Research Article

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Nerve conduction study plays a key role in the correct diagnosis of HNPP

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Abstract

Objective: As nerve conduction study (NCS) is a commonly employed tool in the diagnosis of hereditary neuropathy with liability to pressure palsies (HNPP), we describe the electrophysiological features of our patients, comparing the findings with those of healthy subjects.

Methods: The charts of 19 HNPP patients were reviewed and NCS including residual latency (RL) and terminal latency index (TLI) were compared with the findings of 32 control subjects.

Results: Motor NCS revealed significant differences ($p<0.05$) in all variables except for the tibial distal latency, median compound muscle action potential amplitude, ulnar and peroneal TLI, and tibial RL in the patient cohort compared with healthy controls. Tibial TLI was bigger in the patient cohort ($p<0.05$). Nerve conduction velocity (NCV) slowing of the knee-ankle segments were more marked compared with the elbow-wrist segments ($p<0.05$). NCV of the ulnar nerve was significantly slower in the elbow segment, compared with the below elbow-wrist and axilla-above elbow segments ($p=0.000$). F-responses were prolonged in the lower extremities and RL prolongations were especially prominent in the median nerve ($p<0.05$). TLI values were smaller in the median nerve, compared with all other nerves ($p<0.05$). Sensory NCS were notably abnormal in the patient cohort compared with the healthy controls ($p<0.001$). However, the sural compound nerve action potential amplitude was markedly enlarged compared with the upper extremity nerves ($p<0.01$).

Conclusion: Correct interpretation of the NCS findings plays an essential role in the diagnosis and rational use of mutation analysis in suspected cases.

Keywords: Hereditary neuropathy with liability to pressure palsies, hereditary neuropathy, polyneuropathy, nerve conduction studies

INTRODUCTION

Hereditary neuropathy with liability to pressure palsies (HNPP) is an autosomal dominant demyelinating neuropathy, characterized by recurrent painless mononeuropathies at entrapment sites, following minor trauma or acute compression (1-5). While a heterozygous deletion is present at the chromosome site 17p11.2 encoding peripheral myelin protein (PMP22) gene in 85% of the affected individuals, a point mutation is responsible in approximately 15% (2, 3, 6-8). Nerve conduction studies demonstrate multifocal or segmental abnormalities at compression sites or distal segments of the peripheral nerves (1). In addition to electrodiagnostic investigation, histopathological and genetic tests that have an important place in diagnosis, sonographic and magnetic resonance imaging of compression sites may be of value as complementary diagnostic tools (2,5,7). The electrodiagnostic findings reveal a generalized slowing of the sensory nerve conduction velocities (NCV), reduction of the sensory nerve action potential amplitudes, prolongation of terminal latencies and focal slowing at multiple compression sites, while motor NCVs are mildly slowed (5, 7, 9, 10). Because the clinical picture and evolution of the disease is quite heterogeneous, atypical phenotypes including asymptomatic cases have been reported in the literature (1, 2, 7).

Although the diagnosis is important for prognosis and genetic counseling, it can remain elusive (1). Family history may not always be helpful due to the presence of sporadic cases. Affected individuals can be asymptomatic, without obvious neurological findings (1, 11). Additionally atypical forms may be encountered such as entrapment

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and acute or chronic demyelinating neuropathies (2). Electrodiagnostic studies are important in this setting, being readily available, to exclude other possible causes, as well as to identify the asymptomatic and atypical cases (1). However a certain degree of experience is required to interpret the nerve conduction findings. In this report we aimed to present our experience and describe the clinical and electrophysiological features of our patients, comparing their electrophysiological findings with those of healthy subjects.

METHODS

Patients and Controls

The charts of 19 HNPP (11 female, 8 male) patients, ranging from 16 to 58 years of age with a mean age of 36.5 years, evaluated at the EMG laboratory were retrieved and compared with the findings of 32 healthy control subjects (23 female, 9 male) ranging from 19-68 years of age with a mean age of 36.5 years. There was no statistically significant difference in terms of age (t=-0.009, p=0.993) and gender (chi-square=1.049, p=0.306) between the patient and control groups. Typical HNPP cases presented with acute compression neuropathies and brachial plexopathy. Chronic entrapment neuropathies in the form of carpal tunnel syndrome or ulnar neuropathy at the elbow, polyneuropathy either acute or chronic, fatigue, cramps, nonspecific symptoms such as pain and asymptomatic individuals were considered as atypical phenotypes. Other causes of peripheral neuropathy were ruled out by appropriate laboratory studies, including fasting blood glucose, blood urea nitrogen, creatinine levels, hepatic enzymes, fT3, fT4 and thyroid stimulating hormones, vitamin B12 and folate levels, urinalysis, serologic tests for HBV, HCV and brucella, erythrocyte sedimentation rate, anti SSA, SSB antinuclear (ANA), anti double stranded DNA, anti-neutrophil cytoplasmic (ANCA) antibodies and cerebro spinal fluid analysis in 1 patient. Local ethics committee approved the study. The diagnosis was confirmed with mutation analysis, except for 3 patients, who were demonstrated to have tomaculous neuropathy on sural nerve biopsy.

Electrophysiologic Investigations

Nerve conduction studies were performed utilizing a Neuropack ∑, MEB-5504K (Nihon-Kohden, Tokyo, Japan) EMG machine, employing standard techniques of surface stimulation and recording. Bipolar, felt-tip electrodes were employed for supramaximal stimulation with a pulse duration of 100 μs. Recordings were made with 7x4 mm disposable silver chloride electrodes. Ground electrode was placed on the same limb, usually between the stimulation and recording sites. Belly tendon recordings were obtained for motor nerve conduction studies with a sweep speed was 5 ms, sensitivity of 2 mV, and a bandpass filter of 20-10.000 Hz. Latencies were

Table 1. Clinical characteristics of the patient group

Age/Gender	Symptoms and Findings	Diagnosis	Treatment	Phenotype	Consanguity
19/F	Ulnar neuropathy at the elbow, Carpal tunnel syndrome	PMP22 deletion	Surgical	Atypical	None
21/M	Saturday night paralysis	Tomacula on NB	Conservative	Typical	None
16/M	Acute median and ulnar neuropathy at the wrist	PMP22 point mutation	Conservative	Typical	Mother
54/M	Ulnar neuropathy at the elbow	PMP22 deletion	Surgical	Atypical	Father and daughter
17/F	Paresthesias at the left hand	PMP22 deletion	Preventive measures	Atypical	Mother
37/F	Carpal tunnel syndrome	PMP22 deletion	Surgical	Atypical	None
18/M	Ulnar neuropathy at the elbow	PMP22 deletion	Surgical	Atypical	None
31/F	Ulnar neuropathy at the elbow	PMP22 deletion	Conservative	Atypical	None
58/F	Ulnar neuropathy at the elbow	PMP22 deletion	Conservative	Atypical	None
25/F	Diffuse pain	PMP22 deletion	Preventive measures	Atypical	None
19/M	Brachial plexopathy	PMP22 deletion	Conservative	Typical	None
36/F	Ulnar neuropathy at the elbow	PMP22 deletion	Surgical	Atypical	None
58/F	Ulnar neuropathy at the elbow	PMP22 deletion	Conservative	Atypical	None
57/F	Ulnar neuropathy at the elbow	PMP22 deletion	Conservative	Atypical	None
44/F	Carpal tunnel syndrome	PMP22 deletion	Release operation	Atypical	Daughter
45/M	Peroneal paralysis	PMP22 deletion	Conservative	Typical	None
36/M	Generalized paresthesias	Tomacula on NB	Preventive measures	Atypical	None
49/M	Carpal tunnel syndrome	Tomacula on NB	Surgical	Atypical	None
54/F	Asymptomatic	PMP22 deletion	Preventive measures	Atypical	None

F: female; M: male

Table 2. Comparison of nerve conduction studies between the patient cohort and healthy controls

Patient				Control			
	n	Mean±SD	Range	n	Mean±SD	Range	p
Motor Nerve Conduction Studies							
Terminal Latency (ms)							
Median	34	4.87±1.18	3.2-7.9	32	3.05±0.4	2.4-4.2	p=0.0001
Ulnar	32	3.17±0.74	2-5.2	32	2.61±0.34	2-3.3	p=0.0001
Peroneal	21	6.7±1.62	4.4-9.5	32	4.62±0.74	2.9-6.5	p=0.0001
Tibial	28	5.56±1.5	3.6-9.8	31	5.02±0.65	3.5-6.4	p=0.085
Nerve Conduction Velocity (m/s)							
Median	34	51.22±5.62	38.3-60.5	32	59.68±5.16	46.5-68	p=0.0001
Ulnar	32	55±8.69	39.3-82.6	32	63.44±6.67	51.3-79.1	p=0.0001
Peroneal	21	39.01±7.83	23-49.2	32	50.4±4.3	41.9-57.6	p=0.0001
Tibial	26	38.06±4.89	30.2-55.1	32	46.76±2.99	39.4-52.1	p=0.0001
F Latency (ms)							
Median	34	31.05±3.06	26-38.2	32	25.82±2.29	21.2-30.8	p=0.0001
Ulnar	31	32.27±4.44	24.1-41.6	32	25.71±2.33	21.6-31	p=0.0001
Peroneal	16	58.32±8.72	48.2-81	32	48.51±4.88	39.2-57.6	p=0.0001
Tibial	26	58.41±6.74	42.7-73.2	32	46.68±3.72	38-54.8	p=0.0001
CMAP Amplitude (mV)							
Median	34	11.81±5.03	2.5-21.7	32	13.83±3.89	5.8-22.2	p=0.073
Ulnar	32	12.32±4.34	11.7-20.6	32	14.68±2.55	8.4-22	p=0.011
Peroneal	21	3.99±2.95	0.2-9.3	32	9.96±4.67	4.5-29.6	p=0.0001
Tibial	28	8.74±5.02	1.5-21	32	18.79±9.3	3.6-41.6	p=0.0001
Residual Latency							
Median	34	3.88±1.12	2.3-6.9	32	2.21±0.35	1.6-3.1	p=0.0001
Ulnar	32	2.24±0.74	1-3.9	32	1.82±0.33	1.2-2.5	p=0.005
Peroneal	21	4.56±1.76	2-7.3	32	3±0.72	1.3-5	p=0.001
Tibial	26	2.88±1.64	0.9-6.8	31	2.87±0.68	1.5-4.4	p=0.973
Terminal Latency Index							
Median	34	0.21±0.04	0.1-0.3	32	0.28±0.03	0.2-0.3	p=0.0001
Ulnar	31	0.31±0.08	0.2-0.5	32	0.32±0.04	0.2-0.4	p=0.585
Peroneal	21	0.34±0.12	0.2-0.6	31	0.35±0.07	0.2-0.6	p=0.808
Tibial	26	0.52±0.13	0.3-0.8	31	0.44±0.ü7	0.3-0.6	p=0.008
Sensory Nerve Conduction Studies							
Nerve Conduction Velocity (m/s)							
Median	28	33.68±5.44	22.6-47.1	32	48.22±5.06	39.2-57.6	p=0.0001
Ulnar	22	32.1±3.78	24.9-37.9	32	45.83±4.17	37.5-54.3	p=0.0001
Sural	12	29.84±2.18	26.1-33.8	32	41.44±3.94	34.1-50	p=0.0001
CNAP Amplitude (μV)							
Median	28	9.91±3.77	4-20	32	23.39±8.56	10-39	p=0.0001
Ulnar	22	7.93±3.6	3.4-20	32	18.51.64±9.16	5.2-34	p=0.0001
Sural	12	8.05±2.27	4.8-12	32	23.11±8.84	9.6-46	p=0.0001

CMAP: compound muscle action potential; CNAP: compound nerve action potential; n: number, SD: standard deviation

measured from the first negative deflection. Terminal latency distances were 5 cm for the median and ulnar nerves, 8 cm for the peroneal nerve and 10 cm for the tibial nerve. Motor nerve conduction velocities of the wrist-elbow segment of the median and ulnar nerves, below-above elbow and elbow-axilla segments of the ulnar nerve, knee-ankle segments of the peroneal and tibial nerves were analyzed. Compound muscle action potential (CMAP) was measured from peak to peak. Conduction block was defined as a 50% or more reduction of the CMAP amplitude of the proximal stimulation point, compared to the distal stimulation point, which was required to have a CMAP amplitude of at least 1 mV. Temporal dispersion was defined as greater than 30% prolongation of the negative peak duration of the CMAP obtained at the proximal stimulation point, compared with the distal stimulation point. Minimum F-wave latencies were also obtained. Normal values of our laboratory were used to define nerve conduction abnormalities (12). Motor nerve conduction studies of the median, ulnar, peroneal and tibial nerves were performed and residual latency (RL) and terminal latency index (TLI) for each motor nerve were calculated. Sensory nerve conduction studies of the digit II-wrist segment of the median, digit V-wrist segment of the ulnar and sural-ankle segment of the sural nerves were obtained by a sweep speed of 1 ms, sensitivity of 10 µV, utilizing a bandpass filter of 20-2.000 Hz. While orthodromic technique was utilized for median and ulnar nerves, sural nerve conduction study was performed antidromically. Latency measurements were made to the negative peak of the compound nerve action potential (CNAP), while amplitudes were measured from peak to peak. The skin temperature was monitored. When it fell below 31°C, terminal latencies (TL) were corrected by subtracting from the measured latency 0.2 ms for each degree centigrade and nerve conduction velocities (NCV) were multiplied by constant values defined for each 0.5°C according to DeJesus formula (13). No corrections were made on F-wave latencies.

Statistical Analysis

To check the normality of distribution of the measured variables in patients and controls Kolmogorov-Smirnov test was performed. All tested variables distributed normally in the HNPP group. Parameters of the healthy controls also distributed normally, except for the ulnar terminal latency and TLI of the ulnar and tibial nerves. Therefore comparisons of the means were analyzed by the Student's t-test. Nerve conduction variables in the patient group were expressed by dividing measured variables by the upper or lower limits of our laboratory and calculating the percentages. Group differences of individual nerves were analyzed by the Kruskal-Wallis test. Post-hoc analyses were performed by the Mann-Whitney U test. The significance level was defined as $p<0.05$.

RESULTS

Clinical Findings

Family history was present 4 (21.1%) in the patient group, as 2 being mother and daughter and another 2 had first degree relatives with a history of acute compression neuropathies or chronic sensori-motor peripheral neuropathy of unidentified etiology. Fifteen patients carried deletion of the chromosome 17p22, while 1 patient was found to have a point mutation. Three patients displayed tomaculous changes in the sural nerve biopsy. Four (21%) patients presented with typical phenotypes in the form of acute compression neuropathies or brachial plexopathy, whereas the remaining majority had an atypical presentation including entrapment neuropathies, diffuse pain or paresthesias (Table 1). Treatment consisted of conservative rehabilitative measures or surgical exploration

Table 3. Motor nerve conduction abnormalities in the patient group

Nerve	Slow NCV outside entrapment sites	Slow NCV at entrapment sites	Prolonged terminal latency	Prolonged F-response
Median	23.5% (E-W)	-	88%	29.5%
Ulnar	25% (BE-W)	84% (Elbow)	28%	48.5%
	29.5% (Ax-AE)			
Peroneal	52.5% (K-A)	-	81%	69%
Tibial	69% (K-A)	-	35.5%	84.5%

A: ankle; Ax: axilla; AE: above elbow; BE: below elbow, K: knee, NCV: nerve conduction velocity; W: wrist

Table 4. Sensory nerve conduction abnormalities in the patient group

Nerve	Segment	Slow NCV	Reduced CNAP Amplitude	Absent CNAP	Normal
Median	Digit II-Wrist	85.5%	46.5%	17.5%	12%
Ulnar	Digit V-Wrist	95.5%	32%	35.5%	3%
Sural	Sura-Ankle	91.5%	8.5%	68.5%	2.5%

CNAP: compound nerve action potential; NCV: nerve conduction velocity

Table 5. Nerve conduction studies of the patient cohort expressed in percentages

Motor NCS	n	Mean±SD	Range
Terminal latency (Upper limit %) †			
Median	34	128.17±31.08*	84.2-207.9
Ulnar	32	96.02±22.34	60.61-157.58
Peroneal	21	134±32.46*	88-190
Tibial	28	92.74±24.61	60-163.33
NCV (Lower limit %) †			
Median	34	104.54±11.47	78.16-123.47
Ulnar (BE-W)	32	110.22±17.42	78.76-165.53
Ulnar (AE-BE)	31	81.71±23.87*	34.34-148.23
Ulnar (Ax-AE)	27	105.58±35.05	79.42-136.15
Peroneal	21	95.39±18.69*	56.23-120.29
Tibial	26	96.11±12.10*	76.26-139.14
CMAP amplitude (Lower limit %) †			
Median	34	295.18±125.83	62.5-542.5
Ulnar	32	176±62.02*	16.71-294.29
Peroneal	21	113.91±84.41*	5.14-264.29
Tibial	28	249.83±140.73*	42.86-600
F-response (Upper limit %) †			
Median	34	97.02±9.57	81.25-119.38
Ulnar	31	100.86±13.86	75.31-130
Peroneal	16	112.15±16.24*	92.69-155.77
Tibial	26	112.32±12.72*	82.12-140.77
Residual latency (Upper limit %) †			
Median	34	133.32±37.86*	77.32-235.74
Ulnar	32	90.45±29.42*	38.71-158.47
Peroneal	21	102.18±38.48*	44.39-164.35
Tibial	26	68.15±37.96	21.04-159.57
Terminal latency index (Lower limit %) †			
Median	34	95.64±17.57*	60-135.91
Ulnar	31	118.36±31.39*	64.62-201.15
Peroneal	21	162.84±57.58*	89.05-278.57
Tibial	26	172.37±43.92	97.37-251.61
Sensory NCS			
NCV (Lower limit %)			
Median	28	85.47±13.55	57.36-119.54
Ulnar	22	86.07±9.9	66.77-101.61
Sural	12	88.29±6.16	72.22-100
CNAP amplitude (Lower limit %) †			
Median	28	99.14±37.03*	40-200
Ulnar	22	113.31±50.22*	48.57-285.71
Sural	12	161±43.46	96-240

AE-BE: above elbow-below elbow; Ax-AE: axilla-above elbow; BE-W: below elbow-wrist; CMAP: compound muscle action potential; CNAP: compound nerve action potential; n: number, NCS: nerve conduction study; NCV: nerve conduction velocity
† indicates p<0.01 Kruskal-Wallis test
* indicates p<0.05 Mann-Whitney U test

and release in symptomatic patients, while asymptomatic individuals and patients with ill-defined symptoms received recommendations to prevent compression neuropathies.

Electrophysiological Findings

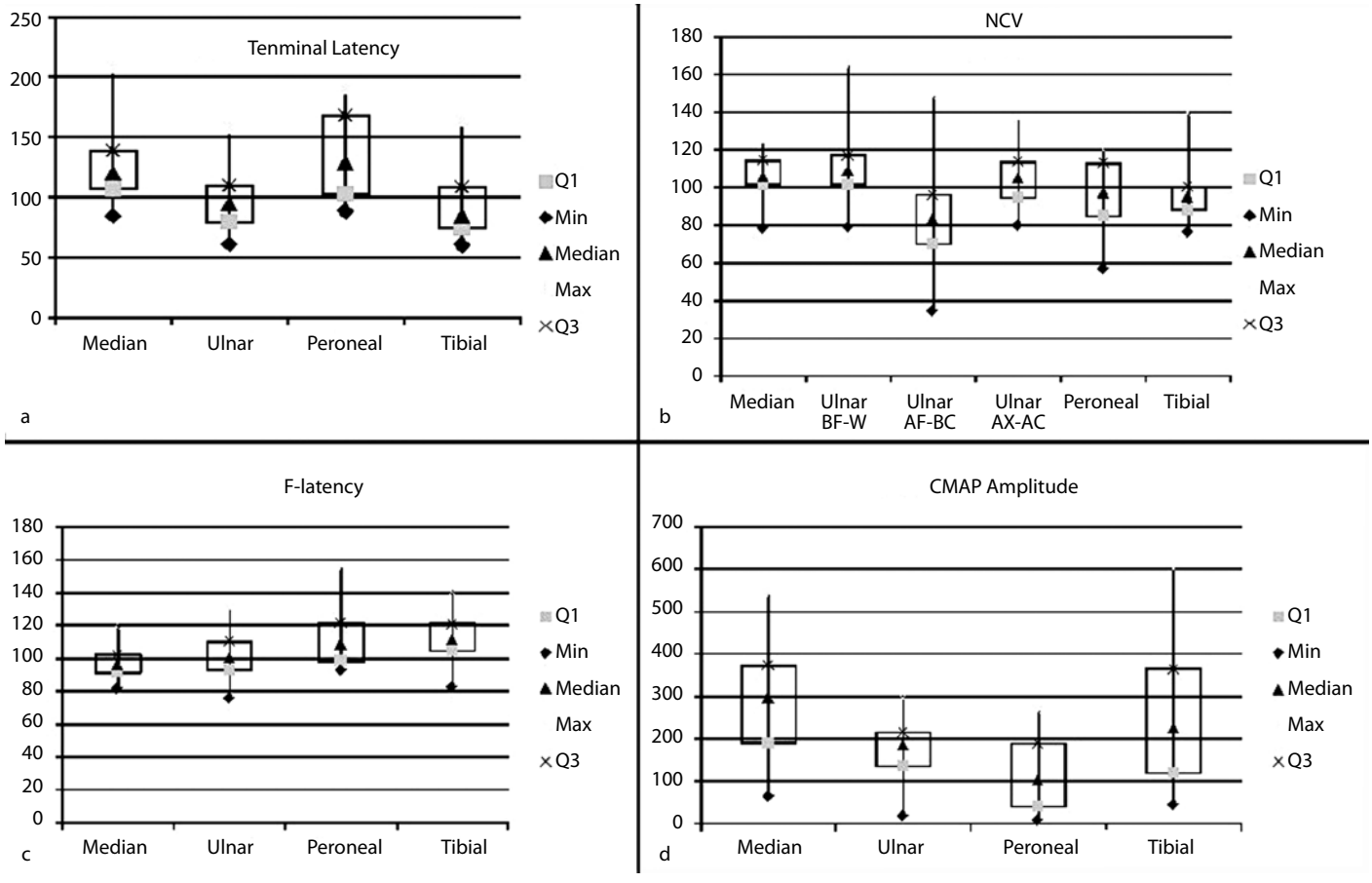
Motor nerve conduction studies revealed significant differences ($p<0.05$) in all variables except for the tibial distal latency ($t=1.772$, $p=0.085$), median CMAP amplitude ($t=-1.820$, $p=0.73$), ulnar ($t=-0.551$, $p=0.585$) and peroneal TLI ($t=-0.245$, $p=0.808$), and tibial RL ($t=0.034$, $p=0.973$) in the patient cohort compared with healthy controls. Tibial TLI value was actually higher in the patient cohort (Table 2). The details of motor NCV slowing in the patient cohort is demonstrated in Table 3. Prolongation of the terminal latencies were mainly observed in the median and peroneal nerves. The slowing of motor NCV, exceeding the lower limit of normal, was most prominent at the elbow segment of the ulnar nerve. NCV slowing and F-wave prolongation were more marked at the lower extremities (Table 3). Out of 31 elbow segments of the ulnar nerves tested, 2 right and 5 left sided conduction blocks (22.5%) was observed. Another patient displayed conduction block at the knee-ankle segment of the left peroneal nerve. One patient with conduction block at the right elbow segment of the ulnar nerve demonstrated conduction block at the knee-ankle segment of the right tibial nerve. Temporal dispersion was not observed.

Sensory nerve conductions in the patient cohort displayed significant abnormalities in all variables compared with the healthy controls ($p<0.001$, Table 2). Patients demonstrated absent sural CNAP in the 68.5% of the tested nerves. The details of the sensory nerve conduction abnormalities are presented in table 4.

Percentages of the nerve conduction variables according to the upper and lower limits are shown in Table 5 and Figure 1. All motor nerve variables demonstrated significant differences by the Kruskal-Wallis test among the nerves tested in the upper and lower extremities. Post hoc analyses were performed by the Mann-Whitney test. In terms of terminal latencies, median and peroneal nerves demonstrated more significant prolongations ($p<0.001$). NCV slowing of the knee-ankle seg-

Figure 1. a-d. Box plot graphics of the most relevant findings in nerve conduction variables expressed as percentages of the upper or lower limits of normal and shown in Table 5. Terminal latency prolongations are most marked in the median and peroneal nerves (a), NCV slowing is prominent at the compression sites and knee-ankle segments of the lower extremity nerves (b), prominent F-wave prolongations are observed in the lower extremity nerves (c), peroneal CMAP amplitude is unproportionally reduced compared to other motor nerves (d)

AE: above elbow; Ax: axilla; BE: below elbow; CMAP: compound muscle action potential; Q1 and Q3: first and third quartiles; Min and Max: minimum and maximum values; W: wrist



ments were more prominent compared with the elbow-wrist segments of the upper extremity nerves ($p<0.05$). NCV of the ulnar nerve was significantly slower at the elbow segment, compared with the below elbow-wrist and axilla-above elbow segments ($p=0.0001$). On the other hand, there was no significant difference in the degree of slowing between the below elbow-wrist and axilla-above elbow segments ($p=0.447$). F-responses were prolonged in the lower extremities ($p<0.05$). Residual latency prolongations were especially prominent in the median nerve compared to all other nerves ($p<0.05$), while the residual latencies of all other nerves were prolonged compared to the tibial residual latency ($p<0.01$). Similarly, terminal latency index values were smaller in the median nerve compared with all other nerves ($p<0.05$), while the ulnar and peroneal nerve values were smaller in comparison with the tibial nerve terminal latency index ($p<0.005$). Peroneal CMAP amplitude was markedly reduced, compared with the CMAP amplitudes of all other nerves ($p<0.05$). NCV of the sensory nerves did not show a significant difference ($p=0.72$). However, the sural nerve CNAP amplitude was markedly bigger compared with the upper extremity nerves ($p<0.01$).

DISCUSSION

Clinically atypical phenotypes were found to be more common and the family history was not conspicuous in our cohort. Luigetti et al. reported typical presentation in 44% of the cases, the most common phenotype being peroneal neuropathy at the level of the fibular head (2). Out of 36 of their atypical patients 18 (50%) had either chronic ulnar neuropathy at the level of the elbow, or carpal tunnel syndrome. Similarly 11 (58%) of our 19 patients had either ulnar neuropathy at the elbow or carpal tunnel syndrome or both reflecting the common occurrence of chronic compression neuropathies in HNPP, necessitating surgery as a therapeutic measure. However this issue remains controversial, as controlled studies concerning surgical decompression have not yet been conducted and some do not recommend surgery in HNPP at all (14). Other atypical cases present with chronic sensory neuropathy, fatigue and cramps, Charcot-Marie-Tooth like phenotype and acute onset of weakness resembling Guillain-Barré syndrome (2). Facial and trigeminal neuropathies have also been reported (11). Non-specific pain and paresthesias were the presenting symptoms in 3 (16%) of our cases. Asymptomatic cases are also encountered, during an electrodiagnostic investigation performed for other reasons. In Luigetti et al. cohort of 73 cases, 32 (44%) had a family history (2). The incidence of sporadic cases is reported to be highly variable, ranging from 20 to 78% of the cases, explained by asymptomatic carriers and de novo mutations (1, 11). The frequent occurrence of atypical patients without a family history often creates a diagnostic dilemma and a need to resort to electrophysiologic methods. Additionally typical cases of acute compression neuropathies may present diagnostic challenge.

In motor nerve conduction studies a prominent prolongation of the terminal latencies of the median and peroneal nerves were noted as previously demonstrated (15). Interestingly, tibial terminal and residual latencies did not show a difference compared to controls. Moreover the tibial nerve terminal latency index was actually higher than the control population. Ulnar nerve terminal latency was also less involved. These findings obviously cannot be explained on the basis of a length dependent neuropathy or a distal myelinopathy. The most likely explanation is the susceptibility to compression of these individual nerves at the level of the wrist and ankle as suggested by Li et al. (15). Although RL and TLI measurements are convincingly abnormal in the median nerve, they do not have an overall diagnostic contribution, probably because slow NCVs influence calculations especially in lower extremity nerves. Motor NCVs show non-homogenous slowing more prominent at the knee-ankle segments of the lower extremity nerves. However NCV slowing was markedly present at the elbow segment of the ulnar nerve as previously demonstrated, being present in the 84% of the segments tested (1, 11). This finding has also been reported in the fibular head segment of the peroneal nerve, but this segment was not checked routinely by us, one of the drawbacks of our study (1, 2). Slow motor NCV markedly present in the lower extremities had not been previously reported. In fact Infante et al. stated that the motor nerve conduction velocities were normal in more than 50% of the cases (11). F-wave prolongation was also more marked at the lower extremities. In Infante's series peroneal F-wave prolongations were also more common compared to those of the upper extremity nerves, which was always in association with increased distal motor latency and motor nerve conduction slowing. This could explain the notable minimal F-wave abnormalities in the lower extremities in our series, due to the prominent motor nerve conduction slowing in peroneal and tibial nerves. Conduction block was almost non-existent except for the elbow segment of the ulnar nerve, which is a common entrapment site. This finding was also observed in other studies (15). It should be noted that temporal dispersion was never observed, unlike acquired demyelinating neuropathies.

Sensory nerve conduction velocities were markedly slow and CNAP amplitudes low both in the upper and lower extremities, as previously demonstrated (1, 15). However sensory nerve conduction velocity slowing calculated as the percentages of the lower limit of normal was uniform compared to previous studies (1). Absent sural CNAP was a notable finding in our study as previously reported by Li et al. (15). CNAP amplitudes calculated as the percentages of the lower limit of normal showed marked reductions in the median and ulnar nerves, whereas the sural nerve amplitudes did not show a comparable reduction, which does not support the presence of a length dependent neuropathy.

In conclusion HNPP patients display marked prolongation of the median and peroneal terminal latencies, as well as peroneal and tibial minimal F-wave latencies. Motor NCV slowing

is prominent at compression sites and lower extremity nerves. Peroneal CMAP amplitude is reduced out of proportion in comparison to other motor nerves. Conduction block is usually observed at sites of compression and hardly present outside these segments. Temporal dispersion is never seen. On the other hand sensory NCV demonstrate diffuse slowing. This combination of findings seems to have a greater diagnostic contribution rather than individual abnormalities of nerve conduction. Previous studies demonstrated that no significant difference exists in terms of nerve conduction studies between typical and asymptomatic cases (11). Therefore, typical nerve conduction studies as described above may guide the clinician to order mutation analysis when confronted with atypical cases.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Ankara Numune Training and Research Hospital (335/2014).

Informed Consent: Due to the retrospective chart review of the study, informed consent was not taken.

Peer-review: Externally peer-reviewed.

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