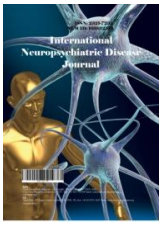

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Clinical and Electrophysiological Aspects of Charcot – Marie Tooth Disease- A Case Report of Two Patients

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Author's contribution

This work was carried by me as I am the only author. I designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. I managed the analyses of the study. I managed the literature searches. I have read and approved the final manuscript.

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Case Report

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ABSTRACT

Aims/ Objectives: To study the importance of electrophysiological tests in diagnosing hereditary motor sensory neuropathy in absence of genetic studies.
Study Design: Cross-sectional study.
Place and Duration of Study: Department of Physiology, Pt. B.D. Sharma Post Graduate Institute of Medical Sciences, Rohtak, Haryana, India.
Methodology: The patients were referred from the Department of Medicine to the Department of Physiology for nerve conduction, F-wave, EMG, VEP & BERA studies.
Results: On electrophysiological examination, there was symmetrical decreased motor conduction velocity of median nerve (less than 38 m/sec), ulnar, tibial and peroneal nerves except in the first patient where the left peroneal nerve conduction velocity was not recordable with decreased amplitude and increased distal motor latencies. Sensory conduction velocities for bilateral median nerves were also decreased with increased latency and decreased amplitude in both the patients. Sensory conduction velocity and amplitudes of bilateral sural nerves were decreased in the first

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patient with increased latencies. However, sensory conduction velocity wasn't recordable for bilateral sural nerves in the other patient. EMG shows decrease in recruitment of motor unit potentials, amplitude in bilateral tibial, peroneous, abductor digiti minimi & 1st dorsal interosseus muscle in the first patient. In proximal upper & lower limb muscles, EMG showed features of denervation. In the second patient, EMG was not advised. VEP in one patient had increased latency of P100 wave & other had normal VEP. Brainstem auditory evoked potential was normal in both patients.

Conclusion: The paper highlights the importance of electrophysiological studies in diagnosis of motor sensory neuropathy in absence of genetic studies. Marked slowing of conduction velocity is the hallmark of CMDT1 [demylinating type].

Keywords: Hereditary neuropathy; EMG; peripheral neuropathy.

1. INTRODUCTION

Charcot-Marie disease (CMT), also called hereditary motor and sensory neuropathy, is the most common inherited peripheral neuropathy, affecting 1 in 2500 [1].

CMT was classically grouped into two main categories according to electrophysiological and nerve biopsy findings:-

(a) CMT1 showing a median nerve conduction velocity of < 38 m/sec, nerve fibre demylination with proliferation of Schwann cells forming onion bulbs.
(b) CMT2 with normal or near normal conduction velocities and pathological signs of axonal degeneration and regeneration [2,3].

CMT produces overall weakness more predominantly seen in distal muscles than proximal muscles, in lower extremities than the upper extremities and motor and sensory deficit. Weakness is present in foot and lower leg muscles but is uncommon in the upper leg or hip girdle muscles. Upper extremity weakness is usually restricted to hand and forearm muscles which may impair hand functions for fine motor and heavy tasks. The sensory loss is glove and stocking in distribution. Patients usually have foot deformities most often pes cavus (high plantar arches), wasting of foot muscles with hammer toe. Wasting of foot and distal lower extremity muscles over time may produce the classical inverted champagne bottle appearance [4,5]. Sensory signs are loss of sensation to touch, pain and vibration distally in lower limbs. Upper limbs are less frequently and less severely affected. Deep tendon reflexes are reduced or absent in most patients with demyelinating CMT [2,6].

Dyck and Lambert [3] classified hereditary motor and sensory neuropathy as:

Marked slowing of motor nerve conduction velocities is a hallmark of CMT1, which serves the basis for differentiation of the demyelinating CMT1 and axonal CMT2 subtypes [7,4].

Demyelination is also manifested by prolonged distal motor latencies [8] and prolonged F wave latencies [9,10].

Electrophysiological criteria used for diagnosis of inherited neuropathies for CMT by me were as per Harding and Thomas guidelines [2]. Thus, median nerve conduction velocity < 38 m/s was considered as demyelinating, 38-45 intermediate (>45 m/s) with low amplitude were considered as axonal neuropathy.

Table 1. Dyck & Lamberts classification of hereditary motor sensory neuropathy

Type	Neuropathy features
HMSN I	Autosomal dominant inheritance
HMSN II	Autosomal dominant inheritance with normal or low NCV
HMSN III	Probable autosomal recessive with very low NCV and very severe clinical abnormality
HMSN IV	Refsum's syndrome
HMSN V	Neuropathy with spastic paraplegia
HMSN VI	Neuropathy with optic atrophy
HMSN VII	Neuropathy with retinitis pigmentosa

2. CASE PRESENTATION

The study was conducted in the department of Physiology on 2 male patients of age groups 20-25 years who were sent from the medicine OPD for electrophysiological evaluation. After taking consent of the patients, the tests performed were:

1. Nerve conduction tests – Motor and sensory. It included bilateral motor median, ulnar, axillary, tibial, peroneal & sensory bilateral median & sural nerves.
2. F wave studies: F wave is a late response resulting from anti-dromic activation of motor neurons including conduction to & from spinal cord.
3. EMG: It measures the electrical activity of muscles using needle electrodes. It shows demyelinating pattern in hereditary motor sensory neuropathy.
4. VEP (Visual Evoked Potential): They are the electrical potential difference recorded from the scalp in response to visual stimuli using surface electrodes. They are primarily reflection of activity originating in the central 3rd to 6th degree of visual fields which are related to the occipital lobe.
5. BERA (Brainstem Evoked Potential): These are the potentials recorded from the ears and vertex in response to brief auditory stimulations to assess the conduction through auditory pathways up to brain using surface electrodes.

The recordings were taken by using RMS EMG EP MK2 machine.

3. RESULTS

Both the patient had similar type of presenting features like weakness of bilateral feet and hands. Age of onset of symptoms was at about 5 years to 15 years. On examination, both the patients had foot drop with pes cavus deformity with wasting of distal muscles of hand and feet with decreased sensation in distal muscles of hand and feet. On electrophysiological examination, there was symmetrical decreased motor conduction velocity of median nerve (less than 38 m/sec), ulnar, tibial and peroneal nerves except in the first patient where the left peroneal nerve conduction velocity was not recordable with decreased amplitude and increased distal motor latencies. Sensory conduction velocities for bilateral median nerves were also decreased with increased latency and decreased amplitude in both the patients. Sensory conduction velocity and amplitudes of bilateral sural nerves were decreased in the first patient with increased latencies. However, sensory conduction velocity wasn't recordable for bilateral sural nerves in the other patient.

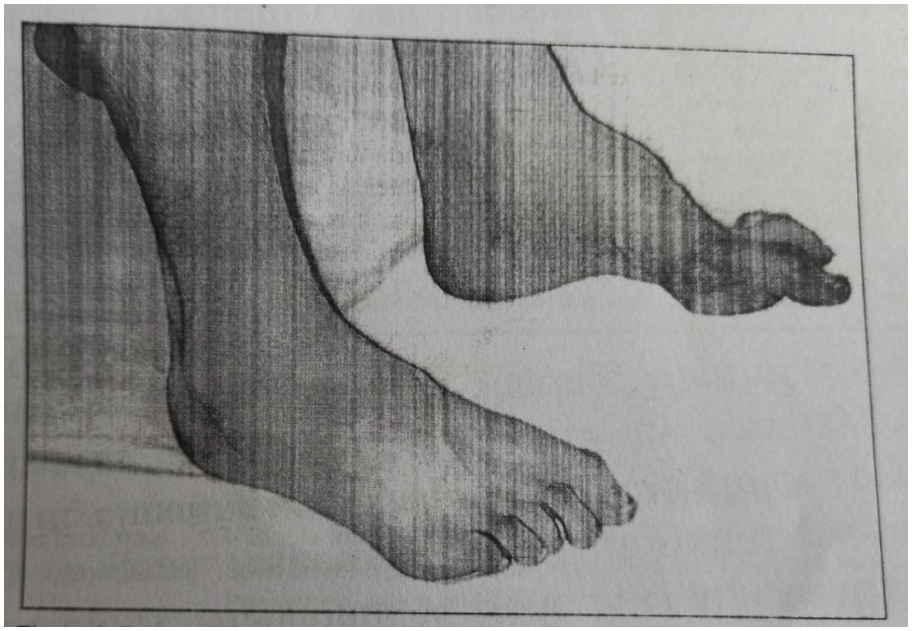

Fig. 1. Pes cavus deformity

Table 2. Features and history of patient

	21 y/M	25 y/M
1. Presenting features and history of patient	Weakness in B/L feet X 4-5 years Weakness in B/L hand X 4-5 months Both feet: weakness gradually progressive, difficulty in holding slippers - No history of difficulty in getting from sitting position to standing - No history of fever. - H/O weakness in BL hands 4-5 months. - gradually progressive, difficulty in gripping objects, buttoning - History of numbness/tingling sensation in B/L hand and feet same duration - No History of respiratory difficulty, urinary incontinence, behavioural abnormalities, visual disturbance, smell, hearing loss or taste sensation, nasal regurgitation of food, nasal twang in voice. No History of difficulty in protruding the tongue,exposure to any drugs like Isoniazide/ Vincristine/toxins or alcohol intake. No History of any chronic illness No History of any similar illness in family	Unsteadiness in walking for 15 years, increased in last 5 years. Weakness in both lower limbs and distal upper limbs. Insidious in onset, gradually progressive difficulty to stand and walk, fear of falling associated with decreased bulk of calf muscles, c/o difficulty in wearing slippers and slipping of slippers. No History of fever, seizure, difficulty in swallowing, in speech or bladder incontinence. Past History:- No history of TB, Hypertension, asthma or epilepsy. No history of drugs like Isoniazide, or anticancer drugs. Personal:- Non smoker, non alcoholic Family history of similar complaints in his sister who is 21 years old.
2. Systemic examination:		
A. Respiratory system exam	Chest Examination- B/L clear, RR 14/min	RR- 15/min, B/L chest clear
B. CVS	Both heart sounds normal, no murmur	Heart sounds normal, no murmur
C. P/A (per abdomen)	soft, non-tender, no organomegaly	Soft, non tender, no organomegaly

F wave conduction velocities and amplitudes were less in upper limbs and absent in lower limbs in both the patients.

EMG studies in distal upper and lower limb muscles showed markedly decreased recruitment and amplitude of motor unit potentials in bilateral peroneal, tibial and first dorsal interosseous muscles in one patient. In the proximal upper and lower limb muscles, needle EMG showed evidence of chronic denervation with spontaneous fibrillation potentials, large polyphasic potentials and reduced recruitment patterns. EMG showed a demyelinating pattern and evidence of denervation in one patient while EMG wasn't advised by the referring physician in the second patient. Brainstem Auditory Evoked Potential showed latencies of all the waves I, II, III, IV and V within normal limits in both the patients with an increased latency of P100 wave observed during VEP recording in one patient. In the other patient, latency of P100 wave was normal.

4. DISCUSSION

The electrophysiological test corresponds to an important step in the evaluation of individuals with suspected hereditary motor-sensory neuropathy and is necessary for the classification of these neuropathies based on genetic studies.

The study of nerve conduction corresponds to the pillar of electrophysiological investigations in these cases.

The main objective is to differentiate between demyelinating and axonal forms [11].

Table 3. CNS findings in the two patients

	Conscious, well oriented in time place & person and has foot drop (claw foot) with wasting of muscles of upper and lower limbs.	**Conscious, well oriented in time place & person and has foot drop (pes cavus) with wasting of muscles of upper and lower limbs.**
Bulk	Right: UL N, LL N; Left: UL N, LL N	Right: UL N, LL N; Left: UL N, LL N
Proximal		
distal	↓ ↓ ↓ ↓	* ↓ ↓ ↓ [*atrophy of distal muscles (thenar)]
Power	Rt: UL N, LL weak; Lt: UL N, LL weak	Rt: UL N, LL weak; Lt: UL N, LL weak
Proximal	N N N N	N N N N
Distal	weak weak weak weak	weak weak weak weak
Tone	N N N N	N N N N
Reflexes	L: - ; R: -	L: + ; R: +
Biceps	- -	+ +
Triceps	- -	+ +
Knee	- -	- -
Ankle	- -	- -
Plantar	- -	- -
Sensory system examinations	Rt: UL N, LL N; Lt: UL N, LL N	Rt: UL N, LL N; Lt: UL N, LL N
Temp	N N N N	N N N N
Pain	- - - -	N N N N
Pressure	N N N N	N N N N
Touch	- - - -	N ↓ N ↓
Joint position	N N N N	N N N N
Cerebellar signs	Dysdydochokinesia + Dysmetria – Nystagmus- Pendullar knee jerk – Romberg sign + No signs of extrapyramidal symptoms Gait- Broad based ataxic gait	Dysdydochokinesia + Dysmetria – Nystagmus- Pendullar knee jerk – Romberg sign +No signs of extrapyramidal symptoms Gait- Broad based ataxic gait

In the current study, marked symmetrical slowing of conduction velocity in bilateral median, ulnar, tibial and peroneal nerves was noticed with increased latency and decreased amplitude which was comparable to the studies by Dubourg [12], Gilliant [7] and Kaku [9].

Marked slowing of motor nerve conduction velocities is a hallmark of CMT1 [7]. Slowing of conduction velocity provides indirect evidence of myelin dysfunction and is usually considered a sign of demyelination or hypomyelination [13]. Uniform slowing of nerve conduction is suggestive of demyelinating neuropathy [14]. Demyelination is also manifested by prolonged distal motor latencies [8] with prolonged F wave latencies which was also seen in this study [9,10].

In the current study, the sensory conduction velocities and amplitudes of bilateral median nerves were decreased with increased latencies in both patients. Decreased conduction velocities and amplitudes of the sural nerves were observed in the first patient while they were absent in the other patient. Both these observations are comparable to the results of the study by Wen et al. [15].

Table 4. Blood profile and nerve conduction tests of the patients

Complete haemogram	Normal			Normal		
Blood sugar (F)	Normal			Normal		
LFT	Normal			Normal		
KFT	Normal			Normal		
Se. Lipid profile	Normal			Normal		
Se Na+/K+	Normal			Normal		
Prothrombin T	Normal			Normal		
S. Protein	Normal			Normal		
Albumin: Globulin	Normal			Normal		
Chest X ray	Normal			Normal		
RA antibody/CRP	Normal levels			Normal levels		
HIV/HBsAg	negative			negative		
Nerve conduction studies	**CV m/sec**	**Latency ms**	**Amplitude mv**	**CV m/sec**	**Latency ms**	**Amplitude mV**
Lt median	29	7.8	.6	36	7.71	5.2
Rt median	27	8.2	1.2	35	7.92	5.3
Lt ulnar	30.7	7.8	3.3	43	8.65	2.7
Rt ulnar	25.6	9.3	4.3	40	8.33	4.9
Rt Axillary	50	5.2	5.2	56	3.2	14
Lt Axillary	52.3	5.4	5.8	54.05	3.33	13.2
Rt Tibial	18	20	.4	26	8.02	0.4
Lt Tibial	19	19	277uv	18	8.75	197.2uv
Rt Peroneal	17.7	21.3	42uv	20	7.29	0.4
Lt Peroneal	NR	NR	NR	22	7.29	1.1
Sensory						
RT Median	16	5.4	85.4uv	15.20	5.92	85.6 uv
Lt Median	17.2	5.3	82uv	15.31	5.88	86 uv
Lt Sural	14	7.2	42uv	Absent	-	-
Rt Sural	12.2	8.2	40uv	Absent	-	-
F wave	CV slower in upper limb and absent in lower limb			CV slower in upper limb and absent in lower limb		
EMG	B/L tibialis anterior 40 % recruitment with giant potential in between with dec amplitude B/L peroneous longus 20% recruitment decreased amplitude. B/L vastus lateralis – 60% recruitment with giant potential in between. B/L Biceps- 60-70% recruitment with mild decrease in amplitude B/L abductor digiti minimi- 50 % recruitment with giant potential in between. B/L first dorsal interosseus- 10% recruitment with decreased amplitude			Not done		
BERA	Latency of all the waves I, II, III, IV and V within N limits			Latency of all the waves I, II, III, IV and V within N limits		
VEP	L Normal latency		R Increased latency of P100 wave	Normal latency of p100 wave		

EMG studies in distal upper and lower limb muscles showed markedly decreased recruitment and amplitude of motor unit potentials in bilateral peroneal, tibial and first dorsal interosseous muscles in one patient. In the proximal upper and lower limb muscles, needle EMG showed evidence of chronic denervation with spontaneous fibrillation potentials, large polyphasic potentials and reduced recruitment patterns which is consistent with the study done by Sevilla et al. [16].

Visual evoked potentials were performed in first patient in which P100 wave latency on the left side was normal while latency of wave P100 was increased on the right side indicating subclinical involvement of the visual pathway which is in accordance with Wen et al. [15].

Brainstem auditory evoked potentials were normal in both the cases which is in contrast with the study by Fusco et al where they got increased latencies in BERA [17].

This study is different from all other studies because of the various neurophysiological tests done on the patients namely, nerve conduction studies, F wave studies, EMG, Brainstem auditory evoked potentials and Visual evoked potential studies in these patients. Most of existing studies in the literature did not conduct all the above tests on single patients.

5. CONCLUSIONS

Hereditary Motor sensory neuropathy should be suspected in children and adults with distal muscle weakness in both upper and lower limbs with areflexia and sensory deficit. Electrophysiological studies are important for differentiating CMT1 (demyelinating form) from CMT2 (axonal) in absence of availability of genetic studies. In the present study electrophysiologic findings showed a diffuse and symmetrical slowing of motor and sensory nerve conduction velocities indicative of a demyelinating type of neuropathy.

CONSENT

As per the international guidelines, an informed and written participant consent explaining all the details has been collected and preserved.

ETHICAL APPROVAL

These patients were referred to me for electrophysiological tests from the Medicine OPD. As such there were no ethical issues involved as the tests were done as prescribed by the treating physician and were a part of the treatment protocol of the patients.

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COMPETING INTERESTS

Author has declared that no competing interests exist.

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