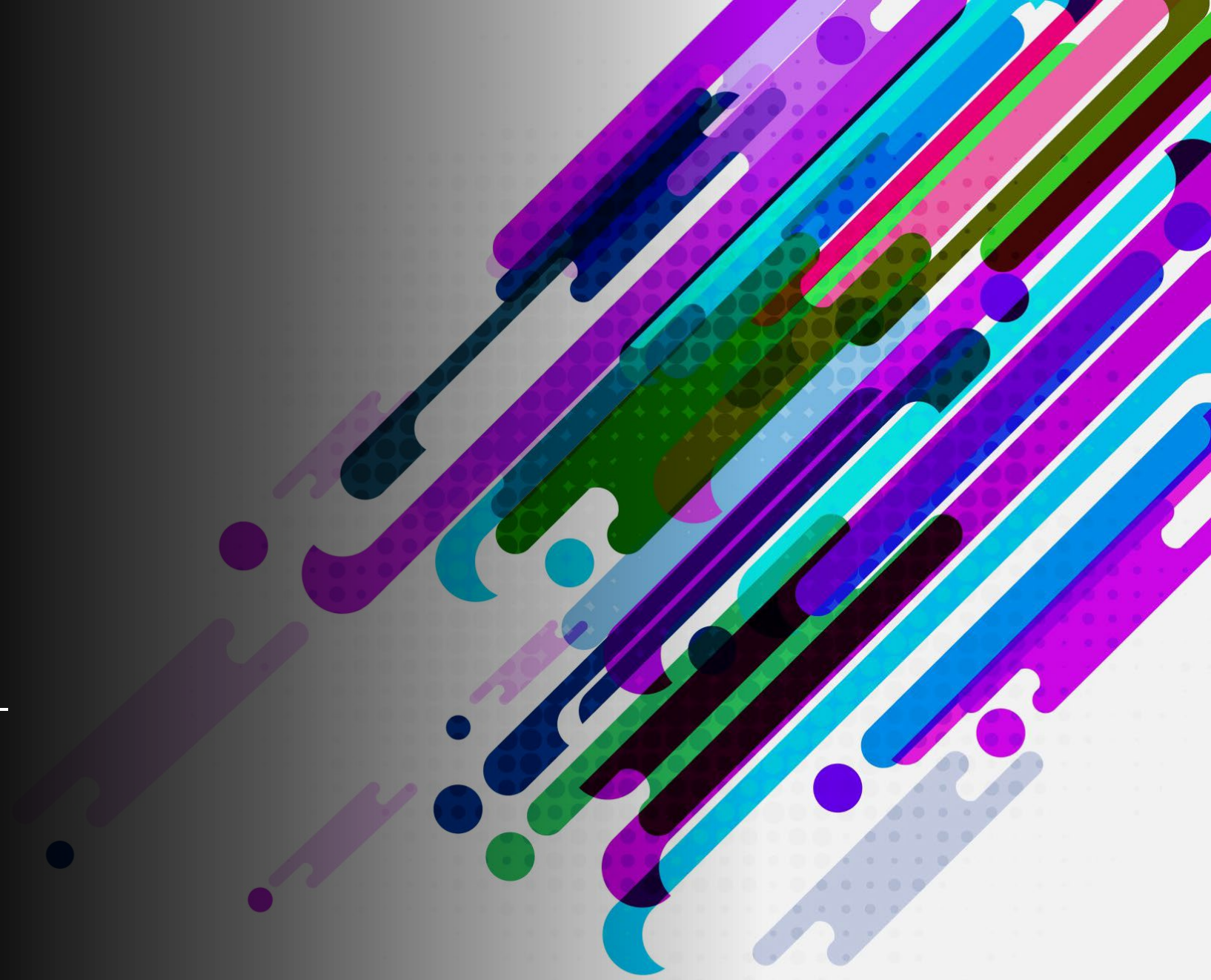
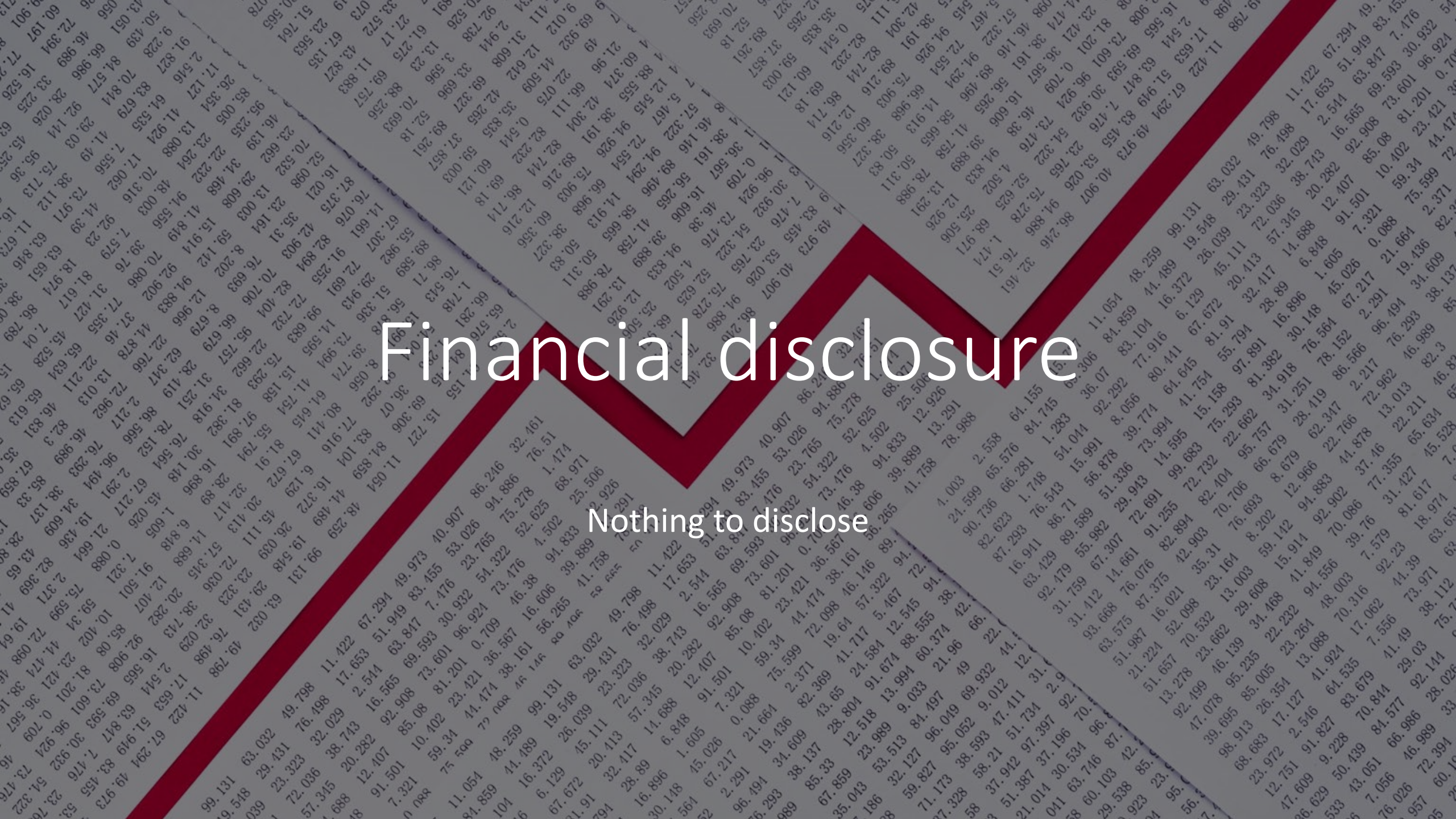
Chronic Inflammatory Demyelinating polyradiculo-neuropathy (CIDP)- diagnosis and treatment

Ehtesham Khalid, MD





Financial disclosure

Nothing to disclose

Definition

Progressive or relapsing, symmetric proximal and distal sensorimotor involvement of 2 limbs with over 8 weeks with absent DTRs.

Immune mediated polyneuropathies with distinctive clinical presentation and electrophysiological features.

CIDP and ‘CIDP Variants’

- Typical CIDP
- Distal CIDP- Distal Acquired demyelinating and Sensory polyneuropathy (DADS)
- Multi-focal CIDP-- Motor acquired Demyelinating sensory and motor Neuropathy (MADSAM)
- Focal CIDP
- Motor CIDP
- Sensory CIDP

Case-1

- 14 years old boy for evaluation of possible hereditary neuropathy. He noticed progressive right leg weakness over 2-3 weeks with difficulty in stride. He noticed improvement for a few days afterwards, but it has been static since then. He is still weak in his right leg after 3 months. He likes to swim and run track. He is currently in ninth grade. Normal birth and developmental history. Negative family history for polyneuropathy.
- On examination-

Motor UE/LE: **5/5 throughout except great toe dorsiflexion is 4/5 bilaterally.** Deep Tendon Reflexes- 1/4 in upper and 2/4 in lower extremities bilaterally

Sensations- Intact.

Nerve conduction study

SNC

Nerve / Sites	Rec. Site	Onset Lat	Peak Lat	NP Amp	PP Amp	Segments	Distance	Velocity	Temp.
		ms	ms	µV	µV		cm	m/s	°C
R Sural - Ankle (Calf)									
Calf	Ankle	3.49	4.38	10.0	7.6	Calf - Ankle	14	40	30.8
Ref.			≤4.40	≥6.0	≥6.0	Ref.		≥40	
R Ulnar - Digit V (Antidromic)									
Wrist	Dig V	3.23	3.96	19.5	32.6	Wrist - Dig V	14	43	31.5
Ref.			≤3.50	≥10.0	≥15.0	Ref.		≥50	
L Sural - Ankle (Calf)									
Calf	Ankle	4.22	7.19	20.8	17.0	Calf - Ankle	14	33	29.6
Ref.			≤4.40	≥6.0	≥6.0	Ref.		≥40	

MNC

Nerve / Sites	Muscle	Latency	Amplitude	Rel Amp	Duration	Segments	Distance	Lat Diff	Velocity	Temp.
		ms	mV	%	ms		cm	ms	m/s	°C
R Peroneal - EDB										
Ankle	EDB	6.51	2.1	100	7.08	Ankle - EDB	9			30.7
Ref.		≤6.50	≥2.0			Ref.				
Fib head	EDB	21.41	0.3	13.8	10.21	Fib head - Ankle	33	14.90	22	30.6
Ref.						Ref.			≥44	
Pop fossa	EDB	22.66	0.4	123	10.63	Pop fossa - Fib head	7	1.25	56	30.3
R Tibial - AH										
Ankle	AH	6.82	1.6	100		Ankle - AH	8			30.4
Ref.		≤5.80	≥4.0			Ref.				
R Ulnar - ADM										
Wrist	ADM	2.86	14.5	100	5.16	Wrist - ADM	7			31.2
Ref.		≤3.30	≥6.0			Ref.				
B.Elbow	ADM	9.58	2.9	19.8	3.39	B.Elbow - Wrist	22	6.72	33	31.3
Ref.						Ref.			≥49	
A.Elbow	ADM	12.60	2.4	82.7	3.75	A.Elbow - B.Elbow	12	3.02	40	31.3
L Peroneal - EDB										
Ankle	EDB	6.25	3.0	100	7.97	Ankle - EDB	9			29.7
Ref.		≤6.50	≥2.0			Ref.				
Fib head	EDB	23.49	0.3	9.83	11.46	Fib head - Ankle	30	17.24	17	29.6
Ref.						Ref.			≥44	
Pop fossa	EDB	26.15	0.3	113	5.94	Pop fossa - Fib head	11	2.66	41	29.7
L Tibial - AH										
Ankle	AH	5.42	8.0	100	8.49	Ankle - AH	8			29.3
Ref.		≤5.80	≥4.0			Ref.				

F Wave

Nerve	F Lat	Ref.	M Lat	Ref.	F-M Lat	Min F Lat	Ref.	Min M Lat	Min F-M
	ms	ms	ms	ms	ms	ms	ms	ms	ms
R Peroneal - EDB	42.5	≤58.0	7.0	≤32.0	35.5	42.8	≤58.0	7.0	35.6
R Tibial - AH	55.3	≤58.0	7.2	≤32.0	48.1	57.4	≤58.0	7.2	50.2
R Ulnar - ADM	25.2	≤32.0	2.7	≤32.0	22.4	27.0	≤32.0	2.7	14.4
L Peroneal - EDB	27.1	≤58.0	7.1	≤32.0	20.0	27.1	≤58.0	7.1	19.8
L Tibial - AH	79.4	≤58.0	5.4	≤32.0	74.0	79.4	≤58.0	5.4	74.0

Case-2

- 16 years old female with progressive leg weakness. She was previously diagnosed with CMT. She was born after 9 months of pregnancy by c-section with no h/o delayed cry. She started to walk at the age of 1 year and to speak at the age of 9 months. Till the age of 5 years she was normal. At the age of 6 years, her family noticed falls during walking without any clear reason. She has difficulty in walking when she was in 6^{th} grade and her ankles started to twist. There is h/o numbness in extremities from last 1 year. There is also h/o symptoms in hands from last 1 year. There is h/o breathing difficulty while sitting and abdominal pain. There is no h/o swallowing difficulty and incontinence. There is no family h/o such condition.

- **On examination**

Generalized moderate muscle loss with atrophy of thenar and hypethenar areaa, legs (distally>proximally). DTRs- 0/4 in upper and lower extremities bilaterally.

- Vibration is reduced up to wrist and up to knees in legs. Pinprick is reduced up to forearm and in legs in upper 1/3 of leg

NCS/EMG

SNC

Nerve / Sites	Rec. Site	Onset Lat ms	Peak Lat ms	Amp µV	Segments	Distance cm	Velocity m/s	Temp. °C
R Median - Digit II (Antidromic)								
Wrist	Dig II	NR	NR	NR	Wrist - Dig II	13	NR	31.2
L Median - Digit II (Antidromic)								
Wrist	Dig II	NR	NR	NR	Wrist - Dig II	13	NR	32.2
R Ulnar - Digit V (Antidromic)								
Wrist	Dig V	NR	NR	NR	Wrist - Dig V	11	NR	31

MNC

Nerve / Sites	Muscle	Latency ms	Amplitude mV	Duration ms	Rel Amp %	Segments	Distance cm	Lat Diff ms	Velocity m/s	Temp. °C
R Median - APB										
Wrist	APB	16.35	1.0	6.77		Wrist - APB	6			31.1
Elbow	APB	23.96	0.7	9.90	73.5	Elbow - Wrist	23	7.60	30	31.1
L Median - APB										
Wrist	APB	16.30	0.8	7.08		Wrist - APB	7			32.2
Elbow	APB	27.08	0.3	5.31	34.7	Elbow - Wrist	23	10.78	21	32
R Ulnar - ADM										
Wrist	ADM	10.21	0.7	11.67	100	Wrist - ADM	7			30.3
B.Elbow	ADM	23.33	0.4	4.53	59.7	B.Elbow - Wrist	17	13.13	13	30.4
A.Elbow	ADM	30.99	0.2	11.41	43.1	A.Elbow - B.Elbow	10	7.66	13	30.4
						A.Elbow - Wrist		20.78		30.4

Epidemiology

- Prevalence-- 1-8.9/100,000
- Peak age- 40-60 years with slight male predominance
- Early recognition can improve prognosis and patient satisfaction.
- The clinical course could be relapsing-remitting or progressive.

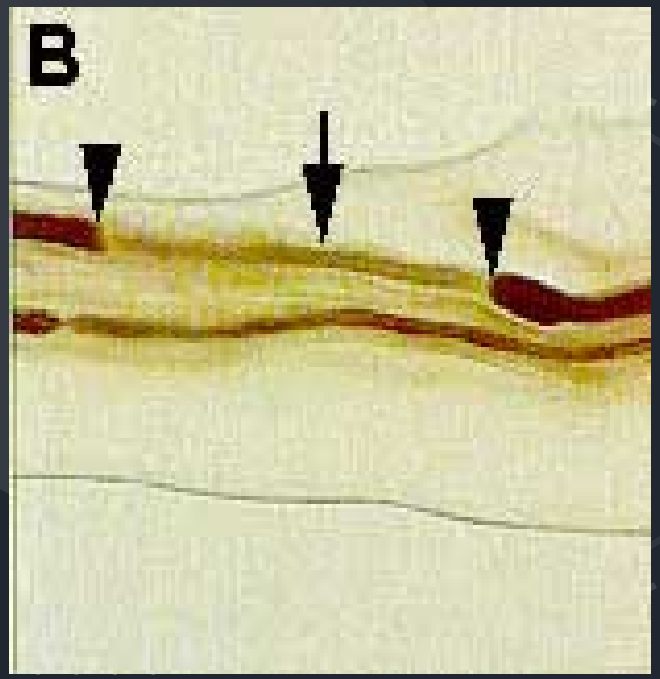
Symptomatology:

A. Weakness
B. Tremors
C. Sensory loss
D. Dysautonomia, respiratory and cranial nerve involvement.

Diagnostic work up

- Fasting blood sugar, Hemoglobin A1c
- Complete blood count
- Inflammatory markers- ESR, CRP
- Chemistry- Urea, creatinine, LFTs, electrolytes.
- Vitamin B12 levels
- Thyroid stimulating hormone level
- Serum and urine electrophoresis, Immunofixation

Diagnostic work up



Courtesy of Y Harati

- HIV and Borrelia Serology
- Free light chains
- Myelin associated Glycoprotein (Anti- MAG)
- Skeletal survey
- Vascular endothelial growth factor level
- Genetic testing for CMT and Transthyretin Familial amyloidosis.
- CSF analysis
- Nerve biopsy

Diagnostic work up

- Nodal-paranodal protein Antibodies.
- ANA, ENA, ANCA.
- Anti- GM1 IgM antibodies.
- CPK
- Acetylcholine receptor Antibodies, MuSK Antibodies.
- Paraneoplastic antibodies.
- Somatosensory Evoked potentials when NCS is normal.

Neurophysiological work up

(a) Motor distal latency prolongation ≥50% above ULN in two nerves (excluding median neuropathy at the wrist from carpal tunnel syndrome), or

(b) Reduction of motor conduction velocity ≥30% below LLN in two nerves, or

(c) Prolongation of F-wave latency ≥20% above ULN in two nerves (≥50% if amplitude of distal negative peak CMAP <80% of LLN), or

(d) Absence of F-waves in two nerves (if these nerves have distal negative peak CMAP amplitudes ≥20% of LLN) + ≥1 other demyelinating

parametera in ≥1 other nerve, or

(e) Motor conduction block: ≥30% reduction of the proximal relative to distal negative peak CMAP amplitude, excluding the tibial nerve, and distal

negative peak CMAP amplitude ≥20% of LLN in two nerves; or in one nerve + ≥ 1 other demyelinating parametera except absence of F-waves in

≥1 other nerve, or

(f) Abnormal temporal dispersion: >30% duration increase between the proximal and distal negative peak CMAP (at least 100% in the tibial nerve) in ≥2 nerves, or

Neurophysiological work up

(g) Distal CMAP duration (interval between onset of the first negative peak and return to baseline of the last negative peak) prolongation in ≥1

Nerve b + ≥1 other demyelinating parametera in ≥1 other nerve

(LFF 2 Hz) median > 8.4 ms, ulnar > 9.6 ms, peroneal > 8.8 ms, tibial > 9.2 ms

- (LFF 5 Hz) median > 8.0 ms, ulnar > 8.6 ms, peroneal > 8.5 ms, tibial > 8.3 ms
- (LFF 10 Hz) median > 7.8 ms, ulnar > 8.5 ms, peroneal > 8.3 ms, tibial > 8.2 ms
- (LFF 20 Hz) median > 7.4 ms, ulnar > 7.8 ms, peroneal > 8.1 ms, tibial > 8.0 ms

- Sensory conduction abnormalities (prolonged distal latency, or
- reduced SNAP amplitude or slowed conduction velocity outside of normal limits) in two nerves.

Neurophysiological work up

CIDP

• Sensory conduction abnormalities (prolonged distal latency, or reduced SNAP amplitude, or slowed conduction velocity outside of normal limits) in two nerves.

Possible CIDP

• As in (1)

• Sensory CIDP with normal motor nerve conduction studies needs to fulfil a. or b.:

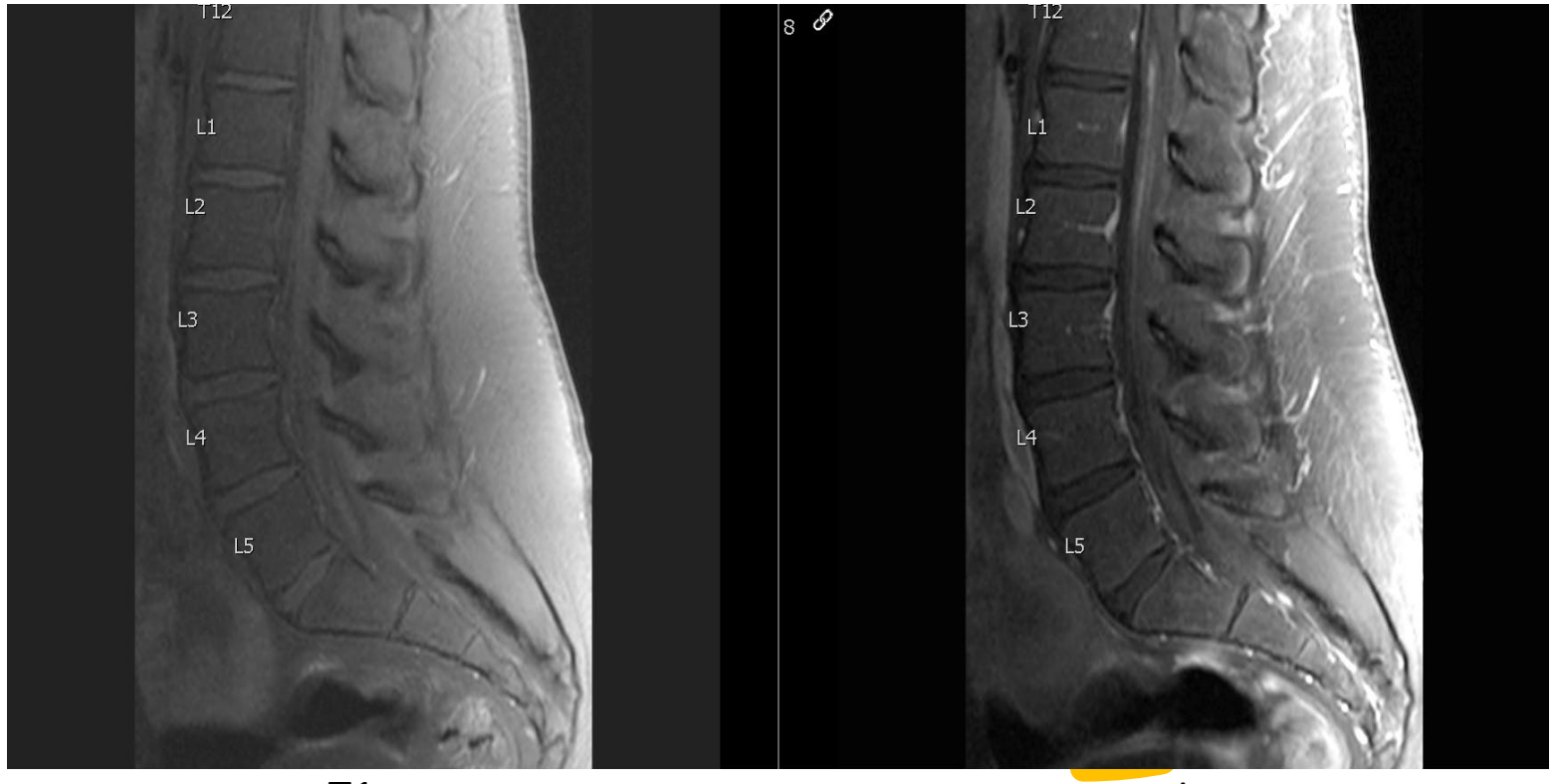
a. sensory nerve conduction velocity < 80% of LLN (for SNAP amplitude >80% of LLN) or < 70% of LLN (for SNAP amplitude <80% of LLN) in at least two nerves (median, ulnar, radial, sural nerve), or

b. sural sparing pattern (abnormal median or radial sensory nerve action potential [SNAP] amplitude with normal sural nerve SNAP amplitude) (excluding carpal tunnel syndrome)

Supportive Work up

- MRI with and without contrast.
- Ultrasound.

Enlarged enhancing nerve roots, plexus and peripheral nerves.



T1

T1 w/con

Treatment

- Morbidity: 76% of patient needed treatment, 31.7% unable to walk.

- Good practice points by EFNS- 2021

1. Intravenous Immunoglobulin (IVIG) or Corticosteroids for initial treatment.
2. Plasma exchange if steroid and IVIG are ineffective.
3. Intravenous immunoglobulin (IVIG) as first line of treatment for motor CIDP.
4. IVIG, ScIG and Steroids for maintenance treatment.
5. If dose is high for either of first line therapy, then consider combination therapy.
6. Symptomatic treatment.

Immunoglobulin

- 2gm/kg course (1gm every 3 weeks to 6 months)
- 2/3 of the patient will notice improvement.
- Single course of intravenous immunoglobulin (IVIg) significantly reduces disability and weakness
- IV or SC (fluctuations in response or did not tolerate)

ICE Trial- Lancet Neurol 2008;7(2):136-144

European Journal of Neurology 2013;20(5):836–42.

Corticosteroids

- Oral prednisone (60-100mg daily or on alternate day)
- Dexamethasone (40mg daily for 4 days/4wk)
- Methylprednisone (500-1000mg as short course)
- Response rate – 65-95%

PREDICT study: Lancet Neurol 2010;9(3):245-253.

Plasma exchange

- 50ml/kg per day for 5 sessions over 7-10 days
- Exchange every 2 weeks
- There is rebound worsening on stopping the therapy

Role of IVIG and PLEX in Neuromuscular conditions. AAN 2018

Other Immuno-modulating therapies

- Azathioprine
- Mycophenolate mofetil
- Ciclosporin
- Methotrexate
- Cyclophosphamide
- Rituximab

Recommendations:

- Response rate 69-81% from first drug to change of therapy to combination of medications.
- Try First line medications followed by combinations of first line medications.
- Second line medication with probable chances of responsiveness can be tried.

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RESEARCH REPORT

WILEY

European Academy of Neurology/Peripheral Nerve Society guideline on diagnosis and treatment of chronic inflammatory demyelinating polyradiculoneuropathy: Report of a joint Task Force—Second revision

Peter Y. K. Van den Bergh[1] | Pieter A. van Doorn[2] | Robert D. M. Hadden[3] | Bert Avau[4] | Patrik Vankrunkelsven[5] | Jeffrey A. Allen[6] | Shahram Attarian[7] | Patricia H. Blomkwist-Markens[8] | David R. Cornblath[9] | Filip Eftimov[10] | H. Stephan Goedee[11] | Thomas Harbo[12] | Satoshi Kuwabara[13] | Richard A. Lewis[14] | Michael P. Lunn[15] | Eduardo Nobile-Orazio[16] |

Case 1

- Glucose- 530mg
- A1c- 13.8

Case 2

RESULT: POSITIVE

One homozygous Likely Pathogenic variant identified in NDRG1. NDRG1 is associated with autosomal recessive Charcot-Marie-Tooth disease.

Additional Variant(s) of Uncertain Significance identified.

GENE	VARIANT	ZYGOSITY	VARIANT CLASSIFICATION
NDRG1	c.595-2A>T (Splice acceptor)	homozygous	Likely Pathogenic
DST	c.1913C>G (p.Thr638Ser)	heterozygous	Uncertain Significance
SPG11	c.3977G>A (p.Ser1326Asn)	heterozygous	Uncertain Significance
SPG11	c.4231C>T (p.Pro1411Ser)	heterozygous	Uncertain Significance

Any Questions

Thank you