A MAN WITH PROGRESSIVE LEG WEAKNESS AND FALLS

Elisabeth P. Golden, MD, Lan Zhou, MD, PhD, Jeffrey Elliott, MD, Lauren Phillips, MD

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CASE PRESENTATION

- 57-year-old man presents with weakness
- Progressive difficulty arising from chairs x3 years
- Increasing frequency of falls, can't run anymore
- Subtle arm weakness
- Feet feel "cold"
- Denies ocular, bulbar, or respiratory symptoms
- Subtle tremor in his hands
- Uses hearing aids

PAST MEDICAL HISTORY

- No childhood concerns
- BPH
- Hearing loss, attributed to working around jet engines x20 years
- Hypertension
- Dyslipidemia, on statin previously
- GERD
- OSA on CPAP
- Meds: iron, fish oil, multivitamins

FAMILY/SOCIAL HISTORY

- Family
  - Father, older brother with CAD
  - Mother with diabetes
  - 3 adult sons, healthy
  - 3 healthy grandchildren
  - No concern for neuromuscular disease
- Social
  - No T/E/D
  - Computer programmer
  - Retired military

EXAM

- Mental status: normal
- Cranial nerves:
  - EOMI, no ptosis
  - 3/5 orbicularis oculi, 4+/5 orbicularis oris
  - 4+/5 tongue (no atrophy or fasciculations)
  - Voice is high-pitched and nasal
- Motor
  - Atrophy of pecs, upper arms
  - Tone normal
  - No scapular winging or scoliosis
  - Neck flexors 4-/5, extensors 5-/5

Muscle group	L	R
Shoulder abductors	5	5-
Elbow flexors	5-	5-
Elbow extensors	5-	4
Wrist flex/ext	5	5
Finger flexors	4+	5-
Finger ext/abd	5	5
Hip flexors	3	3
Hip abd/add	5	5
Knee flexors	5-	5-
Knee extensors	4+	4+
Ankle dorsiflexors	5-	5-
Ankle plantarflexors	5	5
Ankle inv/ev	5	5
Toe flex/ext	5	5

EXAM, CONT.

- Reflexes
  - DTRs trace to absent throughout
  - No UMN signs
- Sensory
  - Pinprick decreased to mid-shins
  - Mild vibratory loss at toes
- Coordination: postural and intention tremor
- Gait: mildly waddling

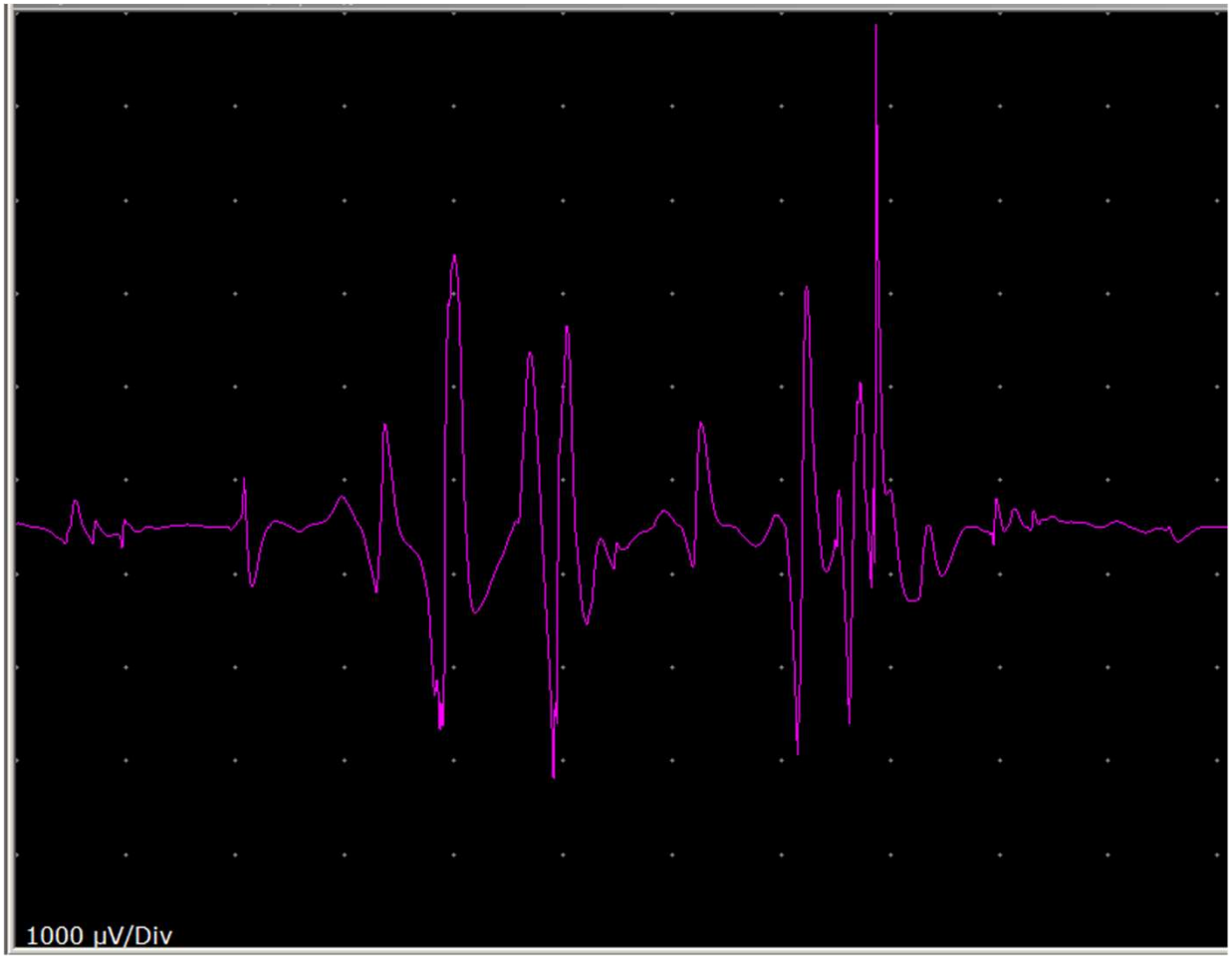
ANCILLARY DATA

- Labs
  - CMP, CBC unremarkable
  - CK 761 (down from 1100 while on statin)
  - TSH 1.76
  - A1c 5.6
- Imaging
  - MR brain: unremarkable
  - MR C spine: multilevel spondylosis, no canal stenosis or significant neural foraminal stenosis

NERVE CONDUCTION STUDIES

- Upper extremity normal
- Lower extremity
  - Decreased peroneal amplitude at EDB (1.6 mV) and TA (2.1), velocity 37 m/s
  - Decreased tibial amplitude (1.0), velocity 37
  - Absent sural and superficial peroneal sensory responses

EMG



EMG

Side	Muscle	Nerve	Root	PSW	Fibs	Fasc	Poly	Amp	Dur	Ins Act	Activa	Recrt	Comment
Left	Deltoid	Axillary	C5-6	Nml	Nml	1+	None	Incr	Incr	Incr	Decr	Decr	very large mup
Left	Triceps	Radial	C6-7-8	1+	Nml	1+	Few	Incr	Incr	Incr	Decr	Decr	pseudomyotonia
Left	Vastus Med	Femoral	L2-4	2+	1+	Nml	Many	Incr	Incr	Incr	Nml	Decr	pseudomyotonia
Left	Ant Tibialis	Dp Br Fibular	L4-5	1+	Nml	Nml	None	Incr	Incr	Incr	Nml	Decr	pseudomyotonia
Left	Orbic Oris	Facial	CN VII	Nml	Nml	1+	None	Incr	Nml	Incr	Decr	Decr	

EMG

- Irritability with pseudomyotonia in all tested limb muscles
- Occasional fasciculations
- Increased insertional activity and fasciculations in the orbicularis oris
- Large motor units with decreased recruitment
- Impression:
  - Diffuse motor axonal process with active and chronic neurogenic changes in limb and facial muscles.
  - Superimposed axonal sensorimotor polyneuropathy.

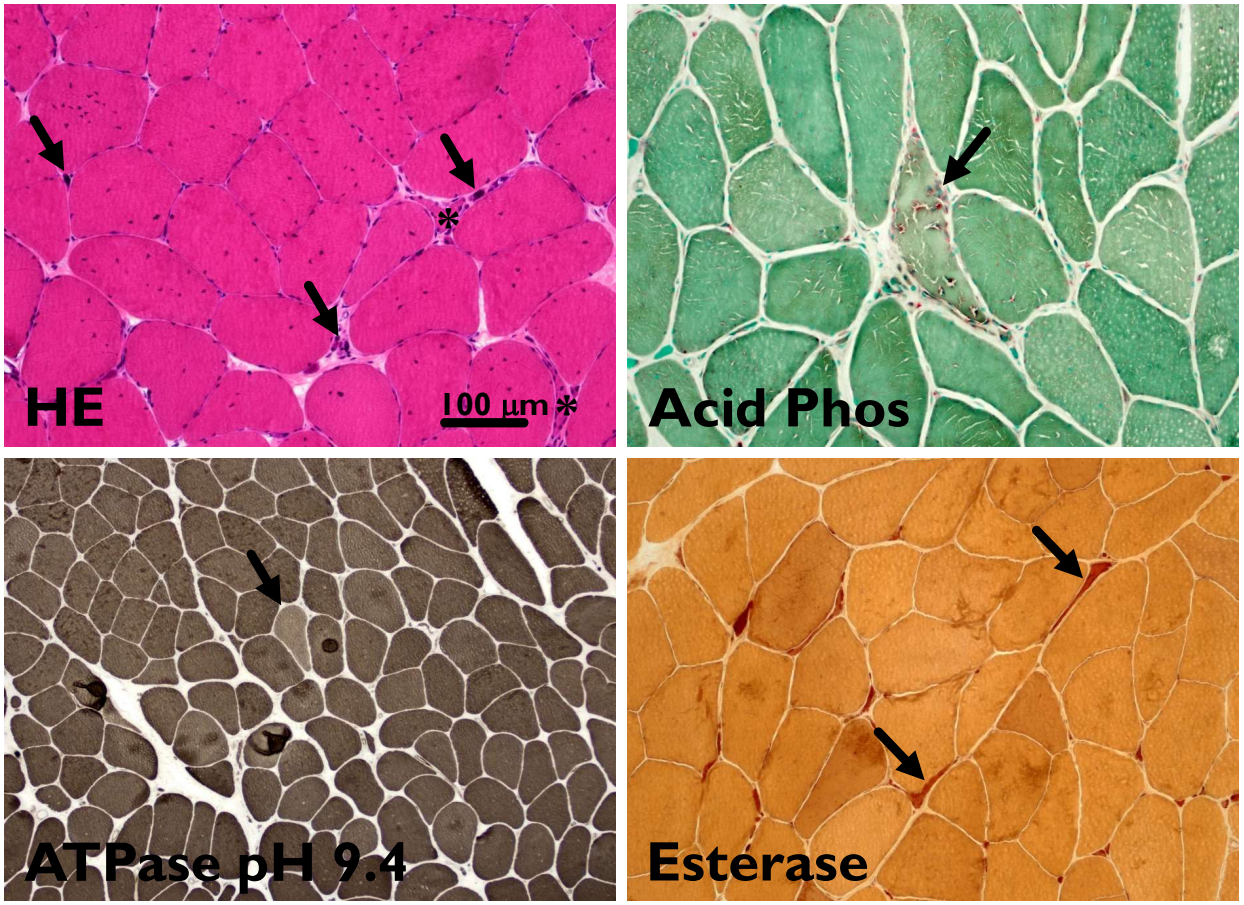
THOUGHTS?

- Localization
  - Anterior horn cells, roots
  - Motor +/- sensory nerves
- Differential diagnosis
  - Spinobulbar muscular atrophy (Kennedy's disease)
  - Adult-onset spinal muscular atrophy
  - Inclusion body myositis
  - LMN predominant ALS
  - Paraneoplastic motor neuronopathy
  - Lyme disease

ADDITIONAL INFORMATION

- Androgen receptor gene testing with 20 CAG repeats (normal)
- *SMN1* no exon 7 deletion
- Muscle biopsy

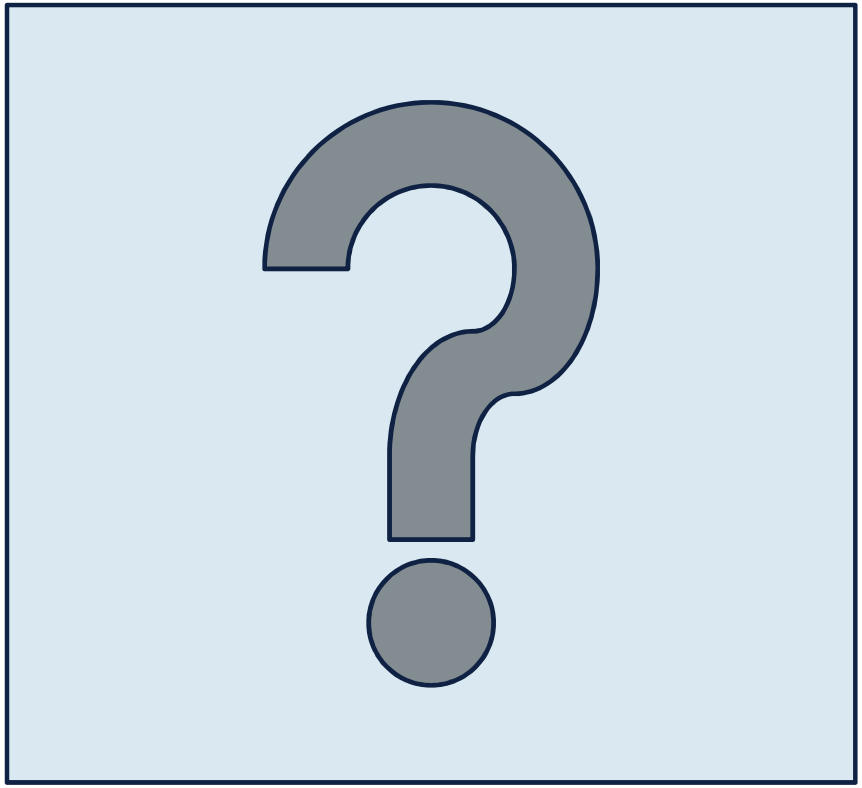
MUSCLE BIOPSY—TRICEPS



MUSCLE BIOPSY

- Mild chronic active myopathy with myofiber hypertrophy, a few degenerating and necrotic fibers, rare myophagocytosis, markedly increased internalized nuclei, and many pyknotic nuclear clumps.
- Remarkable type II fiber predominance.
- No ring fibers.
- Some scattered esterase positive atrophic fibers. No grouped fiber atrophy.

THOUGHTS?



DIAGNOSIS

- CNBP gene analysis: one allele with >75 CCTG repeats
- Myotonic dystrophy type 2

TYPE 2 MYOTONIC DYSTROPHY

- AKA proximal myotonic myopathy (PROMM)
- Autosomal dominant
- Intronic CCTG repeat expansion in CNBP (ZFN9)
  - #repeats =/= severity of disease
  - Somatic instability
  - No anticipation
- Abnormal RNA accumulates in muscle nucleus→abnormal splicing of CLCN1→myotonia
- Abnormal splicing in other tissues→multisystemic disease

DM2 CLINICAL FEATURES

- Adult onset (3rd to 7th decades, mean 34 years)
- Multiple presentations (diagnostic delay 14 years)
  - Lower limb weakness
  - Proximal muscle atrophy, or calf hypertrophy
  - Distal weakness
  - Variable or absent clinical myotonia
  - Prominent muscle pain
- Pattern of weakness
  - Hip flexors/extensors
  - Knee extensors
  - Neck flexors
  - Finger flexors

DM2 EXTRAMUSCULAR FEATURES

- Cataracts
- Hearing loss
- Tremor
- Arrhythmia/cardiomyopathy
- Rare respiratory involvement
- Milder cognitive/sleep disturbances
- Insulin resistance and hypogonadism

DM2 EMG FINDINGS

- Myotonia may be absent, or only detectable in proximal muscles or on repeat testing
- May have "waning only" myotonic discharges
- Myopathic motor units

DM2 BIOPSY FINDINGS

- Internal nuclei, fiber size variation
- Type 2 fiber atrophy and/or hypertrophy with pyknotic nuclear clumps
- Angulated fibers (“denervation-like”)
- Ring fibers

OUR PATIENT

- Supportive of DM2
  - Proximal leg weakness
  - Neck flexion weakness
  - Finger flexion weakness
  - Proximal muscle atrophy
  - Hearing loss
  - Tremor
  - Elevated CK
- Unusual/misleading features
  - Sensory impairment
  - Lack of family history
  - Neurogenic features on EMG
  - Minimal myotonia on EMG
  - Type 2 predominance on biopsy

CONCLUSION

- DM2 has a variety of clinical phenotypes
- Myotonia may be subtle or absent

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