Slow progressive gait impairment with abrupt decompensation

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History of present illness

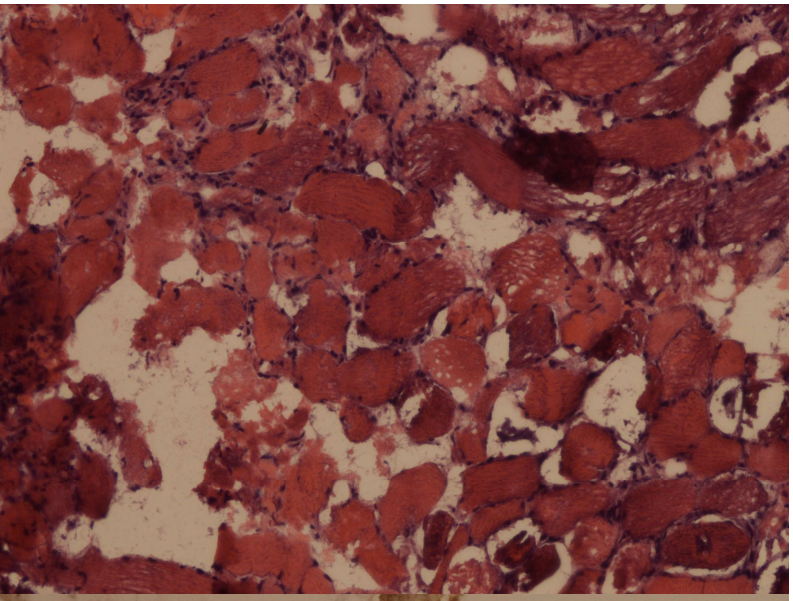
- 24 year old female.
- Worsening of gait over period of 2 weeks.
- Later developed emesis, confusion and lethargy, presented to local ED, and was admitted.
- Initial laboratory evaluation:
  - Severe anion gap metabolic acidosis with pH of 6.95.
  - Leukocytosis to 30K.
  - Normal renal function at presentation.
- Intubated for airway protection shortly after admission.
- Received emergency dialysis for acidosis. Corrected within 2 days.

Acute illness at outside hospital

- CK elevated to 2800 on admission.
- Neurology consulted 2 days after admission for weakness.
  - Exam: No movement in legs. Antigravity movements in arms. Sensory normal. Reflexes absent.
  - Recommended CSF studies, then IVIG for possible AIDP.
- CK elevated up to 18,000 at which time muscle biopsy was recommended.
- Also had elevation of AST and ALT, marked decrease in platelets (467 -> 66K), AKI (Cr 2.8), and elevated INR (2.8) with diagnosis of disseminated intravascular coagulation.

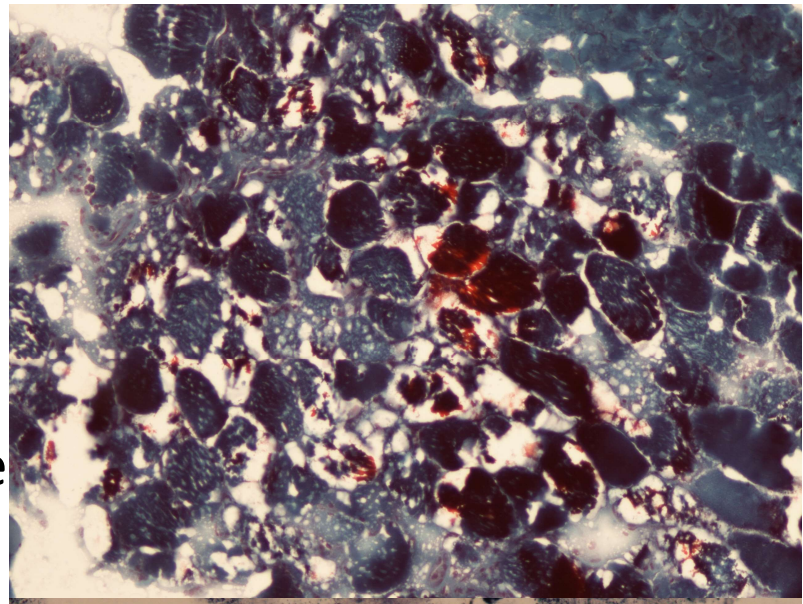
Medical history

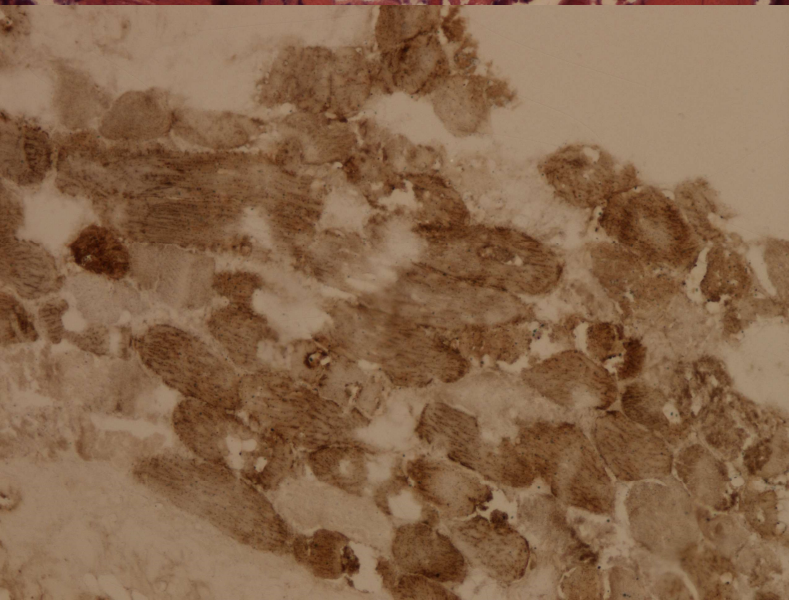
- PMH
  - Generalized anxiety disorder, ankle contractures
- Social Hx
  - Lives with parents, no education beyond high school. Working prior to illness.
- Developmental
  - No delay in motor milestones. Had learning disability and completed high school with IEP.
- Family
  - No family history of neurologic or neuromuscular disorders.



H&E

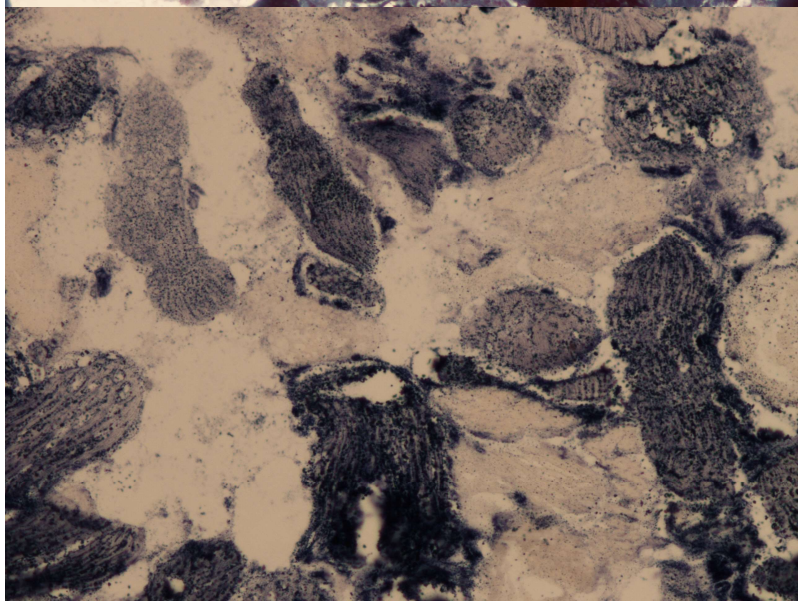
Gomori trichrome

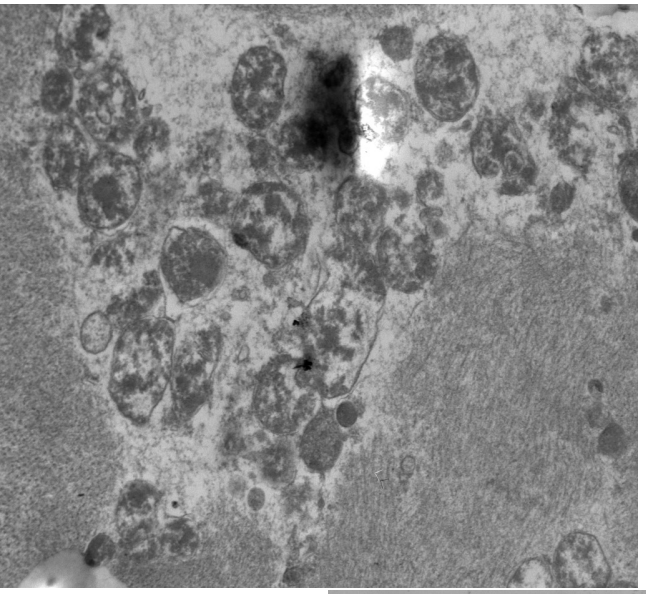


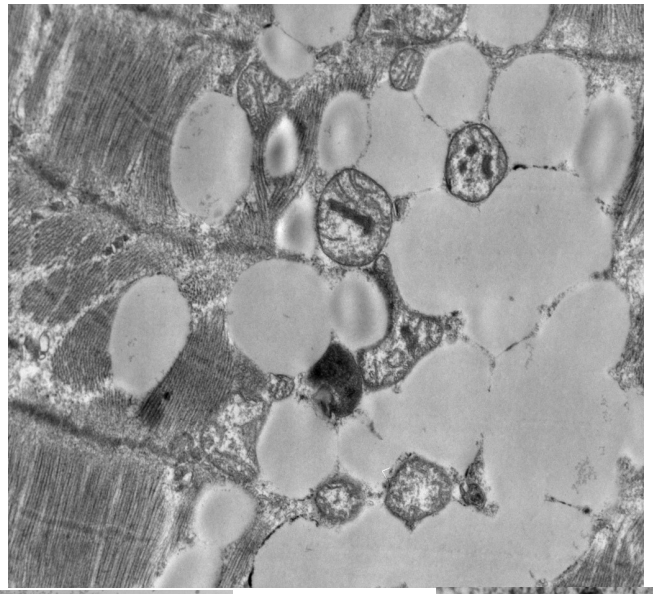


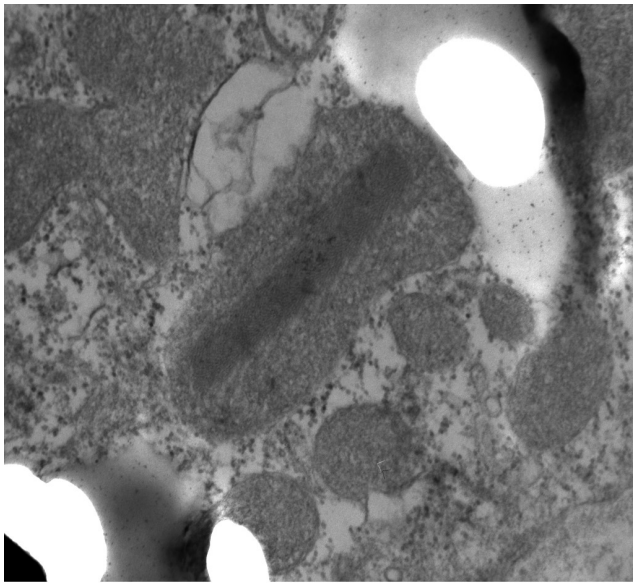
COX/SDH

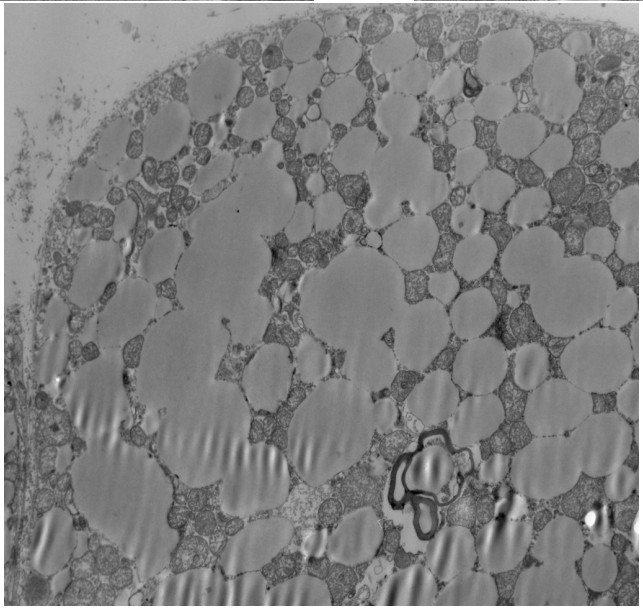
NADH

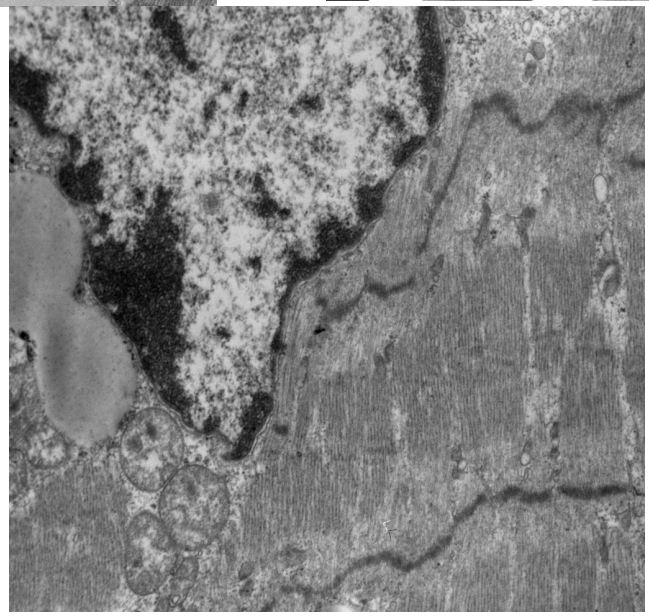












Differential?

Next steps in diagnostic evaluation?

Differential

- CPT II deficiency
- Multiple acyl-CoA dehydrogenase deficiency
- Electron transfer flavoprotein deficiency
- Neutral lipid storage disease with myopathy

Laboratory

- Lipid panel: Normal
- Serum carnitine profile: Normal
- Acylcarnitine profile: Elevation of several acylcarnitine species suggestive of multiple acyl-CoA dehydrogenase deficiency.
- Acylglycine analysis: Minimal elevation of isobutyrylglycine and isovalerylglycine.
- Urine organic acids: “massive elevation of orotic acid” when initially obtained. Later normal.

Genetic testing

- Testing for inherited myopathies showed variants of uncertain significance in RYR1, NEB, and CAPN3.
- Genetic panels for mitochondrial and metabolic myopathies, and lysosomal disorders was negative.
- No mutations identified in CPT2, PNPLA2, ETFA, ETFB, or ETFDH genes.

Diagnosis

- Lipid storage myopathy
  - Are the mitochondrial changes primary or secondary?
- Next steps in evaluation
  - Plan to repeat muscle biopsy with genetic testing of tissue.
  - Whole exome sequencing.
- Referral to Dr. Haller.