Mononeuropathy in Diabetes Mellitus

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SUMMARY

Fifty-one diabetic patients with mononeuropathy were studied to examine possible etiological factors, to determine the relationship with other diabetic complications, and to correlate with the presence and severity of background peripheral and autonomic neuropathy. The median, ulnar, and lateral popliteal nerves were most commonly affected and cranial neuropathy was relatively uncommon. When bilateral involvement of the same nerve was excluded, multiple mononeuropathies were found in only five patients. Median and ulnar mononeuropathy were gradual in onset and affected the dominant limb whereas other types of mononeuropathies were acute in onset with no predilection for either side. No consistent relationship was shown between the onset of mononeuropathy and age, sex, diabetic treatment, duration of diabetes, diabetic control, or other diabetic complications. In particular, there was no significant background peripheral and autonomic neuropathy, as assessed clinically and by objective tests, in almost one-half of the patients studied. It is concluded that diabetic mononeuropathy may occur independently of peripheral and autonomic neuropathy. It is possible, however, that a minimal degree of background damage, known to be present in all diabetic patients, may render them more susceptible than the general population to the various factors causing mononeuropathy. DIABETES 28:96–101, February 1979.

The most common clinical manifestation of the complications of diabetes mellitus is symmetrical peripheral neuropathy.[1] Isolated involvement of individual peripheral or cranial nerves is found less often and has attracted only little attention. The present study reports the clinical features, particularly the mode of onset, distribution, and relationship to other complications, of 51 patients with confirmed diabetic mononeuropathy. We have also attempted to correlate diabetic mononeuropathy with the presence and severity of background peripheral and autonomic neuropathy.

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PATIENTS

Over a 3-yr period in a large diabetes clinic, 59 patients volunteered symptoms suggestive of mononeuropathy involving one or more peripheral or cranial nerves. No attempt was made to actively screen the clinic population. Eight patients were excluded when objective clinical and electrophysiologic testing failed to confirm the diagnosis, leaving a total of 51 patients. The relative frequency of each mononeuropathy is shown in Table 1, together with details of mode of onset, duration of symptoms, sex, age, and treatment of diabetes. The mode of onset was arbitrarily defined as either acute when the symptoms were of sudden onset and present for only 1–3 wk before presentation, or gradual when symptoms had progressed slowly over 3–48 months. Table 2 shows details of duration of diabetes, degree of diabetic control, and the prevalence of other diabetic complications for each type of mononeuropathy. Diabetic control was assessed by the mean plasma glucose concentration obtained 2–3 h postprandially at each clinic attendance over the previous 3 yr, apart from more recently diagnosed patients. A mean plasma glucose of less than 150 mg/100 ml was arbitrarily defined as good, 150–200 mg/100 ml as fair, and greater than 200 mg/100 ml as poor control. The patients were examined for specific microvascular disease, namely diabetic retinopathy (either "background" with microaneurysms and occasional dot hemorrhages and exudates or "more severe changes" with marked exudates, new vessel formation, or venous changes) and nephropathy (as detected by persistent proteinuria of at least 60 mg/100 ml) and also for nonspecific atherosclerosis (symptoms or signs of ischemic heart disease or peripheral vascular disease).

METHODS

Mononeuropathy assessment. The diagnosis of mononeuropathy was made on clinical grounds and confirmed

TABLE 1
Relative frequency of each type of mononeuropathy with details of mode of onset, duration of symptoms, sex, age, and type of diabetic treatment

Type of mononeuropathy	Number of patients	Mode of onset		Duration of symptoms (range)	Sex		Age (yr) mean ± SD (range)	Treatment		
		Acute	Gradual		Male	Female		D	O	I
Median nerve	15	0	15	3–48 months	2	13	52.7 ± 9.7 (35–64)	0	6	9
Ulnar nerve	15	0	15	3–24 months	10	5	54.6 ± 8.4 (40–68)	0	5	10
Lateral popliteal nerve	8	8	0	2–3 wk	4	4	60.6 ± 11.5 (40–73)	1	4	3
Sciatic nerve	3	3	0	1–2 wk	2	1	65.0 ± 7.8 (56–70)	0	1	2
Femoral nerve	3	3	0	2–3 wk	2	1	46.3 ± 11.7 (33–55)	0	0	3
Oculomotor and abducens nerves	4	4	0	1–2 wk	2	2	49.5 ± 20.8 (21 ± 69)	1	0	3
Facial nerve	3	3	0	1–2 wk	2	1	59.0 ± 16.7 (44–77)	1	2	0

D, diet alone; O, oral hypoglycemic agent; I, insulin.

where possible by electrophysiologic testing. All measurements were made by the same investigator in the same environment, with skin temperature maintained at or above 30°C. Surface electrodes were used to stimulate the nerve with 1-cm silver discs placed 5 cm apart. Standard DISA surface recording electrodes and a DISA two-channel electromyograph were used in all studies. Median neuropathy (carpal tunnel syndrome) was considered to be present if terminal latency (TL) from the point of stimulation proximal to the transverse carpal ligament to abductor pollicis brevis muscle was prolonged. In patients with ulnar neuropathy, motor conduction velocity (MCV) was measured in the forearm, transsulcal, and upper arm segments of the nerve to detect possible entrapment at the elbow. Lateral popliteal nerve MCV was measured by stimulating the nerve at the ankle and proximal to the head of the fibula, recording over the extensor digitorum brevis muscle. In patients clinically considered to have femoral neuropathy, femoral nerve conduction velocity was measured as described by Chopra and Hurwitz.[2]

Peripheral neuropathy assessment. Peripheral neuropathy was assessed by clinical examination and by MCV in at least one upper and one lower limb nerve. The degree of clinical peripheral neuropathy was graded into three categories: mild, moderate, or severe (Table 2). Background peripheral neuropathy was assessed electrophysiologically by TL and MCV of the median and/or ulnar nerve in the upper limb and of the lateral popliteal nerve in the lower limb, on the opposite side to the affected nerve. Posterior tibial nerve MCV was used to assess background peripheral neuropathy in the lower limb in those with lateral popliteal nerve palsy. The normal values for our laboratory for TL and MCV are shown in Table 3.

Autonomic neuropathy assessment. The presence of two

TABLE 2
Duration of diabetes, blood glucose control prior to the onset of mononeuropathy, and the frequency of other diabetic complications, both specific (retinopathy, nephropathy, and neuropathy) and nonspecific (atherosclerosis) for each type of mononeuropathy

Type of mononeuropathy	Number of patients	Duration of diabetes (yr)			Blood glucose control			Retinopathy		Nephropathy	Clinical peripheral neuropathy*			Clinical autonomic neuropathy	Atherosclerosis	
		0–9	10–19	20+	Good	Fair	Poor	Background	Severe		Mild	Moderate	Severe		IHD	PVD
Median nerve	15	3	9	3	3	8	4	5	1	0	2	1	0	0	0	0
Ulnar nerve	15	4	5	6	0	10	5	3	6	3	6	6	0	1	4	3
Lateral popliteal nerve	8	5	0	3	2	3	3	1	1	0	5	0	0	0	0	0
Sciatic nerve	3	2	0	1	0	2	1	1	0	0	2	1	0	0	1	0
Femoral nerve	3	1	1	1	0	2	1	1	0	0	2	0	0	0	1	0
Oculomotor and abducens nerve	4	2	2	0	0	3	1	1	1	0	0	0	0	0	0	0
Facial nerve	3	2	1	0	0	2	1	1	0	1	1	1	0	0	0	1
Total	51	19	18	14	5	30	16	13	9	4	18	9	0	1	6	4
(%)	(100)	(37)	(35)	(28)	(10)	(59)	(31)	(25)	(18)	(8)	(35)	(18)	(0)	(2)	(12)	(8)

* The grading of peripheral neuropathy was as follows: mild, absent vibration sense distally and absent ankle jerks bilaterally; moderate, diminished or absent sensation in the lower limbs and/or intrinsic muscle wasting in the feet; severe, neurotropic ulceration in the feet or Charcot arthropathy. IHD, ischemic heart disease; PVD, peripheral vascular disease.

TABLE 3
Results for TL and MCV of all nerves tested in each type of mononeuropathy (mean ± SD)

Type of mononeuropathy	Median nerve		Ulnar nerve				Lateral popliteal nerve		Posterior tibial nerve		Femoral nerve
	TL	MCV	TL	MCV_1	MCV_2	MCV_3	TL	MCV	TL	MCV	MCV
Median nerve											
a	6.4 ± 2.6	46.0 ± 9.2									
b	4.3 ± 0.7	52.3 ± 6.7	2.9 ± 0.2	53.0 ± 4.7			4.7 ± 0.9	45.3 ± 5.2			
Ulnar nerve											
a			4.0 ± 1.1	48.4 ± 7.6	37.1 ± 6.2	49.9 ± 6.1					
b	4.3 ± 0.6	50.0 ± 4.8	2.8 ± 0.4	52.4 ± 2.7	52.2 ± 5.4	54.8 ± 2.6	5.7 ± 1.0	40.8 ± 6.5			
Lateral popliteal nerve											
a							5.2 ± 0.9	35.0 ± 7.5	6.6 ± 1.1	42.6 ± 1.2	
b	3.9 ± 0.4	52.6 ± 2.5	2.8 ± 0.2	53.3 ± 2.9			4.7 ± 0.7	45.6 ± 1.5	6.4 ± 0.9	41.9 ± 2.3	
Sciatic nerve											
a							5.8 ± 1.0	35.0 ± 0.8	7.0 ± 1.3	31.7 ± 4.0	
b	4.3 ± 0.2	50.8 ± 1.4	3.4 ± 0.5	49.9 ± 3.2			5.1 ± 0.9	40.2 ± 2.1	6.5 ± 0.8	38.0 ± 3.3	
Femoral nerve											
a							5.8 ± 1.5	36.8 ± 6.8			43.0 ± 2.8
b	4.2 ± 0.3	52.0 ± 3.1	2.9 ± 0.4	52.9 ± 5.3			5.3 ± 1.0	38.2 ± 9.5			56.2 ± 5.5
Oculomotor and abducens nerve	4.1 ± 0.4	50.5 ± 6.8	3.0 ± 0.3	51.5 ± 7.1			4.5 ± 0.6	44.3 ± 6.0			
Facial nerve	4.3 ± 0.1	50.3 ± 2.8	3.0 ± 0.5	52.7 ± 2.5			5.0 ± 0.7	44.6 ± 9.1			
Normal values	3.5 ± 0.4	54.1 ± 3.0	2.9 ± 0.5	58.4 ± 8.4			4.4 ± 1.3	47.2 ± 5.1	5.1 ± 1.1	49.9 ± 5.7	66.7 ± 7.4

a, affected side; b, nonaffected side; MCV_1, forearm segment; MCV_2, elbow (transsulcal) segment; MCV_3, upper arm segment.

or more of the following features was considered as positive evidence of clinical autonomic neuropathy: male sexual impotence, postural hypotension, intermittent diarrhea, gastric fullness, hypoglycemic unawareness, sweating disturbance, and absent testicular sensation. To confirm that these features were due to autonomic neuropathy, three simple noninvasive tests of autonomic function were carried out: the cardiovascular responses to the Valsalva maneuver and to sustained handgrip, and the postural fall in blood pressure. The Valsalva maneuver was carried out by using a standardized technique as previously described.[3] The heart rate response was measured by a simultaneous electrocardiograph and the results were expressed as the Valsalva ratio (VR), the ratio of the longest R-R interval after the maneuver to the shortest R-R interval during the maneuver. A ratio of 1.10 or less was defined as abnormal, 1.11 to 1.20 as borderline, and 1.21 or more as a normal response. In the standardized sustained handgrip test,[4] the maximum voluntary contraction was first determined, and then handgrip was maintained steadily at 30% of that maximum for as long as possible up to 5 min. Blood pressure was measured with a sphygmomanometer on the nonexercising arm, and observations were made three times at rest, at 1-min intervals during handgrip, and twice more immediately after release. The changes in blood pressure were taken as the difference between the mean of the three resting readings and the last reading before the release of handgrip. A rise in diastolic pressure of less than 10 mm Hg was defined as abnormal, 11–15 mm Hg as borderline, and 16 mm Hg or more as normal. Postural hypotension was defined as a fall in systolic blood pressure of 30 mm Hg or more immediately on standing up from the supine position.

Standard statistical methods were used in analyzing the results, which are expressed as mean ± SD.

RESULTS

The median, ulnar, and lateral popliteal nerves were most commonly affected, accounting for 38 out of 51 cases (75%). In all patients with involvement of the median and ulnar nerves, the dominant limb was affected, symptoms being more marked on the dominant side in those with bilateral involvement. Mononeuropathy of nerves in the lower limb and cranial nerves showed no predilection for either side. Fourteen patients had bilateral involvement of the same nerve (five median, eight ulnar, one lateral popliteal) but only one patient had mononeuropathy affecting two different nerves (ulnar and facial) at the time of presentation. Five patients gave a history of previous episodes of mononeuropathy (single episode in four, three episodes in one) but no patient had suffered a previous mononeuropathy of the currently affected nerve. Median neuropathy and ulnar neuropathy in all cases were gradual in onset with a prolonged duration of symptoms, whereas other mononeuropathies were acute in onset with symptoms for only 1–3 wk before presentation. Involvement of the median nerve was more common in females (13 of 15 patients) whereas ulnar neuropathy was more common in males (10 of 15 patients). Involvement of other nerves showed no predisposition for either males or females. Although the ages of the patients ranged from 21 to 77 yr, 48 patients (94%) were over 40 yr of age. The age distribution was the same in all groups of mononeuropathy. Thirty patients (59%) were being treated with insulin, 18 patients (35%) with oral hypoglycemic agents, and only three patients (6%) with diet alone.

In 19 patients (37%) the mononeuropathy occurred within 10 yr from diagnosis of diabetes (Table 2) and, indeed, in five the mononeuropathy was present at the time of diagnosis of diabetes (three lateral popliteal nerve, one abducens nerve, one facial nerve). Duration of diabetes in the other types of mononeuropathy showed a range from 2–37 yr with an even distribution (mean 15.6 ± 9.3 yr). Diabetic control in terms of blood glucose was graded as good in 10%, fair in 59%, and poor in 31%. Poor control was not associated with any one type of mononeuropathy. Patients with ulnar mononeuropathy were more likely to suffer from other diabetic complications, both specific (retinopathy and

nephropathy) and nonspecific (atherosclerosis), than patients with other types of mononeuropathy. Table 2 also shows the number of patients in each group with background peripheral and autonomic neuropathy assessed clinically. No patient had severe peripheral neuropathy as defined and only one had clinical features of autonomic neuropathy (which was confirmed by abnormal autonomic function tests).

Table 3 shows the results for TL and MCV of both the involved nerve and the nerves used to assess background neuropathy.

DETAILS OF INDIVIDUAL MONONEUROPATHIES

Median nerve (15 patients). Terminal latency of the affected median nerve was prolonged (6.4± 2.6 ms) and MCV was delayed (46.0 ± 9.2 m/s) when compared with the nonaffected side (TL 4.3 ± 0.7 ms, $P < 0.005$; MCV 52.3 ± 6.7 m/s, $P < 0.05$). Clinical peripheral neuropathy was found in three of the 15 patients (mild in two, moderate in one). Results for the group as a whole were within the normal range for both the ulnar nerve (TL 2.9 ± 0.2 ms; MCV 53.0 ± 4.7 m/s) and the lateral popliteal nerve (TL 4.7 ± 0.9 ms; MCV 45.3 ± 5.2 m/s) although the individual values for the three patients with peripheral neuropathy were outside the normal range. No patient had clinical autonomic neuropathy, and the results of autonomic function tests were normal in all except one patient (graded as mild peripheral neuropathy) who had a VR of 1.01 but normal BP response to sustained handgrip and no postural hypotension.

Ulnar nerve (15 patients). On the affected side, TL of the ulnar nerve was prolonged (4.0 ± 1.1 ms), and MCV measured in the forearm segment was delayed (48.4 ± 7.6 m/s) when compared with the nonaffected side (TL 2.8 ± 0.4 ms, $P < 0.001$; MCV 52.4 ± 2.7 m/s, $P < 0.05$). Motor conduction velocity was markedly delayed in the transsulcal (elbow) segment of the affected ulnar nerve (37.1 ± 6.2 m/s) compared with the opposite side (52.2 ± 5.4 m/s, $P < 0.001$). Motor conduction velocity in the upper arm segment of the ulnar nerve was within the normal range on both sides with no significant difference between the affected side (49.9 ± 6.1 m/s) and the nonaffected side (54.8 ± 2.6 m/s). Clinical peripheral neuropathy was found in 12 of the 15 patients (mild in six, moderate in six). In this group recordings from the median nerve were normal (TL 4.3 ± 0.6 ms; MCV 50.0 ± 4.8 m/s) but those from the lateral popliteal nerve were abnormal (TL 5.7 ± 1.0 ms; MCV 40.8 ± 6.5 m/s), consistent with the clinical findings. One patient (with moderate peripheral neuropathy) had clinical autonomic neuropathy confirmed by abnormal results in all three autonomic function tests (VR 1.04; rise in diastolic BP in response to sustained handgrip 8 mm Hg; postural drop in systolic BP 30 mm Hg). The other patients had no clinical autonomic neuropathy but four individuals (all with moderate peripheral neuropathy) had abnormal Valsalva ratios. The other patients in this group had normal Valsalva ratios and normal BP responses to sustained handgrip, and none showed a postural fall in BP.

Lateral popliteal nerve (eight patients). Motor conduction velocity of the affected lateral popliteal nerve was delayed (35.0 ± 7.5 m/s) compared with the nonaffected side (45.6 ± 1.5 m/s, $P < 0.005$). Terminal latency was normal on both sides (affected side 5.3 ± 0.9 ms; nonaffected side 4.7 ± 0.7 ms). Clinical peripheral neuropathy was found in five patients (mild in all five). Normal results were recorded from the median nerve (TL 3.9 ± 0.4 ms; MCV 52.6 ± 2.5 m/s) and ulnar nerve (TL 2.8 ± 0.2 ms; MCV 53.3 ± 2.9 m/s) in this group, but results from the posterior tibial nerve were abnormal on both the affected side (TL 6.6 ± 1.1 ms; MCV 42.6 ± 1.2 m/s) and nonaffected side (TL 6.4 ± 0.9 ms; MCV 41.9 ± 2.3 m/s), consistent with the presence of clinical peripheral neuropathy in five of the eight patients. No patient had clinical autonomic neuropathy, and results of autonomic function tests were normal in all patients.

Sciatic nerve (three patients). On the affected side the MCV recorded from the lateral popliteal nerve (35.0 ± 0.8 m/s) and posterior tibial nerve (31.7 ± 4.0 m/s) were delayed when compared with the nonaffected side (lateral popliteal nerve 40.2 ± 2.1 m/s; posterior tibial nerve 38.0 ± 3.3 m/s). Clinical peripheral neuropathy was present in all three patients (mild in one, moderate in two). Normal results were obtained from the median nerve (TL 4.3 ± 0.2 ms; MCV 50.8 ± 1.4 m/s) and the ulnar nerve (TL 3.4 ± 0.5 ms; MCV 49.9 ± 3.2 m/s). Although results recorded from the lateral popliteal and posterior tibial nerves on the nonaffected side were better than on the affected side, these results were still below the lower limit of the normal range, again consistent with the clinical findings. No patient had clinical autonomic neuropathy, and results of autonomic function tests were normal.

Femoral nerve (three patients). Femoral nerve conduction velocity was delayed on the affected side (43.0 ± 2.8 m/s) when compared with the opposite side (56.2 ± 5.5 m/s). Clinical peripheral neuropathy was present in two of the three patients (both mild) and these patients had delay in MCV of the lateral popliteal nerve on both sides. As a result the mean values for TL and MCV of the lateral popliteal nerve were below the normal range, but there was no difference between the affected side (TL 5.8 ± 1.0 ms; MCV 36.8 ± 6.8 m/s) and nonaffected side (TL 5.3 ± 1.0 ms; MCV 38.2 ± 9.5 m/s). Results recorded from the median nerve (TL 4.2 ± 0.3 ms; MCV 52.0 ± 3.1 m/s) and ulnar nerve (TL 2.9 ± 0.4 ms; MCV 52.9 ± 5.3 m/s) were normal. None of the three patients had clinical autonomic neuropathy, and results of autonomic function tests were normal.

Oculomotor nerve (one patient) and abducens nerve (three patients). No patient had clinical peripheral or autonomic neuropathy. Normal results were recorded for TL and MCV of the median nerve (TL 4.1 ± 0.4 ms; MCV 50.5 ± 6.8 m/s), ulnar nerve (TL 3.0 ± 0.3 ms; MCV 51.5 ± 7.1 m/s) and lateral popliteal nerve (TL 4.5 ± 0.6 ms; MCV 44.3 ± 6.0 m/s). No abnormality of autonomic function tests was found.

Facial nerve (three patients). Clinical peripheral neuropathy was found in two of the three patients (mild in one, moderate in one). Normal results were recorded for TL and MCV of the median nerve (TL 4.3 ± 0.1 ms; MCV 50.3 ± 2.8 m/s), ulnar nerve (TL 3.0 ± 0.5 ms; MCV 52.7 ± 2.5 m/s) and lateral popliteal nerve (TL 5.0 ± 0.7 ms; MCV 44.6 ± 9.1 m/s), apart from delay in lateral popliteal nerve MCV in the patient with moderate peripheral neuropathy. No patient had clinical autonomic neuropathy. The patient graded as having moderate peripheral neuropathy had an abnormal result for VR (1.07). The other two patients had normal values for VR and all three patients had normal BP responses to

sustained handgrip with no evidence of postural hypotension.

DISCUSSION

Diabetic neuropathy may present with diffuse peripheral or autonomic nerve dysfunction but occasionally a single nerve may be involved. In our study of 51 patients, diabetic mononeuropathy, although affecting a variety of nerves, most commonly affected the median, ulnar, and lateral popliteal nerves. All patients had volunteered symptoms suggesting the development of mononeuropathy, and we did not attempt to screen the clinic population for the prevalence of this complication. Eight additional patients, considered on clinical grounds as having possible diabetic mononeuropathy (all median and ulnar nerves), were excluded when results of nerve conduction studies failed to confirm the diagnosis.

We can find no previous study in which a group of patients with proven mononeuropathy has been extensively investigated for the presence and severity of background peripheral and autonomic neuropathy or the relationship to their diabetes and other complications. Mulder et al.[5] examined 103 unselected diabetic patients clinically and with nerve conduction tests, and, although 16 individuals had selective involvement of one or more single nerves, only four would have met our criteria for diabetic mononeuropathy, namely, clinical features confirmed electrophysiologically. It has been stated[6] that median neuropathy (carpal tunnel syndrome) is no more common in diabetic patients than in the general population. We have found that it was present in 29.4% of our patients and Blodgett et al.[7] stated that 59 out of 915 cases (6.4%) of carpal tunnel syndrome were known to be diabetic, suggesting a strong association with diabetes mellitus. Korczyn[8] found that 66% of 130 patients with lower motor neuron paralysis of the facial nerve (Bell's palsy) were diabetic, and other authors have since confirmed the association.[9,10] This condition therefore has also been included in our series. We have shown that the prevalence of cranial nerve involvement in a group of diabetic mononeuropathies was low, accounting for only 7 out of 51 cases (13.7%). Waite and Beetham[11] examined 2002 diabetic patients and found that only 16 had evidence of ocular palsies. Previous reports emphasized the frequent occurrence in the same patient of multiple mononeuropathies.[5,12,13] We found a high incidence of bilateral involvement (27.4%) of the same nerve although only four patients gave a history of previous episodes of mononeuropathy and only one patient had more than one different nerve affected at the time of presentation.

We found median neuropathy to be much more common in females, as indeed is the case in the nondiabetic population,[14] and also that ulnar neuropathy showed a predominance in males. The majority of patients were over 40 yr of age but only a small number had mild diabetes controlled by diet alone. In five patients the symptoms were present at the time of diagnosis of diabetes (lateral popliteal nerve in three, abducens nerve in one, facial nerve in one), similar to the two patients with lateral popliteal nerve palsy described by Shahani and Spalding.[15] Patients with ulnar neuropathy showed a tendency toward longer duration of diabetes and a higher incidence and severity of other complications than the other mononeuropathies. Apart from this we found no relationship between the onset of mononeuropathy and the duration of diabetes or the presence of other diabetic complications (both microvascular and atherosclerosis).

Acute diabetic peripheral neuropathy may follow stress situations such as infection, surgery, or myocardial infarction,[16,17] and mononeuropathies have been described complicating severe ketoacidosis[12,18] and nonketotic coma.[19] In the present series three patients developed acute onset of mononeuropathy (lateral popliteal nerve in one, abducens nerve in two) in association with infection and poor control, one of whom was frankly ketoacidotic. There was no evidence of recent metabolic upset in any of the other patients. Previous blood glucose control, using our method of assessment, seemed to play little part in the etiology of mononeuropathy. Our results suggest that multiple factors may contribute to the development of mononeuropathy and contrast with the findings of other authors in patients with symmetrical peripheral neuropathy. Pirart[20] showed that the incidence of peripheral neuropathy in the diabetic population rises with increasing age and increasing duration of diabetes. He also found a correlation between both asymptomatic and symptomatic peripheral neuropathy and poor diabetic control, and observed an increased incidence of retinopathy, nephropathy, and peripheral vascular disease in patients with diabetic neuropathy. These findings were confirmed by Gregerson[21] who showed impaired motor nerve conduction velocity in diabetic patients in relation to age, duration of diabetes, and metabolic control.

We have shown a relative absence of significant background peripheral and autonomic neuropathy, as assessed clinically and by objective electrophysiologic tests, in almost one-half of our diabetic patients with mononeuropathy. Indeed, in those affected, the majority were assessed as having only mild clinical neuropathy with only minimal impairment of motor nerve conduction velocity. An exception to this is ulnar neuropathy, which was associated with a high incidence of background neurologic damage (12 out of 15 patients). However, some degree of neuropathy exists in all diabetic patients[22] and indeed minimal damage to nerves may be present even at the time of diagnosis of diabetes.[23,24]

The development of mononeuropathy in diabetic patients may represent a combination of metabolic and vascular factors together with the usual daily trauma to nerves, especially pressure at exposed sites such as the median nerve at the wrist, the ulnar nerve at the elbow, and the lateral popliteal nerve at the head of the fibula.[25] Mulder et al.[26] used the term "autogenous mononeuropathy" to describe such patients. Neurologic disorders in diabetes vary in rapidity of onset from acute (within hours) to extremely insidious.[13] In all 15 of our patients with carpal tunnel syndrome, the symptoms were gradual in onset (up to 4 yr before presentation), and the dominant limb was affected. This suggests that mechanical factors may have been important in the etiology of the condition in this group. Similarly, in 15 patients with ulnar neuropathy, symptoms were gradual in onset (up to 2 yr before presentation), and the dominant limb was affected in all cases; symptoms were more marked on the dominant side in those with bilateral involvement. In contrast, lesions of nerves in the lower limb (lateral popliteal, sciatic, femoral) were acute in onset with symptoms for only a few weeks before presentation and showed no predilection for either side. This may be due to the fact that both lower limbs are equally susceptible to

everyday trauma in contrast with the dominant upper limb, or it may possibly support the theory that a vascular lesion is responsible, as has been shown by Raff et al.[27] in femoral neuropathy. The onset of cranial neuropathy was acute in all of our patients, with a duration of symptoms from 1–2 wk only, and frequently associated with systemic upset, especially headache. It is thought that paralysis of nerves supplying the extraocular muscles results from an ischemic lesion,[28] and support for this view comes not only from the acute mode of onset and self-limiting nature of this condition but also from the observation that there is sparing of the pupillary fibers in lesions of the oculomotor nerve,[29] presumed to be due to the peripheral location of these fibers in the nerve trunk as it passes through the cavernous sinus.[31]

There have been few pathologic studies of affected nerves in diabetic mononeuropathy. Dreyfus et al.[30] examined the oculomotor nerve in a diabetic patient who died shortly after developing paralysis of this nerve and concluded that the lesion was compatible with an incomplete ischemic neuropathy. Skanse and Gydell[31] felt that vasa nervorum ischemia may contribute to self-limiting femoral or sciatic neuropathy. Raff et al.[27] studied a patient with mononeuritis multiplex involving the femoral, sciatic, and obturator nerves, and their conclusion was that the lesions that they observed histologically represented infarcts of the affected nerves. It has been suggested that the similarity of diabetic mononeuropathy to the mononeuropathy observed in cases of polyarteritis nodosa, in which nerve infarcts have also been demonstrated,[32] provides further support for the theory that such lesions are vascular in nature. It is thought that Bell's palsy results from an inflammatory lesion, possibly secondary to viral infection,[33] which results in edema of the nerve. In an enclosed space such as the bony canal occupied by the facial nerve this swelling may cause ischemia of the nerve. Similarly, edema secondary to mechanical trauma may cause an ischemic lesion of other nerves in enclosed spaces, such as the median nerve at the wrist, the ulnar nerve at the elbow, and the lateral popliteal nerve at the head of the fibula. This view is supported by the fact that entrapment neuropathy of all types must result from pressure on the vasa nervorum rather than on the nerve fibers themselves.[34]

This study lends support to the view that diabetic mononeuropathy occurs independently of slowly progressive peripheral neuropathy and autonomic neuropathy. While the mode of onset and the natural history of peripheral neuropathy and autonomic neuropathy may point to metabolic factors as important in their etiology, diabetic mononeuropathy is probably a heterogeneous group, the cause varying with the nerve involved and including ischemia, mechanical trauma, acute metabolic upset, and possibly viral infection, all superimposed on minimal background change. Hence we would support the view of Ellenberg,[35] who suggested that one should not regard diabetic neuropathy as a single clinical entity but rather consider diabetic patients as liable to a variety of neuropathies.

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