Title: Guillain-Barre Syndrome Mimicked by Spinal Stenosis in A Case of Chronic Prolapsed Intervertebral Disc: A Case Report

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Author names:

1. Yi Xuan Lee

Degrees and Affiliations:

1. MD. The National University of Malaysia, Kuala Lumpur, Malaysia.

ORCID (Open Researcher and Contributor Identifier):

https://orcid.org/0000-0003-2519-6807

About the author: Yi Xuan is a medical graduate from The National University of Malaysia. She is a passionate volunteer in healthcare and human rights.

Corresponding author email: yixuan005@gmail.com

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Highlights

- Guillain-Barre Syndrome (GBS) is a rare acute autoimmune polyneuropathy that can cause severe complications.
- Broad differentials of neurological signs and symptoms increase the difficulty of diagnosing GBS.
- Comprehensive investigations should be established to rule out GBS, especially in patients with coexisting neurological comorbidities.

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Personal, Professional, and Institutional Social Network accounts.

- **Linkedin:** www.linkedin.com/in/lee-yi-xuan

Discussion Points:

- What are the signs and symptoms of Guillain-Barre Syndrome (GBS)?
- What are the differentials for sensorimotor polyneuropathy?
- How to diagnose and manage Guillain-Barre Syndrome (GBS)?

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ABSTRACT.

Background: Guillain-Barre Syndrome (GBS) is a rare acute autoimmune polyneuropathy which is usually preceded by infections. It can be a difficult diagnosis to establish especially in patients with underlying neurological comorbidities.

The Case: A 54-year-old gentleman with a long history of prolapsed intervertebral disc presented with progressive asymmetrical onset tetraparesthesia for 4 weeks, associated with progressive paraparesis for 2 weeks. The diagnosis of GBS was missed initially due to missing relevant history of prior infection, atypical presentation (asymmetrical limb weakness), and radiological evidence of spinal stenosis. Nerve conduction study, cerebrospinal fluid analysis, and antiganglioside antibodies later confirm the diagnosis of GBS. The patient was started on intravenous immunoglobulin and achieved significant improvement. He was discharged a week later and transferred to a rehabilitation hospital.

Conclusion: GBS should not be excluded a priori diagnostic tests and lab work in neurological patients. Physicians should avoid over-rely on radiological findings to conclude a diagnosis. Comprehensive history and examination to discover reasons behind patients' presentations should be prioritized when developing a diagnosis.

Key Words: Guillain-Barre Syndrome, Polyradiculoneuropathy, Intervertebral Disc Displacement, Spinal Stenosis (Source: MeSH-NLM).

INTRODUCTION.

Guillain-Barre Syndrome (GBS) is a rare acute autoimmune polyneuropathy where its prevalence is only 0.0019% based on the Global Burden of Disease Study (GBD) 2019. [1] However, around 20-30% of cases will develop life-threatening respiratory failure due to severe generalized paralysis. [2] GBS-related year lost due to disability peaks among children aged 5-9 years, subsequently increasing by age among the adult population. Across all age groups, the predisposition of males is higher than females. [3] GBS is usually precipitated by gastrointestinal or respiratory infection, rarely systematic illnesses, post-surgery, trauma, and pregnancy. [4] Several systemic diseases were reported to be related to GBS but mostly are linked to chronic inflammatory demyelinating polyneuropathy. [4] Common presentations of GBS include progressive limb weakness with reduced tendon reflexes, muscle or radicular pain, ataxia, sensory symptoms, and autonomic dysfunctions. [2]

Spinal stenosis is the narrowing of the spinal canal (central canal or neural foramina), subsequently causing compression of the central cord or nerve roots. The most common etiology of spinal stenosis is degenerative spine diseases, including disc herniation, facet joint hypertrophy, ligamentum flavum hypertrophy, osteophyte formation, and spondylolisthesis. [5] Lumbar spinal stenosis is classically presented as lower back and leg pain, lower limb weakness, paresthesia, and loss of balance. In severe cases like cauda equina syndrome, bowel or bladder incontinence can happen due to lumbar-sacral nerve root compression.[5,6]

Although acute ascending sensorimotor polyneuropathy is a distinctive feature of GBS, it is sometimes challenging for physicians to diagnose GBS when there are atypical presentations, rare variants, and heterogeneous manifestations of the disease. Broad differentials, lacking high sensitivity and specificity diagnostic tools further complicate the diagnosis of GBS. [7] This report describes a case of GBS initially misdiagnosed as spinal stenosis in a patient with a long history of a prolapsed intervertebral disc.

THE CASE.

A 54-year-old gentleman with a long history of prolapsed intervertebral disc presented to a tertiary hospital in Kuala Lumpur, Malaysia in June 2022, complaining of progressive worsening bilateral upper and lower limb numbness for the past 5 weeks, associated with bilateral lower limb weakness in the last 3 weeks. He was diagnosed with a slipped disc at L4-L5 level 21 years ago, currently still undergoing physiotherapy. No surgical intervention was done, and he has been asymptomatic since.

5 weeks before admission, the patient had gradual onset of numbness over his right foot, which progressed proximally to his bilateral lower limb until the waist level, associated with bilateral hand numbness up to the elbow. 3 weeks before admission, he started to experience bilateral lower limb weakness which worsens rapidly over a span of 2 weeks, until he was wheelchair-bound. At this point, he was also unable to hold a spoon firmly and button up his shirt. He went to a private hospital and an MRI spine thoracolumbar was done, revealing varying degrees of foramen stenosis due to multiple degenerative changes at L3 to S1 discs. **(Figure 1)** Hence, he was diagnosed with spinal stenosis and surgical intervention was proposed. However, the patient rejected the surgery and opted for medical treatment. He was then given Pregabalin capsule 75mg twice daily, Eperisone tablet 50mg once daily, and Vitamin B-complex tablet once daily.

However, his symptoms persisted despite taking the medication. One week after the start of medical therapy, he came to our centre for a second opinion. Upon thorough questioning, the patient recalled having 3 days of mild cough 2 weeks before the symptoms onset. Otherwise, he had no history of trauma, no back pain, no radiating pain, and no bowel or urinary incontinence. He also had no diplopia, slurred speech, dysphagia, or dyspnea. On upper limbs examination, the tonus was normal, and the sensation was intact. The power of his upper limb was reduced (Medical Research Council scale 4/5, with absent deep tendon reflex). Upper limb proprioception and finger-to-nose test were unremarkable, with no dysdiadochokinesia. The grip-and-release test was negative, but the finger escape test was positive. On lower limb examination sensation was intact. Hypotonia was present in the lower limbs and power was reduced at 4/5 over the hip and knee, 1/5 for dorsiflexion, and 2/5 for plantar flexion. Babinski was equivocal with no clonus response. Lower limb proprioception was impaired, and the patient was unable to perform heel to shin test. All upper and lower limb findings were symmetrical bilaterally.

Magnetic resonance imaging of the cervical and thoracic spine was done, revealing no obvious spinal cord stenosis at the cervical and thoracic level, and no spinal cord lesions were detected. Nerve conduction studies (NCS) showed electrophysiological evidence of bilateral sural sparing, generalized, predominantly demyelinating polyneuropathy, suggestive of Guillain-Barre Syndrome, particularly acute inflammatory demyelinating polyneuropathy (AIDP) subtype. **(Table 1)** The diagnosis was further confirmed by cerebrospinal fluid analysis showing cytoalbuminologic dissociation: normal white cell count (0/mm^3) and elevated total protein (1842mg/dL). Antiganglioside antibodies (anti-GM1 IgG) were also positive. The Modified Erasmus GBS Outcome Score (mEGOS) calculated for this patient was 3, meaning he has a 41% probability of being unable to walk after 4 weeks and 18% after 3 months.

The patient received intravenous immunoglobulin (IVIg) 0.4g/kg daily for 5 days and inpatient physiotherapy. His physiotherapy exercises focused on limb muscle strengthening. Upper limbs proprioceptive neuromuscular facilitation was done on day 1 and day 2 of the admission, while other exercises were continued till discharge at a frequency of 3 times a day. These exercises include bilateral leg bridging with a 10-second hold, straight leg raise of 45 degrees with a 5-second hold, hip abduction and adduction with isometric exercises, and triceps strengthening exercises with 250 g weight. All exercises were repeated 10 times in each training session.

On day 4 of admission, his upper and lower limb power improved significantly after receiving the 4th dose of IVIg. Upper limb power was 5/5, while for lower limb, power was 5/5 over hip and knee, 4/5 for dorsiflexion, and 3/5 for plantar flexion. However, both upper and lower limb numbness persisted. The patient remained areflexic and his lower limb proprioception was still impaired. On day 7 of admission, his condition remained the same, and he was planned for transferring to another rehabilitation hospital for further care. However, due to full bed occupancy in that hospital, he was discharged and scheduled a follow-up there a week later. Before returning home, the patient was confirmed able to perform physiotherapy exercises and all activities of daily living independently. He was recommended to use a walking aid to prevent falls.

DISCUSSION.

The clinical course and severity of GBS vary due to its different pathophysiological processes. In general, the disease progresses through phases. [2] About two-thirds of patients reported respiratory or gastrointestinal symptoms within 4 weeks before the onset of GBS symptoms. This is followed by progressive worsening of symptoms (progressive phase) which peaks at 2-4 weeks. Subsequently, the symptoms plateau from 2 days to 6 months (with median of 7 days) before entering the recovery phase, where 80% of patients will be able to walk independently within 6 months. [8] In this case, the patient came to us 5 weeks after the onset of symptoms, in the plateau phase following 2 weeks of tetraparesthesia and 2 weeks of progressive paraparesis.

In 2011, the Brighton Collaboration GBS Working Group refined the original diagnostic criteria from the National Institute of Neurological Disorders and Stroke by providing the diagnostic level of different symptoms and ancillary examinations. [9-11] It is crucial to diagnose GBS timely due to its rapid disease progression on top of the high mortality (3-10%) once patients develop autonomic dysregulation, causing respiratory failure, arrhythmia, and blood pressure instability. [7] In our case, the respiratory symptom (cough) which is an important hint for GBS, was missed during the first hospital visit. Cough is the most common reason for visits to primary care. [12] Other common complaints include back pain, abdominal symptoms, pharyngitis, dermatitis, fever, headache, and fatigue. Even though the presenting complaint may seem irrelevant, physicians should always conduct systems reviews and screen for common symptoms.

AIDP is the first discovered and most common type of GBS. AIDP is used interchangeably with GBS until the axonal forms of GBS were discovered, namely acute motor axonal neuropathy and acute motor-sensory axonal neuropathy). [4] Subsequently, more variants were classified under the spectrum of GBS which includes paraparesis, pharyngeal–cervical brachial, bilateral facial palsy with paresthesia, pure sensory, Miller Fisher syndrome and Bickerstaff brainstem. [7] Although some variants share similar clinical presentations like flaccid weakness and areflexia, they can be differentiated by respective distinctive pathological characteristics. Diagnosis of GBS and its subtypes can be confirmed by the electrodiagnostic study, cerebrospinal fluid analysis, and serum antiganglioside antibodies analysis. [4,7,8] NCS in this case revealed classic findings in AIDP: prolonged F-waves, reduced compound muscle action potential with motor conduction blocks, reduced motor conduction velocities, prolonged distal sensory latency and reduced sensory nerve action potential. Another important finding in sensory NCS which differentiate demyelination from axonal polyneuropathy is the “sural-sparing pattern” where the sensory action potential of sural nerve is normal or relatively preserved compared to a total absence of median and ulnar sensory nerve action potential. This is the most specific sensory abnormality in AIDP.[3]

Management of GBS patients requires a multidisciplinary approach and patients often warranted intensive care unit admission due to respiratory failure, paralysis, bulbar and autonomic cardiovascular dysfunction. [4] Common complications like atelectasis, aspiration, nosocomial infections, deep venous thrombosis, and pulmonary embolism should be monitored closely to improve the overall outcome and prognosis. [4] Immunomodulatory therapy is best to start within 2 weeks of symptom onset to achieve maximum efficacy. IVIg, plasma exchange or combination therapy are all proven equally effective in treating GBS, though

IVIg is often chosen over plasma exchange due to easier administration, wide availability, and lesser adverse effects. Most patients show substantial recovery and resume walking ability within 6 months. [2,4,7]

The Modified Erasmus GBS Outcome Score (mEGOS) is a validated tool used to predict the prognosis of GBS patients. [13, 14] A lower score might prompt physicians to take more aggressive treatment in the early phase of diagnosis. [13] However, a second IVIg course should not be given as it does not benefit patients and causes more severe adverse events instead, as suggested by the Netherland's SID-GBS RCT trial. [15] The study's international version, the I-SID-GBS study, is currently ongoing as part of the International Guillain-Barré Syndrome Outcome Study (IGOS), which is expected to complete in September 2024. [16]

GBS can be a difficult diagnosis, especially in patients with co-existing neurological comorbidities. Established diagnostic criteria of GBS should be checked when patients with limb weakness develop new symptoms atypical with their current diagnosis, such as leg pain (the most common symptom of spinal stenosis) that is absent in this case. [4,5] Also, physicians should refrain from over-rely on radiological findings to conclude a diagnosis. Comprehensive history and examination to discover reasons behind patients' presentation should be the mainstay when making a diagnosis.

SUMMARY - ACCELERATING TRANSLATION

Guillain-Barre Syndrome (GBS) is a rare neurological disease. Its complications can range from limb weakness, muscle pain, loss of balance, and abnormal sensations, to life-threatening ones such as autonomic dysfunctions in more severe cases. Diagnosing GBS in patients with existing neurological conditions can be challenging due to overlapping symptoms and signs. When developing a diagnosis, comprehensive history and examination to discover reasons behind patients' presentations should be prioritized. Also, GBS should not be excluded before diagnostic tests and laboratory investigations. Careful evaluation and managing GBS patients with multidisciplinary care ensure optimal patient recovery.

REFERENCES.

1. Vos T, Lim SS, Abbafati C, Abbas KM, Abbasi M, Abbasifard M, Abbasi-Kangevari M, Abbastabar H, Abd-Allah F, Abdelalim A, Abdollahi M. Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. The Lancet. 2020 Oct 17;396(10258):1204-22.
2. Willison HJ, Jacobs BC, Doorn PA van. Guillain-Barré syndrome. The Lancet. 2016 Aug 13;388(10045):717–27.
3. Bragazzi NL, Kolahi AA, Nejadghaderi SA, Lochner P, Brigo F, Naldi A, et al. Global, regional, and national burden of Guillain–Barré syndrome and its underlying causes from 1990 to 2019. J Neuroinflammation. 2021 Nov 11;18(1):264.
4. Piccione EA, Salame K, Katirji B. Guillain-Barré Syndrome and Related Disorders. In: Katirji B, Kaminski HJ, Ruff RL (eds.) Neuromuscular Disorders in Clinical Practice. Springer, New York; 2014. p. 573–603.
5. Alvarez JA, Hardy RH. Lumbar spine stenosis: a common cause of back and leg pain. Am Fam Physician. 1998 Apr 15;57(8):1825–34, 1839–40.
6. Katz JN, Zimmerman ZE, Mass H, Makhni MC. Diagnosis and Management of Lumbar Spinal Stenosis: A Review. JAMA. 2022 May 3;327(17):1688–99.
7. Leonhard SE, Mandarakas MR, Gondim FAA, Bateman K, Ferreira MLB, Cornblath DR, et al. Diagnosis and management of Guillain–Barré syndrome in ten steps. Nat Rev Neurol. 2019 Nov;15(11):671–83.
8. van den Berg B, Walgaard C, Drenthen J, Fokke C, Jacobs BC, van Doorn PA. Guillain–Barré syndrome: pathogenesis, diagnosis, treatment and prognosis. Nat Rev Neurol. 2014 Aug;10(8):469–82.
9. Asbury AK, Cornblath DR. Assessment of current diagnostic criteria for Guillain-Barré syndrome. Ann Neurol. 1990;27(S1):S21–4.
10. Fokke C, van den Berg B, Drenthen J, Walgaard C, van Doorn PA, Jacobs BC. Diagnosis of Guillain-Barré syndrome and validation of Brighton criteria. Brain. 2014 Jan 1;137(1):33–43.
11. Sejvar JJ, Kohl KS, Gidudu J, Amato A, Bakshi N, Baxter R, et al. Guillain-Barré syndrome and Fisher syndrome: case definitions and guidelines for collection, analysis, and presentation of immunization safety data. Vaccine. 2011 Jan 10;29(3):599–612.
12. Finley CR, Chan DS, Garrison S, Korownyk C, Kolber MR, Campbell S, Eurich DT, Lindblad AJ, Vandermeer B, Allan GM. What are the most common conditions in primary care? Systematic review. Can Fam Physician. 2018 Nov;64(11):832-840.
13. Walgaard C, Lingsma HF, Ruts L, van Doorn PA, Steyerberg EW, Jacobs BC. Early recognition of poor prognosis in Guillain-Barre syndrome. Neurology. 2011 Mar 15;76(11):968-75.
14. Doets AY, Lingsma HF, Walgaard C, Islam B, Papri N, Davidson A, et al. Predicting Outcome in Guillain-Barré Syndrome: International Validation of the Modified Erasmus GBS Outcome Score. Neurology. 2022 Feb 1;98(5):e518-e532.
15. Walgaard C, Jacobs BC, Lingsma HF, Steyerberg EW, van den Berg B, Doets AY, et al. Second intravenous immunoglobulin dose in patients with Guillain-Barré syndrome with poor prognosis (SID-GBS): a double-blind, randomised, placebo-controlled trial. Lancet Neurol. 2021 Apr;20(4):275-283.

16. Jacobs BC, van den Berg B, Verboon C, Chavada G, Cornblath DR, Gorson KC, et al. International Guillain-Barré Syndrome Outcome Study: protocol of a prospective observational cohort study on clinical and biological predictors of disease course and outcome in Guillain-Barré syndrome. J Peripher Nerv Syst. 2017 Jun;22(2):68-76.

FIGURES AND TABLES.

Figure 1. T2 weighted MRI of the lumbar spine. (A) Sagittal image shows foraminal stenosis (white arrows) at L3-L4, L4-L5, and L5-S1 levels. (B) Sagittal image shows lumbar spinal stenosis (white arrows) at L3-L4, L4-L5, and L5-S1 levels. (C) Sagittal image shows disc herniation (white arrow) at L5-S1 level. (D) Axial image at L5-S1 level shows bilateral foraminal stenosis (left>right, white arrows), ligamentum flavum hypertrophy (red arrow) and facet joint arthropathy (yellow arrow).

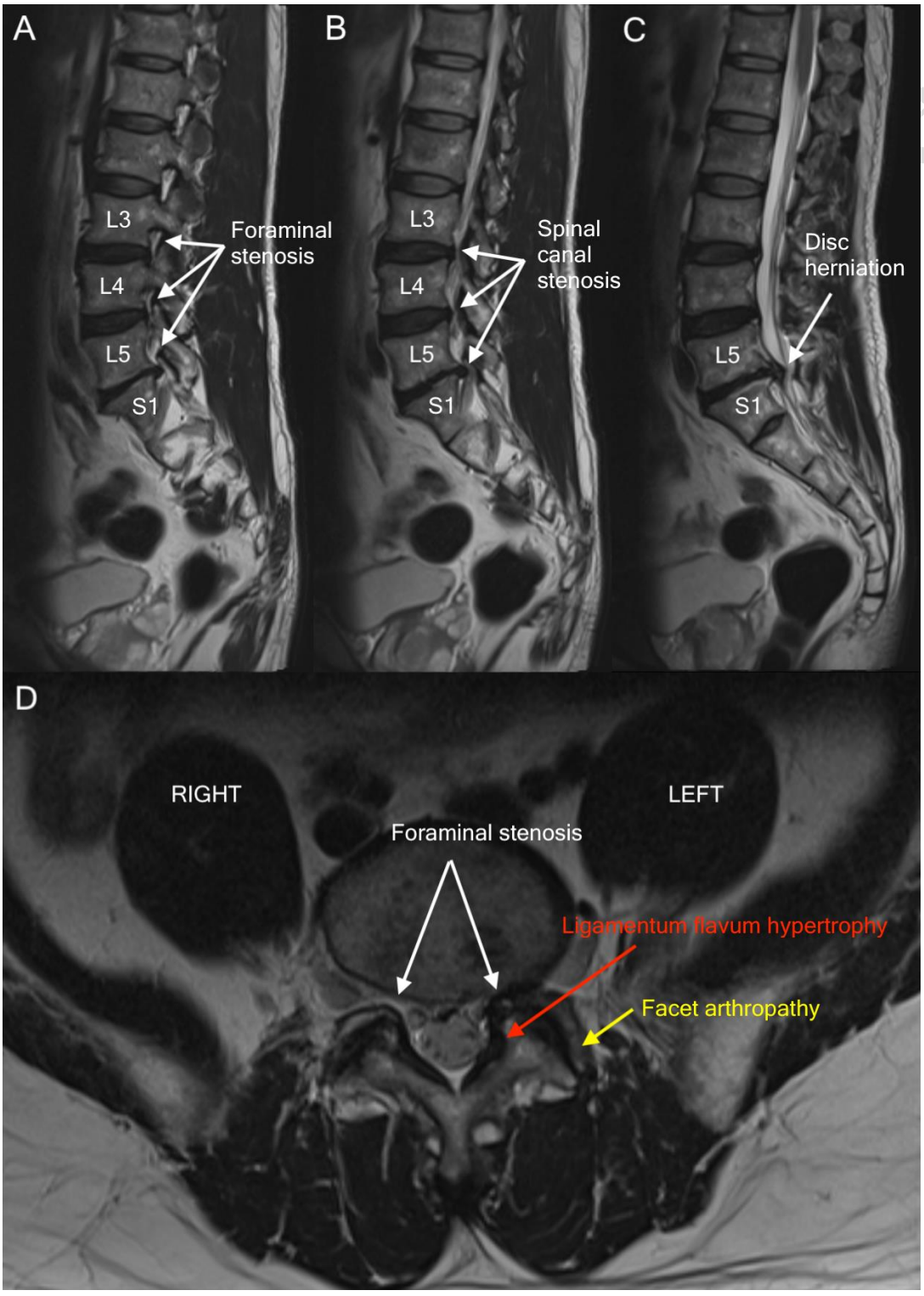

Table 1. Nerve conduction studies (NCS) result.

Motor					
Nerve/ Site	**Latency (ms)**	**Amplitude (mV)**	**Conduction Velocity (m/s)**	**F wave (ms)**	**Interpretation**
Median – Abductor Pollicis Brevis (Left/ Right)					DML: severely prolonged CMAP: reduced MCV: reduced F-wave: prolonged
Wrist	5.65/10.35	3.5/3.9	-	38.31/37.78	
Elbow	11.60/16.80	3.0/2.5	40.3/40.3		
Reference	<4.7	>4.2	>47	-	
Ulnar – Abductor Digiti Minimi (Left/ Right)					DML: severely prolonged CMAP: reduced MCV: reduced F-wave: prolonged
Wrist	7.60/5.15	3.3/2.6	-	45.08/40.50	
Elbow	12.20/12.00	2.1/1.7	45.7/32.1		
Ant. elbow	16.70/17.00	1.6/1.0	31.1/30.0		
Reference	<3.7	>7.9	>52	-	
Peroneal – Extensor Digitorum Brevis (Left/ Right)					DML: severely prolonged CMAP: reduced MCV: reduced F-wave: prolonged
Ankle	8.30/8.40	1.2/0.8	-	NR	
Fib. head	NR/NR	NR/NR	0/0		
Knee	NR/NR	NR/NR	0/0		
Reference	<6.5	>1.1	>42	-	
Tibial – Abductor Hallucis (Left/ Right)					DML: severely prolonged CMAP: reduced with conduction block MCV: reduced F-wave: prolonged
Ankle	7.75/8.20	1.6/1.0	-	68.5/68.83	
Knee	23.00/25.75	0.5/0.1	27.5/23.9		
Reference	<6.1	>5.3	>37	-	
Sensory					
Nerve/ Site	**Rec. Site**	**Latency (ms)**	**Peak-Peak Ampl. (μV)**	**Velocity (m/s)**	**Interpretation**
Median – Digit II (Left/ Right)					DSL: absent SNAP: absent
Digit II	Wrist	NR/NR	NR/NR	0/0	
Reference		<3.3	>15	-	
Ulnar – Digit V (Left/ Right)					DSL: absent

Digit V	Wrist	NR/NR	NR/NR	0/0	SNAP: absent
Reference		<3.1	>13	-	
Sural – Lateral Malleolus (Left/ Right)					DSL: normal SNAP: reduced
Calf	Lat. malleolus	2.10/1.95	2.0/2.5	66.7/71.8	
Reference*		<3.6	>4	-	

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