CMT phenotype with scapular winging

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Disclosure Information

Gil I. Wolfe MD et al.

Disclosure of Relevant Financial Relationships

None

Disclosure of Off-Label and/or investigative Uses

None

History and PE

- 22 yo Dutch man
  - >12 yrs of ankle instability, slowly progressive distal weakness
    - First noted while ice skating; played hockey through age 16
    - Tremor at age 20
    - No CN, bulbar, respiratory issues
  - FHx: PE-confirmed scapular winging in mother
  - PE
    - Bilateral distal tapering, pes cavus, scapular winging
    - MRC 4+ finger extension/abduction; 4 ankle df/eversion; 3 toe extension; ankle pf normal
    - DTRs absent at ankles
    - Sensory loss to light touch below ankles; timed vibration 5 secs at great toes

Laboratory evaluation

- NCS showed axonal SMPN
  - NCS normal in both parents
- Routine labs
  - Normal metab panel, ESR 1, TSH 0.9, B12 1040, ANA neg, etc.
- Case discussion

Scapular winging: neurogenic causes

Scapula key for shoulder abduction and rotation

- Unilateral
  - Long thoracic neuropathy (medial winging)
  - Spinal accessory neuropathy (lateral winging esp with shoulder abduction; depressed shoulder)
  - Dorsal scapular neuropathy (lateral winging)
  - Plexopathies involving above (Parsonage Turner)
  - MND sometimes
- Bilateral (SPS)
  - MND (ALS, SMA type 4)
  - Davidenkow syndrome
    - AD SPS, distal sensory loss, pes cavus
      - Davidenkow S. *Arch Neurol Psychiatry* 1939;41:694-701
    - Distinct from CMT?
      - Con: Harding & Thomas
      - Pro: Schwartz & Swash
    - HNPP forms
      - Wong E et al. *Muscle Nerve* 2018; epub before print

- Shaibani A. *A Video Atlas of Neuromuscular Disorders* Oxford 2014
- Silvestri NJ. *Neuromuscular Disorders: A Symptoms & Signs Approach to Differential Diagnosis & Treatment* Springer/Demos Medical 2018

Scapuloperoneal syndromes

- Myopathic
  - Myotonic dystrophy
  - FSHD
  - LGMD 2A
  - Desminopathy
  - IBM
  - Myophosphorylase deficiency
  - Polymyositis
  - Congenital myopathies
  - Nonaka myopathy
  - Scapuloperoneal MD (hyaline body myopathy)
    - X-linked: *FHL1* (EDMD), *LAMP-2* (Danon dz)
    - AD, AR: *MYH7*
      - Shaibani A. *A Video Atlas of Neuromuscular Disorders*. Oxford 2014

Genetic studies

- Unrevealing
  - PMP-22
  - Axonal CMT panel (MFN2, MPZ, NEFL, GDAP1, Lamin A/C)
  - GJB1, TRPV4, HSPB1
  - WES
- mtDNA sequencing
  - *ATP6* m.9025G>A novel mutation predicting Gly167Ser substitution
    - Conserved region of ATP synthase membrane subunit 6 component of Complex V
  - WGS confirmed *ATP6* mutation
    - Homoplasmic mutant loads in pt; high heteroplasmic mutant loads in mother

(MT)ATP6 neurogenic variants

- Distal HMN (1st to 2nd decade) ⟵
  - 1% of unclassified CMT2
  - UMN features/extensor plantar responses (30%)
  - Pes cavus (50%); kyphoscoliosis (10%); sensory loss (30%)
  - Proximal weakness in 8/27 by my count
  - Axonal NCS
  - Lower mutant loads can be asymptomatic
    - Pitceathly et al. *Neurology* 2012;79:1145-1154
- Neuropathy + ataxia (childhood to adult)
  - Dysarthria, horizontal gaze-evoked nystagmus, migraine, optic atrophy
  - Axonal NCS
- CNS + motor (2nd to 3rd decade)
  - Cognitive impairment, exercise intolerance, proximal weakness, ataxia
  - EMG neurogenic