Abstract The objective of this study was to assess the long-term course and treatment of chronic inflammatory demyelinating polyradiculoneuropathy (CIDP). We evaluated, according to a predefined protocol, a series of 60 CIDP patients who received a long-term course of steroids and immunosuppressants. Eighteen of them also had monoclonal gammopathy of undetermined significance (MGUS). Mean follow-up was 4.4 years and was similar for CIDP and CIDP-MGUS patients. At the end of the follow-up, improvement was ascertained in 60% of patients (69% CIDP, 39% CIDP-MGUS). Complete remission was achieved in 13%.

Out of 26 patients receiving steroids as a monotherapy, 19 improved (73%). The following variables were predictive of a better outcome: female gender, younger age at onset, relapsing-remitting course, and absence of axonal damage at neurophysiologic study. In the multivariate analysis, younger age at onset and demyelination without axonal damage still retained an independent positive value.

Key words Chronic inflammatory demyelinating polyradiculoneuropathy • CIDP • Dysimmune neuropathy • Steroids • Plasmapheresis • MGUS

Introduction Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is an immune-mediated disease [1]. Although steroids are an acknowledged treatment [2-4], their efficacy is limited and they can cause side effects in the long term. The effectiveness of immunosuppressant agents has not been definitively proved [5-9] and they also may cause serious side effects. Repeated courses of plasma exchange (PEX) or intravenous immunoglobulins (IVIG) are efficacious [10-14]. IVIG have few side effects; as for PEX, the major drawbacks include high costs and the necessity of patients' hospitalization. This is why steroids still have a significant role in the treatment of CIDP. Clinical studies aimed at assessing the long-term efficacy and tolerability of different therapeutical regimens are relatively rare and not conclusive [15-22]. Consequently, there is room for doubt regarding the best therapeutical approach to this disease.

Materials and methods Sixty consecutive patients who met the diagnostic criteria for probable or definite CIDP [23] were included in the study. Presence of monoclonal gammopathy of undetermined significance (MGUS) was not an exclusion criterion. All of the patients were evaluated in our hospital over a period of 11 years (1987-1997) according to a predefined protocol. At the time of diagnosis, all patients underwent: clinical evaluation, laboratory tests, and complete electrophysiologic and cerebrospinal fluid (CSF) examinations. In 16 patients diagnosis was confirmed by sural nerve biopsy.

Clinical evaluation Patient disability was assessed at baseline, after six and 12 months, and at the end of follow-up, according to a modified Rankin scale [11]. The modified Rankin scale scores were: 0 = asymptomatic;
Laboratory tests

All patients underwent a complete laboratory work-up to exclude other causes of neuropathy. Serum and urine immunofixation was performed. Anti-MAG and anti-GM1 antibodies were also determined. Patients with MGUS were submitted to skeletal X-ray examination, abdominal computed tomography (CT) and, if required, bone biopsy.

Electrophysiologic examination

All patients had needle electromyographic examination of the first dorsal interosseous muscle of the hand and of the anterior tibial muscle. Conduction studies were performed using standard techniques. Motor conduction of median, ulnar, peroneal and tibial nerves was assessed. For motor nerves, F response latencies, compound muscle action potential (CMAP) amplitudes and duration, conduction velocities, distal latencies, and the proximal/distal CMAP amplitude ratios were evaluated. Sensory nerve action potentials (SNAPs), and amplitude and conduction velocities (onset latencies) were recorded from the median or ulnar nerves and from the sural nerves. Forty-four patients had repeat electrophysiologic examinations.

Demyelination was defined according to the criteria depicted by the Ad Hoc Subcommitte [23]. Demyelination with secondary axonal involvement was defined by the presence of fibrillation potentials on needle electrode examination or of low compound muscle action potential amplitudes without significant temporal dispersion [24].

Treatment

Therapy was established according to the general principles of immune disease drug therapy. Prednisone (1-1.5 mg/kg day) was the first-line drug. Once sustained improvement had been achieved for at least 2-3 months, dosage was tapered by 10% every 3-5 weeks to the effective maintenance dose. Patients at increased risk of steroid side effects, such as men over 55 years or post-menopausal women, were given lower doses (≤ 50 mg/day). In these patients, immunosuppressive drugs (azathioprine (AZA), 1-3 mg/kg day; cyclophosphamide (CTX), 1-1.5 mg/kg day) were added to steroids from the beginning of therapy. Immunosuppressants were also added to steroids if they were ineffective or caused relevant side effects. Thirteen patients received plasmapheresis (PEX) plus steroids from the beginning of the treatment. Three patients were also treated with IVIG. All patients receiving steroids also had calcium and either vitamin D or short repeated courses of sodium etidronate.

Clinical outcome

Disease course was defined as chronic progressive-monophasic, or relapsing-remitting according to Dyck et al. [1]. Clinical improvement or worsening was defined as a decrease or increase of at least one step on the Rankin scale persisting for at least six months, respectively.

Statistical analysis

Proportions were compared according to the chi-square or Fisher’s exact test. Continuous data were compared using the two-sample t test for parametric data, or Wilcoxon rank-sum statistics for non-parametric data. Logistic regression method was used to analyse categorical outcome variables. Statistical analyses were carried out using Stata Statistical Software, release 5.0.

Results

Forty-two patients had pure CIDP and 18 had CIDP associated with MGUS (CIDP-MGUS). Six CIDP-MGUS patients had IgM-κ gammopathy; three IgM-λ; four IgG-κ; three IgG-λ; one patient had both IgG-λ and IgM-κ gammopathy and another patient had both IgG-λ and IgG-κ.

Clinical features and disease course are summarized in Table 1. Age at onset had a bimodal distribution with a first peak at 20-25 years and a second at about 50 years. Disease onset occurred earlier in CIDP patients as compared to CIDP-MGUS (p = 0.001): in the latter group only three patients had disease onset before age 45 years. Clinical disability was mild (Rankin ≤ 2) in 67% of patients, moderate (Rankin = 3) in 25%, and severe (Rankin = 4) in 8%. There was no difference between CIDP and CIDP-MGUS patients regarding disability score and clinical signs at study entry.

Thirty patients (50%) had both motor and sensory involvement, 21 (35%) had predominant motor deficits, while nine (15%) had mainly sensory symptoms. Lower limbs were predominantly involved in 35 cases (58%), all limbs resulted similarly affected in 22 patients (37%), and upper limbs were mainly affected in 3 patients (5%). Five patients had also bulbar involvement. Disease course was monophasic in 29 patients, and relapsing-remitting in the remaining 31.

Anti-GM1 antibodies were detected in five patients (one improved). Anti-MAG antibodies were found in three cases (two had IgM-λ MGUS; the one who had IgM-κ gammopathy improved). CSF studies demonstrated increased protein concentration in 56 patients (93%). Oligoclonal bands in CSF were detected in 12 of 42 CIDP patients (28.6%), and in five of them the same pattern was found in the serum.

Electrophysiologic studies demonstrated signs of primary demyelination in 37 patients (62% of CIDP; and 61% of CIDP-MGUS) and demyelination associated with secondary axonal involvement in the remaining patients (Table 1).