FIG. 3. Sural nerve biopsy from a patient with CIDP. A few mononuclear inflammatory cells surround the endoneurial blood vessel (curved arrow). There is a decrease in the number of large myelinated fibers. Some thinly myelinated fibers have excessive Schwann cell process proliferation ("onion bulbs") (arrowhead) (toluidine blue stain). (From Brey RL, Barohn RJ, et al. Neurologist 1996;2:25–52, with permission, Williams & Wilkins.)

TABLE 12. Diagnostic criteria for CIDP

<table>
<thead>
<tr>
<th>Mandatory clinical features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Progression of muscle weakness in proximal and distal muscles of upper and lower extremities for 2 months</td>
</tr>
<tr>
<td>Areflexia or hyporeflexia</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Major laboratory features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Evidence of demyelination on nerve conduction studies (see Table 10)</td>
</tr>
<tr>
<td>Cerebrospinal fluid (CSF) studies</td>
</tr>
<tr>
<td>CSF protein &gt; 45 mg/dL</td>
</tr>
<tr>
<td>Cell count &lt; 10/mm³</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Nerve biopsy features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nerve biopsy with predominant features of demyelination that include segmental demyelination, remyelination, onion-bulb formation, and inflammation.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mandatory exclusion criteria (patients must be devoid of these features)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical features of a hereditary neuropathy or history of exposure to drugs or toxins known to cause peripheral neuropathy.</td>
</tr>
<tr>
<td>Laboratory evidence from blood, urine, or CSF examination of a potential etiology for the neuropathy other than CIDP.</td>
</tr>
<tr>
<td>Evidence on nerve biopsy for a potential etiology for neuropathy other than CIDP.</td>
</tr>
<tr>
<td>Electrodiagnostic features of neuromuscular transmission defect, myopathy, or anterior horn cell disease.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Diagnostic categories (must meet all mandatory exclusion criteria)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definite CIDP</td>
</tr>
<tr>
<td>Mandatory clinical features</td>
</tr>
<tr>
<td>All major laboratory features</td>
</tr>
<tr>
<td>Probable CIDP</td>
</tr>
<tr>
<td>Mandatory clinical features</td>
</tr>
<tr>
<td>2 of 3 major laboratory features</td>
</tr>
<tr>
<td>Possible CIDP</td>
</tr>
<tr>
<td>Mandatory clinical features</td>
</tr>
<tr>
<td>1 of 3 major laboratory features</td>
</tr>
</tbody>
</table>

Adapted from Refs. 5, 43, and 81.

CIDP with a benign monoclonal gammopathy generally does not reveal an underlying lymphoma, osteosclerotic myeloma, or another malignancy to account for the paraprotein. The treatment of these patients should be similar to those without paraproteins.

Pure sensory and axonal variants of CIDP have been reported and both apparently respond to immunosuppressive therapy (33,94–96). These patients do not meet the diagnostic criteria for CIDP, and the existence of these variants is somewhat controversial.

Patients with subacute weakness of 4 to 8 weeks, so-called subacute demyelinating polyneuropathy (97), have also been reported. Treatment can be the same as that used for CIDP, although it is interesting that three of the cases reported by Hughes et al. (97) had spontaneous recoveries, suggesting a similarity to GBS.

TABLE 13. CIDP with concurrent illness

| HIV infection |
| Monoclonal gammopathy |
| Chronic active hepatitis |
| Inflammatory bowel disease |
| Connective tissue disease |
| Bone marrow and organ transplants |
| Lymphoma |
| Hereditary neuropathy |
| Diabetes mellitus |
| Thyrotoxicosis |
| Nephrotic syndrome |
| CNS demyelination |

CNS, central nervous system.

TABLE 14. Therapeutic options in CIDP

| First line |
| Prednisone |
| ? IVlg |
| Second line |
| Plasmapheresis |
| IVlg |
| Azathioprine |
| Third line: |
| Cyclosporine |
| Cyclophosphamide |
| Experimental: |
| Interferon |

IVlg, intravenous immunoglobulin.
6 months, the prednisone dose can be slowly tapered by 5 mg every 2 to 3 weeks. Some patients can be tapered off completely, but relapses often occur. It is important for both the patient and physician to realize that CIDP is a chronic disorder and may require one or more years of immunosuppressive therapy.

PE was more effective than “sham” pheresis for CIDP in two important studies (99,100). PE is typically used if patients are severely weak or if they relapse on prednisone. Five to 10 treatments are usually performed over 1 to 4 weeks at the initiation of therapy. Unlike the situation in GBS, however, there is no benchmark goal of how much total fluid to remove. We generally do not routinely repeat PE at fixed intervals but instead use repeat courses of five or six PE treatments as needed if the patient deteriorates again. When we initiate PE in a patient who has worsened while on prednisone, we usually increase the steroid dose or add a second oral immunosuppressive agent; otherwise, the patient may relapse when the effect of PE has worn off, usually in 4 to 8 weeks.

IVIg was recently introduced for the treatment of CIDP. Although early studies showed variable results (102–104), two important recent studies convincingly showed that IVIg had an important role in the treatment of CIDP. Dyck et al. (105) compared PE with IVIg in 20 patients with CIDP and found that both therapies were equally effective. In the report by Hahn et al. (101), 30 patients received IVIg at doses of 2 g/kg over 5 days or an intravenous placebo in a randomized, double-blind, crossover study. Nineteen of 30 patients improved on IVIg, including 9 chronic progressive and 10 patients with relapsing CIDP, whereas all worsened on placebo alone. Similar improvement was seen both on neurologic disability scale scores and nerve conduction studies. Eight of nine patients with chronic progressive CIDP improved to normal function and maintained this level with the single 5-day course of IVIg; five were maintained on small doses of oral prednisone.

The patients studied by Dyck et al. (105) and Hahn et al. (101) were generally not new in onset, and many had already been tried on prednisone therapy. A randomized placebo-controlled study of IVIg in CIDP patients who never received prior immunosuppressive therapy was just completed in North America, and the data are currently being analyzed. This study was designed to determine if IVIg should be a first-line therapy in CIDP. It is currently difficult to convince third-party payers to cover IVIg in CIDP. Hopefully, this will be less of a problem as further evidence accumulates regarding the effectiveness of IVIg therapy in CIDP. After 6 months of IVIg therapy, we generally try to stop the IVIg or extend the treatments by 1 to 2 months. The optimal duration of treatment with IVIg in this disorder is not known. Some chronic progressive patients in the study by Hahn et al. (101) required only the induction therapy; however, most were also on prednisone (101).

In the single controlled study of azathioprine in CIDP, the drug was no more effective than placebo (106). However, it is still occasionally used as a second-line therapy in patients who relapse on prednisone therapy, especially if IVIg cannot be used. Cyclosporine (107,108) and, less often, cyclophosphamide are third-line oral therapies that can be tried. Several small reports described benefit of interferon-α (109,110) or interferon-β (111). A recent open-label study of interferon-α treatment in 16 patients followed for 6 weeks found improvement in 56% (112). Although encouraging, further studies involving placebo control, larger patient members, and larger follow-up are needed.

**Prognosis**

In our retrospective series, greater than 90% of patients with CIDP initially improved with immunosuppressive treatment; however, the relapse rate was high, approaching 50% (5). Only 30% of patients in this series achieved a complete remission off medication (5). Two patients (3.3%) died. It appears the longer patients are followed, the more likely they will relapse (5). In the series of Dyck et al. (4), 64% of patients were improved or in remission and able to return to work, 8% were ambulatory but unable to work, 11% were bedridden or wheelchair bound, and 11% died of the disease. Gorson et al. (113) found that, overall, 66% of their patients responded to prednisone, PE, or IVIg. These three retrospective series found no factors predictive of a poor response. Two recent prospective studies may provide more reliable numbers regarding how often patients respond to treatment. In the controlled trial of IVIg in CIDP patients performed by Hahn et al. (101), 63% (19/32) responded favorably. Patients with an acute relapse or with a disease duration of 1 year or less were more likely to respond. In a separate study by this group (100), 80% (12/15) of patients who received PE also responded.

Most patients with monoclonal proteins and CIDP have the same response to therapy as CIDP patients without paraproteins. Patients with IgM paraproteins, particularly those that are anti-MAG, may be more resistant to therapy (114–117). However, much of this data is based on studies of patients with monoclonal protein-associated polyneuropathies, not patients meeting the diagnostic criteria for CIDP. A retrospective review comparing CIDP patients with a paraprotein with those without found no difference between patients with IgM, IgG, or IgA gammapathies (118,119). Some authors advocate treating neuropathy patients with IgM paraproteins with chemotherapeutic agents such as chlorambucil or cyclophosphamide (120–122). IVIg appeared beneficial in two small open studies of neuropathy patients with IgM gammapathies (123,124), whereas a small controlled trial (117) found a much more modest response. A recent controlled study comparing IVIg and interferon-α treatment
in IgM gammopathy patients found little benefit from IVlg, whereas there was improvement in 80% of the interferon-treated group (125). There have been no prospective studies addressing treatment of CIDP with a monoclonal gammopathy of uncertain significance (MGUS); we currently treat them no differently from other CIDP patients.

REFERENCES


