Neuromuscular Disease: PNS and CNS Manifestations!

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Case 1

• **CC:** Weakness/numbness/pain in bilateral arms for 2 months
• **HPI:** 44 yo RH CF with a h/o ulnar neuropathy, fibromyalgia pain started abruptly in bilateral arms, has been going on for the past 2 months, worse with chores
• Denies neck pain
• Referred from MS specialist after MRI brain imaging not explaining her symptoms
HPI

- In the past, she has had recurrent episodes of numbness/tingling/weakness/pain in bilateral median, ulnar distributions with episodic numbness in peroneal distributions that would last weeks to months.
- Denied bowel/bladder involvement
- Also reports multiple neurologic complaints of transient diplopia, tremors, dysautonomia, and gait instability in the past year
History

**PMHx/Pshx**: as per HPI; Cervical decompression following neck injury

**FHx:**

**Maternal Aunt**: Multiple Sclerosis

Maternal grandmother and mother had foot deformities (hammertoes).

*19 year-old son has difficulty with his ankles (frequent ankle sprains)*
Neuro Exam

MENTAL STATUS: WNL
(subjective complaints)

CNs: WNL

MOTOR EXAM

STRENGTH

BUE: FDI & interossei 4/5
APB 2/5

BLE: 5/5

REFLEXES:

Diminished in BUE
Present in BLE

SENSATION: Reduced LT, PP and temp in the B/L median and ulnar nerve distributions distally

Other findings: + Tinel's BUE wrists and elbows; High arched feet, hammer toes
MRI Brain
### Sensory and Mixed Nerve Conduction:

<table>
<thead>
<tr>
<th>Nerve and Site</th>
<th>Onset Lat ms</th>
<th>Peak Lat ms</th>
<th>Amp µV</th>
<th>Segment</th>
<th>Dist mm</th>
<th>CV m/s</th>
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<tbody>
<tr>
<td><strong>Median.R</strong> to Digit II (index finger).R</td>
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<td></td>
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<td>Wrist-Digit II (index finger)</td>
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<tr>
<td>Wrist</td>
<td>NR</td>
<td>NR</td>
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<td><strong>Ulnar.R</strong> to Digit V (little finger).R</td>
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<td>Wrist</td>
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<td>14</td>
<td>Digit V (little finger)-Wrist</td>
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<td>Ankle-Lower leg</td>
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<td>Ankle-Lower leg</td>
<td>140</td>
<td>44</td>
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<td><strong>Median.L</strong> to Digit II (index finger).L</td>
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<tr>
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<td>Wrist</td>
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<tr>
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<tr>
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## Motor Nerve Conduction:

<table>
<thead>
<tr>
<th>Nerve and Site</th>
<th>Lat ms</th>
<th>Amp mV</th>
<th>Segment</th>
<th>Dist mm</th>
<th>Lat Diff ms</th>
<th>CV m/s</th>
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<td><strong>Median.R to APB. (C8-T1).R</strong></td>
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<td>Palm</td>
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<td>Wrist</td>
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<td>2.1</td>
<td>Palm-Wrist</td>
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<td>9.4</td>
<td>Abductor digiti minimi m. (C8-T1)-Wrist</td>
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<td>Below elbow</td>
<td>7.5</td>
<td>5.0</td>
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<td>4.3</td>
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<td>Above elbow</td>
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<td>Below elbow-Above elbow</td>
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</tr>
<tr>
<td>Median Elbow</td>
<td>10.7</td>
<td>1.7</td>
<td>Median Wrist-Median Elbow</td>
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</table>
Multiple bilateral

• SIGNIFICANT improvement in entrapment neuropathies and resolution of partial motor conduction blocks!
Case 2

- **CC:** Left lower extremity weakness
- **HPI:** 39 yo RH CM with history of Cervical Transverse Myelitis presents for left foot drop.
- He had an episode of legs crossed while sitting down and shortly after standing up, he was unable to lift his foot up, felt like it went to sleep.
- Of note, he had an episode of cervical myelitis at age 35 the night after eating spicy shrimp tacos at Papasitos; 2-3 days later, difficulty with balance, progressive weakness (tripping, dropping objects), entire body felt numb including torso.
Neuro Exam

MENTAL STATUS: WNL

CNs: WNL

MOTOR:

STRENGTH

BUE normal except b/l interossei 4/5

BLE normal except b/l DF/eversion 4/5

REFLEXES: Normal uppers, 2+ patellar, absent ankle jerks

SENSATON: Stocking glove decreased sensation below knees and elbows bilaterally Gait: steppage gait
Genetics: +PMP-22 gene deletion

Multiple entrapment neuropathies in upper and lower
Hereditary Neuropathy with Liability to Pressure Palsies (HNPP)

- Rare, Autosomal Dominant, Inherited neuropathy characterized by painless recurrent entrapment neuropathies

- Initially described by De Jong in 1947 as “Potato-grubbing Palsy”
  - Family of 4 generations with recurrent entrapment neuropathies
  - Associated with prolonged kneeling during the “potato grab”.

[Logo of UTH Health]
Peripheral Myelin Protein-22 (PMP-22)

• **What causes HNPP?**
  – Deletion of 1.5-mb deletion on chromosome 17p11.2
  – Heterozygous deletion of PMP-22 (duplication in CMT1A)

• **Function**: Uncertain but thought to be important in myelin stabilization.

• CNS involvement in HNPP is rare
In our cases...

• In both our cases, clinical and subclinical CNS damage seen

• CNS involvement?
  – In early development, in the CNS, **PMP22 mRNA** may be expressed in **very low levels in the oligodendrocytes**
  – Thus, studies have suggested a role in CNS myelin development

CNS involvement rarely reported in HNPP; is there an association?
Mutations with CNS involvement
Cases Reports

- **1995**: Case report by Dr. Barohn et al on a patient with HNPP and CNS demyelination; transient facial/truncal/perineal numbness, CNS demyelination on MRI
- **2005**: Case report by Dr. Sanahuja et al on a family pedigree (18 members) with MRI abnormalities; 9/18 had HNPP, 6/6 with HNPP had MRI abnormalities, nml MRI in 2/2 without HNPP.
- **2006**: Case report by Dr. Tackenberg et al on 7 patients with MRI abnormalities and prolonged mean latencies in blink reflex, jaw-opening reflex, and acoustic evoked potentials; **Subclinical CNS demyelination**
Case Reports

• **2013**: Dr. Chanson et al on 15 patients with HNPP all with abnormal DTI, neuropsych testing and volume of GM/WM c/w notable CNS changes

• **2015**: Case report by Dr. Wang et al, on 12 observed to have decreased FA on DTI in Cerebral Normal-Appearing White Matter in HNPP
DISCUSSION

- Important to consider HNPP in those with CNS demyelination
- Opposing points?
  - Bias: publication bias, population
  - The role of PMP22 in the CNS has not been established in humans as of yet.
  - Occurrence by chance?
- Create registry for cases to establish association of CNS and PNS in HNPP
ACKNOWLEDGMENTS

• I thank Dr. Thy Nguyen and Dr. Biliciler for their help in preparing this presentation, they’re the best!

QUESTIONS?

I think we’ve run out of time…
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REFERENCES


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