

Case Report

A family with Charcot-Marie-Tooth disease (type 1): evaluating diagnostic role of nerve conduction studies

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ABSTRACT

We aimed to report a case history of a family with Charcot-Marie-Tooth disease and to assess the role of nerve conduction studies in the diagnosis. A 10-year-old girl presented with difficulty in walking with a history of delayed motor milestones and slowly progressive weakness in distal muscles of both the lower limbs, with similar group of complaints in her father and a younger brother. Clinical examination of the patients was done and nerve conduction studies were performed. Clinical features and nerve conduction studies suggested the diagnosis as Charcot-Marie-Tooth disease with characteristic electro-diagnostic findings of Charcot-Marie-Tooth disease type-1. Charcot-Marie-Tooth disease is a rare disorder found in India. Although genetic tests form the basis of accurate diagnosis, yet nerve conduction studies, to a great extent, prove to be remarkable in approaching the diagnosis and distinguishing the common subtypes of this rare condition.

Keywords: Charcot-Marie-Tooth disease, Nerve conduction studies

INTRODUCTION

Charcot-Marie-Tooth (CMT) disease refers to a group of inherited peripheral neuropathies with a worldwide prevalence of 10 per 100,000.¹ It is a heterogeneous group of hereditary motor and sensory neuropathies. The inheritance pattern is autosomal dominant in majority of CMT patients, although X-linked and autosomal recessive forms also exist. Dyck and Lambert subdivided Hereditary Motor and Sensory Neuropathies (HMSNs) into dominantly inherited demyelinating HMSN-I (CMT-1) and dominantly inherited axonal HMSN-II (CMT-2) forms based on electrophysiological and neuropathological criteria.² Other types were classified as HMSN-III to VII depending on the inheritance type and associated features.

Although genetic tests are definitive for the diagnosis, yet a role of nerve conduction studies in diagnosing and distinguishing the subtypes of this disorder has been creditable, especially, where cost of the test serves as a major hindrance. This report presents such a case of a rare peripheral neuropathy found in a family and role of nerve conduction studies in diagnosing the condition.

CASE REPORT

This is a case history of three members of the same family: father (40-year-old), daughter (10-year-old) and son (3-year-old) presenting with similar group of complaints, suggesting a hereditary pattern. A 10 year old girl belonging to Muslim community, born out of non-consanguineous marriage presented with difficulty in walking. As per mother she had delayed development

with neck holding achieved at 1 year, sitting at 2 years and walking at approximately 5 years. She takes support while climbing up and down. She cannot run or stand up on her own. The symptoms were slowly progressive. There was no history of hearing and speech problems, involuntary movements or any autonomic disturbances. The past history was not significant. The family history revealed the presence of similar complaints in her father, now presenting with difficulty in walking and easy fatigability. Her 3-year-old younger brother had delayed motor milestones. Other two siblings were normal.

General physical examination revealed pes-cavus deformity in the feet. On neurological examination, higher mental functions were found to be normal. Bilateral calf muscles showed signs of wasting. The power in the muscles of the hand was reduced, with normal power in the other upper limb muscles. The lower limb muscles also had reduced power in the distal group, while muscles of thighs had normal power. All the Deep Tendon Reflexes (DTR) were absent, bilaterally. Superficial reflexes were present. Sensory examination was normal except the impairment of vibration sense. Similar clinical findings were observed in her father, with characteristic presence of pes-cavus deformity (Figure-1). Reduced power in the distal group of muscles was found. Investigations in both the patients showed normal fasting and post-prandial blood sugar, normal serum creatinine, sodium, potassium, Liver function tests and Rheumatoid factor. Serum CPK-MB (Creatine phosphokinase) of the girl was 369 IU. CSF examination of the girl was done which was normal. Muscle biopsy of only girl's father could be performed as consent was not given for the girl. Histopathology report suggested the features of muscular dystrophy in the form of mild variability in the muscle fiber size, internalization of nuclei, necrotic muscle and fibro-adipose tissue infiltrating the muscle. However, absence of dystrophin could not be confirmed.



Figure 1: Pes-cavus in patient's father (a deformity associated with Charcot-Marie-Tooth disease type 1) with wasting of the calf muscles.

Nerve conduction studies

Nerve Conduction Velocity (NCV) (sensory and motor) of the girl showed almost uniform slowing (similar nerve conduction changes in different nerves and in different segments of the same nerve), to about 37 m/sec in upper and lower limbs. Median motor nerve conduction velocity in the forearm segment was 37.12 m/sec. No evidence of conduction block (defined as a 20-50% drop in the amplitude of negative peak on proximal stimulation compared to distal) was found.³ Temporal dispersion (in which negative and positive phases of action potential overlap due to variable conduction velocity in demyelinating fibres) was also absent (Figure-2). The amplitudes (base to peak) for both Sensory Nerve Action Potential (SNAP) and compound muscle action potential (CMAP) were within normal range for all the nerves.

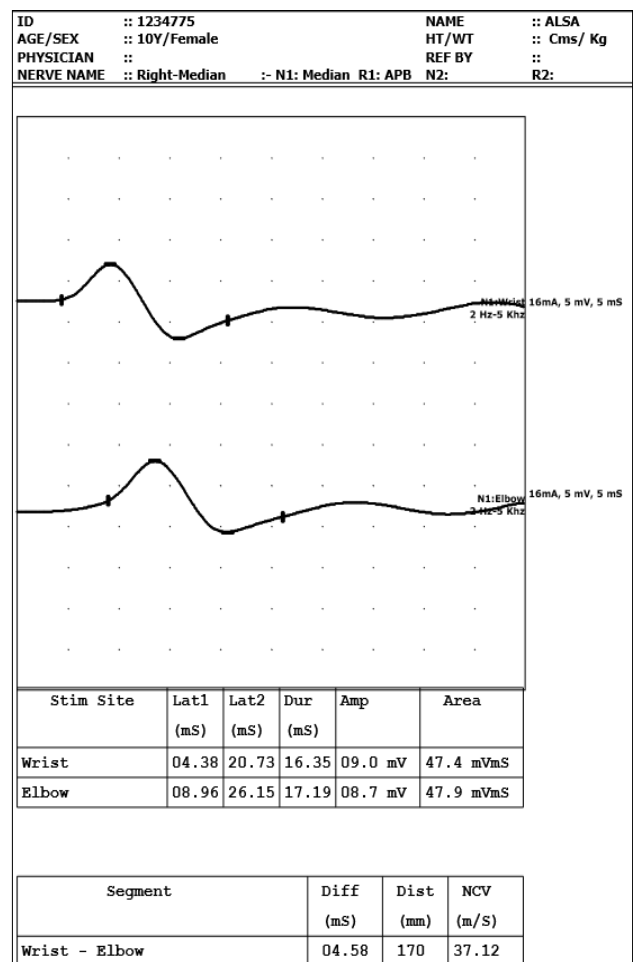


Figure 2: Median motor nerve-conduction recordings of the patient (10-year-old female): The median motor nerve conduction velocity is 37.12 m/sec (<38 m/sec, suggestive of CMT-1) with normal amplitude at proximal and distal stimulation sites. No evidence of conduction block (amplitudes at proximal and distal sites were 9 mv and 8.7 mv respectively) or temporal dispersion: electro-diagnostic feature, distinguishing hereditary demyelinating neuropathy from acquired type.

Nerve conduction studies of her father revealed almost similar findings. A uniform slowing of nerve conduction, to about 23.8 m/sec was found. Median motor forearm conduction was 22.86 m/sec with no evidence of conduction block or temporal dispersion (Figure-3). The amplitudes (base to peak) for Compound Muscle Action Potential (CMAP) were slightly reduced while for SNAP no definite wave-form could be recorded. Hence, owing to the above mentioned characteristic neurophysiological findings, our diagnosis was Charcot-Marie-Tooth disease type 1 in the patient and her father. Chromosomal analysis, however, could not be done due to patient's unaffordability.

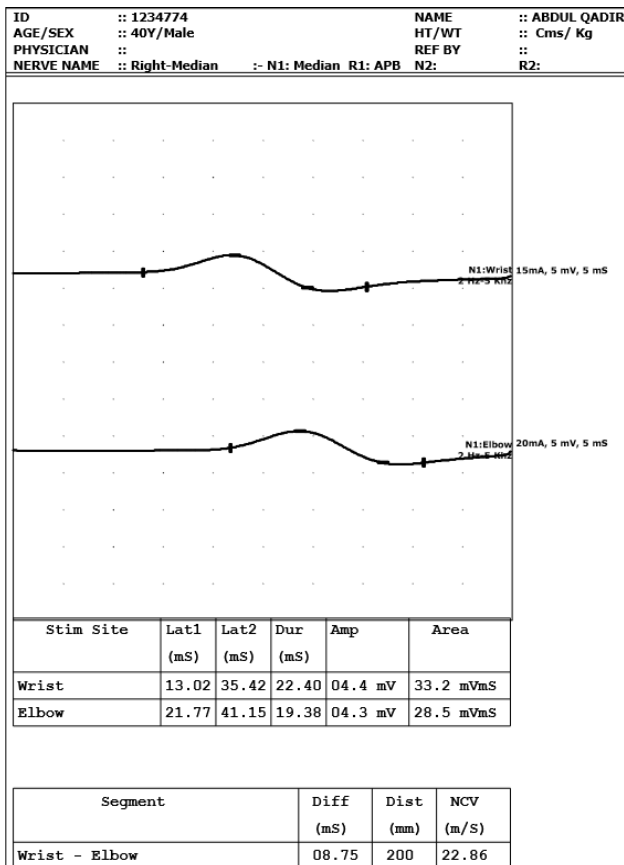


Figure 3: Median motor nerve conduction recordings of the patient's father (40-year-old): The median motor nerve conduction velocity is 22.86 m/sec (markedly reduced, suggesting CMT-1), with slightly reduced amplitude (normal laboratory range: 9 mv ± 2) at both proximal and distal stimulation sites. No evidence of conduction block or temporal dispersion (electro- diagnostic feature, distinguishing hereditary demyelinating neuropathy from acquired type).

DISCUSSION

Charcot-Marie-Tooth disease type 1 (CMT-1), the commonest form of CMT neuropathies, usually autosomal dominant, slowly progressive, with age of onset as first or second decade of life and strong family history, presents with distal symmetrical lower limb

weakness, associated pes-cavus foot deformity, absent DTR and variable sensory loss with loss of vibration and proprioception affected early. In both the patients, all the above clinical findings were present.

Nerve conduction studies revealing a uniform slowing of conduction in our case (37 m/sec in the girl and 23.8 m/sec in the father), absence of conduction block and temporal dispersion exclude the possibility of an acquired demyelinating neuropathy (Chronic inflammatory demyelinating neuropathy), which is further supported by a normal CSF examination and presence of a family history.⁴ Uniform slowing of NCV also excludes HNPP (Hereditary neuropathy with pressure palsies), in which a characteristic asymmetric pattern of slowing is found, along with a history of entrapment neuropathy, which was absent in our case.⁵

CMT-2 (autosomal dominant CMT) presents in a manner, clinically indistinguishable from CMT-1. An accurate diagnosis is impossible without NCV tests. Reduced CMAP and SNAP amplitudes with normal or mildly reduced NCV (>38 m/sec in median motor forearm conduction) are the hallmarks.⁶ Sural nerve biopsy showing axonal loss without the evidence of demyelination; and genetic tests, further confirms the diagnosis. A reduction in CMAP and SNAP amplitudes have also been reported in CMT-1 in previous studies, which are in accordance with the unobtainable SNAP amplitudes found in NCS of girl's father in our case.⁷ Other rare forms of CMT (HMSN-III and CMT-4) are autosomal recessive, severe forms with early age of onset. Charcot-Marie-Tooth disease has great genetic heterogeneity which renders the molecular diagnosis complex and time consuming and many molecular geneticist take into account the type of CMT (axonal or demyelinating) based on the motor NCV of the median nerve.

Regarding the treatment of this disease, no specific cure exists. Physical therapy in the form of active feet stretching and ankle bracing can be beneficial. Early diagnosis and physical therapy can help patient remain ambulatory throughout their lives.

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REFERENCES

- Emery AE. Population frequencies of inherited neuromuscular diseases: a world survey. *Neuromuscul Dis.* 1991;1(1):19-29.
- Dyck, PJ, Lambert, EH. Lower motor and primary sensory neuron diseases with peroneal muscular atrophy. II. Neurologic, genetic, and electrophysiologic findings in various neuronal degenerations. *Arch Neurol.* 1968;18(6):619-25.

3. Oh SJ, Kim DE, Kuruoglu HR. What is the best diagnostic index of conduction block and temporal dispersion? *Muscle Nerve.* 1994 May;17(5):489-93.
4. Lewis RA, Sumner AJ. The electrodiagnostic distinctions between chronic familial and acquired demyelinating neuropathies. *Neurol.* 1982 Jun;32(6):592-6.
5. Li J, Krajewski K, Shy ME, Lewis RA. Hereditary neuropathy with liability to pressure palsy: the electrophysiology fits the name. *Neurol.* 2002 Jun;58(12):1769-73.
6. Harding AE, Thomas PK. The clinical features of hereditary motor and sensory neuropathy types I and II. *Brain.* 1980 Jun;103(2):259-80.
7. Krajewski KM1, Lewis RA, Fuerst DR, Turansky C, Hinderer SR, Garbern J, Kamholz J, Shy ME. Neurological dysfunction and axonal degeneration in Charcot-Marie-Tooth disease type 1A. *Brain.* 2000 Jul;123(Pt 7):1516-27.

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