Hereditary Neuropathy with Analysis of Electrophysiological Findings:
A Case Report

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Abstract
The hereditary motor and sensory neuropathies (HMSN) represent a genetically heterogeneous collection of disorders in which patients develop a progressive muscular atrophy and sensory neuropathy of the distal extremities. There are abnormalities of axons or Schwann cells and their myelin sheaths resulting in peripheral nerve dysfunction. These disorders are also known as Charcot-Marie-Tooth (CMT) disease, which is divided into seven distinct subtypes based on inheritance pattern (dominant, recessive, or X-linked) and whether the primary pathology is located in the myelin or axon. Each of these CMT types are further divided based on their specific molecular and genetic findings. Here we report a case which was diagnosed on the basis of clinical history and neurophysiological testing. Although genetic analysis is the gold standard for diagnosis we could not do it due to lack of availability of genetic testing in our country at this moment. [Journal of National Institute of Neurosciences Bangladesh, 2016;2(1): 43-45]

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Introduction
Hereditary motor-sensory neuropathies are abnormalities of axons or Schwann cells and their myelin sheaths resulting in peripheral nerve dysfunction1. They are characterized by non typical neural development, and degradation of neural tissue. The two common forms of hereditary motor and sensory neuropathies (HMSN) are either hypertrophic demyelinated nerves or complete atrophy of neural tissue. Hypertrophic condition causes neural stiffness and a demyelination of nerves in the peripheral nervous system, and atrophy causes the breakdown of axons and neural cell bodies2. These disorders are also known as Charcot-Marie-Tooth (CMT) disease, which is divided into seven distinct subtypes based on inheritance pattern like dominant, recessive, or X-linked and whether the primary pathology is located in the myelin or axon. Each of these CMT types are further divided based on their specific molecular and genetic findings3. Most forms of HMSN affect males earlier and more severely than females, but others show no predilection to either sex.
Onset of HMSN is most common in early childhood, with clinical effects occurring before the age of 10, but some symptoms are life-long and progress slowly. Four genes have been identified that are related to these disorders which are peripheral myelin protein 22, myelin protein zero, gap junction protein connexin 32 and early growth responsive gene 2. The purpose of the present work was to describe a clinically suspected case of hereditary motor and sensory neuropathies (HNSN) which has later been supported by electrophysiological tests.

Case Presentation
A 35 year old man presented with the complaints of difficulty in walking due to weakness and wasting of the muscles since the age of eleven (11) years. This was more marked over the last 8 years with involvement of the upper limbs. Initially the patient could perform the daily activities independently; however, for the last five years the patient needed support for the activities of daily living. The patient had not given any history of fasciculation, sensory symptoms, ocular problem or any symptom of bladder and bowel involvement. One of the maternal uncles of the patient had been suffering from similar illness. On examination the vitals were within normal limit. Neurological examination revealed a normal higher psychic function including the speech. All cranial nerves including the fundus were normal. Upper limbs revealed wasting of both hand muscles with deformity of fingers, more marked in right hand.

All deep tendon reflexes (DTR) in the upper limb (U/L) were absent. In the lower limbs there were pes cavus and hammer toe deformity with ulceration over right great toe. Bulk of muscle was reduced in both lower limb with a distal prominence giving the appearance of inverted champagne bottle. All deep tendon reflexes were reduced. Sensory examination revealed no abnormality. Gait was high stepping. Both heel and toe walking were impaired bilaterally. No nerve was found to be thickened. Cerebeller examination revealed no abnormality. Routine blood chemistry and cerebrospinal fluid (CSF) examination was unremarkable. The nerve conduction study (NCS) revealed a non recordable compound muscle action potential (CMAP) in the median, tibial and peroneal nerves on both sides. Ulnar compound muscle action potential (CMAP) amplitude was reduced together with a prolonged distal latency and reduced conduction velocity (<35m/s) on both sides. SNAPs could not be recorded in the studied nerves (median, ulnar and sural) on either side. These electrophysiological findings are consistent with sensory motor polyneuropathy with involvement of axons predominantly. Absence of conduction block & presence of relative symmetry is suggestive of Hereditary sensory motor polyneuropathy (HMSN type 2).

Discussion
The clinical symptoms of HMSN usually have onset in childhood or young adulthood. Symptoms are variable. Motor symptoms seem to be more predominant than sensory symptoms. Symptoms are fatigue, pain, lack of balance, lack of feeling, lack of reflexes and hearing, which results from muscle atrophy. Patients also presents with high arched feet, stork leg or inverted champagne bottle appearance, hammer toes, foot drop...
and scoliosis. Weakness of the intrinsic hand muscles generally occurs late in the course of the disease but is not usually related to the degree of leg weakness or atrophy or to the age of the patient. Muscle stretch reflexes disappear early in the ankles and later in the patella and upper limbs

The diagnosis of these neuropathies is based on clinical and ancillary examination. In demyelinating CMT neuropathies, nerve conduction studies show marked slowing of conduction velocity, usually below 75% of the lower limit of normal. Slowing is uniform in all nerves, without evidence of temporal dispersion or conduction block. Motor responses may be very low or absent in the lower extremities. In nearly all cases, slowing can be demonstrated in the upper extremities (median motor conduction velocity <38m/s). Sensory studies are usually abnormal and generally show low or absent amplitude. Sural nerve biopsy reveals features of demyelination and remyelination, with indications of Schwann cells disturbances. Genetic studies are of value not only for diagnosing these diseases, but also for better understanding the molecular events that result in the clinical symptoms.

Charcot–Marie–Tooth disease was first described in 1886 by Jean-Martin Charcot, Pierre Marie, and independently Howard Henry Tooth. In the 1950s, further classification occurred and separated patients into two distinct groups. Group one was characterized by slow nerve conduction velocities and demyelinating neuropathy. Group two was characterized by mostly normal nerve conduction velocities and degeneration of axons. In 1968, HMSN were classified again into seven groups.

HMSN1 is the type of Charcot–Marie–Tooth disease type 1A and 1B. This is hypertrophic demyelinating type and affected individuals experience weakness and atrophy in the lower legs in adolescence, and later develop weakness in the hands. This is the most common type of CMT. HMSN2 (Charcot–Marie–Tooth disease type 2) is the neuronal type in which symptoms are similar to type 1 and onset is in adolescence.

HMSN3 variant is known as Dejerine–Sottas disease (Charcot–Marie–Tooth type 3) and onset is in infancy and results in delayed motor skills, much more severe than types 1 & 2. HNSN4 is also known as Refsum disease. In this spinal type muscular weakness and atrophy is similar to that of other types of CMT, but set apart by being autosomal recessive inheritance. HMSN5 is also known as Charcot–Marie–Tooth with pyramidal features. This is pyramidal type and onset is between ages 5–12 years. Lower legs are affected first by muscle weakness and atrophy one is followed by the upper extremities. Type 5 is also associated with visual and hearing loss. HMSN6 is also known as Charcot–Marie–Tooth type 6. This variant early onset muscular weakness and atrophy is followed by optic atrophy resulting in vision loss and possibly blindness. HMSN 7 is also known as HMSN+ retinitis pigmentosa. This is represented with a later onset with muscular weakness and atrophy mostly in the lower limb.

**Conclusions**

Patients of peripheral neuropathy are quite common in our day to day practice. However, due to widespread unavailability of neurophysiological tests many a times the diagnosis remains speculative. In this case electrophysiological testing has supported the clinical diagnosis of hereditary motor and sensory neuropathies (HMSN). Although genetic analysis is the gold standard for confirmation of HMSN, it has not been done in our case due to lack of availability of genetic testing in our country at this moment.

**References**