Demyelinating Neuropathy in Diabetes Mellitus

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Background: Recent studies have reported that patients with diabetes mellitus (DM) have a predisposition to develop chronic inflammatory demyelinating polyneuropathy (CIDP).

Objectives: To determine whether patients with DM have a polyneuropathy fulfilling electrophysiologic criteria for CIDP, and whether CIDP is more frequent in patients with type 1 than in patients with type 2 DM.

Methods: We prospectively studied the frequency of electrophysiologic changes meeting the criteria for CIDP in patients with DM seen in our electrophysiology laboratory during a 51-month period (period 1). To evaluate the relationship between DM and CIDP, we prospectively determined during a 14-month period (period 2) the frequency of DM in patients seen in our electrophysiology laboratory with other neuromuscular diseases, and the frequency of idiopathic CIDP.

Results: During period 1, 120 patients with DM met the electrophysiologic criteria for CIDP (DM-CIDP). The most frequent clinical features of DM-CIDP were those of a predominantly large-fiber sensorimotor neuropathy, with recent motor deterioration and a moderately increased cerebrospinal fluid protein concentration. Twenty-six of the 120 patients were given intravenous immunoglobulin (400 mg/kg per day for 5 days), and 21 patients (80.8%) had significant improvement in the neurologic deficit at the end of 4 weeks of therapy. The DM-CIDP occurred equally in type 1 and type 2 DM. During period 2, 1127 patients were seen. Of these, 189 (16.8%) had DM with various neurologic disorders, including 32 patients (16.9%) with DM-CIDP. Among the remaining 938 patients without DM, 17 (1.8%) had idiopathic CIDP. The odds of occurrence of DM-CIDP was 11 times higher among diabetic than nondiabetic patients ($P<.001$).

Conclusions: Demyelinating neuropathy meeting the electrophysiologic criteria for CIDP occurred in both types of DM, and its occurrence was significantly higher in diabetic than in nondiabetic patients.

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Peripheral neuropathies of several types are common in diabetes mellitus (DM), including symmetric sensorimotor polyneuropathy, single or multiple mononeuropathy, autonomic neuropathy, truncal radiculopathy, plexopathy, and proximal motor neuropathy. Pathological studies of diabetic nerves have shown segmental demyelination, in addition to axonal loss, vasculopathy, and inflammatory infiltrates. Peripheral sensorimotor demyelinating neuropathy indistinguishable from idiopathic chronic inflammatory demyelinating polyneuropathy (I-CIDP) has been reported in patients with both type 1 and type 2 DM by some authors, but not by others. We shall apply the term DM-CIDP to patients with both conditions. Patients with diabetic neuropathies have been reported to respond to various therapies directed at immunologic disorders. Thus, it is unclear whether CIDP occurs more frequently than would be expected by chance in DM, and whether the clinical characteristics of the neuropathy in patients with DM-CIDP differ from those in patients with “pure” diabetic neuropathy. To answer these questions, we have compared the frequency of DM in CIDP with that in other neuromuscular disorders in a population of patients seen in our electrophysiology laboratory, and compared the characteristics of DM-CIDP with those of I-CIDP.

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RESULTS

PERIOD 1

We identified 120 patients with DM who met the EP criteria for demyelination during the period from June 1, 1996, to August 31, 2000.
**PATIENTS AND METHODS**

**PATIENT SELECTION**

All patients with peripheral sensorimotor neuropathy related to DM, referred for electrophysiological (EP) examination to the Neurology Electrophysiology Laboratory at University of Miami–Jackson Memorial Medical Center, Miami, Fla, between June 1, 1996, and August 31, 2000 (period 1), were examined prospectively. Exclusionary criteria were a clinical picture of diabetic amyotrophy or lumbo-sacral plexopathy; a typical picture of diabetic chronic distal sensory neuropathy, unless there were new symptoms of progressive weakness involving proximal and distal muscles; concomitant disease (paraproteinemia, endocrinopathy other than diabetes, connective tissue disorder, vitamin B₁₂ and folic acid deficiency, heavy metal intoxication, human immunodeficiency virus infection, hepatitis, Lyme disease, cancer, and kidney failure); or a family history of neuropathy.

To evaluate the relative frequency of L-CIDP and DM-CIDP, and the relative frequency of DM in other neuromuscular diseases, we prospectively obtained data to determine the total number of patients with each condition seen in our electrophysiology laboratory between July 1, 1999, and August 31, 2000, and whether they had DM (period 2).

**DIAGNOSTIC CRITERIA FOR DM-CIDP**

Patients underwent EP testing to evaluate whether the peripheral neuropathy was predominately demyelinating and met the EP criteria for the diagnosis of CIDP. The criteria were based on those recommended by the American Academy of Neurology (AAN) Ad Hoc Subcommittee AIDS Task Force 1991,29 except that the criteria for partial conduction block were more stringent, as recommended by the American Association of Electrodiagnostic Medicine30 and other investigators.31,32 As recommended by Saperstein et al,32 we did not require cerebrospinal fluid (CSF) examination and sural nerve biopsy. We did adopt more stringent diagnostic criteria for CIDP (modified from AAN 199129; see next paragraph).

The diagnosis of diabetic demyelinating peripheral neuropathy was established by (1) the presence of proved DM33; (2) the presence of a chronic, progressive or relapsing, motor, sensory, or sensorimotor polyneuropathy of at least 2 months’ duration associated with hyporeflexia or areflexia; and (3) EP criteria for demyelinating neuropathy as defined by the AAN Ad Hoc Subcommittee on AIDS and adapted by the American Association of Electrodiagnostic Medicine.30 Partial conduction block was diagnosed when the amplitude and area of the compound muscle action potential (CMAP) were decreased by more than 50% on proximal compared with distal stimulation across a standard peripheral nerve segment, when the distal CMAP amplitude was greater than 1 mV, and the duration was increased by less than 30% of the distal CMAP amplitude duration. Abnormal temporal dispersion was diagnosed when the proximal CMAP duration was increased by more than 30%, but where the proximal CMAP amplitude and area were not decreased by more than 50% across a standard peripheral nerve segment with a distal CMAP amplitude of more than 1 mV. For patients without partial conduction to be diagnosed as having a demyelinating neuropathy, they were required to have all 3 of the following abnormalities: (1) prolonged distal motor latency (as defined in the AAN 1991 criteria for CIDP29) in at least 2 motor nerves; (2) slowed conduction velocity (as defined in the AAN 1991 criteria for CIDP29) in at least 2 motor nerves; and (3) delayed (as

Continued on next page
had a CSF examination. The results of CSF cell count and IgG index were normal in these patients.

EP Studies

Nerve conduction study findings are summarized in Table 2. All patients fulfilled at least 3 of the 4 criteria for demyelination (conduction block, prolonged distal motor latency, slowed conduction velocity, delayed or absent F waves), but there was a wide range of EP abnormalities (Table 3). A total of 630 motor nerves were examined (Table 2, which does not include details of 8 facial nerves studied; Table 3). Distal latencies were prolonged in 292 (46.3%) of 630 nerves tested; conduction velocity was slowed in 375 (59.5%) and F waves were prolonged or absent in 445 (70.6%; Table 3). Partial conduction block was demonstrated in at least 1 nerve in 48 of the total 120 patients (40.0%; Table 3). Temporal dispersion was observed in at least 1 nerve in 58 patients (46.7%); 46 patients had type 2 DM, and 16 of these patients with temporal dispersion also had associated partial conduction block (Table 3). The mean summated CMAP amplitude (normalized for number of nerves studied in a patient) tended to be higher in patients with conduction block (5.4±2.0 mV) than in patients without conduction block (4.4±1.6 mV; P = .049). There was no difference in motor deficit score between those with (43.5±24.1) and those without (40.0±19.4) conduction block (P = .4). Linear regression analysis showed a significant inverse correlation (r = −0.4, P = .006) between the summated CMAP amplitude and the motor deficit score in patients with and without conduction block. Conduction block occurred equally among patients with mild (21 of 45 patients [46.7%]), moderate (16 of 44 patients [36.4%]), and severe (11 of 31 patients [35.9%]) neuropathy (P = .51).

Response to Intravenous Immunoglobulin

The details of the results are reported elsewhere.35 In brief, the average NIS of the 26 patients improved significantly from baseline (39.6±26.7; range, 25-125) to 4 weeks after the intravenous immunoglobulin therapy (33.0±29.6; range, 3-119; P <.001). The improvement in NIS (motor component) was observed on the third day of the treatment in 3 patients (11.5%), on the fifth day of the treatment in 4 patients (15.4%), and after the completion of the 5-day course in the remainder. In 21 (80.8%) of the 26 patients, the improvement in NIS was more than 5 points after 4 weeks. There was significant

definition in the AAN 1991 criteria for CIDP39) or absent F waves in at least 2 motor nerves.

NEUROLOGIC ASSESSMENT

All patients had quantitative evaluation by means of the Neuropathy Impairment Score (NIS),34 which summates deficits in strength, sensation, and reflexes found on neurologic examination. Deficits in strength were scored from 1 (25% deficit) to 4 (100% deficit); deficits in sensation and reflexes were scored as 0 (no deficit), 1 (decreased function), or 2 (absent function). The neuropathy severity was graded as mild with an NIS score of 15 to 25, moderate with an NIS score of 26 to 50, and severe with an NIS score of higher than 50.

EP STUDIES

Nerve conduction and electromyographic studies were performed in at least 3 limbs, which included 1 affected and the contralateral limb, by means of standard techniques. If 2 limbs were affected, a 4-extremity study was performed. We measured motor nerve conduction and corresponding F waves in 4 or more of the following nerves: tibial, peroneal, median, and ulnar. The radial motor nerve was studied in patients in whom the median and ulnar motor responses could not be obtained, or were less than 1 mV because of associated compressive neuropathies. The radial nerve was stimulated by the near nerve needle electrode technique distally in the forearm, at the elbow, and at midarm, recording over the extensor indicis muscle. Similarly, the sciatic nerve, stimulated at the popliteal fossa and gluteal fold by near nerve needle stimulation with recording over the medial gastrocnemius muscle, was studied in patients in whom the distal tibial motor response could not be obtained or was less than 1 mV. Needle electromyography was performed in affected limbs. The skin temperature was maintained above 32°C in the upper extremities and above 31°C in the lower extremities.

LABORATORY EVALUATION

All patients underwent screening laboratory examination, including anti-GM1 and anti–myelin-associated glycoproteins antibody titers and glycosylated hemoglobin level. A CSF examination, including cell count, glucose level, protein level, and IgG index, was performed in 49 patients. No patient had a nerve biopsy (reasons as described in the “Comment” section).

STUDY DESIGN FOR A SUBGROUP OF PATIENTS FOR INTRAVENOUS IMMUNOGLOBULIN THERAPY

The details of design for this component of the study are reported elsewhere.35 In brief, the study was a 4-week, open-label pilot study of intravenous immunoglobulin with serial quantitative measures of neurologic impairment. The primary outcome measure in this study was changes from baseline to 4 weeks in mean NIS. We defined the criterion indicating improvement as more than a 3-point decrease in NIS.36,37

STATISTICAL ANALYSIS

StatView II (Abacus Concepts Inc, Berkeley, Calif) was used for data analysis. We determined the statistical significance of differences between categorical variables by means of a χ² or Fisher exact test as appropriate and for differences between continuous variables by means of 2-tailed paired or unpaired t test. All data are expressed as mean±SD. The data were adjusted for multiple comparisons (Bonferroni correction). Statistical significance for all analyses was defined as P <.05.
(P = .01) improvement in lower limb motor function 4 weeks after the intravenous immunoglobulin therapy compared with baseline as indicated by the number of patients in the following groups: able to walk without aid (13 of 26 patients [50.0%] at 4 weeks vs 30.8% at baseline), requiring an aid to walk (10 of 26 patients [38.5%] vs 19.2% at baseline), and requiring a wheelchair (3 of 26 patients [11.5%] vs 50% at baseline). A greater proportion of patients with conduction block (11 of 11) showed an improvement in NIS in response to the intravenous immunoglobulin therapy than of those without conduction block (10 of 15; P = .03). Similarly, relapses occurred less often in the responders with conduction block (1/11 [9.1%]) than in responders without conduction block (5/10 [50.0%]; P = .04). Twenty-one (80.8%) of the 26 patients who responded to intravenous immunoglobulin treatment were followed up for a mean duration of 26±10.6 (range, 1-42 months). Fifteen of the patients had no relapse of the DM-CIDP and required no further immunotherapy. Six patients had a relapse of the DM-CIDP from 9 to 19 months after initial intravenous immunoglobulin treatment. Intravenous immunoglobulin therapy was generally well tolerated. Three patients (11.5%) developed a reversible decrease in renal function.

PERIOD 2

Relative Frequency of I-CIDP
and That Associated With Types 1 and 2 Diabetes

During period 2, 1127 patients were seen in our electrophysiology laboratory. Of these, 189 (16.8%), 15 with type 1 diabetes and 174 with type 2, had DM with various neurologic disorders. Of these 189, 32 (16.9%) had DM-CIDP. The proportion of patients with DM-CIDP was not different in type 1 (4/15 [26.7%]) and type 2 (28/174 [16.1%]; P = .49) diabetes. Among the 938 patients without DM, 17 (1.8%) had I-CIDP. Looked at another way, during period 2 a total of 49 patients meeting EP criteria for CIDP were seen, of whom 32 (65.3%) had associated DM. The odds of the occurrence of CIDP was 11 times higher in patients with DM than in patients without DM (odds ratio, 11.04; 95% confidence interval, 6.1-11.5; P < .001).

Frequency of Diabetes in Various Neuromuscular Diseases

During period 2, 9 (7.5%) of the 120 patients with amyotrophic lateral sclerosis (ALS) had DM, and 9 (6.6%) of 136 patients with myasthenia gravis (MG) had DM. The odds of the occurrence of DM in patients with CIDP was more than 20 times higher than that in patients with MG (odds ratio, 28.2; 95% confidence interval, 10.7-76.9; P < .001) and in those with ALS (odds ratio, 24.7; 95% confidence interval, 9.3-67.4; P < .001). There was no age difference among the patients with ALS (63.0±12.5 years; range, 32-86 years), the patients with MG (60.0±18.3 years; range, 15-90 years), and all the patients (n = 49) with demyelinating peripheral neuropathy meeting EP criteria for CIDP (56±13.8 years; range, 18-90 years; P = .06). Similarly, there was no difference among these 3 groups with respect to the sex ratio.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Finding</th>
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<tr>
<td>Sex, No. M/F</td>
<td>74/46</td>
</tr>
<tr>
<td>Type of DM, No. of patients</td>
<td>2</td>
</tr>
<tr>
<td>Type of DM, No. of patients</td>
<td>1</td>
</tr>
<tr>
<td>Age, y</td>
<td>Mean ± SD 57 ± 11.4</td>
</tr>
<tr>
<td>Duration of symptoms at presentation, mo</td>
<td>Mean ± SD 23.4 ± 28.3</td>
</tr>
<tr>
<td>Pattern of presenting symptoms, No. (%)</td>
<td></td>
</tr>
<tr>
<td>Sensory symptoms in hands and feet</td>
<td>40 (33.3)</td>
</tr>
<tr>
<td>Sensory symptoms in hands and feet, weakness</td>
<td>28 (23.3)</td>
</tr>
<tr>
<td>Sensory symptoms in hands, weakness in UE</td>
<td>26 (21.7)</td>
</tr>
<tr>
<td>Sensory symptoms in hands and feet, weakness in UE and LE</td>
<td>14 (11.7)</td>
</tr>
<tr>
<td>Weakness in LE</td>
<td>6 (5.0)</td>
</tr>
<tr>
<td>Poor balance†</td>
<td>6 (5.0)</td>
</tr>
</tbody>
</table>

†Four patients also had numbness in the feet.

Table 1. Clinical Features and Laboratory Data for 120 Patients

The main focus of this study was on the EP abnormalities and clinical profile of patients with DM. We did not require CSF examination or sural nerve biopsy, and we agree with the recommendations of Saperstein et al. The CSF protein level is increased in a significant proportion of patients with other types of diabetic neuropathy (axonal neuropathy or lumbosacral plexopathy) and is normal in a significant proportion (10%-21%) of patients with I-CIDP. Sural nerve biopsy abnormalities as criteria for demyelination lack sensitivity and specificity (40%-50%), and endoneurial inflammatory
infiltrates (mononuclear cells) occur infrequently (7%-18%).22,39,42

Dyck et al40 coined the term CIDP for a large cohort of patients (N = 53) with a clinical picture of a predominantly motor symmetric weakness, proximal and distal, associated with hyporeflexia or areflexia and a relapsing or a chronic progressive course. After this initial report, although often considered under the rubric of CIDP, many subtypes of CIDP have been reported,22,29,32,42 including our recently published review of the atypical cases of CIDP,24 suggesting that the spectrum of CIDP is much broader than the restrictive one initially proposed from the point of view of the presence of pain, asymmetry, radicular distribution, etc. In this study, we have restricted inclusion of cases to those fulfilling the clinical criteria recommended by the AAN Ad Hoc Committee,29 and we have adopted more stringent EP criteria for the diagnosis of CIDP (see the “Patients and Methods” section). All patients had motor involvement, 94% involving proximal muscles to some extent (Table 1). Sensory symptoms were present in 93% of cases, including pain in feet and hands in 41% of cases. Pain is not a major symptom in patients with I-CIDP; the occurrence of pain in hands and feet varies from 3% to 42%,22,39,40 and radicular pain or truncal numbness varies from 6% to 7.5%.22,40

We found that 16.9% of patients with DM met the EP criteria for CIDP, which occurred equally frequently in patients with type 1 and type 2 DM. The odds of the occurrence of CIDP were 11 times higher in diabetic than nondiabetic patients. We also found that the odds for the occurrence of DM among patients with CIDP were more than 20 times higher than in patients with MG and in those with ALS. Diabetes mellitus (especially type 1) has been associated with MG,43 the reported frequency ranging from 0.6% to 7%,44-47 which is similar to that found in our study (6.6%). The frequency of DM in patients with ALS has been reported to be from 2.1% to 28.9%,48-51 which compares with 7.5% in our study.

However, our study has limitations due to the potential bias of patient referral. Most of the patients referred to

<table>
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<tr>
<th>Table 2. Results of Electrodiagnostic Studies*</th>
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<tbody>
<tr>
<td><strong>Nerve Tested</strong></td>
</tr>
<tr>
<td>(Reference Value)†</td>
</tr>
<tr>
<td>Median</td>
</tr>
<tr>
<td>Ulnar</td>
</tr>
<tr>
<td>Radial</td>
</tr>
<tr>
<td>Tibial</td>
</tr>
<tr>
<td>Peroneal</td>
</tr>
<tr>
<td>Sciatic</td>
</tr>
<tr>
<td>Sural</td>
</tr>
</tbody>
</table>

*DML indicates distal motor latency; CV, conduction velocity; and CMAP, compound muscle action potential. Means and ranges were calculated only for recordable potentials (see Table 3 for unrecordable potentials).
†Normal values for our laboratory for various parameters for each nerve. All amplitude values are given as millivolts for motor nerves and microvolts for sensory nerves.
‡Values indicate the number of patients tested.
§Value indicates bilateral measurement.
bias may explain to some extent the results of previous diabetic neuropathy have varied from no conduction block. Previous reports of EP studies in peripheral neuropathy. Many of these patients (40%) with DM have a predominantly demyelinating neuropathy meeting EP criteria for CIDP is not rare in diabetic patients.9,11,15-17,19,24,53 In these studies, conduction block was defined as a greater than 20% decline in SNAPS.

We found that DM-CIDP occurred equally in patients with type 1 and type 2 diabetes. While our study is potentially subject to referral bias, the proportion of cases with type 1 and type 2 diabetes was similar in our study to that in the US diabetic population. Selection bias may explain to some extent the results of previous reports of a preponderance of either type 1 DM11,13,14 or type 2 DM15-18 with demyelinating neuropathies, or the report that demyelinating neuropathy is rare in DM.27 Miyasaki et al33 studied the specificity of EP diagnostic criteria for CIDP in 543 patients (307 male; age, 60.4 ± 11.1 years) with diabetic neuropathy. There were 169 patients with moderate to severe neuropathy. Among these 169 patients, 20 (11.8%) met the EP criteria for CIDP. They concluded that demyelinating peripheral neuropathy meeting EP criteria for CIDP is not rare in diabetic patients.

Our data demonstrated that a subgroup of patients (16.9%) with DM have a predominantly demyelinating peripheral neuropathy. Many of these patients (40%) had conduction block. Previous reports of EP studies in diabetic neuropathy have varied from no conduction block, or its rare occurrence, to the frequent finding of conduction block. In these studies, conduction block was defined as a greater than 20% decline in proximal CMAP compared with distal, with less than 15% increase in CMAP duration in the proximal CMAP.29 We have adopted the stricter criteria recommended by Cross et al, Rotta et al, and Notermans et al, defining conduction block as at least a 30% decline in proximal CMAP compared with distal, with less than 30% increase in CMAP duration with proximal stimulation. Conduction block has been correlated with segmental demyelination in pathological studies.35

The 2 main pathophysiologic mechanisms proposed for diabetic neuropathy are nerve ischemia (microangiopathy) and metabolic derangement of nerves. However, DM is one of the group of autoimmune disorders, and there is growing evidence that immune and inflammatory processes play a role in some of the neuropathies occurring in DM, including demyelinating polyneuropathy.1,6-15,57-60 Mitchell et al7 reported finding major histocompatibility class II antigen expression on Schwann cells, similar to that found in I-CIDP, in the nerves of patients with diabetic amyotrophy. Younger et al8 found that up to 60% of sural nerve biopsy specimens from 20 diabetic patients with various types of neuropathy had lymphocytic microvasculitis or perivasculitis, and endoneurial T-cell infiltrates, with increased expression of tumor necrosis factor α, cytokines, and components of the membrane attack complex. Several studies have suggested that autoantibodies directed against phospholipid,63 gangliosides,66 sulphatide,55 nerve growth factor, and advanced glycation end products may play a role in the pathogenesis of diabetic neuropathy.

Immunotherapy, including intravenous immune globulin, has been shown to be effective in some patients with several types of diabetic neuropathy.9,10,12,16-23 Menkes et al21 reported that 8 (25.8%) of 31 patients with acquired demyelinating polyneuropathy had DM and that, although these patients were thought to have untreatable "axonal diabetic neuropathy," all responded to immunotherapy.23 In our study, 26 patients, all but 1 of them with type 2 DM, were treated with intravenous immunoglobulin, and 21 of them improved.24 The mechanism of action of intravenous immunoglobulin in treating the autoimmune disorders is uncertain. Proposed mechanisms include the neutralization of the pathogenic antibodies by anti-idiotype antibodies, attenuation of complement-mediated tissue damage, and saturation or functional

### Table 3. Summary of Abnormal Nerve Conduction Findings

<table>
<thead>
<tr>
<th>Nerve</th>
<th>No. of Nerves Studied</th>
<th>Conduction Block</th>
<th>Temporal Dispersion</th>
<th>Distal Latency</th>
<th>Conduction Velocity</th>
<th>F-Wave Study</th>
<th>SNAP Amplitude</th>
<th>CMAP Amplitude</th>
<th>Conduction Velocity</th>
<th>H-Reflex Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median</td>
<td>118 (27%)</td>
<td>106/118 (89.8%)</td>
<td>19 (1%)</td>
<td>91 (93%)</td>
<td>81 (79%)</td>
<td>98 (16%)</td>
<td>46 (35 NR: 11)</td>
<td>68 (44)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ulnar</td>
<td>100 (15%)</td>
<td>87/100 (87.0%)</td>
<td>19 (1%)</td>
<td>18 (59%)</td>
<td>73 (96%)</td>
<td>87 (11%)</td>
<td>54 (34 NR: 18)</td>
<td>31</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Radial</td>
<td>7</td>
<td>4/7 (57.1)</td>
<td>0</td>
<td>1</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tibial</td>
<td>115 (80%)</td>
<td>92/115 (80.0%)</td>
<td>9 (1%)</td>
<td>41 (44%)</td>
<td>83 (59%)</td>
<td>89 (50%)</td>
<td>42 (22 NR: 16)</td>
<td>NE</td>
<td>120 (97: 95 NR)</td>
<td></td>
</tr>
<tr>
<td>Peroneal</td>
<td>93 (23%)</td>
<td>74/93 (79.6%)</td>
<td>5</td>
<td>8</td>
<td>48 (44%)</td>
<td>65 (51%)</td>
<td>56 (33 NR: 17)</td>
<td>NE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sciatic</td>
<td>31 (13%)</td>
<td>21/32 (65.6%)</td>
<td>5</td>
<td>3 (1%)</td>
<td>17 (14%)</td>
<td>15 (9%)</td>
<td>18 (3%)</td>
<td>15 (1%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Facial</td>
<td>8</td>
<td>5/8 (62.5)</td>
<td>5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sural</td>
<td>120†</td>
<td>95 (65 NR†)</td>
<td>25</td>
<td></td>
<td></td>
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*For conduction block, temporal dispersion, distal latency, and F wave, "abnormal" refers to values meeting the criteria for demyelination outlined in the "Patients and Methods" section. CMAP indicates compound muscle action potential, SNAP, sensory nerve action potential; NR, no response; and NE, not examined.

†Value indicates number of patients who had bilateral measurements.

‡Value indicates number of patients with bilateral abnormality.
blockade of Fc receptors on macrophages that are the major effectors of demyelination.72-74 Other mechanisms may include the functional modulation of T lymphocytes and their production of proinflammatory cytokines,73 and the binding of anti-idiotype antibodies to antigen receptors on B cells, thus decreasing autoantibody production.76 It is likely that several of these mechanisms contribute to the short-term and long-term effects of intravenous immunoglobulin therapy in many autoimmune diseases. The results presented in this article support the contention that DM-CIDP responds as well as I-CIDP to intravenous immunoglobulin therapy, although a controlled trial will be needed to prove this. While therapeutic response cannot be used to prove a pathophysiologic mechanism, it provides further supporting evidence for the autoimmune hypothesis of the occurrence of DM in CIDP.

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Author contributions: Study concept and design (Drs Sharma and Farronay); acquisition of data (Drs Sharma, Cross, Farronay, Ayyar, and Shebert); analysis and interpretation of data (Drs Sharma, Farronay, and Bradley); drafting of the manuscript (Drs Sharma, Farronay, and Bradley); critical revision of the manuscript for important intellectual content (Drs Sharma, Cross, Farronay, Ayyar, Shebert, and Bradley); statistical expertise (Dr Sharma); administrative, technical, or material support (Drs Sharma, Cross, Farronay, Ayyar, Shebert, and Bradley); study supervision (Drs Sharma and Bradley).

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