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Clinical characteristics in a cohort of patients with chronic inflammatory demyelinating polyneuropathy: a retrospective study

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Abstract

Objective: *The objective of the study is to evaluate the chronic inflammatory demyelinating polyneuropathy (CIDP) clinical spectrum in a cohort of Mexican patients who benefit from social security.* **Methods:** *A retrospective study of CIDP patients from 2010 to 2021. We documented neurological deficits, electrophysiological and laboratory parameters, diagnostic characteristics, disease activity, and clinical outcomes.* **Results:** *36 cases met the criteria of the EAN/PNS 2021, the mean age was 58.25 ± 10.10 years, 50% were women, and 69.4% used intravenous immunoglobulin (IVIG). Concerning functional status, 63.9% had an independent walk and 86.1% had mild weakness in manual skills. The analysis of functional status showed better results in the IVIG treatment group.* **Conclusions:** *Similar to previous literature reports, 50% of our patients had stable active disease. Considering the heterogeneity of the disease, more research about treatment initiation and long-term results is warranted.*

Keywords: *Chronic inflammatory demyelinating polyneuropathy. Polyneuropathy. Treatment. Functional status. Outcome characteristics.*

Características clínicas en una cohorte de pacientes con polineuropatía desmielinizante inflamatoria crónica: un estudio retrospectivo

Resumen

Objetivo: *Evaluar el espectro clínico de la polineuropatía desmielinizante inflamatoria crónica (PDIC) en una cohorte de pacientes mexicanos beneficiarios de la seguridad social.* **Métodos:** *Estudio retrospectivo de pacientes con PDIC durante el período 2010-2021. Documentamos déficits neurológicos, parámetros electrofisiológicos y de laboratorio, características de diagnóstico, actividad de la enfermedad y resultados clínicos.* **Resultados:** *36 casos cumplieron con los criterios de la EAN/PNS 2021, la edad promedio fue de 58,25 ± 10,10 años, el 50% eran mujeres y el 69,4% utilizaban inmunoglobulina intravenosa. En cuanto al estado funcional, el 63,9% presentaba marcha independiente y el 86,1% presentaba debilidad leve en las habilidades manuales. El análisis del estado funcional mostró mejores resultados en el grupo de tratamiento con inmunoglobulinas intravenosa.* **Conclusiones:** *Al igual que en informes de la literatura, el 50% de nuestros pacientes tenían enfermedad activa estable. Teniendo en cuenta la heterogeneidad de la enfermedad, se justifica realizar más investigaciones sobre el tratamiento y los resultados a largo plazo.*

Palabras clave: *Polineuropatía desmielizante inflamatoria crónica. Polineuropatía. Tratamiento. Estado funcional. Características de resultado.*

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Introduction

Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is a disorder of the peripheral nerves and nerve roots causing limb weakness, sensory deficits, hyporeflexia/areflexia with a progressive or relapsing form[1,2]. However, atypical features such as cranial nerve involvement, dysautonomia, and tremor are also reported[3]. CIDP is an immune-mediated disorder with macrophages inducing myelin damage, with consequent activation of complement-dependent antibodies, although its complete pathogenesis and etiology remain uncertain[4]. The USA and Europe report a prevalence of 3-5 cases/100,000 habitants/year and an incidence of 0.5-1 cases/100,000 habitants/year, being more frequent in men[1,5]. In Latin America, few studies describe the CIDP population; the first epidemiological study in South America and the Caribbean in 2019 reported a prevalence of 2.95 per 100,000 habitants[6]. In Mexico, two studies focus on the clinical characteristics and the type of clinical response to treatment[3,7].

There are two widely accepted guidelines for diagnosis: one proposed by the American Academy of Neurology, described in 2012, and the other from the European Academy of Neurology (EAN) and Peripheral Nerve Society (PNS)[1,2]. At present, the 2021 European criteria are a high-sensitivity diagnostic tool, with definite CIDP and possible CIDP, integrating clinical and neurophysiological findings and supporting criteria[1]. The comparison and validity of functional results in other studies are difficult due to different treatment responses and clinical and electrophysiological characteristics among published studies[8]. A standardized metric for disease severity and assessment of treatment effectiveness has been attempted in a series of grading systems such as inflammatory neuropathy cause and treatment, Inflammatory Rasch-built Overall Disability Scale, and CIDP disease activity status (CDAS)[9,10]. The response to medical treatment is adequate for intravenous immunoglobulin (IVIG) and corticosteroids. CIDP efficacy (study) reported on the long-term efficacy benefits of IVIG treatment. After treatment, 41.5% of patients presented independent walking, and up to 75.6% had manual skills weakness[11,12].

The study aims to evaluate the CIDP clinical spectrum in a cohort of Mexican patients who benefit from social security and free medical treatment, approaching their clinical and functional status.

Methods

We performed a retrospective study in a cohort of patients with CIDP diagnosis.

Patients

We recruited patients with a CIDP diagnosis who regularly attended neurology services at the High Specialty Hospital National Medical Center La Raza in Mexico City from 2010 to 2021. All diagnoses were performed by a neurologist team following the 2021 EAN/PNS criteria for CIDP and possible CIDP[1]. We analyzed clinical records, demographics, clinical presentation, nerve conductions studies (NCS), and laboratory parameters to determine diagnostic characteristics, disease activity, and post-treatment response. We classified patients according to the immunosuppressive treatment received: IVIG, corticosteroid, and other immunomodulatory treatments such as azathioprine and mycophenolate mofetil.

We evaluated disability by applying classical clinical measurement scales and other validated scales in the first visit and during follow-up using CDAS[13]. Then, for analysis, we divided the modified Rankin Scale (mRS) into three categories: 1-2 for mild, 3 for moderate, and 4-5 for severe. We classified manual skills disability using the Medical Research Council scale (MRC) according to hand muscle strength examination, dividing them into three categories: mild for strength 4-5, 3 for moderate, and 2-1 for severe. Finally, for independent walking, we made two groups: one with support walker use and the other without.

For a bivariate analysis and comparison, we classified patients into typical CIDP and its varieties: distal, focal, multifocal, motor, and sensory (previously called atypical). Response to treatment was judged based on the neurologist team's conclusion according to the follow-up data, dividing them into two groups. We considered those with preserved gait, manual skills, and a RANKIN > 3 in the satisfactory response group and another with an unsatisfactory response; we compared our results with previously published series.

Ethics

We conducted the study following the Declaration of Helsinki, and the local ethics committee approved the investigation protocol.

Samples

We obtained cerebrospinal fluid (CSF) samples and performed their subsequent analysis with cell and protein quantification to support CIDP criteria, defining albumin-cytological dissociation as a protein level: > 45 mg/dl and a white blood cell count ≤ 50 cells/μL.

The NCS recordings were conducted and reported by a certified neurophysiologist.

Statistical analysis

For the statistical analysis, we performed descriptive statistics using the SPSS 20 version on Windows. We described cohort characteristics using proportions, mean ± SD for continuous data, frequency, and percentage for categorical data. Also, for normality assessment, we used the Shapiro–Wilk test and for bivariate analysis, χ^2 test, Student t-test, Mann–Whitney U-test, or Kruskal–Wallis test according to its distribution groups. We consider statistically significant differences with $p < 0.05$.

Results

From a sample of 70 patients with suspected CIDP, 36 patients met the criteria for probable and definite CIDP, 50% were female, mean age 58.25 ± 10.10 years (range 35-81), mean disease duration of 93 ± 45.11 months, time to diagnosis 8.53 ± 8.1 months (range 2-48), 25% of patients presented with diabetes mellitus, and 11.1% with another immune-mediated pathology. Lumbar puncture was performed on 35 patients, and 74.2% had albumin-cytological dissociation, with mean proteins in CSF of 96 ± 82.26 mg/dL. Initial symptoms showed weakness as the first symptom in 88.9% of the patients. Paresthesia or dysesthesia in 80.6% was the second most common symptom. The most common initial presentation was four-limb involvement in 72.2% and lower limbs only in 19.4%. We showed the rest of the demographic, clinical, and NCS characteristics in table 1.

Regarding the current functional scales, we found that 41.7% had CDAS 3A (stable active disease > 1 year, on treatment with normal examination), 41.7% CDAS 5C (unstable active disease: abnormal examination with progressive or relapsing course, on treatment), and 8.3% CDAS 3B (stable active disease > 1 year, on treatment with abnormal examination).

Regarding the functionality scales and treatment response, although it did not reach statistical significance, the bivariate analysis showed better functional scores (manual skills, independent walking, mRS) in patients treated with IVIG than other immunosuppressive agents. We represent these results in Fig 1.

We analyzed the treatment response in two separate groups: adequate and unsatisfactory responses. According to functional scales, the results showed statistically significant differences in the mRS scale, independent gait, manual skills, and CIDP variant (Table 2).

Table 1. Clinical, demographic, and functional characteristics of patients with CIDP

Variables	n = 36 (%)
CIDP variant	
Typical	26 (72.2 %)
Multifocal	3 (8.3 %)
Distal	7 (19.4 %)
Current treatment	
IVIG	25 (69.4%)
Prednisone	2 (5.6%)
Nonsteroidal immunosuppressant	8 (22.3%)
Rituximab	1 (2.8%)
Comorbidities	
Diabetes mellitus	10 (27.8%)
Hypothyroidism	6 (16.7%)
Other autoimmune diseases	4 (11.1%)
CSF (proteins mg/dL)	96 ± 82.26 (range 14 - 474)
Prior steroid use	23 (63.9%)
Current functional status	
mRS	
Mild (0-2)	31 (86.1%)
Moderate (3)	5 (13.9%)
Severe (4-5)	0
Independent walk	23 (63.9%)
Manual skills	
Mild (5-4)	31 (86.1%)
Moderate (3)	2 (5.6%)
Severe (2-1)	3 (8.3%)

IVIG: intravenous immunoglobulin; CSF: cerebrospinal fluid; mRS: modified Rankin scale; CIDP: chronic inflammatory demyelinating polyneuropathy.
Other autoimmune diseases: autoimmune thrombocytopenia (2), ankylosing spondylitis (2).

Discussion

Few studies report the prevalence of CIDP in the US, Europe, and Latin America, being around 2.81/100,000 habitants[1,5,6].

The heterogeneity in their data may be explained by different diagnostic criteria used. CIDP characteristics are weakness, paresthesia, and dysesthesia in a classically proximal distribution that was present in all our patients. Our CIDP patients share similar characteristics with previous reports: age at presentation, gender, and typical variant predominance[7]. CIDP variants in other series represented 49% and 21.3%, similar to ours with 27.7%[7,8].

The association between CIDP and diabetes is discussed in two retrospective studies conducted in Europe. It is considered a common and treatable inflammatory neuropathy in these groups of patients[14,15]. Furthermore, a study in Mexico found that diabetes is the main associated comorbidity.7 In our study, diabetes was present in 27.8% of the patients, similar to other

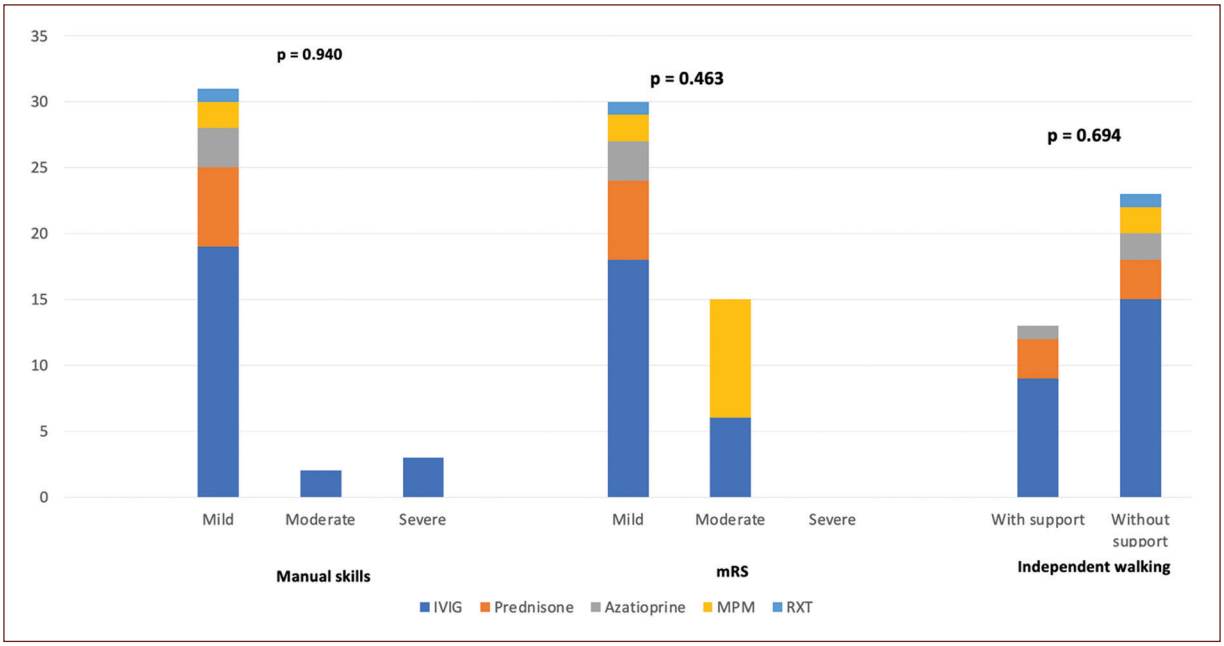

Figure 1. Comparative column chart between functionality scales and actual treatment.

cohorts (20%, 30.4%, and 18%)[14-16]. Other associated factors have been studied: diet, smoking, alcohol consumption, fatigue, toxic exposure, and disability progression and quality of life[17-19].

The standard recommended treatment by the European and American guidelines is composed of immunomodulatory drugs that have been reported beneficial. IVIG and oral corticosteroids are first-line treatments for CIDP (Class II)[12,20-23]. As part of a public health program, IVIG is more accessible in our hospital than in other centers, where 69.4% of our patients were under this kind of treatment, compared with 21.3 % of another Mexican reference center, 59.3% in the UK, and 42.2% in Serbia[7,14].

The evaluation of the treatment results for CIDP relies on the neuromuscular expert judgment considering clinical, functional, and electrophysiological evaluation. Patients in other cohorts report different functionality: 23% without symptoms, 50.4% stable active disease with abnormal examination[9]. In our cohort, 50% retain walking and 52.7% manual skills. However, as mentioned in the results, although patients with IVIG and prednisone had improved functional scales, this was not statistically significant. We found no sociodemographic or comorbidity variables significantly associated with disability scales. CDAS is an easy-to-apply tool used to classify long-term outcomes and responses to treatment in patients by a single observer[13]. Albulaihe et al. reported a prevalence of CDAS-3 (stable active disease with > 1 year on treatment) of 50%, followed by CDAS1-2 of 23%,9 while for other series CDAS-3 ranged from 26% to 53%[10], similar to our results of 41.7% for CDAS-3 and CDAS-5 (unstable active disease: abnormal examination with progressive or relapsing course) 41.7%. Of the latter, 80% were under immunoglobulin treatment, 6% with corticosteroid, and the rest on other treatments. We made a comparison between adequate and unsatisfactory treatment responses. Although not significant, patients with unsatisfactory responses were younger, with more delay in diagnosis, longer duration of illness, and more protein in their CSF.

Conclusions

More than 50% of patients have stable active disease with or without abnormalities on examination, but another 40% still have unstable disease despite treatment.

Limitations: first, it is retrospective design. Second, some functional scales already established for CIDP patients were not calculated because of not previously having the appropriate handgrip measuring device. Third, some old files failed to have a complete physical examination or sufficient medical scale information. However, our findings agree with previous scientific descriptions and show the advantages of treatment with IVIG concerning good functional results.

Table 2. Comparison between adequate and unsatisfactory treatment response according to its functional scales, clinical evolution

Variables	Adequate response (n = 20)	Unsatisfactory response (n = 16)	p
Age (years)	60.45 ± 8.2	55.5 ± 11.7	0.147
Time to diagnosis (months)	6.5 ± 3.5	7.06 ± 4.05	0.662
Disease duration (months)	90 ± 43.09	96.75 ± 48.6	0.662
CSF (proteins mg/dL)	82.58 ± 46.17	113.91 ± 113.3	0.270
mRS			
Mild	20	10	0.003
Moderate	0	6	
Severe	0	0	
Independent walking		13	0.000
With support	0	3	
Without support	20		
Manual skills			
Mild	20	11	0.027
Moderate	0	2	
Severe	0	3	
Actual treatment			
IVIG	12	12	0.570
Prednisone	3	3	
AZT	2	1	
MPM	2	0	
RTX	1	0	
CIDP variant			
Typical	16	10	0.022
Multifocal	3	0	
Distal	1	6	

IVIG: intravenous immunoglobulin; MPM: mycophenolate mofetil; RXT: rituximab; mRS: modified Rankin Scale; AZT: azathioprine; CIDP: chronic inflammatory demyelinating polyneuropathy.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

Use of artificial intelligence for generating text. The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript nor for the creation of images, graphics, tables, or their corresponding captions.

References

1. Van den Bergh PY, van Doorn PA, Hadden RD, Avau B, Vankrunkelsven P, Allen JA, et al. European academy of neurology/peripheral nerve society guideline on diagnosis and treatment of chronic inflammatory demyelinating polyradiculoneuropathy: report of a joint task force-second revision. J Peripher Nerv Syst. 2021;26:242-68.
2. Van den Bergh PY, Hadden RD, Bouche P, Cornblath DR, Hahn A, Illa I, 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 peripheral nerve society-first revision. Eur J Neurol. 2010;17:356-63.
3. San-Juan OD, Castro-Macías JI. Chronic inflammatory demyelinating polyradiculoneuropathy. 10 years' experience in a Mexican centre. Rev Neurol. 2008;46:656-9.
4. Dziadkowiak E, Waliszewska-Prosół M, Nowakowska-Kotas M, Budrewicz S, Koszewicz Z, Koszewicz M**.** Pathophysiology of the different clinical phenotypes of chronic inflammatory demyelinating polyradiculoneuropathy (CIDP). Int J Mol Sci. 2022;23:179.
5. Broers MC, Bunschoten C, Nieboer D, Lingsma HF, Jacobs BC. Incidence and prevalence of chronic inflammatory demyelinating polyradiculoneuropathy: a systematic review and meta-analysis. Neuroepidemiology. 2019;52:161-72.
6. Cea G, Idiáquez JF, Salinas R, Matamala JM, Villagra R, Stuardo A. Epidemiology of chronic inflammatory demyelinating polyneuropathy in the South-Eastern area of Santiago, Chile. J Clin Neurosci. 2020;74:271-3.
7. López-Hernández JC, Mercado-Pompa A, Pérez-Torres T, Galnares-Olalde JA, Vargas-Cañas ES. Efficacy of long-term prednisone therapy in patients with chronic inflammatory demyelinating polyneuropathy (CIDP): a retrospective cohort study. Rev Neurol. 2021;73:275-81.
8. Bril V, Banach M, Dalakas MC, Deng C, Donofrio P, Hanna K, et al. Electrophysiologic correlations with clinical outcomes in CIDP. Muscle Nerve. 2010;42:492-7.
9. Albulaihe H, Alabdali M, Alsulaiman A, Abraham A, Breiner A, Barnett C, et al. Disease activity in chronic inflammatory demyelinating polyneuropathy. J Neurol Sci. 2016;369:204-9.
10. Rajabally YA, Cassereau J, Robbe A, Nicolas G. Disease status in chronic inflammatory demyelinating polyneuropathy: inter-centre comparative analysis and correlates. Eur J Neurol. 2015;22:1469-73.
11. Hughes RA, Donofrio P, Bril V, Dalakas MC, Deng C, Hanna K, et al. Intravenous immune globulin (10% caprylate-chromatography purified) for the treatment of chronic inflammatory demyelinating polyradiculoneuropathy (ICE study): a randomised placebo-controlled trial. Lancet Neurol. 2008;7:136-44.
12. Oaklander AL, Lunn MP, Hughes RA, van Schaik IN, Frost C, Chalk CH. Treatments for chronic inflammatory demyelinating polyradiculoneuropathy (CIDP): an overview of systematic reviews. Cochrane Database Syst Rev. 2017;1:CD010369.
13. Gorson KC, van Schaik IN, Merkies IS, Lewis RA, Barohn RJ, Koski CL, et al. Chronic inflammatory demyelinating polyneuropathy disease activity status: recommendations for clinical research standards and use in clinical practice. J Peripher Nerv Syst. 2010;15:326-33.
14. Rajabally YA, Peric S, Cobeljic M, Afzal S, Bozovic I, Palibrk A, et al. Chronic inflammatory demyelinating polyneuropathy associated with diabetes: a European multicentre comparative reappraisal. J Neurol Neurosurg Psychiatry. 2020;91:1100-4.
15. Rajabally YA, Stettner M, Kieseier BC, Hartung HP, Malik RA. CIDP and other inflammatory neuropathies in diabetes-diagnosis and management. Nature Rev Neurol. 2017;13:599-611.
16. Hiew FL, Ong JJ, Viswanathan S, Puvanarajah S. Outcome in chronic inflammatory demyelinating polyneuropathy from a Malaysian centre over sixteen years. J Clin Neurosci. 2018;50:203-7.
17. Doneddu PE, Bianchi E, Cocito D, Manganelli F, Fazio R, Filosto M, et al. Impact of environmental factors and physical activity on disability and quality of life in CIDP. J Neurol. 2020;267:2683-91.

18. Bozovic I, Kacar A, Peric S, Nikolic A, Bjelica B, Cobeljic M, et al. Quality of life predictors in patients with chronic inflammatory demyelinating polyradiculoneuropathy. J Neurol. 2017;264:2481-6.
19. Boukhris S, Magy L, Gallouedec G, Khalil M, Couratier P, Gil J, et al. Fatigue as the main presenting symptom of chronic inflammatory demyelinating polyradiculoneuropathy: a study of 11 cases. J Peripher Nerv Syst. 2005;10:329-37.
20. Lo YL, Fook-Chong S, Wong PS, Tien SL, Ratnagopal P. Intravenous immunoglobulin for chronic inflammatory demyelinating polyradiculoneuropathy: a multiracial Asian perspective. Eur J Neurol. 2008;15:e81-2.
21. Perraudin C, Bourdin A, Vicino A, Kuntzer T, Bugnon O, Berger J. Home-based subcutaneous immunoglobulin for chronic inflammatory demyelinating polyneuropathy patients: a swiss cost-minimization analysis. PLoS One. 2020;15:e0242630.
22. Godil J, Barrett MJ, Ensrud E, Chahin N, Karam C. Refractory CIDP: clinical characteristics, antibodies and response to alternative treatment. J Neurol Sci. 2020;418:117098.
23. Oaklander AL, Gimigliano F. Are the treatments for chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) effective and safe?-a cochrane overview summary with commentary. NeuroRehabilitation. 2019;44:609-12.