Case Report

Electrophysiological and radiological diagnosis of hereditary motor and sensory polyneuropathy

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Abstract

Hereditary motor and sensory neuropathy (HMSN), also known as Charcot-Marie-Tooth disease (CMT), is a member of the inherited neuropathy family with specific clinical and genetical manifestations. More than twenty genes have been linked to HMSN, and the number might increase. Regarding diagnosis, a healthcare provider should be suspicious if the patient is young with a family history. Integrative diagnosis, which includes electrophysiological, radiological, and genetic screening, is of great value to exclude metabolic, nutritive-toxic, infectious, and inflammatory or autoimmunological causes and to reach the exact subtype of hereditary neuropathy. Nowadays, next-generation sequencing-based analysis is becoming a routine diagnostic tool for inherited neuropathy, but if this facility is not available, electrophysiological and radiological diagnoses are the best diagnostic tools to be used. Differentiation between hereditary neuropathy and diabetic neuropathy is essential for primary care physicians to have the right plan.

Keywords: Hereditary motor and sensory polyneuropathy, nerve conduction velocity, pulmonary function test, radiological findings

Introduction

Hereditary motor and sensory neuropathy (HMSN), also known as Charcot-Marie-Tooth disease (CMT), is a member of the inherited neuropathy family with specific clinical and genetical manifestations. More than twenty genes have been linked to HMSN, and the number might increase. Inherited neuropathies are categorized as follows: 1) HMSN if there is muscle weakness and sensory loss, 2) hereditary motor neuropathy (HMN) if it is mainly motor deficit, 3) hereditary sensory neuropathy (HSN) if it is mainly sensory deficit, 4) hereditary sensory and autonomic neuropathy (HSAN) if it is mixed sensory and autonomic deficit (less common), and 5) small fiber neuropathy (SFN), which is manifested by burning and periodic pain.[1,2] HMSN is considered to be among the most common inherited neuromuscular disorders (its prevalence of 17–40/100,000).[3-5]

Several clinical manifestations can be seen in HMSN, including progressive weakness and atrophy of distal muscles, which start from the lower extremities and eventually reach the upper extremities, walking in a step gait pattern, loss of sensory sensation distally, and hyporeflexia. In addition, HMSN is usually accompanied by pes cavus and claw toes. Moreover, it could be accompanied by neuropathic pain, scoliosis, skeletal deformities, deafness, cognitive deficits, tremor, impaired speech and dysphagia, breathing difficulties, or structural changes in the central nervous system.[6,7] Due to the similarities between the subtypes of hereditary neuropathy and neuropathy as a consequence of metabolic syndromes, it is of great value for

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primary care physicians to differentiate and deal correctly with the various types of neuropathy.

Case Report

A 52-year-old Saudi woman, with a weight of 60 Kg and a height of 157 cm, came to the emergency room with numbness in the upper limbs with difficulty to make hand grips associated with pain in the cervical region starting for the last 15 years. She has no seizures, headache, decrease in vision power, dysphagia, and urine and stool incontinence. Simultaneously with the upper limb symptoms, she developed numbness in both lower limbs and difficulty to walk with slurred speech, which were neglected in the primary investigations. Symptoms progressed to worsen with years but were stable in the last 5 years. The muscle power of the upper limb was 4/5, while the muscle power of the lower limb was 3/5, with mild wasting of both thenar and hypothenar of upper limbs and lower limbs. Diminished upper and lower reflexes were observed. Her sister has similar signs and symptoms. She has normal blood levels of B12, calcium, HbA1c, and other blood elements with no history of diabetes and other medical complaints.

Nerve conduction studies

The upper limb nerve conduction study showed median, ulnar, and radial sensory latency, and conduction velocities were completely absent bilaterally [Table 1]. Table 2 shows normal motor conduction velocities bilaterally in all these nerves (right median: 52 m/s, right ulnar: 57 m/s, right radial: 72 m/s, left median: 55 m/s, left ulnar: 50 m/s, and left radial: 72 m/s). Also, Table 2 shows that F-wave responses were normal (right median: 31.4, right ulnar: 27.8, left median: 28, and left ulnar: 31.7 milliseconds). In lower limb nerve conduction studies, common peroneal nerve distal latency was normal (right: 5.21 and left: 5.63), with absent conduction velocities bilaterally and F wave [Table 3 and Figure 1]. Sural and tibial nerve distal latency and conduction velocities were absent bilaterally. F-wave responses were absent bilaterally, with the conclusion suggestive of sensory neuropathy involving median, ulnar, and radial nerves in the upper limbs. However, polyneuropathy involving common peroneal, tibial, and sural nerves in lower limbs was present.

Magnetic resonance imaging (MRI) findings

A plain brain MRI showed foci of non-enhancing abnormal signal intensities in the left centrum semiovale, bilateral anterior frontal lobes, and right parietal lobe. All of them were hypointense on T1 weighted (T1WI) and hyperintense on T2 weighted (T2WI) or fluid-attenuated inversion recovery (FLAIR) without demonstration of diffusion restriction. No perilesional edema was associated with any of them [Figures 2 and 3]. A plain MRI of the cervical and lumbar spine was also performed, which depicted hypertrophy of bilateral C7-T1-level exiting nerve roots along with signs of paraspinal muscle atrophy and their fatty infiltration, indicating denervation myopathy [Figures 4 and 5].

Table 1: Nerve conduction studies of sensory nerves of upper and lower limbs

Sensory				
	Right		Left	
	Latency (ms)	CV (m/s)	Latency (ms)	CV (m/s)
Median	Absent	Absent	Absent	Absent
Ulnar	Absent	Absent	Absent	Absent
Radial	Absent	Absent	Absent	Absent
Sural	Absent	Absent	Absent	Absent

Table 2: Nerve conduction studies of motor nerves of upper limbs

Motor						
Ulnar nerve						
Right upper limb				Left upper limb		
	Latency ms	CV (m/s)	F wave	Latency (ms)	CV (m/s)	F wave
At wrist	2.6	57	27.8	2.55	50	31.7
At elbow	7.19			8.7		
Median nerve						
Right upper limb				Left upper limb		
	Latency ms	CV (m/s)	F wave	Latency ms	CV (m/s)	F wave
At wrist	2.24	52	31.4	3.81	55	28
At elbow	7,92			8.28		
Radial nerve						
Right upper limb				Left upper limb		
	Latency ms	CV (m/s)	F wave	Latency ms	CV (m/s)	F wave
At wrist	2.34	72	-	2.5	72	-

Pulmonary function test

Spirometry was performed with a conclusion of a moderate degree of obstructive and restrictive lung impairment (Forced expiratory volume in one second [FEV1] = 63%, forced vital capacity (FVC) = 54%, FEV1/FVC = 85%, forced expiratory flow (FEF) max = 25%-50%-75%, FEF 25% = 36%, FEF 50% = 36%, and FEF 75% = 62%).

Genetic screening

Genetic screening was not available to confirm the diagnosis. Therefore, we had to rely on electrophysiological and radiological findings in concomitant with signs and symptoms.

Outcome and follow-up

Even though hereditary neuropathy has no cure for the time being, it is important to have the exact diagnosis for a better prognosis and future plan for the patient and the family.

Discussion

Healthcare provider, in particular primary care and family physicians, should be suspicious if the patient is young with

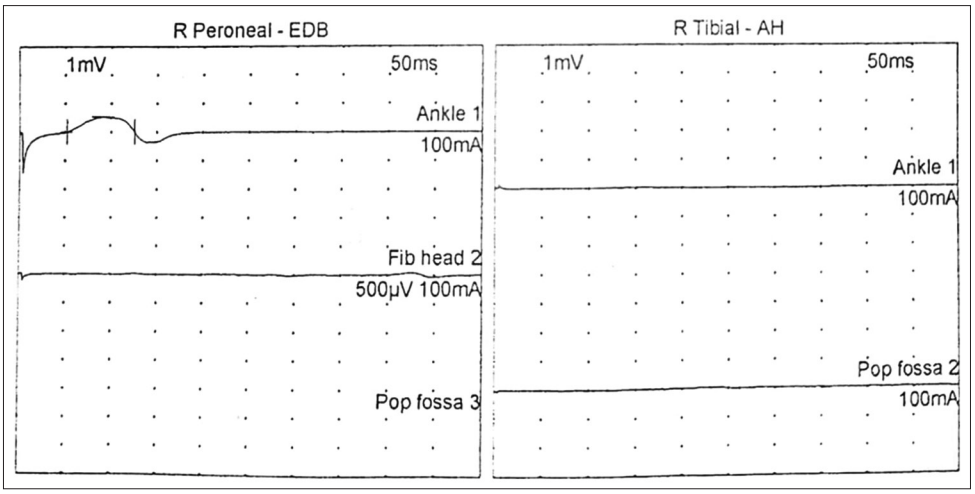

Figure 1: Right tibial and peroneal motor conduction study

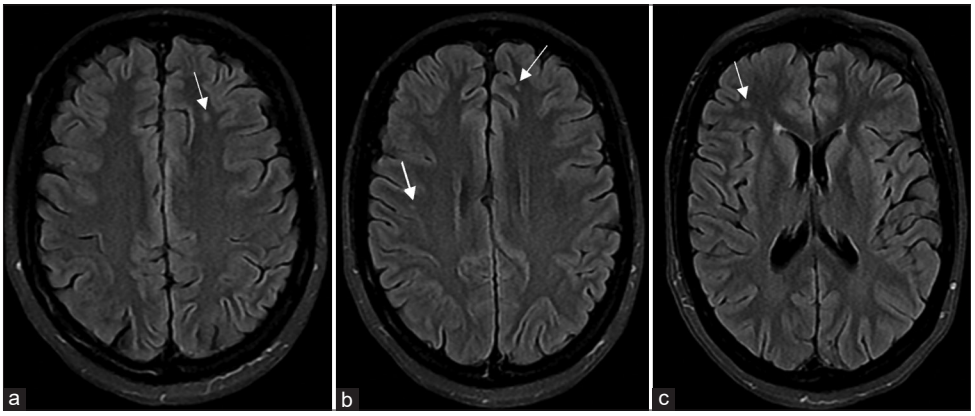

Figure 2: Axial sections of plain MRI brain fluid-attenuated inversion recovery (FLAIR) sequences showing the tiny focus of hyperintensity in left centrum semiovale (a), left anterior frontal lobe and right parietal lobe (b), and right frontal lobe (c)

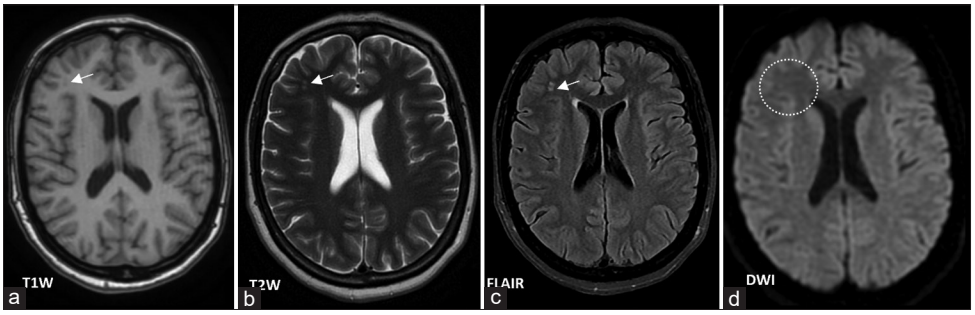

Figure 3: Axial sections of plain MRI brain showing two foci of abnormal signals in the right frontal lobe, which are hypointense on T1 weighted (T1WI) [a] and hyperintense on T2 weighted (T2WI) and fluid-attenuated inversion recovery (FLAIR) sequences [b, c]. They do not show restricted diffusion on diffusion-weighted images (DWIs) [d]

a family history. The aim of this case report is to differentiate between various types of hereditary neuropathy and diabetic neuropathy. Moreover, an integrative diagnosis, which includes electrophysiological, radiological, and genetic screening, is of great value to exclude metabolic, nutritive-toxic, infectious, and inflammatory or autoimmunological causes and to reach the exact subtype of hereditary neuropathy. Nowadays, next-generation sequencing-based analysis is becoming a routine diagnostic tool for inherited neuropathy. Approximately 20–70% of HMSN acquired duplicate PMP22 gene. Electrophysiological diagnosis and radiological findings are useful diagnostic tools, but the genetic study will confirm the conclusion and hence can help in the prognosis and the expectations of the patient's future.[8] For this patient specifically, it seems from the nerve conduction studies of the upper and lower limbs that all sensory nerves are involved with the lower limb's motor nerves affected only. With the prognosis of the disease, we think that upper motor nerves eventually will be affected as well.

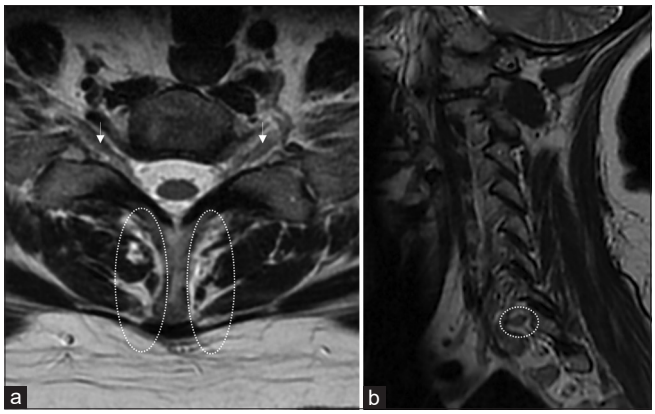

Figure 4: Plain T2W MRI cervical spine (axial section, a) and upper thoracic level (sagittal section, b) showing hypertrophic bilateral nerve roots at the level of C7-T1 in the axial plane (arrows). Right parasagittal MRI showing right-sided hypertrophic nerve root in the neural foramen at the same level (dotted circle). Paraspinal thoracic muscle atrophy and fatty infiltration (white fat) are also shown (dotted oval)

Radiological imaging features, although not diagnostic and specific for HMSN, assist clinical examination findings, genetic testing, and nerve conduction study in delineating the final diagnosis by identifying the distribution of disease and its pattern of involvement. Imaging has also contributed to monitor the progression of disease and response to treatment. Computed tomography (CT) scan and myelogram are limited, while MRI has a promising role in the assessment of diseases.[9]

MRI may show smooth thickening of the involved nerves due to repeated cycles of demyelination and remyelination. This is analogous to other hypertrophic neuropathies. In the spine, ganglia, exiting nerve roots, and cauda equina may be involved, leading to neural foramina and spinal canal stenosis.[10]

The involvement of cranial nerves in HMSN is uncommon. In case they are affected, a CT scan bone window shows enlarged cranial foramina due to hypertrophy of the nerves.[11] Infrequently, brain parenchymal changes and their coexistence with multiple sclerosis have also been reported in different types of HMSN. MRI may show scattered foci of T2 or FLAIR hyperintense signals in deep white matter with or without contrast uptake and diffusion restriction. These foci may be representative of demyelination as seen in our patient as well.[11-13]

Diffuse white matter hyperintense signals in the posterior white matter, centrum semiovale, and corpus callosum of a child mimicking leukodystrophy have also been mentioned in the literature.[14] Depending on the region of the diseased nerve, MRI may show indirect signs of denervation myopathy, which is a part of many other neuropathies as well. It includes T2 or short tau inversion recovery hyperintense signals of muscles due to muscle edema in the acute phase, followed by muscle atrophy and T1 hyperintense fatty infiltration in the chronic stage.[9,10,15,16]

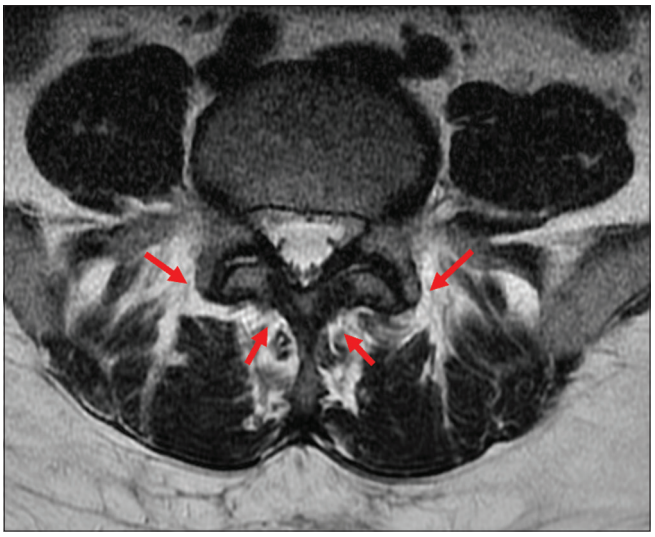

Figure 5: Axial section T2WI plain MRI lower lumbar spine showing paraspinal muscle atrophy and fatty infiltration (white fat) (red arrows)

Table 3: Nerve conduction studies of motor nerves of lower limbs

Peroneal nerve			
Right lower limb	**Value**	**Left lower limb**	**Value**
Distal latency (ms)	5.21	Distal latency (ms)	5.63
Proximal latency (ms)	Absent	Proximal latency (ms)	Absent
CV (m/s)	Absent	CV(m/s)	Absent
F wave	Absent	F wave	Absent
Tibial nerve			
Right lower limb	**Value**	**Left lower limb**	**Value**
Distal latency (ms)	Absent	Distal latency (ms)	Absent
Proximal latency (ms)	Absent	Proximal latency (ms)	Absent
CV (m/s)	Absent	CV (m/s)	Absent
F wave	Absent	F wave	Absent

Conclusion

Integrative diagnosis, which includes electrophysiological, radiological, and genetic screening, is of great value to exclude metabolic, nutritive-toxic, infectious, and inflammatory or autoimmunological causes and to reach the exact subtype of hereditary neuropathy. Nowadays, next-generation sequencing-based analysis is becoming a routine diagnostic tool for inherited neuropathy, but if this facility is not available, electrophysiological and radiological diagnoses are the best diagnostic tools to be used. Differentiation between hereditary neuropathy and diabetic neuropathy is essential for primary care physicians to have the right plan.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and

due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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