Neuromuscular Disease: PNS and CNS Manifestations!

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UTHealth
The University of Texas Health Science Center at Houston
Medical School

Mischer Neuroscience Institute
MEMORIAL HERMANN

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:

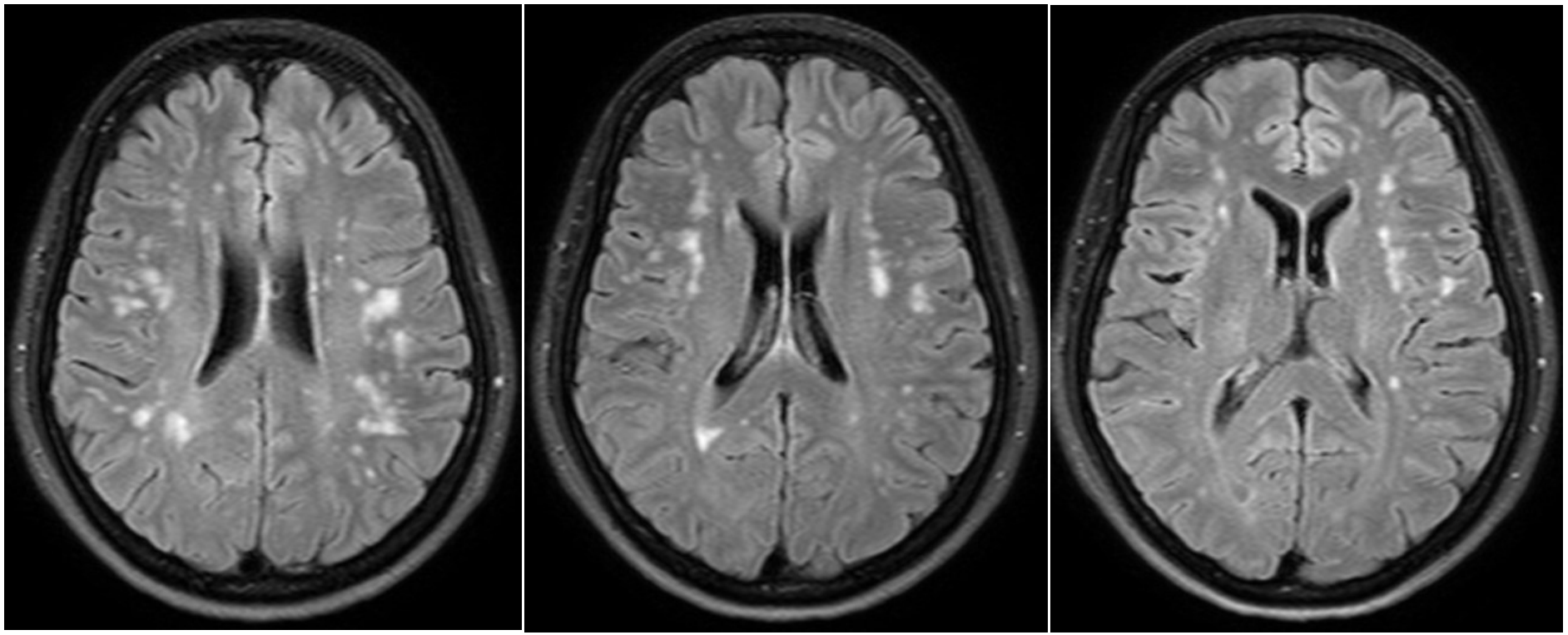
Diminished in BUE

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:

Nerve and Site	Onset Lat ms	Peak Lat ms	Amp µV	Segment	Dist mm	CV m/s
Median.R to Digit II (index finger).R						
Wrist	NR	NR	NR	Wrist-Digit II (index finger)	130	
Ulnar.R to Digit V (little finger).R						
Wrist	2.4	3.0	14	Digit V (little finger)-Wrist	110	46
Radial.R to Anatomical snuff box.R						
Forearm	1.8	2.4	13	Anatomical snuff box-Forearm	100	56
Forearm	1.4	2.3	21	Anatomical snuff box-Forearm	100	71
Sural.R to Ankle.R						
Lower leg	2.9	3.6	6	Ankle-Lower leg	140	48
Lower leg	3.2	3.8	5	Ankle-Lower leg	140	44
Median.L to Digit II (index finger).L						
Wrist	NR	NR	NR	Wrist-Digit II (index finger)	130	
Ulnar.L to Digit V (little finger).L						
Wrist	2.6	3.3	10	Digit V (little finger)-Wrist	110	42
Wrist	2.5	3.2	9	Digit V (little finger)-Wrist	110	43
Radial.L to Anatomical snuff box.L						
Forearm	1.5	2.2	32	Anatomical snuff box-Forearm	100	66

Motor Nerve Conduction:

Nerve and Site	Lat ms	Amp mV	Segment	Dist mm	Lat Diff ms	CV m/s
Median.R to APB. (C8-T1).R						
Palm	1.9	3.0				
Wrist	5.8	2.1	Palm-Wrist	70	3.9	17
Elbow	10.9	2.0	Wrist-Elbow	225	5.1	44
Ulnar.R to Abductor digiti minimi m. (C8-T1).R						
Wrist	3.2	9.4	Abductor digiti minimi m. (C8-T1)-Wrist	70	3.2	
Below elbow	7.5	5.0	Wrist-Below elbow	220	4.3	51
Above elbow	10.1	4.7	Below elbow-Above elbow	100	2.6	38
Median Wrist	NR	NR	Median Wrist			
Median Elbow	9.6	2.9	Median Wrist-Median Elbow			
Median.L to APB. (C8-T1).L						
Palm	2.1	7.6				
Wrist	5.8	4.4	Palm-Wrist	70	3.7	19
Elbow	11.4	4.3	Wrist-Elbow	10	5.6	39
Ulnar.L to Abductor digiti minimi m. (C8-T1).L						
Wrist	2.8	7.5	Abductor digiti minimi m. (C8-T1)-Wrist	70	2.8	
Below elbow	7.6	1.9	Wrist-Below elbow	218	4.8	45
Above elbow	10.5	1.7	Below elbow-Above elbow	100	2.9	34
Median Wrist	NR	NR	Median Wrist			
Median Elbow	10.7	1.7	Median Wrist-Median Elbow			

Multiple bilateral

- SIGNIFICANT improvement in entrapment neuropathies and resolution of partial motor conduction blocks!

Test(s) Requested: PMP22 Gene / ExonArrayDX Analysis to Evaluate for Gene Deletion or Duplication / Hereditary Neuropathy with Liability to Pressure Palsy (HNPP) / Charcot-Marie-Tooth 1A (CMT1A)

Result: **POSITIVE: Heterozygous for a Deletion of the Entire PMP22 Gene.**

Case 2

- **CC**:
- **HPI**: Myelitis pres
- He h nd shortly after ke it went to sl
- Of n 5 the night after ater, diffic dropping obje

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

Motor Nerve Conduction:

Nerve and Site	Lat ms	Amp mV	Segment	Dist mm	Lat Diff ms	CV m/s
Median.L to Abductor pollicis brevis (C8-T1).L						
Wrist	6.1	6.9	Abductor pollicis brevis (C8-T1)-Wrist	70	6.1	
Elbow	11.4	6.6	Wrist-Elbow	250	5.3	47
Ulnar.L to Abductor digiti minimi m. (C8-T1).L						
Wrist	3.4	12.3	Abductor digiti minimi m. (C8-T1)-Wrist			
Below elbow	8.1	11.0	Wrist-Below elbow	215	4.7	46
Above elbow	14.2	5.3	Below elbow-Above elbow			
Peroneal.L to Extensor digitorum brevis (L4-S1).L						
Ankle	6.2	0.8	Extensor digitorum brevis (L4-S1)-Ankle	90	6.2	
Fibula (head)	18.7	0.7	Ankle-Fibula (head)			27
Popliteal fossa	23.6	0.2	Fibula (head)-Popliteal fossa			29
Peroneal.L to Tibialis anterior (L4-L5).L						
Fibula (head)	3.3	2.0	Tibialis anterior (L4-L5)-Fibula (head)			
Popl						
Til						
An				90	4.6	
Po					14.4	27
Pe						
An				90		
Fit						
Pe						
Fit					2.3	
Po				130	3.0	43
Tib						
Ankle	4.4	3.0	Abductor hallucis (S1-S2)-Ankle	90	4.4	
Popliteal fossa	17.5	1.2	Ankle-Popliteal fossa	430	13.1	33

Genetics: +PMP-22 gene deletion

Multiple entrapment neuropathies in upper and lower

stitute

Health Science Center at Houston
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MRI CERVICAL SPINE WO CONTRAST

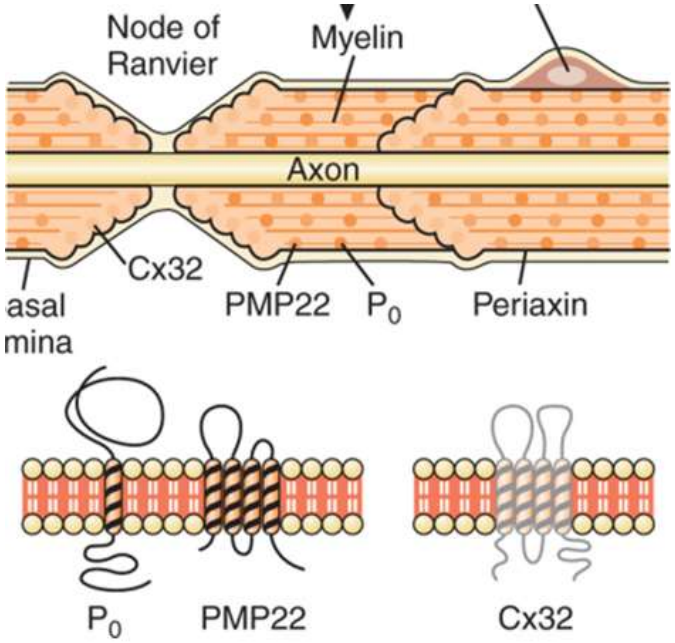
Hereditary Neuropathy with Liability to Pressure Palsies (HNPP)

- 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”.

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

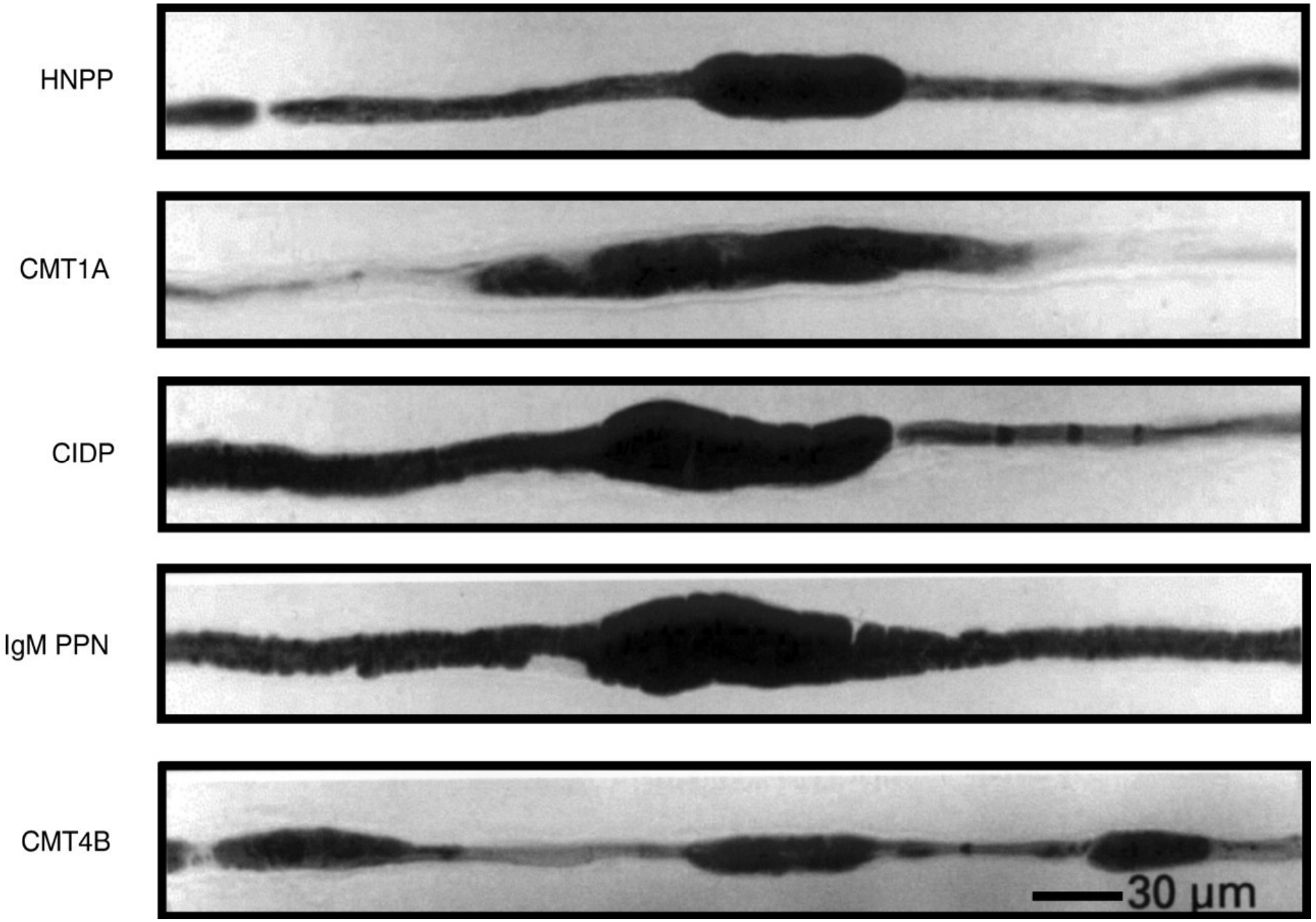


In our cases…

- 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?


HNPP
CMT1A
CIDP
IgM PPN
CMT4B
30 µm

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

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QUESTIONS?

I think we've run out of time…

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