The (mis)diagnosis of CIDP
The high price of missing the mark

Chronic inflammatory demyelinating polyneuropathy (CIDP) is an immune-mediated peripheral nervous system disorder classically presenting with progressive, symmetrical limb weakness including the proximal muscles, generalized areflexia, and large fiber sensory loss.\(^1\) Electrodiagnostic studies show unequivocal segmental demyelination in multiple motor nerves or nerve roots, and the CSF protein level is usually elevated. In addition to classical CIDP, there are many variant presentations, so-called atypical forms, such as pure motor, pure sensory, regional (restricted to the upper or lower limbs), multifocal (Lewis-Sumner syndrome), and distal patterns.\(^2\) The diagnosis of CIDP can be established when patients meet carefully delineated clinical, electrodiagnostic, and laboratory criteria,\(^1,2\) but may be more challenging in cases with atypical presentations. Further difficulties arise when nerve conduction studies are inadequately performed or trivial nerve conduction abnormalities are labeled demyelinating. Misdiagnosis of CIDP leads to inappropriate and often long-term use of corticosteroids and IV immunoglobulin (IVIg), with the potential for adverse effects and an enormous financial burden to the health care system.

There has been increasing concern about the frequent misdiagnosis and inappropriate treatment of patients labeled CIDP in the neurologic community.\(^3\) In our experience, we have seen misdiagnosed patients treated with IVIg for up to 12 years. Misdiagnosis usually occurs when other peripheral nerve disorders, such as diabetic, hereditary, or toxic neuropathies, or cervical and lumbar polyradiculopathy, are misclassified as CIDP. In this issue of Neurology\(^8\), Allen and Lewis\(^4\) analyzed the accuracy of the diagnosis in 58 patients referred for CIDP. Patients were classified according to the European Federation of Neurological Societies/Peripheral Nerve Society (EFNS/PNS) diagnostic criteria.\(^1\) After review of all available clinical, electrodiagnostic, CSF, MRI, and nerve biopsy data, an astounding 47% of these patients failed to meet the criteria for CIDP; the majority had received prolonged treatment with IVIg or corticosteroids for periods of 3 months–5 years. Many patients misdiagnosed with CIDP had other unrelated neurologic disorders, ranging from amyotrophic lateral sclerosis to diabetic polyneuropathy, fibromyalgia, small fiber neuropathy, and even psychogenic conditions. Patients referred by a neuromuscular specialist were almost twice as likely to have a correct diagnosis. Following treatment, 85% percent of patients without CIDP reported at least some nonspecific subjective improvement (e.g., “feeling better”), yet only 19% reported better strength or sensation, and all had an alternative inflammatory disorder (e.g., multiple sclerosis, neurosarcoïdosis), highlighting the challenges of patient self-reporting in this population. The authors noted that the principal causes of misdiagnosis were failure to apply clinical and electrodiagnostic criteria, improperly performed and interpreted electrodiagnostic studies, and excessive reliance on minimally elevated CSF protein levels. Although not addressed in this study, we postulate that in some cases misaligned incentives related to the profitability of physician-owned IVIg infusion centers may be a contributing factor.

This study has limitations, including retrospective analysis, limited objective treatment response data, and evaluation limited to only one US referral center, and the results may not be applicable to other countries, especially those with strict controls on the utilization of IVIg. Nonetheless, these results largely confirm the anecdotal shared experiences of many US CIDP investigators.

The fact that so many patients labeled with CIDP had non-neuropathic conditions is worrisome, raising fundamental questions regarding the adequacy of neuromuscular education and practice of contemporary neurologists that will not be remedied easily. This study implies that the educational curriculum of neurology residency programs should be strengthened in neuromuscular disease and electrodiagnosis. There are several additional implications from the Allen and Lewis article that can improve performance in routine practice. Clinicians should adopt and adhere to one of the established diagnostic guidelines for CIDP (EFNS/PNS or others)\(^5,6\); electrodiagnosticians should test enough nerves and utilize stringent cutoff values to be confident that observed nerve...
conduction abnormalities meet demyelinating criteria; and referral to a neuromuscular specialist should be considered in atypical cases or when there is diagnostic uncertainty. For example, the GBS/CIDP Foundation International has established Centers of Excellence in the United States and Europe to assist patients and clinicians in establishing the correct diagnosis and treatment plan. Physicians treating patients with CIDP should follow proper dosing regimens with durations that have been derived from published protocols, and discontinue therapy following a sustained period of meaningful clinical improvement. Properly treated patients with CIDP have a sustained remission after as little as 6 months of treatment with IVIg or corticosteroids, and many do not require lifelong treatment. Treatment also should be discontinued when patients fail to respond after an adequate trial. An alternative proven therapy may be offered, and perhaps the accuracy of the diagnosis should be reviewed. In nonresponders with aggressive or longstanding CIDP, the possibility of permanent secondary axonal injury should be considered. Finally, proper objective metrics, such as grip dynamometry and the Rasch-built Overall Disability Scale, should be utilized routinely before and after therapy to assess for change; it is not sufficient to make conclusions regarding treatment responses based solely upon subjective impressions.

The proper diagnosis and management of CIDP is essential for patients and the management of increasingly scarce medical resources. As the US health care system continues to evolve towards quality-based care, the use of IVIg and other emerging and expensive immunomodulatory therapies for CIDP will come under greater scrutiny. If the physician community fails to insure that these resources are used appropriately, the health insurance industry or governmental agencies may do so on our behalf, perhaps to the detriment of our patients.

STUDY FUNDING
No targeted funding reported.

DISCLOSURE
K. Gorson serves as a consultant and on a data safety monitoring board for a study sponsored by CSL Behring and has served as a consultant for Baxter Pharmaceuticals. C. Gooch has served as a consultant in neuromuscular therapeutics for Baxter and CSL Behring and on the data safety monitoring board for NeuralStem. Go to Neurology.org for full disclosures.

REFERENCES
ABSTRACT

Objective: We aimed to explore the diagnosis and misdiagnosis of chronic inflammatory demyelinating polyneuropathy (CIDP) and to identify pitfalls that erroneously lead to a misdiagnosis.

Methods: A retrospective study of 59 consecutive patients referred with a diagnosis of CIDP was performed. Patients were classified as having or not having CIDP according to European Federation of Neurological Societies/Peripheral Nerve Society (EFNS/PNS) criteria. Diagnostic and treatment data were compared in the 2 groups.

Results: Forty-seven percent of patients referred with a diagnosis of CIDP failed to meet minimal CIDP diagnostic requirements. All misdiagnosed patients who satisfied EFNS/PNS clinical criteria would be considered atypical as defined by the EFNS/PNS. CSF cytoalbuminologic dissociation was present in 50% of those without CIDP, although protein elevations were generally mild. Nerve conduction studies in patients without CIDP were heterogeneous, but generally showed demyelinating features better explained by a process other than CIDP. Patients frequently reported improvements after being treated with immunotherapy, even if the CIDP diagnosis was incorrect.

Conclusions: CIDP misdiagnosis is common. Over-reliance on subjective patient-reported perception of treatment benefit, liberal electrophysiologic interpretation of demyelination, and placing an overstated importance on mild or moderate cytoalbuminologic dissociation are common diagnostic errors. Utilization of clear and objective indicators of treatment efficacy might improve our ability to make informed treatment decisions.

GLOSSARY

CIDP = chronic inflammatory demyelinating polyneuropathy; CMAP = compound motor action potential; CV = conduction velocity; EFNS/PNS = European Federation of Neurological Societies/Peripheral Nerve Society; IVIg = IV immunoglobulin; MAG = myelin-associated glycoprotein; MMN = multifocal motor neuropathy; MS = multiple sclerosis; R-ODS = Rasch-built Overall Disability Scale; SFN = small fiber neuropathy; SMA = spinal muscular atrophy; SPS = stiff-person syndrome.

Chronic inflammatory demyelinating polyneuropathy (CIDP) is a treatable immune-mediated peripheral nerve disorder that affects 1.0 to 8.9 persons per 100,000. In the early 20th century, the cardinal clinical features of what we now call CIDP were described, and since that time the electrodiagnostic, histopathologic, and therapeutic features of the disorder have been defined. Over 15 sets of CIDP diagnostic criteria have been developed, a fact that points to the difficulties in defining a disorder without reliable biologic markers. The recognition that CIDP is a syndrome, including multifocal, pure sensory, and other variants, further complicates the diagnostic picture. While early diagnosis and treatment are critical to prevent potentially irreversible deficits, equally problematic is the growing realization that many patients are misdiagnosed with CIDP and subsequently treated for long periods of time without clear evidence of therapeutic effect. The cost to patients and society is substantial.

Our objective was to determine the extent of accurate CIDP diagnosis, identify pitfalls that erroneously led to misdiagnosis, and correlate subjective treatment response with diagnostic accuracy. In doing so, we aim to refocus the diagnostic process with heightened clinical diligence and more objective measures to guide our treatment approaches.

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Go to Neurology.org for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article.
METHODS

Identification of patients. Included in this retrospective review were consecutive new patient referrals to Northwestern University with a diagnosis of CIDP between September 2012 and February 2014. All patients were evaluated by one of the authors (J.A.A.).

Clinical data collection. Clinical and electrodiagnostic data were recorded from all patients. Clinical diagnosis of typical or atypical and electrodiagnostic designation of definite, probable, or possible were determined as defined by European Federation of Neurological Societies/Peripheral Nerve Society (EFNS/PNS) criteria.11 Nerve conduction studies were performed at Northwestern University at the time of the clinical consultation whenever possible. Electrophysiologic studies in patients without CIDP were categorized by the most salient abnormality. CSF, MRI of spinal root, and nerve biopsy were not required for diagnosis in all cases, but were recorded if obtained. After integration of the data, patients were diagnosed with definite, probable, or possible CIDP according to EFNS/PNS criteria. Diagnoses alternative to CIDP were determined when possible. All charts were blinded and independently reviewed by an external evaluator (R.A.L.). Only charts in which the diagnosis was agreed upon by both authors were included in this analysis.

Beneficial response to immunotherapy was carefully reviewed. All patients treated with immunotherapy were asked if they improved. As a matter of standard clinical practice, patients were asked to broadly define what symptom improved and the level of confidence that improvement occurred. Patients reporting subjective improvement of any symptom were categorized as either “subjective improvement, probable or definite” or “subjective improvement, definite” depending on the patient’s degree of certainty. Patients were then asked to report only definite improvements in strength and/or sensation. These patients were categorized as “strength/sensation improvement, definite.” For both groups, charts were reviewed for documented objective interval changes in strength and sensation.

Immunotherapy prescribing patterns were recorded. If IV immunoglobulin (IVIg) frequency or dose were variable during the treatment course, then the most common dosing schedule was recorded. Because the type of corticosteroid was not uniform and stable doses were rarely prescribed, only treatment duration was recorded.

Statistical analysis. Descriptive statistics include counts and percentages for nominal or dichotomous variables. Categorical variables were analyzed using the Pearson χ² and Fisher exact test. Continuous variables were analyzed with Student 2-tailed t test. p < 0.05 Was considered significant.

Standard protocol approvals, registrations, and patient consents. The study was approved by the Northwestern Institutional Review Board.

RESULTS

Demographic and clinical features. A total of 59 patients with the referring query of CIDP were evaluated. Diagnostic agreement was reached in all but 1 case, leaving 58 available for analysis. EFNS/PNS criteria were met in 31 patients (53%), satisfying definite (87%), probable (3%), or possible (10%) requirements. Twenty-seven patients (47%) failed to meet minimal CIDP diagnostic standards. Prior to the study evaluation, patients with CIDP were managed by a neuromuscular specialist at a teaching hospital in 68% of cases, compared to 37% without CIDP (p = 0.034). There was no single clinician who provided a disproportionate number of referrals to either group. Thirty-six percent of those with CIDP were seen at Northwestern University as a single consultation, compared to 48% without CIDP (p = 0.42). Remaining patients were managed by one of the authors (J.A.A.), often in collaboration with the patient’s local continuity neurologist. Alternative diagnoses for patients without CIDP are shown in the figure. Alternative diagnosis was reached after review of external records and collection of additional data as needed. Two patients were believed to have a hereditary neuropathy. In both, the clinical course, family history, and additional testing supported that diagnosis, but prohibitive barriers precluded confirmatory genetic testing.

Table 1 shows demographic and diagnostic data for the CIDP and not CIDP groups. Age, sex, and geographic residence distribution were similar. Patients without CIDP tended to have symptoms for longer and a diagnosis for shorter than the CIDP group, although differences were not statistically significant. Misdiaognosed patients satisfied EFNS/PNS clinical criteria in 44% of cases. In all 44%, the clinical characteristics would be considered atypical as defined by the EFNS/PNS. CSF cytologic and/or dissociation as a categorical variable was common in both groups, occurring in 50% of those without CIDP and 90% with CIDP. However, protein elevations in the not CIDP group were generally mild, with only 2 of 20 being greater than 100 mg/dL (mean 61.4 mg/dL). In the CIDP group, 17 of 31 were greater than 100 mg/dL (mean 156.3 mg/dL).

<table>
<thead>
<tr>
<th>Clinical and electrodiagnostic data</th>
<th>Definite (87%), probable (3%), or possible (10%) requirements.</th>
<th>Twenty-seven patients (47%) failed to meet minimal CIDP diagnostic standards.</th>
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<tr>
<td>Alternative diagnoses for patients without CIDP</td>
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Electrophysiologic studies. All but 3 electrophysiologic studies were performed at Northwestern University (2 not CIDP, 1 CIDP group). Electrodiagnostic criteria were met by 100% of CIDP confirmed vs 14.8% of patients without CIDP (table 1). Electrophysiologic findings and clinical diagnosis in patients without CIDP are shown in table 2. The most common finding (6 patients) was a length-dependent axonal polyneuropathy, sometimes with mild to moderate degrees of conduction velocity slowing coexisting with either reduced compound motor action potential (CMAP) amplitudes or associated with a systemic condition known to be associated with conduction velocity slowing (e.g., diabetes). Five patients demonstrated focal or multifocal demyelination, but limited to compressible sites. Axonal abnormalities restricted to motor nerves were appreciated in 4 patients, all of whom had a motor neuron disease. In 2 of these patients, mild conduction velocity (CV) slowing was appreciated in motor nerves with severely reduced CMAPs. In 3 patients, deep peroneal abnormalities were most apparent, often with a lesser finding at another site. All 3 of these patients also had reduced peroneal CMAP amplitudes. Electrophysiologic studies were normal in 5 patients.

Response to immunotherapy. At the time of referral, 29 of 31 patients in the CIDP group and 21 of 27 patients in the not CIDP group had received either IVIg or corticosteroids (table 3). When improvement was defined in subjective patient-reported terms, 89% of patients with CIDP and 85% of patients without CIDP reported at least a probable perception of benefit. When patients were asked to include only symptoms that definitely improved, 66% of patients without CIDP responded affirmatively. Only when improvement in symptoms and signs was unequivocal and limited to strength or sensation did a difference between the groups emerge ($p < 0.01$). When IVIg and corticosteroids were considered independently, similar trends were appreciated. In the not CIDP group, 4 patients (19%) demonstrated definite improvement in strength or sensation (IVIg = 2, corticosteroids = 2). These 4 patients, although diagnosed with and treated as having CIDP, were reclassified by the authors as having multifocal motor neuropathy (MMN), multiple sclerosis (MS), neurosarcoidosis, and stiff-person syndrome (SPS).

Table 4 describes the prescribing patterns in those patients with and without CIDP. Although patients with CIDP received IVIg for twice as long, even the misdiagnosed group was treated for an average of 1.5 years. IVIg frequency and total monthly dose were similar between groups. Corticosteroids were prescribed for a longer duration in the group with CIDP, although this difference was not statistically significant. Because of wide variability in corticosteroid prescribing practices, an accurate average dose could not be calculated. When considering aggregated use of immunotherapy, IVIg was prescribed for a combined 32.5 years and corticosteroids for a combined 13.5 years for patients without CIDP.

DISCUSSION Within this retrospective review, we find that almost half of patients incorrectly carry a diagnosis of CIDP. Alternative diagnoses were heterogeneous. While most had some type of large-fiber neuropathic process, it is remarkable that 22% of...
misdiagnosed patients had generalized chronic pain syndromes without any of the trademark clinical or electrophysiologic CIDP features. Another large portion (44%) satisfied EFNS/PNS clinical criteria, each of which would be considered atypical under the EFNS/PNS definition. Atypical presentations include those with pure motor, pure sensory, and distal predominant clinical features. Only 4 of these also satisfied EFNS/PNS electrodiagnostic criteria. These 4 patients were reclassified as MMN (2), anti-MAG neuropathy, and suspected Charcot-Marie-Tooth. It has previously been shown that a CIDP diagnosis can accurately be made in patients with polyneuropathy progressing for more than 8 weeks if the pattern of weakness is symmetric, proximal, and distal (i.e., typical CIDP), even in the absence of electrophysiologic studies.12 Our findings support that claim. The more challenging scenario arises in patients with atypical clinical features, and it is in this group that clinicians have too often taken diagnostic liberties. The observation that misdiagnosed patients were less likely to undergo an evaluation by a neuromuscular specialist at a teaching hospital emphasizes the diagnostic difficulties in these complex patients. The failure to focus on symptoms and signs distinct to CIDP may be one reason for misdiagnosis. Failure to adhere to well-defined electrodiagnostic guidelines may be another. It is critical that the CIDP diagnosis with atypical clinical features be based on both clinical and electrophysiologic abnormalities.

Nerve conduction studies were found to be a major factor in misdiagnosis. Four patterns in the misdiagnosed group emerged: length-dependent axonal, preferential peroneal, motor axonal, and compressible sites. Often 1 or more “demyelinating” features were concomitantly observed. In all cases the “demyelinating” features were mild to moderate and better explained by a condition other than CIDP. Although it is beyond the scope of this article to go into the sources of electrodiagnostic confusion, it is clear that careful attention need be given to unequivocal evidence of segmental demyelination. Vulnerability to electrodiagnostic errors increases when (1) equipodal degrees of CV slowing occur with length-dependent axonal neuropathies, (2) deep peroneal nerve findings to the extensor digitorum brevis muscle are used as the focal diagnostic abnormality, (3) mild CV slowing is observed in motor neuron disease, and (4) when clear CV slowing is present but it is limited to compressible sites.

We also show that spinal fluid analysis has the potential to confuse, rather than clarify, the diagnosis. Fifty percent of our patients without CIDP demonstrated cytoalbuminologic dissociation, but in only 2 was the level greater than 100 mg/dL. Certainly atypical CIDP can occur. It is also well-appreciated that not all patients with CIDP have cytoalbuminologic dissociation17 and that rare patients with potentially treatable dysimmune polyneuropathy may not satisfy strict CIDP electrodiagnostic criteria.18,19 We do not suggest that we abort the notion that these diagnostically challenging patients exist, but rather advise heightened caution when interpreting electrophysiologic and laboratory data in atypical clinical settings.

We found that both patients with and without CIDP believed that IVIg or corticosteroids were beneficial, and this often led to prolonged treatment courses. The challenge of interpreting and reacting to perception of benefit is neither easy nor trivial. Symptoms like fatigue20 and pain21 may be prominent in CIDP, and should not be dismissed. However, hypervigilance of improvement only of these nonspecific symptoms absent improvement in the
Clinical hallmarks of CIDP may have erroneous consequences. Diagnostically, improvement following immunotherapy is considered supportive of the CIDP diagnosis. Subjective response to any treatment is complicated by placebo response, desire of the patient and physician to change the course of the illness, and nonspecific treatment effects unrelated to disease response. Even objective response is not disease-specific. Perception of benefit drives treatment plans and can lead to long-term immunotherapy with perpetuation of the wrong diagnosis. In this small single-center cohort, patients were treated for a combined 32 years with IVIg and 13 years with corticosteroids for a disease they did not have. Although we cannot exclude the possibility that some of our misdiagnosed patients had ill-defined immune-mediated processes that improved with immunomodulating therapy, these findings suggest that subjective patient experiences after treatment may contribute to CIDP misdiagnosis.

Our findings imply that too often objective indicators of improvement following immunotherapy are not documented as is required within the EFNS/PNS diagnostic guideline. In 2013, the Peripheral Neuropathy Outcome Measures Standardization collaboration concluded that disability measured by the Rasch-built Overall Disability Scale (R-ODS) and strength measured by grip strength dynamometer are useful metrics by which CIDP can be assessed and treatment responses can be defined. It is also notable that over 90% of patients with CIDP who respond to IVIg (2 g/kg followed at 3-week intervals at 1 g/kg) do so by the third infusion. We recommend inclusion of disease-specific outcomes (i.e., R-ODS and quantitative grip strength) within the EFNS/PNS guideline and utilization of these metrics during routine clinical care as a way to reliably document treatment benefit. We also suggest that if an IVIg trial be undertaken it be conducted for a maximum of 3 months with frequent collection of objective disease-specific indicators of treatment efficacy. If response to immunotherapy is to be used as a diagnostic indicator, improvements (i.e., benefit) should be reflected in the obtained outcome measures.

The objective of this study was not to determine efficacy of CIDP treatment. This is better addressed in other publications. We instead sought to provide insight into how patients feel when treated. Eighty-five percent of patients without CIDP felt better with immunotherapy when benefit was broadly and subjectively defined. Even when restricted to definite subjective improvement, 66% of patients without CIDP felt better. This observation might ostensibly support liberal immunotherapy in unconfirmed cases. However, our therapeutic options for CIDP are not benign, and long-term utilization of immunomodulation as a means to treat a symptom absent a defined disease process can be risky. The long-term medical and financial burdens of chronic corticosteroid or IVIg use are not insignificant. We argue that supportive and symptomatic management strategies would be better employed under these circumstances. We also observed that treatment of the poorly defined CIDP case has the potential to misdirect the immunotherapy treatment plan. Four of our patients who did not have CIDP experienced definite improvement in strength or sensation with immunotherapy. This small but notable proportion of patients who did not have CIDP felt better. This observation might provide insight into how patients feel when treated.

### Table 3: Treatment response to immunotherapy in patients with and without CIDP

<table>
<thead>
<tr>
<th></th>
<th>CIDP</th>
<th>Not CIDP</th>
<th>p Value</th>
</tr>
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<tbody>
<tr>
<td>Subjective improvement, definite, %</td>
<td>86.9 (29)</td>
<td>85.7 (21)</td>
<td>0.69</td>
</tr>
<tr>
<td>Subjective improvement, definite, %</td>
<td>89.6</td>
<td>66.7</td>
<td>0.07</td>
</tr>
<tr>
<td>Strength/sensation improvement, definite, %</td>
<td>68.9</td>
<td>19.0</td>
<td>&lt;0.01</td>
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<tr>
<td>IVIg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subjective improvement, definite, %</td>
<td>82.1 (28)</td>
<td>75.0 (20)</td>
<td>0.72</td>
</tr>
<tr>
<td>Subjective improvement, definite, %</td>
<td>78.6</td>
<td>55.0</td>
<td>0.11</td>
</tr>
<tr>
<td>Strength/sensation improvement, definite, %</td>
<td>57.1</td>
<td>10.0</td>
<td>&lt;0.01</td>
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<td>Corticosteroids</td>
<td></td>
<td></td>
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<tr>
<td>Subjective improvement, definite, %</td>
<td>66.7 (24)</td>
<td>66.7 (12)</td>
<td>&gt;0.99</td>
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<tr>
<td>Subjective improvement, definite, %</td>
<td>66.7</td>
<td>50.0</td>
<td>0.47</td>
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<tr>
<td>Strength/sensation improvement, definite, %</td>
<td>45.8</td>
<td>16.7</td>
<td>0.14</td>
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### Table 4: Treatment characteristics in patients with and without CIDP

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<th></th>
<th>CIDP</th>
<th>Not CIDP</th>
<th>p Value</th>
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</thead>
<tbody>
<tr>
<td>IVIg duration, mo, average (range)</td>
<td>41.5 (3-144)</td>
<td>18.6 (3-60)</td>
<td>0.04</td>
</tr>
<tr>
<td>IVIg frequency, wk, average (range)</td>
<td>3.1 (1-6)</td>
<td>3.62 (1-8)</td>
<td>0.18</td>
</tr>
<tr>
<td>IVIg dose per month, g/kg, average (range)</td>
<td>1.16 (0.3-2)</td>
<td>1.15 (0.2-4)</td>
<td>0.93</td>
</tr>
<tr>
<td>Corticosteroid duration, mo, average (range)</td>
<td>22.4 (3-132)</td>
<td>16.2 (3-48)</td>
<td>0.52</td>
</tr>
</tbody>
</table>

Abbreviations: CIDP = chronic inflammatory demyelinating polyneuropathy; IVIg = IV immunoglobulin.
portion of patients reporting benefit may be skewed by including these patients with well-defined autoim-mune disease in the not CIDP group, the analysis was not significantly impacted if these patients were excluded (data not shown).

This retrospective analysis used EFNS/PNS criteria (81% sensitivity and 96% specificity) as a benchmark for CIDP diagnosis. We attempted to minimize diagnostic errors by strictly adhering to this criterion. All clinical data were blinded and reviewed (by R.A.L.) for an independent diagnostic interpretation. Although we cannot exclude the possibility that some of our patients were misclassified, EFNS/PNS criteria adherence and our agreement in 58 of 59 cases suggests otherwise. The arbitrary way in which we defined response to immunotherapy might also be questioned. We broadly defined subjective improvement based on symptom type and patient confidence of improvement. Our findings imply that many patients who receive IVIg or corticosteroids feel better. This does not necessarily mean that they have CIDP or even that the neuropathy has improved. Our analysis does not include an assessment of immunotherapies other than IVIg and corticosteroids. While treatment with other agents may conceivably augment the subjective effect of IVIg or corticosteroids, in no case was a second-line agent started before IVIg or corticosteroids and use of second-line agents was infrequent. As such, we believed it unlikely that another intervention could explain the subjective experiences of IVIg and corticosteroids.

Our findings suggest that CIDP diagnostic points of weakness include (1) hypervigilance of subjective patient-reported perception of treatment benefit, (2) misinterpretation of electrodiagnostic studies, and (3) placing an overstated importance on mild or moderate cyroalbuminologic dissociation. These errors are especially magnified in clinically atypical patients. Further study is needed to determine the source of electrophysiologic errors (e.g., technique or interpretation) and how those errors can be avoided. Our data are supportive of opinions previously expressed by several leaders within the CIDP community. Based on our findings, we encourage utilization of existing CIDP diagnostic criteria as a means to improve diagnostic accuracy and heightened diagnostic diligence for patients with atypical clinical features. We strongly encourage well-defined and carefully observed treatment trials in all our patients, utilizing objective measures to determine efficacy and avoidance of nonspecific subjective perception of benefit as means to aid diagnosis or guide continuation of treatment. For patients where diagnostic or treatment questions persist, obtaining consultations from specialized centers may be particularly helpful.

REFERENCES


AUTHOR CONTRIBUTIONS

J. Allen: data collection, data analysis and interpretation, manuscript preparation. R. Lewis: data analysis and interpretation, manuscript preparation.

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DISCLOSURE

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This Week’s Neurology® Podcast
CIDP diagnostic pitfalls and perception of treatment benefit (see p.498)

This podcast begins and closes with Dr. Robert Gross, Editor-in-Chief, briefly discussing highlighted articles from the August 11, 2015, issue of Neurology. In the second segment, Dr. Michelle Mauermann talks with Dr. Jeffrey Allen about his paper on chronic inflammatory demyelinating polyneuropathy diagnostic pitfalls and perception of treatment benefit. Dr. Adam Numis reads the e-Pearl of the week about exam findings in hemifacial spasms. In the next part of the podcast, Dr. Alberto Espay focuses his interview with Dr. Howard Weiner on his Frontiers in Neuroscience Lecture at the AAN Annual Meeting on the topic of immune mechanisms in neurologic diseases.

Disclosures can be found at Neurology.org.

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