch F, Rahne T, Plontke SK. Prevalence of hearing loss in patients with late-onset Pompe disease: audiological and otological consequences. *Int J Audiol*. 2013;52(12):816-823. 6. El-Gharbawy AH, Bhat G, Murillo JE, et al. Expanding the clinical spectrum of late-onset Pompe disease: dilated arteriopathy involving the thoracic aorta, a novel vascular phenotype uncovered. *Mol Genet Metabol*. 2011;103(4):362-366. 7. Jones HN, Crisp KD, Asrani P, Sloane R, Kishnani PS. Quantitative assessment of lingual strength in late-onset Pompe disease. *Muscle Nerve*. 2014;51(5):731-735.

### Discussion

#### Atypical presentation of LOPD

- Classical LOPD usually presents with slowly progressive pelvic girdle and respiratory muscle weakness
- Ptosis, an unusual presentation, has a prevalence of about 7%<sup>1</sup>
- Several uncommon presentations have been described including distal muscle wasting, waddling gait, rigid spine syndrome, and oropharyngeal dysphagia<sup>1-4</sup>
- Non-neurological features may also be present, such as cerebrovascular arteriopathy, hearing loss and gastrointestinal symptoms<sup>5,6</sup>
- Tongue weakness and/or hypertrophy are uncommon features with tongue atrophy occasionally leading to an alternative diagnosis such as motor neuron disorders or oculopharyngeal muscular dystrophy (PABP2 gene showed normal numbers of repeats, which excludes oculopharyngeal muscular dystrophy)

#### Respiratory involvement may be a subtle feature of LOPD

- Respiratory muscle involvement is often insidious and may not be spontaneously reported by the patient
- The diaphragm is prominently affected with symptoms of nocturnal hypoventilation (fatigue, morning headaches, etc) or orthopnea
- A reduction of the forced vital capacity (FVC) between upright and supine of >10%, often >20%, is indicative of diaphragmatic weakness

#### Diagnostic delays

- The variability of phenotypes for LOPD overlap significantly with other progressive genetic muscle diseases, resulting in poor recognition and diagnostic delays
- DNA-based diagnostic testing is an established method for discerning LOPD

#### Critical aspects of atypical LOPD

- Non-neurologic symptoms such as oropharyngeal and respiratory abnormalities are part of the expanding phenotype of LOPD and require a high index of suspicion