Motor chronic inflammatory demyelinating polyneuropathy (CIDP) in 17 patients: Clinical characteristics, electrophysiological study, and response to treatment

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Running title: Motor CIDP in 17 patients

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Abstract :

Background and Aims: Motor chronic inflammatory demyelinating polyneuropathy (CIDP) is a rare poorly described subtype of CIDP. We aimed to study the clinical and electrophysiological characteristics and as response to treatment.

Methods: From a prospective database of CIDP patients, we included patients with definite or probable CIDP with motor signs and without sensory signs/symptoms at diagnosis. Patients were considered to have pure motor CIDP (PM-CIDP) if sensory conductions were normal or to have motor predominant CIDP (MPred-CIDP) if ≥2 sensory nerve action potential amplitude were abnormal.

Results: Among the 700 patients with CIDP, 17 (2%) were included (PM-CIDP n=7, MPred-CIDP n=10); 71% were male, median age at onset was 48 years (range:13-76 years), 47% had an associated inflammatory or infectious disease or neoplasia. At the more severe disease stage, 94% of patients had upper and lower limb weakness, with distal and proximal weakness in 4 limbs for 56% of them. Three-quarters (75%) responded to intravenous immunoglobulins (IVIg) and 4/5 patients to corticosteroids including 3/3 patients with MPred-CIDP. The most frequent conduction abnormalities were conduction blocks (CB, 82%) and F-wave abnormalities (88%). During follow-up, 4/10 MPred-CIDP patients developed mild sensory symptoms; none with PM-CIDP did so. Patients with PM-CIDP had poorer outcome (median ONLS:4, range:2-5) compared to MPred-CIDP (2, range:0-4;p=0.03) at last follow-up.

Conclusions: The present study found a progressive clinical course in the majority of patients with motor CIDP as well as frequent associated diseases, CB, and F-wave abnormalities. Corticosteroids might be considered as a therapeutic option in resistant IVIg patients with MPred-CIDP.

Key words: motor CIDP; pure motor CIDP; motor predominant CIDP; corticosteroid; cancer

Introduction

Chronic inflammatory demyelinating polyneuropathy (CIDP) is a treatable autoimmune acquired neuropathy with heterogeneous presentation. [1,2] Motor CIDP is one form of atypical CIDP which is described by the joint task force of the EFNS/PNS. [3] However, the clinical characteristics, electrophysiological features, and response to treatment of patients with motor CIDP have been poorly reported given the rarity of this CIDP subtype (only 1-10% of patients with CIDP). [4-12] An early age at onset is probably more frequent compared to other types of CIDP [5,9] and clinical course can be progressive or relapsing-remitting. [5,7,9,10] Electrophysiological studies show frequent conduction blocks (CB). [5,7,9,10] Finally, intravenous immunoglobulins (IVIg) treatment should be the first choice and corticosteroids have been shown to potentially lead to deterioration.[3,5,9,10] However, the definition of motor CIDP is not precise according to the EFNS/PNS 2010 guidelines and it remains unclear whether diagnosis of motor CIDP should only be based on clinical findings or whether the presence of normal sensory nerve conduction is required. [11]

The aims of the present study were therefore to describe the clinical and electrophysiological characteristics, as well as the response to treatment of a cohort of patients with motor CIDP.

Materials and methods

Patients

Data were extracted from a prospective single center (Pitié-Salpêtrière hospital, Paris, France) database which includes all consecutive patients with CIDP between January 1st 2008 and October 31st 2018. Detailed material and methods have been reported elsewhere. [13]

Patients with definite or probable CIDP according to the EFNS/PNS 2010 guidelines, [3] having a motor CIDP with motor signs (weakness, cramps, fasciculations, motor cranial nerve palsy), in a symmetric or asymmetric polyneuropathic distribution [7] with no sensory symptoms or signs at diagnosis (including normal light touch, pinprick, temperature, vibratory sensations, normal gait, and negative Romberg sign), were included. Patients with focal (involvement of the brachial or lumbosacral plexus or of one or more peripheral nerves in one upper or lower limb), multifocal acquired demyelinating sensory and motor neuropathy (MADSAM)/Lewis-Sumner syndrome, [3] or multifocal motor neuropathy (MMN) [14] were excluded.

Patients with motor CIDP were classified into 2 groups according to sensory explorations upon electrodiagnostic examination (EDX): patients with normal sensory conduction studies were classified as having pure motor CIDP (PM-CIDP). Patients with at least 2 sensory nerves with sensory nerve action potential (SNAP) amplitude under the lower limit of normal value of the EDX laboratory were classified as having motor predominant CIDP (MPred-CIDP).

Data collection

Disease course and response to treatment as well as laboratory workup and nerve biopsy were retrospectively collected from medical files. Antiganglioside antibodies including anti-GM1, -GM2, -GM3, -GD1a, -GD1b, -GT1b and GQ1b antibodies of both IgM and IgG isotypes were detected by using immunodot assay.

Asymmetrical weakness was defined by a difference of 1 medical research council (MRC) grade if strength was MRC > 3, and 2 MRC grades if strength was MRC ≤ 3, as is used in MMN. [14] The course of the disease was classified as either progressive or relapsing-remitting (defined as 2 episodes with intervening remission and relapse unrelated to a change in treatment). A positive response to treatment was defined as an improvement by at least 2 MRC grades in any muscle and/or by 1 point improvement in the overall neuropathy limitations scale (ONLS). A treatment-dependent patient was one who needed regular administration of his/her treatment to maintain its benefit and to avoid the risk of rapid relapse.

Neurophysiological investigations

EDX was performed - as previously described - [15] by an experienced electromyographer using a Viking Nicolet electromyograph. Demyelinating features (including definite and probable partial motor conduction block, CB) on motor nerves were defined according to the EFNS/PNS 2010 guidelines. [3] The first EDX performed at the Pitié-Salpêtrière Hospital for each patient was considered in the present study. An inversed sensory ratio was defined by a median/sural or ulnar/sural or radial/sural SNAP amplitude ratio <1, without median or ulnar nerves with entrapment. Somatosensory evoked potentials (SSEP) were performed for certain patients.

Proximal conduction was suggestive of demyelination if it showed abnormal conduction in the N8-N22 segment or N18-N22 conduction time. [16]

Statistical analyses

Continuous variables were compared using Student's test or Wilcoxon rank sum test, and discrete variables using Chi-squared test or Fisher's exact test. The level of significance was set at $p<0.05$. All calculations were performed using the statistical software R* (R core team, 2017).

Ethics statement

Clinical data were obtained in accordance with ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. All patients were informed and gave their consent. For this retrospective study, no authorization from an ethics committee was required.

Results

Among 700 patients with CIDP in the database, 17 (prevalence of 2%) were included in the present study: 7 had PM-CIDP and 10 MPred-CIDP. All but 1 patient were classified as having definite CIDP (Patient #3 with PM-CIDP had probable CIDP; Table 1).

Clinical features

There were 5 women and 12 men (Table 1). The median age at onset was 48 years (range: 13-76 years), 6/17 patients (35%) were less than 30 years old at onset. In most patients, onset was chronic (12/16 patients [75%]). The initial symptom was lower limb (LL) weakness in 10/16 patients (59%, Table 1). At the more severe disease stage, the majority of patients had 4-limb weakness (15/16 patients [94%], Table 1). The median ONLS at the more severe disease stage was 4 points (range: 3-10) and 3 patients used a single crutch (patient #2, #12, and #13). Median ONLS at last follow-up was 3 (range: 0-5); 4 patients had a ONLS score of 0 or 1. An associated disease was found in 8/17 patients (47%), including 4/17 patients (24%) presenting with cancer (Table 1). In 2 patients (patient #7 and #8), cancer was diagnosed during CIDP investigations (B-cell lymphoma, and epidermoid carcinoma of lung) and in 2 others, it was diagnosed 1 year (patient #11 with palate cancer) and 11 years (patient #5 with generalized cancer) after CIDP diagnosis.

Disease course and response to treatment

The median follow-up duration was 4 years (47 months, range: 1-153 months). During follow-up, 2 patients (patients #5 and #11) died due to cancer complications and 1 was lost to follow-up (patient #8). Clinical course was progressive in most patients (12/17 patients; 71%) and relapsing-remitting in 5/17 patients (29%, Table 2). Spontaneous improvement occurred at the

beginning of disease in 3/17 patients (18%; patient #6, #14 and #17). Among those concerned, 12/16 patients (75%) had a positive response to IVIg, 4/5 (80%) to corticosteroids (including 3/3 with MPred-CIDP and 1/2 with PM-CIDP; the patient with PM-CIDP who did not respond to corticosteroids did not show clinical deterioration), and 2/5 (40%) to plasma exchange (PE; patient #7 had a lymphoma treatment (splenectomy) associated with PE, Table 2). Only 4/13 patients (31%) experienced successful treatment discontinuation with a median duration of 12 months (range: 7-42, Table 2).

Paraclinical exams

Neurophysiological investigations

In 11/17 patients (65%), EDX was performed before the onset of immunomodulatory treatment. Among all 17 patients, 15 (88%) had definite CIDP (Table 3). The median interval between first clinical signs and EDX was 24 months (range: 3-72 months). The median number of motor nerves tested was 8 (range: 5-8) and sensory nerves tested was 8 (range: 5-10).

The 2 most frequent demyelinating features on motor nerves were F wave abnormalities (prolongation or absence) and CB; F wave abnormalities were found in 15/17 patients (88%) representing 53/100 nerves (53%) and multifocal CB in 14/17 patients (82%) representing 58/95 nerves (61%, Table 3). The median number of CB per patient was 4 (range: 0-8). In total, 34/64 CB were definite (53%) and 30/64 were probable (47%). Among the 64 CB, 26 (41%) were located in the ulnar nerve (Table 3). In the 37 nerves without CB, 21 had abnormal F waves (57%). Prolonged DL and reduced CV were rare and found in 3/17 (18%) and 6/17 (35%) patients respectively (Table 3, mostly on nerves with CB).

The median number of reduced distal compound muscle action potential (CMAP) amplitude per patient was 4 (range: 0-8). Fibrillation potentials or positive sharp waves at rest were found in 11/17 patients (65%). A total of 5/17 (29%) patients had fasciculations in 1 muscle, and 1 patient (patient #11) had fasciculations in 4 muscles (Table 3).

Among patients with MPred-CIDP, the median number of abnormal SNAP amplitude was 4.5 (range: 2-9), 9/10 patients (90%) had an inversed sensory ratio.

Five patients (all were MPred-CIDP) had data for SSEP and 3/5 (60%) had proximal conduction abnormality suggestive of demyelination.

Other paraclinical exams

Two patients (patients #11 and #14,) had IgM anti-GM1 antibodies (patient #11 had associated anti-GQ1b antibodies) and 1 patient had IgM anti-GM2 antibodies (patients # 4, Table 1). The mean CSF protein concentration was 73 mg/dl (range: 0.36-150 mg/dl) and CSF protein was mildly elevated (>50 mg/dl) in 11/14 patients (79%; Table 1). Nerve biopsy was performed in 3 patients (all had MPred-CIDP) and found absence of inflammatory infiltrate in 3 patients and evidence of demyelination or remyelination in 2 patients.

Comparison of PM-CIDP and MPred-CIDP patients

During follow-up, 4/10 (40%) patients with MPred-CIDP developed mild sensory symptoms, none of those with PM-CIDP did so ($p < 0.001$, Table 4). These sensory symptoms consisted in tingling in extremities which appeareared with a median delay of 18 months (range: 8-216 months), but none had gait or limb ataxia nor hypoesthesia (patients #14 and #16 : tingling in 4 extremities, patients #15 and #17: tingling limited to hands). Median follow-up duration was similar for patients with PM-CIDP (47 months, range: 1-81) and patients with MPred-CIDP (44

months, range: 3-153, Table 4). The median follow-up of the 4 patients with mild sensory symptoms was 57 months (range: 39-153). The median ONLS at last follow-up in patients with PM-CIDP was 4 (range: 2-5) compared to 2 (range: 0-4) for those with MPred-CIDP ($p = 0.03$); 4 patients with MPred-CIDP had an ONLS of 0 or 1 while none of those with PM-CIDP did so (Table 4). Concerning the response to treatments, response to IVIg was not significantly different between PM-CIDP and MPred-CIDP patients ($p=1$, Table 4). Among the patients treated by corticosteroids, 1/2 PM-CIDP patients responded compared to 3/3 MPred-CIDP patients ($p=0.4$; Table 4).

Discussion

The present study shows that motor forms of CIDP can be considered as variants of CIDP that present with specific clinical, electrophysiological, and response to treatment courses. More precisely, the present study confirms that motor CIDP seem to be (i) rare; [4-12] (ii) tend to occur more often in males; [5,8,10] (iii) at a young age at onset; [5,9] (iv) present with frequent and multifocal CB [5,7,9,10] and F wave abnormalities [5,7,10] on EDX; and (v) respond well to IVIg. [5,7, 9,10]

Other potential features of motor CIDP are highlighted herein. First, a high proportion of patients (almost half of them) presented with associated diseases. Three patients were diagnosed with cancer, either during CIDP investigations or in the first year of evolution. It is difficult to conclude on a possible link between cancer and motor CIDP given that tumors were diverse and not necessarily known to be associated with paraneoplastic neurologic disorders. Demyelinating neuropathy with predominantly motor form has been reported in association with lymphoma. [17] Melanoma, lung or esophageal cancer, have also been described in motor CIDP. [18,19] In a previous cohort of CIDP patients (not only motor CIDP), our group reported a concurrent illness in only one quarter of patients. [13] Therefore, thorough investigations aiming at identifying diseases associated with motor CIDP are required. Second, in agreement with two previous studies, [5,7] a majority of patients herein experienced a progressive clinical course. Conversely, all patients from the studies by Kimura *et al.* [10] and Sabatelli *et al.* [9] presented with a relapsing-remitting course. Finally, despite the use of various immunomodulatory treatments, the majority of patients experienced a poor clinical outcome: only a small quarter of patient had an acceptable ONLS score at 0 or 1 at the end of follow-up. This is discordant with the results from Kimura *et al.* who reported that patients with motor CIDP experienced very good outcome, better than patients with other CIDP types. [10]

From an electrophysiological point of view, the finding of recurrent and multifocal CB in almost all nerves in which abnormal CV and DL were found indicates that CB are the cause of these demyelinating parameters and therefore should not be considered alone. Furthermore, in this context and with an objective of diagnosis, it is of note that the ulnar nerve was the most affected by CB, but also that CB can be present only in proximal segments. Conversely to CV and DL, F wave abnormalities were found both in nerves with and without CB, which should also be kept in mind during diagnostic workup.

No consensual definition is available concerning the diagnosis of pure motor CIDP. The EFNS/PNS guidelines, which provide a more precise definition of motor CIDP, are currently under review. In the present study a clinical definition of motor CIDP, at diagnosis, was used and patients were included independently of sensory conduction abnormality upon EDX. Thus, 2 groups were identified herein, patients without sensitive nerve abnormalities (PM-CIDP) and those with (MPred-CIDP), as assessed by EDX. There was no significant difference in terms of clinical and paraclinical features between the 2 groups, except for outcome (patients with PM-CIDP had poorer outcome), and the development of sensory symptoms during follow-up (all patients who developed subtle sensory signs had MPred-CIDP). Some of the MPred-CIDP patients who developed mild sensory symptoms did not however develop ataxia or hypoesthesia as in common CIDP, and remained motor predominant. It is possible that these patients have an intermediate and milder form, which lies on the spectrum between the motor and typical forms. Donnedu *et al*. had previously reported the possibility that atypical CIDP, including motor CIDP, evolved towards typical CIDP. [7] The higher proportion of patients (more than half of patients) moving towards a typical form of CIDP observed by the authors could be explained in part by the longer median follow-up (6 years as opposed to 4 years herein).[7] Taken together, for a patient

with a motor form, the existence of a sensory involvement upon EDX might be a predictive factor for moving towards a typical CIDP. In a similar way, patients with other atypical CIDP forms (pure sensory CIDP, MADSAM/Lewis-Sumner, distal acquired demyelinating symmetric neuropathy [DADS]*)* can evolve into typical CIDP. [7,15,20]

Finally, pure motor CIDP has been frequently reported as a steroid unresponsive pathology. [5,9,10,21] In the present study however, the majority of patients who underwent corticosteroid treatment showed improvements, but these concerned mainly patients with MPred-CIDP group. This result is in line with the study by Doneddu *et al.* which reported a beneficial effect of corticosteroids in 3/7 patients, but exclusively in patients with MPred-CIDP. [7] Using these recent data, corticosteroids might be considered as a therapeutic option in resistant IVIg motor CIDP patients, at least for patients with abnormal sensory conduction. More data are needed to rule on the efficiency of corticosteroid in PM-CIDP patients.

The current body of data indicates that 2 main alternative diagnoses of neuropathy could be considered in the context of motor deficits: MMN and motor neuron disease. Motor CIDP and MMN share several features: pure motor involvement, young age at onset, good response to IVIg therapy, possible antiganglioside antibodies, and multiple CB on EDX. However, they differ on 3 major aspects: motor CIDP is associated with diffuse weakness, more diffuse electrophysiological damage, and a possible improvement using corticosteroids. However, some MMN patients may develop a more diffuse distal and proximal weakness later in the disease course indicating that a continuum may exist between MMN and motor CIDP. The association of pure motor deficit, amyotrophy, and sometimes diffuse cramps and fasciculation (as in patient #11), suggests motor neuron disease. Motor neuron disease and motor CIDP can share common

EDX abnormalities, for instance, reduced distal CMAP, fibrillation, fasciculations, and CB; the latter are reported transitory in patients with rapidly progressive motor neuron disease. [22-24]

The present study has several limitations inherent to its retrospective observational design and the fact that it is based on a small number of patients because of the rarity of the disease. Furthermore, due to our expert center status, the first EDX was performed after immunomodulatory treatment initiation in a third of patients which could affect results. Finally, after initial investigations and treatment introduction, some patients were redirected to their local center which explains a shorter follow-up period.

To conclude, beyond the previously reported features of motor CIDP including its low prevalence, good response to IVIg, and frequent CB and F wave abnormalities upon EDX, the present study found a progressive clinical course in the majority of patients and frequent associated diseases. In contrast to MPred-CIDP patients, PM-CIDP patients seem to have poorer outcome and did not develop sensory symptoms during follow-up. Corticosteroids might be considered as a therapeutic option in resistant IVIg patients with MPred-CIDP but more data are needed to rule on the efficiency of corticosteroids in PM-CIDP patients.

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Reference

1. Vallat J-M, Sommer C, Magy L. Chronic inflammatory demyelinating polyradiculoneuropathy: diagnostic and therapeutic challenges for a treatable condition. The Lancet Neurology. 2010 Apr;9(4):402–12.

2. Rabin M, Mutlu G, Stojkovic T et al. Chronic inflammatory demyelinating polyradiculoneuropathy: search for factors associated with treatment dependence or successful withdrawal. Journal of Neurology, Neurosurgery & Psychiatry. 2014 Aug 1;85(8):901–6.

3. Van den Bergh PYK, Hadden RDM, Bouche P, et al. European Federation of Neurological Societies/Peripheral Nerve Society Guideline on management of chronic inflammatory demyelinating polyradiculoneuropathy: Report of a joint task force of the European Federation of Neurological Societies and the Peripher: EFNS/PNS CIDP guideline - first revision. European Journal of Neurology. 2010 Mar;17(3):356–63.

4. Gorson KC, Allam G, Ropper AH. Chronic inflammatory demyelinating polyneuropathy: clinical features and response to treatment in 67 consecutive patients with and without a monoclonal gammopathy. Neurology. 1997 Feb;48(2):321–8.

5. Busby M, Donaghy M. Chronic dysimmune neuropathy. Journal of Neurology. 2003 Jun 1;250(6):714–24.

6. Mahdi-Rogers M, Hughes RAC. Epidemiology of chronic inflammatory neuropathies in southeast England. European Journal of Neurology. 2014 Jan;21(1):28–33.

7. Doneddu PE, Cocito D, Manganelli F, et al. Atypical CIDP: diagnostic criteria,

progression and treatment response. Data from the Italian CIDP Database. Journal of Neurology, Neurosurgery & Psychiatry. 2019 Feb;90(2):125–32.

8. Ikeda S, Koike H, Nishi R et al. Clinicopathological characteristics of subtypes of chronic inflammatory demyelinating polyradiculoneuropathy. J Neurol Neurosurg Psychiatry. 2019 Jun 21;

9. Sabatelli M, Madia F, Mignogna T, Lippi G, Quaranta L, Tonali P. Pure motor chronic inflammatory demyelinating polyneuropathy. J Neurol. 2001 Sep;248(9):772–7.

10. Kimura A, Sakurai T, Koumura A et al. Motor-dominant chronic inflammatory demyelinating polyneuropathy. Journal of Neurology. 2010 Apr;257(4):621–9.

11. Nobile-Orazio E. Chronic inflammatory demyelinating polyradiculoneuropathy and variants: where we are and where we should go. J Peripher Nerv Syst. 2014 Mar;19(1):2–13.

12. Querol L, Rojas-Garcia R, Casasnovas C, et al. Long-term outcome in chronic inflammatory demyelinating polyneuropathy patients treated with intravenous immunoglobulin: A retrospective study: Long-Term Effectiveness of IVIg in CIDP. Muscle & Nerve. 2013 Dec;48(6):870–6

13. Viala K, Maisonobe T, Stojkovic T et al. A current view of the diagnosis, clinical variants, response to treatment and prognosis of chronic inflammatory demyelinating polyradiculoneuropathy. Journal of the Peripheral Nervous System. 2010 Mar;15(1):50–6.

14. Joint Task Force of the EFNS and the PNS. European Federation of Neurological

Societies/Peripheral Nerve Society Guideline on management of multifocal motor neuropathy. Report of a Joint Task Force of the European Federation of Neurological Societies and the Peripheral Nerve Society - first revis. Journal of the Peripheral Nervous System. 2010 Dec;15(4):295–301.

15. Viala K. Follow-up study and response to treatment in 23 patients with Lewis-Sumner syndrome. Brain. 2004 Aug 2;127(9):2010–7.

16. Koutlidis RM, Ayrignac X, Pradat P-F et al. Segmental somatosensory-evoked potentials as a diagnostic tool in chronic inflammatory demyelinating polyneuropathies, and other sensory neuropathies. Neurophysiol Clin. 2014 Sep;44(3):267–80.

17. Viala K, Behin A, Maisonobe T, et al. Neuropathy in lymphoma: a relationship between the pattern of neuropathy, type of lymphoma and prognosis? Journal of Neurology, Neurosurgery & Psychiatry. 2008 Jul 1;79(7):778–82.

18. Rajabally YA, Attarian S. Chronic inflammatory demyelinating polyneuropathy and malignancy: A systematic review: CIDP and Malignancy: a Review. Muscle & Nerve. 2018 Jun;57(6):875–83.

19. Mostoufizadeh S, Souri M, de Seze J. A Case of Paraneoplastic Demyelinating Motor Polyneuropathy. Case Reports in Neurology. 2012;4(1):71–6.

20. van Dijk GW, Notermans NC, Franssen H, Wokke JH. Development of weakness in patients with chronic inflammatory demyelinating polyneuropathy and only sensory symptoms at presentation: a long-term follow-up study. J Neurol. 1999 Dec;246(12):1134–9.

21. Molenaar DS, van Doorn PA, Vermeulen M. Pulsed high dose dexamethasone treatment in chronic inflammatory demyelinating polyneuropathy: a pilot study. Journal of Neurology, Neurosurgery & Psychiatry. 1997 Apr 1;62(4):388–90.

22. Echaniz-Laguna A, Degos B, Mohr M, Kessler R, Urban-Kraemer E, Tranchant C. A study of three patients with amyotrophic lateral sclerosis and a polyneuropathy resembling CIDP. Muscle & Nerve. 2006 Mar;33(3):356–62.

23. Rajabally YA, Jacob S. Chronic inflammatory demyelinating polyneuropathy–like disorder associated with amyotrophic lateral sclerosis. Muscle & Nerve. 2008 Jul;38(1):855–60.

24. Ahdab R, Créange A, Saint-Val C, Farhat W-H, Lefaucheur J-P. Rapidly progressive amyotrophic lateral sclerosis initially masquerading as a demyelinating neuropathy. Neurophysiologie Clinique/Clinical Neurophysiology. 2013 Jun;43(3):181–7.

Tables

Table 1: Clinical and laboratory characteristics

Patient	Age at onset (years)/ sex	Clinical diagnostic criteria (EFNS/PNS 2010)	Category (PM/MPred-CIDP)	Onset	Localization of initial symptom	UL or LL involve-ment	P or/and D weakness	Cranial nerve palsy	Diffuse areflexia	Sensory symptoms during disease course (months, after onset)	ONLS at the more severe disease stage	ONLS at last follow-up	Anti-ganglioside antibodies	CSF protein level (g/L)	Associated diseases
1	44/F	Definite	PM-CIDP	Chronic	r LL	a UL+LL	D	-	+	-	4	4	-	1.5	-
2	23/M	Definite	PM-CIDP	Subacute	b LL	UL+LL	P+D	VII*, XII	-	-	10	5	-	0.52	Ileitis
3	30/F	Probable	PM-CIDP	Chronic	b LL	UL+LL	P+D	-	+	-	5	2	-	0.97	Inflammatory bowel disease
4	59/F	Definite	PM-CIDP	Chronic	b LL	UL+LL	P+D	-	-	-	4	4	GM2	0.67	-
5	66/M	Definite	PM-CIDP	NA	NA	NA	NA	-	+	-	3	2**	NP	1	Generalized cancer
6	40/M	Definite	PM-CIDP	Subacute	l LL	a UL+LL	D in UL P+D in LL	-	-	-	5	4	-	0.36	-
7	62/F	Definite	PM-CIDP	Chronic	b UL	a UL+LL	P+D in UL P in LL	-	-	-	5	5	-	0.61	B-cell lymphoma
8	58/M	Definite	MPred-CIDP	Chronic	l LL	a UL+LL	D		+	-	4	4	-	1.2	Epidermoid Carcinoma of lung
9	69/M	Definite	MPred-CIDP	Chronic	b UL	UL+LL	P+D	-	+	-	5	1	-	0.64	-
10	13/M	Definite	MPred-CIDP	Chronic	l UL	a UL	P+D	-	+	-	3	0	-	NP	-
11	51/M	Definite	MPred-CIDP	Chronic	Diffuse (cramp, fasciculation)	UL+LL	P+D	-	+	-	3	3**	GM1, GQ1B	0.87	Palate cancer
12	76/M	Definite	MPred-CIDP	Chronic	b LL	UL + LL	D in UL	-	+	-	3	2	NP	0.55	-
13	63/M	Definite	MPred-CIDP	Acute	b LL+ b UL	UL + LL	P+D	-	-	-	5	0	-	0.51	-
14	25/M	Definite	MPred-CIDP	Chronic	b LL	a UL+LL	P+D	VI *	-	+ (NA)	7	4	GM1	0.45	Atypical mycobacteria, HIV
15	48/M	Definite	MPred-CIDP	Chronic	b LL	UL+LL	P+D	-	-	+ (216)	4	2	-	0.4	-
16	28/F	Definite	MPred-CIDP	Subacute	b LL	UL+LL	P+D	-	+	+ (18)	4	3	-	NP	Sjögren, HCV, SCD
17	26/M	Definite	MPred-CIDP	Chronic	b UL (Tremor)	UL+LL	P+D in UL D in LL	-	-	+ (8)	4	0	-	NP	-

a: asymmetrical, b: bilateral, CIDP: chronic inflammatory demyelinating polyneuropathy, CSF: Cerebrospinal fluid, D: distal, F: female, HCV: Hepatitis C virus, HIV: Human immunodeficiency virus, l: left, LL: lower limbs, M: male, MPred-CIDP: motor predominant CIDP, NA: not available, NP: not performed, ONLS: Overall Neuropathy Limitations Scale, P: proximal, PM-CIDP: pure motor CIDP, r: right, SCD: Sickle cell disease, UL: upper limbs, *: bilateral, +: present, -: absent, **: at last follow-up before the death

Table 2: Disease course and response to treatment

Patient	Category (PM/MPred-CIDP)	Duration of follow-up (months)	Disease course	Response to IVIg	Response to CS	Response to PE	Other IS treatments	Successful discontinuation of IVIg, CS, or PE without relapse (months #)	Current therapy
1	PM-CIDP	81	Progressive	+	NT	-	MM	-	IVIg+MM
2	PM-CIDP	56	Progressive	+	-	NT	MM	+ (42)	0
3	PM-CIDP	12	Progressive	+	NT	NT	NT	-	IVIg
4	PM-CIDP	1	Progressive	+	NT	NT	NT	-	IVIg
5	PM-CIDP	47	Progressive	-	+	+	Az	-	PE*
6	PM-CIDP	60	RR	+	NT	NT	NT	-	IVIg
7	PM-CIDP	16	Progressive	-	NT	+	NT	NT	PE
8	MPred-CIDP	3	Progressive	NT	NT	NT	NT	NT	NT
9	MPred-CIDP	36	Progressive	+	+	-	MM	+ (12)	MM
10	MPred-CIDP	56	Progressive	-	+	-	NT	-	CS+IVIg
11	MPred-CIDP	120	Progressive	+	NT	NT	NT	-	IVIg*
12	MPred-CIDP	4	Progressive	+	NT	NT	NT	NT	IVIg
13	MPred-CIDP	15	Progressive	+	NT	NT	NT	NT	IVIg
14	MPred-CIDP	153	RR	-	+	NT	NT	-	CS
15	MPred-CIDP	49	RR	+	NT	NT	NT	-	IVIg
16	MPred-CIDP	39	RR	+	NT	NT	Rituximab	+ (7)	0
17	MPred-CIDP	65	RR	+	NT	NT	NT	+ (12)	0

Az: azathioprine, CIDP: chronic inflammatory demyelinating polyneuropathy, CS: corticosteroids, IS: immunosuppressive, IVIg: intravenous immunoglobulins, MM: mycophenolate mofetil, MPred-CIDP: motor predominant CIDP, NT: not tried, PE: plasma exchange, PM-CIDP: pure motor CIDP, RR: relapsing-remitting, +: yes, -: no, *: last follow up before death, #: months since stopping treatment without relapse

Table 3: Electroneuromyography data

Patient	Category (PM/MPred-CIDP)	Electro-diagnostic criteria (*, in months)	Demyelinating features on motor nerves				Topography of CB				Number of motor nerve with abnormal CMAP amplitude	Number of sensory nerves with abnormal SNAP amplitude	Fibrillation or PSW at rest	Fasciculation at rest
			Prolonged DL	Reduced CV	Abnormal F waves	Number of CB	Median	Ulnar	Common fibular	Tibial				
1	PM-CIDP	Definite (48)	+	-	-	5	2 (D)	3 (2D, I)			7	0	+	-
2	PM-CIDP	Definite (7)	-	-	+	0					8	0	+	-
3	PM-CIDP	Possible (3)	-	-	+	3	1 (D)		2 (D)		4	0	+	-
4	PM-CIDP	Definite (5)	+	-	+	8	1 (D)	3 (2D, I)	2 (D)	2 (D)	8	0	+	-
5	PM-CIDP	Definite (72)	-	-	+	0					0	0	-	-
6	PM-CIDP	Definite (60)	-	+	+	3		2 (I)	1 (D)		2	0	+	+
7	PM-CIDP	Definite (36)	-	-	+	3		2 (D)	1 (D)		4	0	+	-
8	MPred-CIDP	Definite (3)	-	+	+	4	2 (D)	2 (D)			6	9	+	+
9	MPred-CIDP	Definite (36)	-	+	+	0					3	6	-	-
10	MPred-CIDP	Definite (72)	-	+	+	6	4 (2D, 2I)	2 (D)			4	2	-	+
11	MPred-CIDP	Definite (4)	-	-	+	7	2 (I, P)	3 (I, 2P)	2 (D)		4	5	+	+
12	MPred-CIDP	Definite (12)	+	-	+	4	1 (D)	2 (D)	1 (D)		8	7	+	-
13	MPred-CIDP	Definite (6)	-	+	+	6	2 (D)	3 (D, 2P)	1 (D)		2	4	-	-
14	MPred-CIDP	Probable (24)	-	-	-	3		1 (I)	2 (D)		1	3	-	-
15	MPred-CIDP	Definite (30)	-	-	+	4			2 (D)	2 (D)	3	2	+	+
16	MPred-CIDP	Definite (24)	-	-	+	1	1 (D)				8	5	+	-
17	MPred-CIDP	Definite (14)	-	+	+	7	2 (D)	3 (2D, I)	2 (D)		2	3	-	-

CB: conduction block, CIDP: chronic inflammatory demyelinating polyneuropathy, CMAP: compound muscle action potential, CV: conduction velocity, D: distal (forearm: below elbow-wrist, or leg: below the fibular head-feet for fibular common nerve or under the knee-feet for tibial nerve), DL: distal latency, I: intermediate (arm: axillary-above the elbow), MPred-CIDP: motor predominant CIDP, PM-CIDP: pure motor CIDP, P: Proximal (Erb'point-axillary), PSW: Positive sharp wave, SNAP: sensory nerve action potential, *: delay between first clinical signs and EDX, +: present, - : absent

Table 4: Characteristics of patients with PM-CIDP and MPred-CIDP

	PM-CIDP	MPred-CIDP	p value
Sex male/female	3/4	9/1	0.1
Age at onset, years, median (range)	44 (23-66)	49.5 (13-76)	1.0
Progressive onset	4 (67%)	8 (80%)	0.6
Development of sensory symptoms	0 (0%)	4 (40%)	0.1
Disease course and response to treatment			
Duration of follow-up, months, median (range)	47 (1-81)	44 (3-153)	0.7
RR disease course	1 (14%)	4 (40%)	0.3
Response to IVIg	5/7 (71%)	7/9 (78%)	1
Response to CS	1/2 (50%)	3/3 (100%)	0.4
ONLS at the more severe disease stage (range)	5 (3-10)	4 (3-7)	0.29
ONLS at last follow-up (range)	4 (2-5)	2 (0-4)	0.03*
Electroneuromyography			
Abnormal F waves	6 (86%)	9 (90%)	1.0
Number of CB, median (range)	3 (3-8)	4 (0-7)	0.3
Prolonged DL	2 (29%)	1 (10%)	0.54
Reduced CV	1 (14%)	5 (50%)	0.3
Abnormal CMAP amplitude, median (range)	4 (0-8)	3.5 (1-8)	0.6
Abnormal SNAP amplitude, median (range)	0 (0-0)	4.5 (2-9)	< 0.001*
Fibrillation or positive sharp wave at rest	6 (86%)	5 (50%)	0.3
Fasciculation at rest	1 (14%)	4 (40%)	0.3

CB: conduction block, CIDP: chronic inflammatory demyelinating polyneuropathy, CMAP: compound muscle action potential, CS: corticosteroids, CV: conduction velocity, DL: distal latency, IVIg: intravenous immunoglobulin, MPred-CIDP: motor predominant CIDP, ONLS: overall neuropathy limitations scale, PM-CIDP: pure motor CIDP, RR: relapsing-remitting, SNAP: sensory nerve action potential, *: $p<0.05$