ORIGINAL RESEARCH

Ulnar Neuropathy at Elbow in Patients With Type 2 Diabetes Mellitus

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Purpose: In diabetes mellitus (DM), upper extremity entrapment neuropathies are suggested to be a component of polyneuropathy (PNP). Our aim is to examine the presence of ulnar neuropathy at the elbow (UNE) and its relation to other findings including PNP in symptomatic and asymptomatic type-2 DM patients who were admitted for routine examinations.

Methods: The study included all cases referred for electromyography because of type-2 DM between November 2017 and May 2018. Demographic and clinical characteristics were recorded. Routine electromyography examinations in all cases included the following: bilateral motor conduction of the median, ulnar, peroneal, and tibial nerves and sensory conduction of the median, ulnar, and sural nerves. For ulnar nerve examination, stimuli were given at the wrist, below the elbow, and above the elbow. Electrophysiological findings were evaluated according to the American Association of Neuromuscular and Electrodiagnostic Medicine criteria.

Results: Eighty-two patients with type-2 DM and 144 upper extremities were included in the study. Of the 82 patients who participated in the study, 3 had findings suggesting ulnar neuropathy, and electrophysiology confirmed UNE in only one. Electrophysiological studies showed UNE in 36 patients. Other diagnoses identified by electrophysiology were carpal tunnel syndrome and PNP. Ulnar neuropathy at the elbow was more commonly associated with PNP compared with carpal tunnel syndrome. Gender and PNP were independent risk factors for the development of UNE.

Conclusions: Although the majority of diabetic patients were asymptomatic for the UNE, approximately one third of all patients with DM were found to have UNE. Ulnar neuropathy at the elbow is closely related with PNP.

Key Words: Type-2 diabetes mellitus, Polyneuropathy, Ulnar neuropathy at the elbow.

(J Clin Neurophysiol 2020;37: 220–224)

The most common neurologic complications in diabetes mellitus (DM) are focal neuropathies and length-dependent symmetrical sensorimotor polyneuropathy.[1,2] Entrapment neuropathies, particularly in the upper extremities (UE), are frequently seen in any stage of diabetes[3,4] and may be one of the early neurophysiological markers of the peripheral nerve involvement in diabetes. Because of the metabolic changes and abnormal glucose metabolism, even in the preclinical period, functional impairment and structural changes in the peripheral nerves are seen. Because of the anatomic considerations, some peripheral nerves are more vulnerable to peripheral nerve entrapments.[1] In entrapment neuropathies, a progressive and slow onset is seen if no measures are taken.[5]

The most common entrapment neuropathies in patients with DM are carpal tunnel syndrome (CTS) (30%) and ulnar neuropathy at the elbow (UNE) (2.1%).[5] In the presence of diabetic polyneuropathy (PNP), UNE may be difficult to diagnose just by using reduction in motor conduction in the elbow segment because the motor conduction velocity may be reduced throughout the whole ulnar nerve. Furthermore, especially in patients with DM-PNP who do not have symptoms and signs of ulnar neuropathy, ulnar nerve conduction may be abnormally slowed in the elbow segment.[6]

In this study, we aimed to investigate the presence of UNE in all patients with DM who were admitted to our electromyography (EMG) laboratory for routine examinations and to determine the ratio of asymptomatic patients who were shown to have UNE by electrophysiology.

PATIENTS AND METHOD

Patients

The study included all consecutive patients who were admitted to our electrophysiology laboratory between November 2017 and May 2018 for a routine electrophysiological evaluation in the course of type-2 DM. Patients with type-I DM, connective tissue disorders, trauma of UE, untreated hypothyroidism, cervical radiculopathy, brachial plexopathy, and any surgery related to UEs or with electrophysiological findings indicating Martin-Gruber anastomosis were excluded.

The study was approved by the institutional review board of Cerrahpasa School of Medicine, and all participants gave informed consent.

METHODS

Clinical Assessments

A neurologist (F.C., A.G., F.U.) examined each patient using the same assessment sheets, with regard to the age, sex, disease duration, presence and, if present, characteristics, localization, and triggering factors of the sensory symptoms, weakness and pain, and medications. A detailed neurologic examination was done including fine touch, vibration and position sense, strength of intrinsic hand and foot muscles, and

The authors have no funding or conflicts of interest to disclose.

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ISSN: 0736-0258/19/3703-0220
DOI 10.1097/WNP.0000000000000629

deep tendon reflexes. The presence of other complications related to DM was also noted.

Electrophysiological Assessments

Nerve conduction studies were performed using Ag-AgCl surface EMG recording electrodes (Neuropack Σ-MEB-5504K; Nihon Kohden Corporation, Tokyo, Japan) according to standard techniques.[7]

In all cases, routine EMG examination included the following measurements: motor conduction of the median, ulnar, peroneal, and tibial nerves and sensory conduction of the median, ulnar, and sural nerves. Motor and sensory nerve conduction studies were performed bilaterally as previously described.[7] To evaluate motor responses of ulnar nerve, ulnar nerve was evaluated while the patient's palm was facing up and elbow was flexed in 90°. Ulnar nerve was stimulated at three points: at the wrist, 3 cm distal to the medial epicondyle, and 7 cm proximal to the medial epicondyle. The compound muscle action potentials (CMAP) on the abductor digiti minimi muscle were recorded using surface electrodes. The latency was measured at the beginning of the CMAP, and amplitude was measured from the baseline to the negative peak. For sensory response of ulnar nerve, a ring electrode was placed on the fifth finger, and ulnar nerve was stimulated at wrist. The temperature of the skin in the extremities was maintained at about 32 to 34°C.

In case of clinical necessity, inching examination (2-cm intervals; beginning at 4 cm distal of medial epicondyle till 3 cm proximal of medial epicondyle, a total of 8 measurements) was performed. We performed needle EMG of deltoid, biceps brachii, triceps brachii, extensor digitorum, first dorsal interosseous muscle, and flexor carpi ulnaris muscles to exclude the involvement of other parts of the peripheral nervous system and to contribute the lesion localization and the prognosis of ulnar nerve involvement. The electrophysiological findings were evaluated according to the criteria of the American Association of Neuromuscular and Electrodiagnostic Medicine.[8,9]

We made the diagnosis of CTS if the latency of sensory response of median nerve recorded on the second finger was prolonged compared with that of ulnar nerve recorded on fifth finger. If the latency of sensory response was normal, we continued with the recording of median and ulnar nerve sensory responses on forth finger. In the case of median nerve sensory latency being ≥ 0.5 milliseconds longer than the ulnar nerve latency, we made the diagnosis of CTS. The criteria for the diagnosis of axonal neuropathy included the decrease in the amplitudes of CMAP or sensory nerve action potentials (SNAP) below a 50% of the lower normal value with normal or near-normal conduction velocities and distal latencies. For demyelinating neuropathy, conduction velocities were slower more than 75% and distal latencies were longer than 125% of the normal values of the laboratory without a severe reduction in amplitudes.

Statistical Analysis

We first determined mean age, gender distribution, disease duration, other microvascular complications (retinopathy or nephropathy), and electrophysiological diagnosis (UNE, CTS, and PNP) in the whole group. In the second step, we performed a statistical analysis between patients with and without UNE comparing mean age, gender distribution, disease duration, other microvascular complications, and other electrophysiological diagnosis (CTS and PNP). We also performed a regression test to identify independent risk factors of UNE in our patient population. The entered variables were gender, other microvascular complications, presence of CTS, and presence of PNP. Finally, we conducted an analysis to compare the clinical and electrophysiological features between patients having UNE with or without PNP.

Analysis was performed with SPSS software version 20.0 (SPSS Inc, Chicago, IL). The χ^2 test and *t*-test were used for independent groups, or Mann–Whitney *U* test was used to compare demographic data, diagnostic criteria, and electrophysiological parameters. Fisher exact test was used to compare the demographic data and diagnostic criteria when the number of cells with an expected frequency of less than 5 was 25% or more. For risk analysis, we used logistic regression test. The significance level was set at 0.05.

RESULTS

Among the total number of 2,400 patients who were examined in the study period for peripheral nervous system disorders and analysis of movement disorders in our laboratory, there were 182 patients with DM. Among them, 82 patients with type-2 DM were included in the study and 144 UE were studied. We excluded patients with type-1 DM ($n = 76$) and those who had comorbidity, that is, electrophysiological findings indicating radiculopathy ($n = 11$), history of fracture in the UE ($n = 4$), Martin-Gruber anastomosis ($n = 2$), chronic inflammatory polyradiculoneuropathy ($n = 2$), multiple sclerosis ($n = 1$), arthritis or rheumatological disorder ($n = 1$), motor neuron disorder ($n = 1$), Fabry disease ($n = 1$), surgery for sarcoma in the UE, and use of chemotherapeutics ($n = 1$). The major referral complaints of the patients included were burning, tingling, and numbness of the feet in 49 patients (59.8%). Other patients described numbness of hands ($n = 24$, 29.3%), imbalance ($n = 1$, 1.2%), and symptoms suggestive of restless legs syndrome ($n = 1$, 1.2%). Three patients had symptoms suggestive of UNE. Four patients did not have any symptoms and were only referred for a routine examination.

The mean age was 60.7 ± 8.9 years (range, 43–80 years), and there were 52 women. The mean duration of DM was 12 ± 8 years (range, 0.5–30 years). Twenty-six patients were using insulin with oral antidiabetics, whereas others used oral antidiabetic drugs. Table 1 demonstrates demographic and clinical findings.

Only three patients had complaints suggestive of UNE. A total of 25 patients had numbness of unilateral or bilateral hands that suggested CTS, whereas 55 patients had symptoms such as distal paresthesia and/or weakness suggestive of polyneuropathy. Among those, eight had symptoms suggestive of both PNP and CTS.

Of the 82 patients and 144 UE studied, UNE was identified in 36 patients (43.9%) and in 48 UE (33.3%), respectively. However, only one of these cases had symptoms that could have suggested UNE. Ulnar neuropathy at the elbow was bilateral in 12 cases (33.3%). Two more patients had findings suggesting

TABLE 1. Demographic and Clinical Findings in the Whole Group, in the Group With UNE, and in the Group Without UNE

	Whole Group $n = 82$	UNE+ $n = 36$	UNE− $n = 46$	P*
Gender (M/F), n	52/30	22/14	8/38	0.000
Age (year), mean ± SD	60.7 ± 8.9	61.5 ± 9.3	60.1 ± 8.5	0.476
DM duration (year), mean ± SD	12.0 ± 8.0	13.1 ± 7.6	11.0 ± 8.6	0.254
PNP presence, *n* (%)	22 (26.8)	18 (50)	4 (8.7)	0.000
CTS presence, *n* (%)	43 (52.4)	15 (41.7)	28 (60.9)	0.084
PNP duration, (months), mean ± SD	23.5 ± 25.2	28.3 ± 31.9	19.5 ± 17.5	0.198
CTS duration, (months), mean ± SD	16.4 ± 20.9	19.2 ± 26.2	14.9 ± 18.2	0.629
UNE duration, (months), mean ± SD†	0.4 ± 0.5	0.5	—	NA
Retinopathy and/or nephropathy, *n* (%)	10 (12.2)	4 (11.1)	6 (13.0)	0.534
Diabetic foot, *n* (%)	4 (4.9)	4 (11.1)	0	0.059

*Comparisons between patients with and without UNE.
†Only three patients.
M, male; F, female; UNE, ulnar neuropathy at the elbow; CTS, carpal tunnel syndrome; PNP, polyneuropathy.

ulnar neuropathy with no electrophysiological findings confirming UNE. Eighteen patients (22.5%) had other microvascular complications (retinopathy or nephropathy). Other diagnoses identified by the electrophysiology were CTS ($n = 43$, 52.4%) and PNP ($n = 22$, 26.8%). Figure 1A shows graphical representation of all electrophysiological diagnoses in the group.

The mean age and disease duration of groups with and without UNE were similar. The number of male patients was significantly higher in those with UNE ($P = 0.000$) or PNP ($P = 0.011$), whereas the number of women was higher in CTS group ($P = 0.002$, Fig. 1B). When we dichotomized the group of UNE into unilateral or bilateral involvement, the mean age and disease duration of groups were still similar. Other microvascular complications were also similar between patients with or without UNE (Table 1) or between patients with unilateral or bilateral UNE.

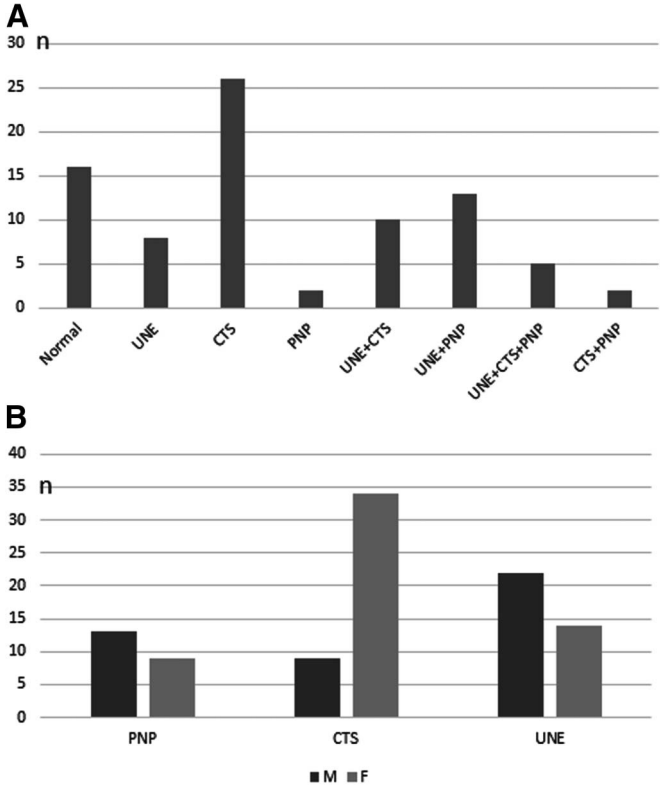

FIG. 1. Graphical representation of all electrophysiological diagnoses (**A**). Graphical representation of gender distribution according to electrophysiological diagnosis (**B**).

The number of UNE cases with demyelinating features were more common than cases with pure axon loss. However, axon loss accompanied demyelination in more than half of the cases with UNE. Reduction in SNAP amplitude was more common than that in CMAP amplitude. The needle EMG showed motor unit potentials suggestive of chronic neurogenic involvement. Figure 2 shows recordings of a normal motor response of ulnar nerve and a conduction block at the level of elbow.

Ulnar neuropathy at the elbow was found to be more frequent in patients with PNP ($P = 0.000$), whereas CTS was more common among DM patients without PNP ($P = 0.002$). Logistic regression test showed that PNP and gender were independently related to the presence of UNE ($P = 0.002$ and $P = 0.001$, respectively). In all cases with severe PNP, severe reduction in conduction velocity at the elbow was determined (Table 2). Patients with PNP had reduction in SNAP or CMAP amplitude more commonly compared with those without PNP.

DISCUSSION

The most important findings of our study are as follows: (1) the prevalence of UNE, determined by electrophysiology among DM patients who were admitted to our laboratory, was high (43.9%), (2) although UNE was the second most common entrapment neuropathy in DM, it was more closely related to PNP compared with CTS, (3) the electrophysiological findings of UNE was more severe in the presence of PNP, and (4) gender and presence of PNP were independent risk factors for the development of UNE.

In routine EMG examinations in diabetic patients, we often encounter electrophysiological findings suggesting asymptomatic ulnar neuropathy or CTS despite the absence of PNP findings.

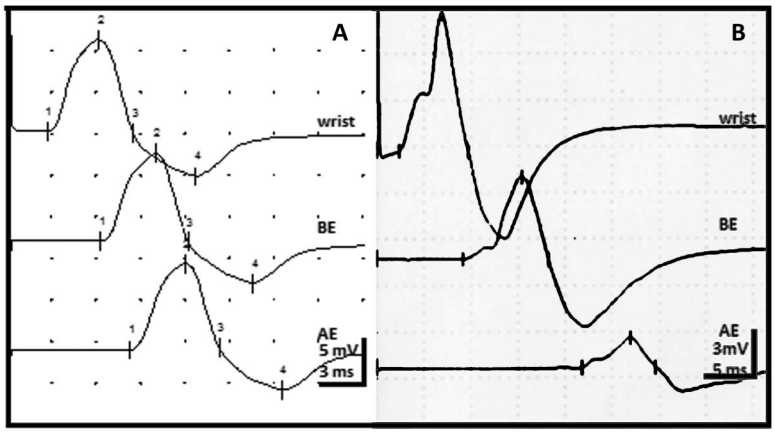

FIG. 2. **A**, A representative recording of normal motor response of left ulnar nerve (65-year-old woman with one-year history of DM). **B**, A representative recording of conduction block left ulnar nerve (62-year-old man with 10-year history of DM and PNP). BE, below elbow; above elbow; DM, diabetes mellitus; PNP, polyneuropathy.

However, subclinical ulnar neuropathy or CTS are difficult to diagnose in patients with diabetic PNP. Although ulnar neuropathy is the second most common entrapment neuropathy in patients with diabetes,[5] no specific electrophysiological criterion has yet been described to identify focal lesions of the ulnar nerve in DM or in patients with diabetic polyneuropathy. For this reason, to predict the UNE diagnosis best, we used the American Association of Neuromuscular and Electrodiagnostic Medicine guidelines.[8,9] Conduction block or changes in the waveform and amplitude of SNAPs can be used as the important indicators of UNE.[9] Although the predictive value of the reduction in the amplitude of the ulnar SNAP was reported to be the best in patients with idiopathic UNE,[10] its predictive value is reduced in the presence of PNP. However, abnormalities in sensory conduction precede significant changes in motor conduction in patients with diabetic PNP.[11] We had patients with reduced sensory amplitudes who did not have changes in motor conduction and whom we did not classified as UNE. Therefore, we may have probably missed some cases with UNE in the early stages in our study. We did not include patients with pure reduced ulnar nerve SNAP amplitude in the UNE group because we did not measure the sensory conduction velocity across the elbow, which is a limitation of our study. Without measurement of conduction velocity, reduction in SNAP amplitude cannot be localized to the elbow. Therefore, measurement of ulnar nerve sensory conduction velocity should be performed in all patients with DM.

The exact prevalence of any form of PNP in diabetic patients is not known exactly. It was estimated to be between 5% and 66%.[12,13] The prevalence of diabetic PNP and UNE in our cohort were 2.4% and 1.5%, respectively. However, the prevalence of UNE among patients with DM is quite high. In our study, the prevalence of UNE was higher in the diabetic PNP group than in the non-PNP group. Although the risk of UNE increases with longer disease duration,[1] it is not always a late complication of diabetes, and it is frequently an early finding.

In the majority of patients with idiopathic UNE, the initial symptoms are usually numbness and tingling, which are in the ulnar nerve distribution and intermittent, are often associated with elbow flexion, and become more evident at night. The severity of pain and paresthesia varies, and sensory loss is not disturbing in some patients. Interestingly, in our cohort of patients with DM, only one patient with UNE had relevant symptoms. Other studies also reported patients with UNE having no symptoms suggestive of it.[6,14] In the study of Rota et al.,[14] subclinical UNE was also detected in a very high percentage of DM patients, suggesting that the ulnar nerve is very susceptible to focal entrapment in DM as the median nerve. Pain in CTS, which appears in the course of DM, is usually a prominent feature, but pain is less pronounced in UNE in patients with DM and, frequently, there is no pain.[6,14] Motor weakness may not be noticed for months or years.[8] Additionally, in a previously published study on severe ulnar neuropathy in patients with DM, it was reported that motor deficit was more than sensory

TABLE 2. Electrophysiological Findings in Elbows With UNE in Patients With or Without PNP

	Patients With PNP ($n = 41$ UE)	Patients Without PNP ($n = 103$ UE)	*P*
Patients with UNE, *n* (%)	28 (68.3%)	22 (21.4%)	0.000
Patients with CTS, *n* (%)	12 (29.3)	62 (60.2)	0.002
Patients with reduction in MCV at elbow, *n* (%)	37 (90.2)	1 (9.7)	0.000
Patients with MCV <35 m/s at elbow, *n* (%)	11 (26.8)	0	0.000
Patients with conduction block at elbow, *n* (%)	9 (21.9)	6 (5.8)	0.007
Patients with reduction in CMAP amplitude, *n* (%)	6 (14.6)	4 (3.9)	0.032
Patients with reduction in SNAP amplitude, *n* (%)	23 (56.1)	9 (8.7)	0.000

CMAP, compound muscle action potential; CTS, carpal tunnel syndrome; MCV, motor conduction velocity; PNP, polyneuropathy; SNAP, sensory nerve action potential; UE, upper extremity; UNE, ulnar neuropathy at elbow.

involvement,[15] which may be associated with increased sensory threshold in diabetic patients with PNP.[16] As a matter of fact, motor symptoms and signs such as weakness or atrophy of the intrinsic hand muscles, without sensory symptoms, may go unnoticed in DM. Therefore, it is important to recognize UNE in DM and to avoid the risk factors such as external compression or continuous elbow flexion. However, we should emphasize that the study of Mondelli et al.[4] reported sensory loss in all cases with UNE in DM and no case with motor deficit alone. But the study design was quite different. They retrospectively analyzed the ratio of patients with DM among cases of UNE diagnosed in an electrophysiology laboratory. When they compared the frequency of elbow pain between UNE in DM and idiopathic UNE or posttraumatic UNE, the elbow pain was significantly uncommon in patients with DM.

Similar to what was previously reported in idiopathic UNE,[17] cases with demyelinating lesion was more common in our cohort. Although one previous study reported that axonal damage was more common in UNE of patients with DM,[15] a consecutive study[4] showed that the percentage of axonal forms in UNE of DM was similar to those found in UNE related to the other etiologies and suggested that it was related to the severity of UNE. Our study also supported the idea that axonal form would be related to the severe involvement of the nerve.

There are certain limitations to the study. This was a hospital-based study, and the included patients were limited with the patients referred for the examination. Therefore, we should keep in mind, the number of UNE cases may not correctly reflect the actual number in the population with DM. Despite the bias in the prevalence, it is clear that DM selectively affects both sensory and motor fibers of ulnar nerve at the elbow and causes insidious motor findings. In our opinion, DM makes the ulnar nerve more vulnerable to the daily movements of the elbow joint. Patients with DM may be warned about the habits that may increase the tension in the canal. Because of the high number of PNP and sensory deficit in those cases, the patients are not aware of the sensory symptoms.

In conclusion, our findings suggest that UNE is common in patients with DM, even if they report no symptoms suggestive of UNE. Thus, all patients should be referred for regular examinations, and electrophysiological examination should involve motor and sensory nerve conduction studies across elbow.

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