Efficacy of Intravenous Immunoglobulin in Patients With IgG Monoclonal Gammopathy and Polyneuropathy

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Context: The optimal treatment of patients with neuropathy associated with IgG monoclonal gammopathy of undetermined significance is unknown. Plasma exchange has been shown to be effective but alternative therapies have not been systematically evaluated.

Objective: To report our experience with intravenous immunoglobulin (IVIG) in patients with IgG monoclonal gammopathy of undetermined significance polyneuropathy.

Design: Retrospective review of clinical and electrodiagnostic features of 20 consecutive patients treated with IVIG over an 8-year period.

Setting: Academic medical center.

Main Outcome Measures: Medical Research Council strength (maximum, 40 points) and sensory (maximum, 26 points) scores, modified Rankin Disability Scale score.

Results: There were 14 men and 6 women (mean age, 65 years; age range, 36-82 years). The mean strength score was 35.6 points and the mean sensory score was 15.8 points prior to therapy. After IVIG therapy, the mean strength score increased by 1.1 points ($P = .22$) and the sensory score increased by 1.7 points ($P = .11$). Eight patients (40%) improved by 2 points or more in their motor or sensory score and 1 point or more in the modified Rankin Disability Scale score and were considered IVIG therapy responders. They had a shorter duration of symptoms ($P = .03$), numb hands ($P = .02$), and falling episodes ($P = .02$), and had greater proximal leg weakness ($P = .02$) compared with nonresponders. In IVIG therapy responders, the ulnar motor conduction velocity was slower, ulnar and peroneal distal motor latencies were prolonged, and the frequency of conduction block was higher (13 of 36 motor nerves in responders vs 6 of 53 in nonresponders, $P = .008$).

Conclusions: Intravenous immunoglobulin therapy was beneficial in 8 (40%) of our 20 patients with polyneuropathy and IgG monoclonal gammopathy of undetermined significance. Proximal leg weakness, short duration of symptoms, and demyelinating features on electrodiagnostic studies were associated with a response to IVIG therapy.

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THE POLYNEUROPATHY associated with monoclonal gammopathy of undetermined significance (MGUS) is thought to be immune-mediated in some cases.1-3 The evidence for a connection between MGUS and a neuropathy is strongest for those patients with an IgM paraprotein; approximately half of these patients have antibodies directed against epitopes on peripheral nerve myelin (eg, antimyelin-associated glycoprotein antibodies).2,5 The relationship between IgG-MGUS and polyneuropathy is less certain, and many of the latter cases have been considered indistinguishable from idiopathic chronic inflammatory demyelinating polyneuropathy (CIDP).5-11 Although plasma exchange apparently has been effective in the polyneuropathy associated with IgG-MGUS,12 the role of other immunomodulating therapies has not been evaluated systematically. There have been reports of patients improving with corticosteroid therapy, alone or in combination with cytotoxic therapy,13-16 and with intravenous immunoglobulin (IVIG).10,11,16 We reviewed our treatment experience with IVIG in patients with IgG-MGUS polyneuropathy with attention to clinical, electrodiagnostic, and immunological features that may have been associated with a response to treatment.

RESULTS

PATIENTS

There were 14 men and 6 women with a mean age of 65 years (age range, 36-82 years). The average duration of symptoms prior to treatment with IVIG was 27
PATIENTS AND METHODS

PATIENT SELECTION

Clinical, laboratory, and electrophysiological information were collected uniformly and reviewed retrospectively for consecutive patients with an IgG-MGUS neuropathy who were seen by the Neuromuscular Service at St Elizabeth’s Medical Center, Boston, Mass, from January 1, 1992, through December 31, 2000 and were treated with IVIG. Immunoelctrophoresis or immunofixation electrophoresis with quantitation of serum immunoglobulins and κ and λ light chains was obtained in all patients using a high-resolution agarose gel technique according to the procedure described previously.7 Monospecific antisera to IgM, IgG, IgA, and κ and λ light chains were used and immunoglobulins were quantified with nephelometry. The amount of the IgG monoclonal protein was less than 3.0 g/L and the level of the paraprotein remained stable on repeated testing in all patients. Serum autoantibodies directed against myelin-associated glycoprotein, sulfatide, and GM1 were measured in 19 patients. One patient had a low titer (1:2700) of antisialyllactoside antibodies; in the remaining 18 patients, antibodies were not detected. Most patients were evaluated by a hematologist (R.W.) and underwent a radiographic skeletal survey, bone marrow aspirate and biopsy, fat pad biopsy, urine immunoelctrophoresis, and chest and abdominal computed tomographic scans that excluded a plasma cell dyscrasia and lymphoproliferative disorder, and none developed such a condition at the time of last follow-up. Those with a history of concurrent medical illnesses associated with polyneuropathy (eg, diabetes mellitus, nutritional deficiencies, malignancy, human immunodeficiency virus infection, alcohol dependence, or connective tissue diseases), medication or toxic exposures known to cause neuropathy, or a family history of neuropathy also were excluded.

Eleven patients received 1 or more immunomodulating therapies before treatment with IVIG: 7 were treated with plasma exchange, 4 with corticosteroids, 3 with azathioprine, and 2 with cyclophosphamide. Five patients improved transiently but they developed a relapsing course, warranting a trial of an alternative therapy (IVIG); the remainder failed to respond to therapy. None received immunotherapy for at least 2 months prior to treatment with IVIG.

CLINICAL ASSESSMENT

Strength was assessed using the Medical Research Council (MRC) grading scale (0-5 points) in 8 muscles in the arms and legs (ie, deltoid, extensor digitorum communis, psoas, and tibialis anterior muscles, on both sides) with a maximum possible MRC strength score of 40 points, comparable to previous studies.7,8,13,18-24 Vibration, joint position, and pinprick sensation were graded semiquantitatively in the first distal interphalangeal and metatarsal joints bilaterally using a modified version of the Neurological Impairment Scale as follows: 2 points, normal; 1 point, reduced; and 0 points, absent. The presence of sensory ataxia was assessed by the Romberg sign, graded as present (0 point), equivocal (swaying with eyes closed but able to maintain balance for 5 seconds; 1 point), or absent (2 points); the maximum possible sensory score was 26 points.7,8,13,18-24

To assess the effect of the neuropathy on daily functional activities, the modified Rankin Disability Scale was used, similar to prior neuropathy studies,7,8,13,17,20-24 as follows: 0 indicates asymptomatic; 1, nondisabling symptoms that do not interfere with daily activities; 2, slight disability, unable to carry out all activities but still able to look after oneself; 3, moderate disability, requiring assistance with some activities but able to walk without assistance; 4, moderately severe disability, unable to walk without assistance and unable to attend to one’s own bodily needs without assistance; and 5, severe disability, totally dependent, requiring constant nursing care and attention.

ELECTROPHYSIOLOGICAL ASSESSMENT

Electrophysiological studies were performed at the time of initial evaluation according to methods previously described.25 Motor conduction studies were performed using supramaximal percutaneous stimulation with surface electrode recordings. Sensory nerve action potentials were recorded following antidromic stimulation using ring (median and ulnar) or bar (sural) electrodes; skin temperature was maintained at 32°C. The median, ulnar, and peroneal motor nerves and median, ulnar, and sural sensory nerves were sampled in most patients. Partial conduction block was defined as a 20% or more baseline-to-peak amplitude reduction between proximal and distal sites of motor nerve stimulation, excluding sites prone to compression.27 Needle electrode examination included sampling of at least one distal and proximal muscle in the arm and leg, using a semi-quantitative assessment of motor unit potentials and abnormal spontaneous activity.

IVIG THERAPY

All patients were treated with at least 1 course of IVIG at a dosage of 2 g/kg, administered over 2 to 5 days. Twelve patients received 1 course of IVIG therapy, 3 received 2 courses, and 5 had 3 cycles of therapy (administered monthly for 3 consecutive months). To assess a response to treatment, motor and sensory scores and the modified Rankin Disability Scale score were determined at the time of the maximum deficit before the initial treatment and at the time of maximal improvement after IVIG therapy, or at the last follow-up for patients who did not respond to IVIG therapy. Because most patients had a predominantly sensory neuropathy, improvement was defined as an increase of 2 points or more in the motor or sensory score, and improvement of 1 point or more in the modified Rankin Disability Scale score. Patients were classified as treatment responders or nonresponders. The mean duration of follow-up was 44 months (median, 33 months; range, 4-144 months). Relapse after receiving IVIG therapy was defined as worsening after improvement with a decline of 2 points or more in either the motor or sensory score, and increase (worsening) of 1 point or more in the modified Rankin Disability Scale score.

STATISTICAL ANALYSIS

Intravenous immunoglobulin therapy responders were compared with nonresponders to identify clinical, laboratory, or electrophysiological features that may have been associated with a response to IVIG therapy. The Fisher exact test (2-sided) was used to compare categorical responses and the Kruskal-Wallis analysis of variance or Wilcoxon-matched sign rank test was used to compare nonparametric ordinal and continuous variables. P≤.05 was considered statistically significant.
months (range, 1-120 months). Most had a preponderantly sensory polyneuropathy with reports of numbness (17 patients), gait unsteadiness (16 patients), paresthesias (14 patients), and neuropathic pain (9 patients). Fifteen reported weakness in the hands (9 patients) or legs (15 patients).

**RESPONSE TO IVIG THERAPY**

The initial mean MRC score was 35.6 points and the follow-up score improved by an average of 1.1 points (follow-up mean MRC score, 36.7 points; \( P = .22 \), Table 1). The MRC score improved by 2 or more points in 7 patients, remained unchanged in 7, and worsened in 6 after IVIG therapy (Table 2). The initial mean sensory score was 15.8 points and improved by an average of 1.7 points (follow-up mean sensory score, 17.5 points; \( P = .11 \)). The sensory score improved by 2 points or more in 9 patients, was unchanged in 7, and worsened in 4 (Table 2).

Eight patients (40%) had a 2-point or greater improvement in either the sensory or motor score, and all 8 had a 1-point or greater improvement (reduction) in the modified Rankin Disability Scale score, and were, therefore, classified as IVIG therapy responders (Table 2 and Table 3). These patients had a shorter duration of symptoms at the time of the initial evaluation (mean, 7 months vs 41 months for nonresponders, \( P = .03 \)), and more often reported numbness in the hands and episodes of falling (Table 3). The IVIG therapy responders also had greater proximal leg weakness (mean psoas MRC score, 3.9 points vs 4.8 points for nonresponders, \( P = .02 \)) prior to therapy. In the IVIG responder group, the mean MRC score improved by 4.4 points (vs −1.1 points in nonresponders, \( P < .001 \)), and the mean sensory score improved by 6.5 points (vs −1.4 points for nonresponders, \( P < .001 \), Table 3).

The 12 patients who had only 1 IVIG infusion had a mean improvement of the MRC score of 2.7 points compared with a mean decrease of 1.3 points in those who received 2 or 3 infusions (\( P = .01 \)). Similarly, the mean sensory score increased by 3.5 points in patients who received 1 infusion compared with a mean reduction of 0.9 points in patients who received 2 or 3 infusions (\( P = .03 \)).

**ELECTRODIAGNOSTIC AND LABORATORY FEATURES**

Several electrodiagnostic abnormalities were associated with a response to IVIG therapy (Table 4). In those who responded to IVIG therapy, the mean ulnar motor amplitude was lower, the ulnar conduction velocity was substantially slower, the ulnar and peroneal motor distal latencies were prolonged, and the frequency of conduction block was higher (Table 4). Sensory nerve action potentials were frequently absent in both groups.

Nine patients had at least 1 demyelinating abnormality on electromyographic (EMG) studies. Using strict research criteria for the diagnosis of CIDP,\(^27\) we found that only 2 patients fulfilled criteria for definite CIDP (clinical, electrodiagnostic, cerebrospinal fluid, and nerve biopsy requirements), and neither improved with IVIG therapy, although both also had substantial axon loss seen on EMG and in nerve biopsy specimens. Three patients had probable CIDP (a nerve biopsy specimen was not obtained but all other criteria were satisfied), and all improved after IVIG therapy; 2 others had possible CIDP (the result of a cerebrospinal fluid sample was normal or a lumbar puncture was not performed, neither had a nerve biopsy specimen obtained, but clinical and EMG criteria were satisfied), and both responded to IVIG therapy. Two others had a mixed axonal and demyelinating polyneuropathy that did not satisfy EMG criteria for CIDP, and neither patient’s condition improved with treatment. In summary, 7 patients fulfilled the criteria for possible or probable CIDP (lacking cerebrospinal fluid or biopsy material to qualify for definite CIDP), and 5 (71%) improved with IVIG therapy.

Three IVIG therapy responders (patients 5, 9, and 12, Table 2) had an axonal neuropathy. In 2, gait disorder was the primary problem, with imbalance and sensory ataxia related to impaired proprioception and the presence of the Romberg sign that improved after receiving IVIG therapy. One patient had distal, symmetric sensory loss and pain in the feet and legs that resolved after receiving IVIG therapy. Electrodiagnostic studies showed slightly reduced motor amplitudes in the legs, mild slowing of conduction velocities, little or no denervation potentials in distal leg muscles, and absent sural sensory potentials. There were no demyelinating features.

There were no differences in the mean amount of the IgG monoclonal protein (IVIG therapy responder group, 1.4 g/L; IVIG nonresponder group, 1.3 g/L, \( P = .75 \)) or cerebrospinal fluid protein concentration (IVIG therapy responder group, 0.77 g/L; IVIG nonresponder group, 0.52 g/L, \( P = .56 \)).

**TIMING OF IMPROVEMENT, RELAPSE AFTER RECEIVING IVIG THERAPY, AND FOLLOW-UP**

In those who responded to IVIG therapy, we observed the onset of improvement a mean of 3 weeks (range, 1-8 weeks) after receiving IVIG treatment, with maximum improvement after an average of 6 weeks (range, 2-12 weeks). Six patients in the IVIG therapy responder group developed a relapsing course and required periodic maintenance therapy. The mean time to relapse for these
patients was 9 weeks (range, 2-16 weeks, Table 2). The remaining 2 patients (patients 5 and 10, Table 2) had sustained improvement of their condition at the most recent follow-up (range, 22-48 months).

Three of 12 patients in the nonresponder group have remained stable at last follow-up and have not received further therapy. The remaining 9 patients had slowly progressive motor or sensory deficits.

**COMMENT**

There have been only a few case reports or small case series alluding to the efficacy of IVIG therapy in patients with IgG-MGUS associated polyneuropathy. Our systematic review of a larger number of patients indicates that approximately 40% responded to IVIG therapy. The treatment had a positive effect in the activities of daily living of the 8 patients who responded to IVIG therapy, as measured by an improved modified Rankin Disability Scale score, and corroborated by increased strength and sensory scores after receiving therapy compared with the nonresponders. The improvement we observed in this group was similar to that of others. Hermosilla et al also noted significant clinical improvement in 4 of 5 patients with IgG-MGUS-associated demyelinating neuropathy who were treated with IVIG, although most developed a long-term, relapsing course, comparable to that of most of our patients who responded to IVIG therapy. Other reports have indicated that the neuropathy of an additional 5 patients improved following treatment with IVIG, but further details were not provided.

Data provided in Table 1 suggest that IVIG therapy was not effective in producing statistically significant improvement in the mean motor or sensory scores of the entire cohort. However, although ours is the largest report of patients with IgG-MGUS who were treated with IVIG, the sample size of 20 patients is small and, therefore, clinically meaningful effects in some patients may be obscured by larger group analysis. This only can be clarified by appropriately powered, prospective studies.

Although both motor and sensory scores improved in the subset of patients who responded to IVIG therapy, the magnitude of improvement was greatest for the sensory score. This probably reflects the nature of IgG-MGUS neuropathy as a preponderantly sensory condition; maximum improvement for the motor and sensory scores was greater for those patients who had 1 infusion compared with patients who had 2 or 3 infusions. It may

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**Table 2. IgG-MGUS Polyneuropathy: Clinical Features**

<table>
<thead>
<tr>
<th>Patient No./Age, y/Sex</th>
<th>Duration of Symptoms, mo</th>
<th>Initial No. of IVIG Cycles Administered</th>
<th>MRC Muscle Score†</th>
<th>Sensory Score†</th>
<th>Modified Rankin Disability Scale Score†</th>
<th>IVIG Therapy Responder</th>
<th>Relapse</th>
<th>Time to Relapse, mo</th>
<th>Follow-up, mo</th>
</tr>
</thead>
</table>
| 1/78/F 1 2 30/28 20/20 3/3 No … … 27 | 2/53/F 3 3 33/39 12/22 4/2 Yes Yes 3 72 | 3/44/M 3 3 33/39 6/16 3/2 Yes Yes 1.5 60 | 4/61/M 5 3 40/40 20/16 1/1 No … … 18 | 5/69/M 6 1 38/40 20/24 2/0 Yes No … … 22 | 6/68/M 6 2 34/33 14/14 2/2 No … … 39 | 7/54/M 6 6 28/39 18/24 3/1 Yes Yes 0.5 6 | 8/73/M 6 1 23.5/28.5 16/20 5/3 Yes Yes 1.0 60 | 9/66/M 9 1 36/40 12/20 4/1 Yes Yes 4.0 18 | 10/64/M 12 3 38/40 18/20 2/1 Yes No … … 48 | 11/44/F 12 1 38/38 10/2 2/3 No … … 84 | 12/70/M 12 1 40/40 22/24 2/1 Yes Yes 3.0 48 | 13/56/M 22 3 34/33 4/2 3/4 No … … 144 | 14/78/F 36 1 40/40 22/22 1/1 No … … 21 | 15/76/M 36 2 35/27 16/16 2/2 No … … 84 | 16/72/M 36 1 38/38 12/12 2/2 No … … 26 | 17/36/M 60 1 36/35 26/26 2/3 No … … 72 | 18/82/F 72 1 40/40 20/20 2/2 No … … 12 | 19/75/M 84 3 39.5/39 15/12 2/3 No … … 24 | 20/78/M 120 3 38/38 14/16 2/2 No … … 4

*†IgG-MGUS indicates IgG monoclonal gammopathy of undetermined significance; IVIG, intravenous immunoglobulin; MRC, Medical Research Council; and ellipses, not applicable.

†Values indicate the pretherapy/posttherapy IVIG scores for each evaluation. See the “Clinical Assessment” subsection of the “Patients and Methods” section for an explanation of the scoring methods used.
be that those who did not respond to the first course were simply less likely to respond to additional infusions, perhaps due to associated axonal degeneration. The timing of improvement in the IVIG therapy responders is comparable to what has been reported in patients with CIDP. However, 6 of the 7 patients who improved after 1 infusion developed a relapsing course, and it may be that patients with demyelinating neuropathies and IgG-MGUS are more likely to respond to treatment with IVIG early (ie, after a single infusion) and require periodic retreatment due to relapse.

Although most of our patients who responded to IVIG therapy had a demyelinating neuropathy, it is of some interest that 3 IVIG therapy responders had electrodiagnostic features of an axonopathy. Clinically, 2 had a large-fiber, sensory ataxic neuropathy, and 1 has developed a long-term relapsing course requiring periodic treatment with IVIG every few months. The timing and degree of improvement is inconsistent with axonal regeneration, and we can only speculate about the nature of the clinical response. We did not obtain nerve biopsy specimens in these patients and, therefore, cannot exclude a

Table 3. IgG-MGUS Polyneuropathy: IVIG Therapy Responders vs Nonresponders

<table>
<thead>
<tr>
<th>Variable</th>
<th>IVIG Therapy</th>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Responder</td>
<td>Nonresponder</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>(n = 8)</td>
<td>(n = 12)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>62 (10)</td>
<td>67 (15)</td>
<td>.15</td>
<td></td>
</tr>
<tr>
<td>Male sex, No.</td>
<td>5</td>
<td>9</td>
<td>.64</td>
<td></td>
</tr>
<tr>
<td>Symptom duration, mo</td>
<td>7.1 (3.6)</td>
<td>40.8 (36.7)</td>
<td>.03</td>
<td></td>
</tr>
<tr>
<td>Weak feet, No.</td>
<td>5</td>
<td>6</td>
<td>.99</td>
<td></td>
</tr>
<tr>
<td>Weak hands, No.</td>
<td>5</td>
<td>4</td>
<td>.36</td>
<td></td>
</tr>
<tr>
<td>Numb feet, No.</td>
<td>8</td>
<td>8</td>
<td>.12</td>
<td></td>
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<tr>
<td>Numb hands, No.</td>
<td>7</td>
<td>3</td>
<td>.02</td>
<td></td>
</tr>
<tr>
<td>Ataxia, No.</td>
<td>6</td>
<td>3</td>
<td>.06</td>
<td></td>
</tr>
<tr>
<td>Falls, No.</td>
<td>7</td>
<td>3</td>
<td>.02</td>
<td></td>
</tr>
<tr>
<td>Pre-IVIG therapy MRC score, points</td>
<td>33.7 (5.6)</td>
<td>36.9 (3.1)</td>
<td>.16</td>
<td></td>
</tr>
<tr>
<td>Change in MRC score after IVIG therapy, points</td>
<td>4.4 (3.3)</td>
<td>−1.1 (2.3)</td>
<td>.001</td>
<td></td>
</tr>
<tr>
<td>Pre-IVIG therapy sensory score, points</td>
<td>14.8 (4.5)</td>
<td>16.1 (5.9)</td>
<td>.61</td>
<td></td>
</tr>
<tr>
<td>Change in sensory score after IVIG therapy, points</td>
<td>6.5 (3.0)</td>
<td>−1.3 (2.7)</td>
<td>.001</td>
<td></td>
</tr>
<tr>
<td>Pre-IVIG therapy modified Rankin Disability Scale score, points</td>
<td>3.1 (1.1)</td>
<td>2.0 (0.6)</td>
<td>.02</td>
<td></td>
</tr>
<tr>
<td>Change in modified Rankin Disability Scale score after IVIG therapy, points</td>
<td>−1.8 (0.7)</td>
<td>0.3 (0.5)</td>
<td>.001</td>
<td></td>
</tr>
</tbody>
</table>

*Continuous data are given as mean (SD) unless otherwise indicated. IgG-MGUS indicates IgG monoclonal gammopathy of undetermined significance; IVIG, intravenous immunoglobulin; and MRC, Medical Research Council.

**Boldfaced P values indicate statistical significance.

Table 4. IgG-MGUS Polyneuropathy: Nerve Conduction Studies

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total No. of Patients</th>
<th>IVIG Therapy Responder (n = 8)</th>
<th></th>
<th></th>
<th>IVIG Therapy Nonresponder (n = 12)</th>
<th></th>
<th></th>
<th>P Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motor Studies</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Median</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Distal amplitude, (nl &gt; 4.0 mV)</td>
<td>7</td>
<td>3.6 (2.2)</td>
<td>12</td>
<td>4.8 (2.5)</td>
<td>.24</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Conduction velocity, m/s (nl &gt; 49 m/s)</td>
<td>7</td>
<td>34 (17)</td>
<td>11</td>
<td>49 (6)</td>
<td>.08</td>
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<tr>
<td>Distal latency, ms (nl &lt; 4.4 ms)</td>
<td>7</td>
<td>8.0 (5.6)</td>
<td>11</td>
<td>4.7 (1.5)</td>
<td>.11</td>
<td></td>
<td></td>
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<tr>
<td>Ulnar</td>
<td></td>
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<tr>
<td>Distal amplitude, mV (nl &gt; 6.0 mV)</td>
<td>8</td>
<td>4.9 (2.7)</td>
<td>11</td>
<td>8.6 (2.7)</td>
<td>.01</td>
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<tr>
<td>Conduction velocity, m/s (nl &gt; 50 m/s)</td>
<td>8</td>
<td>35 (19)</td>
<td>11</td>
<td>55 (6)</td>
<td>.04</td>
<td></td>
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<tr>
<td>Distal latency, ms (nl &lt; 3.2 ms)</td>
<td>8</td>
<td>4.7 (2.3)</td>
<td>11</td>
<td>2.9 (0.5)</td>
<td>.01</td>
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<tr>
<td>Peroneal</td>
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<tr>
<td>Distal amplitude, mV (nl &gt; 2.0 mV)</td>
<td>8</td>
<td>1.2 (0.6)</td>
<td>11</td>
<td>2.4 (3.0)</td>
<td>.20</td>
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<tr>
<td>Conduction velocity, m/s (nl &gt; 40 m/s)</td>
<td>8</td>
<td>30 (9)</td>
<td>10</td>
<td>37 (10)</td>
<td>.99</td>
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<td></td>
<td></td>
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<tr>
<td>Distal latency, ms (nl &lt; 6.1 ms)</td>
<td>8</td>
<td>6.5 (2.4)</td>
<td>10</td>
<td>4.4 (0.9)</td>
<td>.04</td>
<td></td>
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<tr>
<td>No. of nerves with conduction block‡</td>
<td>13/36</td>
<td></td>
<td>6/53</td>
<td></td>
<td>&lt;.008</td>
<td></td>
<td></td>
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<tr>
<td>Sensory Studies‡</td>
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<td></td>
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<tr>
<td>Median absent</td>
<td>4/6</td>
<td></td>
<td>3/11</td>
<td></td>
<td>.38</td>
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<td>Ulnar absent</td>
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<td></td>
<td>2/11</td>
<td></td>
<td>.14</td>
<td></td>
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<tr>
<td>Sural absent</td>
<td>5/6</td>
<td></td>
<td>8/12</td>
<td></td>
<td>.99</td>
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</table>

*Continuous data are given as mean (SD) unless otherwise indicated. IgG-MGUS indicates IgG monoclonal gammopathy of undetermined significance; IVIG, intravenous immunoglobulin; and nl, normal.

†Boldfaced P values indicate statistical significance.

‡The numerator indicates the number of patients in the subsample; the denominator, the total number of patients in the sample.
demyelinating sensory polyneuropathy or polyradiculoneuropathy, similar to prior reports. Most such cases have little or no weakness but demyelinating abnormalities are found on motor nerve conduction studies, and the diagnosis is usually confirmed by sensory nerve biopsy specimens demonstrating pathological features of demyelination. We postulate that our axonal cases represent a sensory ataxic polyradiculoneuropathy due to sensory nerve demyelination with loss of the sural sensory nerve action potential, comparable to the sensory ataxic variant of CIDP that has been reported to be steroid responsive.

The patients whose conditions improved with IVIG therapy had more frequent falls at baseline, probably as a consequence of more severe proximal leg weakness compared with the nonresponders. These observations, along with a higher frequency of reports of hand numbness, are clinical features that have been commonly associated with an acquired demyelinating polyneuropathy. In the IVIG therapy responder group, 4 of 10 nerve conduction parameters indicated more severe demyelination compared with nonresponders: specifically, the average ulnar motor nerve conduction velocity was slower, ulnar and peroneal distal motor latencies were more prolonged, and the frequency of motor nerve conduction block was higher. Indeed, we found that 5 (62%) of the 8 IVIG therapy responders fulfilled strict EMG research criteria for CIDP. In contrast, there was no relationship between the amount of the IgG protein and a response to IVIG therapy. Demyelinating features on EMG studies may be more relevant than the presence of an IgG monoclonal protein for predicting a response to IVIG therapy.

Several investigators have suggested that there are few salient features that distinguish IgG-MGUS neuropathy from idiopathic CIDP. Both disorders are associated with sensory and motor deficits (although sensory features seem to predominate in patients with MGUS), a progressive or relapsing course, demyelinating changes on electrophysiological and pathological studies, and improvement following treatment with corticosteroids, plasma exchange, or IVIG. The rate of response to IVIG therapy in our patients with IgG-MGUS is comparable to patients with idiopathic CIDP. Although proximal and distal limb weakness has been considered a characteristic feature of CIDP and generally distinguishes these patients from those with demyelinating IgG-MGUS polyneuropathy, as previously noted, pure sensory variants of CIDP also have been recognized, making distinction from patients with IgG-MGUS difficult in individual cases. We conclude that in patients with a polyneuropathy and IgG monoclonal protein, IVIG therapy is a reasonable alternative to plasma exchange.

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