

# Chronic inflammatory demyelinating polyneuropathy. A case description

MARIA GARCIA CASTILLO<sup>1</sup>

<sup>1</sup>CARLOS ANDRADE MARIN

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Garcia-Castillo M.

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

### Authors information

Garcia-Castillo María Ariana.

Mail: [magarciacastillo@gmail.com](mailto:magarciacastillo@gmail.com)

Affiliation: No affiliation.

Orcid ID: <https://orcid.org/0000-0003-4962-9582>

### Correspondence

Garcia-Castillo María Ariana.

Address: Hernández de Girón y Pedregal. Conjunto San Martin. Torre 1 PB01. Quito 170509, Ecuador. Tel: +593 98 767 61 63

E-mail: [magarciacastillo@gmail.com](mailto:magarciacastillo@gmail.com)

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MAGC: designed the research, analyzed all magnetic resonance studies; wrote and reviewed the manuscript.

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### Introduction

Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is clinically defined as a “chronically progressive, stepwise or recurrent proximal and distal weakness and sensory dysfunction of all extremities, developing over at least 2 months, with absent or reduced tendon reflexes in all limbs and sometimes with cranial nerve involvement”<sup>1</sup>.

Chronic inflammatory demyelinating polyneuropathy (CIDP) is an acquired autoimmune disorder directed against the myelin sheath of peripheral nerves.<sup>1</sup> It was initially characterized as chronic inflammatory polyradiculoneuropathy by Dyck et al in 1975, but cases consistent with probable CIDP were described as early as 1958<sup>2,3</sup>.

CIDP is difficult to diagnose, but early diagnosis can be crucial to prevent permanent nerve damage.<sup>4</sup>

Although CIDP is the most common treatable chronic neuropathy worldwide, it is still a rare disease.<sup>5</sup>

The reported prevalence of CIDP ranges from 0.7 to 10.3 cases per 100,000 people<sup>6</sup>. There is a male predominance, with a gender rate ratio ranging from 1.5 to 4. CIDP primarily affects adults and the incidence rises with advancing age. The median age of onset is not well established. No specific predisposing risk factors for CIDP have been clearly identified<sup>6,7</sup>.

There are several clinical presentations, and sensory dysfunction is frequently present, most usually affecting joint position and vibration submodalities. Wasting is not prominent early in the disease. There are atypical forms, such as multifocal acquired demyelinating sensory and motor neuropathy (MADSAM, or Lewis–Sumner syndrome), pure sensory or pure motor CIDP and focal or distal forms (distal acquired demyelinating sensory polyneuropathy (DADS))<sup>8</sup>.

Most people with CIDP have a progressive rather than a spontaneously relapsing and remitting course, with a variable balance between motor and sensory symptoms. The American Academy of Neurology established diagnostic research criteria for CIDP in 1991<sup>9</sup>.

However, there is still no gold-standard set of diagnostic criteria for the electrophysiologic identification of demyelination, or for the clinical diagnosis of CIDP and its variants, even though multiple sets of diagnostic criteria have been published<sup>10-22</sup>.

Differences between these sets are related to definitions of the clinical picture, the requirements for nerve biopsy, electrodiagnostic criteria for demyelination, and the number of features required to make the diagnosis. The plethora of criteria sets for CIDP illustrate the difficulty of developing precise standards for problems that have multiple variations.

When independently validated in a retrospective study, the 2006 EFNS/PNS criteria had a sensitivity and specificity of 81 and 97 percent, respectively<sup>23</sup>. The most frequently used CIDP criteria in clinical practice and research are the revised European Federation of Neurological Societies/Peripheral Nerve Society 2010 criteria<sup>24</sup>.

These and other proposed criteria typically comprise a combination of clinical and electrophysiological features (there have been 15 formal sets of published electrophysiological criteria for the diagnosis of CIDP<sup>25</sup>). Cases are classified as definite, probable or possible, depending upon the number of criteria fulfilled. In most cases, finding a raised CSF protein without CSF leucocytosis<sup>26</sup> further supports the diagnosis. Clear evidence of macrophage-associated demyelination and remyelination, with or without a T-cell inflammatory endoneurial infiltrate in a sensory nerve biopsy, remains the gold standard supportive criterion. There have been several validations of these diagnostic criteria, though none is 100% sensitive or specific<sup>1,9</sup>; for example, the EFNS/PNS criteria show a positive predictive value of 97% and negative predictive value of 92%,<sup>6</sup> and different validation cohorts give widely varying sensitivities and specificities<sup>27</sup>.

### Case description

A 47-year-old woman presented to acute care with ataxia, nystagmus, vertigo, and diffuse burning tingling sensations, and weakness of all limbs, of greater frequency and intensity in the lower limbs.

Symptoms progressed over the course of 3 months.

Initially, weakness was most obvious when going up and down the stairs, but 2 weeks before going to the hospital, the weakness aggravated, with difficulty in walking.

*Family personal history:*

Three maternal aunts: Hashimoto's thyroiditis, with subsequent development of carcinoma (follicular in two, medullary in one).

Sister: multiple sclerosis, Hashimoto's thyroiditis

Sister: rheumatoid arthritis under biological treatment.

Grandmother: Akinetic Parkinson's

*Physical examination*

*Muscular strength:* according to Medical Research Council's scale (MRC Scale)

Upper left limb Proximal: 3/5 Trapezius: 4-/ 5 Wrist: 5/5 Finger flexors: 4-/5

Left Lower Limb Proximal: 4-/5 Knee Flexor: 3/5

Distal: 3/5

Proximal right upper limb: 3/5 Trapezius: 4 / 5 Wrist: 5/5 Finger flexors: 4-/5

Right lower limb Proximal: 4-/5 Knee flexor: 3/5 Distal: 3/5

*Surface Sensitivity:*

Hypoesthesia of the internal face of the arm, forearm and hand (cubital)

Hypoesthesia of the lateral face of the right leg (external popliteal)

Preserved temperature and pain perception. Bilateral indifferent skin plantar reflex.

Deep sensitivity: kinesthesia, palesthesia normal in the 4 extremities

Complex Sensitivity: preserved stereoagnosia, normal tactile discrimination.

Osteotendinous reflexes: generalized areflexia.

Coordination: altered bilateral finger nose test. Heel-Knee test normal. Truncal ataxia accented with closed eyes, in seating and bipedestation. Walking: lateralization on both sides during point-heel, Romberg +

Following admission, MRI showed areas of scattered T2 and FLAIR signal hyperintensity in midbrain, anterior and posterior pons, in the distal medulla oblongata, and in the spinal cord, in C2-C3 and C6, suspicious of demyelinating process.

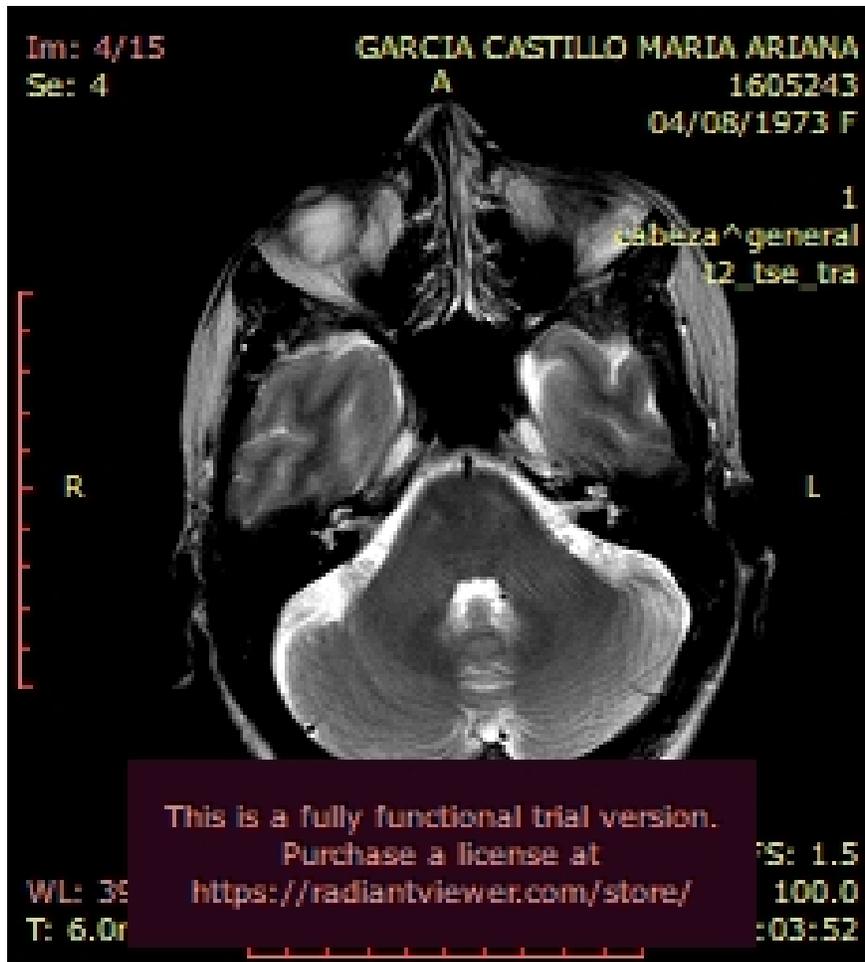
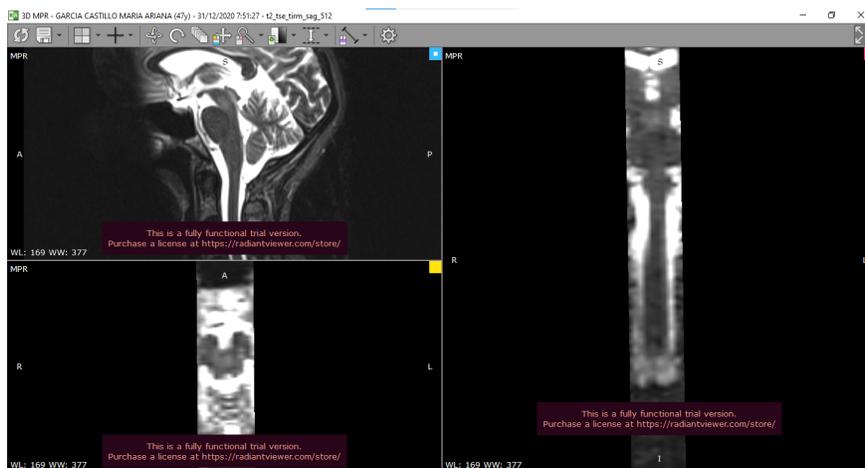


Fig. 1

Scattered T2 hyperintensities in ventral pons (axial)





a.

b.

*Fig. 2*

*Scattered T2 hyperintensities in midbrain. a. Sagittal b. Coronal reconstruction*

Thickening in the distal course of the left C3 branch.

In cerebrospinal fluid, glucose 54 mg/dL, protein 284 mg/dL, no red blood cells, no white blood cells. Gram staining negative, and absent oligoclonal bands.

Meningitis panel, including: Escherichia coli K1, Haemophilus influenzae, Listeria monocytogenes, Neisseria meningitidis, Streptococcus agalactiae, Streptococcus pneumoniae, Cytomegalovirus, Enterovirus, Herpes simplex: virus 1 (HSV-1), Herpes simplex virus 2 (HSV-1), Herpes simplex virus 2 (HSV-1) Human herpes 6 (HHV-6), Human Parechovirus, Varicella Zoster Virus, Cryptococcus neoformans / gattii, negative

The serologic evaluation for immunological markers of disease, including ANA, AntiDNA, AntiANCA PR3, AntiANCA MPO, C3, C4, AntiRO, AntiLA, B2 glycoprotein, AntiTPO, antithyroglobulin was normal.

Rheumatoid factor was borderline

Patient tested negative for endocrinological and tumoral markers of disease.

Markers for neurotropic viruses and Toxoplasma were negative.

*Electromyography (EMG) showed axonal demyelinating polyradiculoneuropathy, abnormal distal latency with very low amplitude, disappearance of F waves, and numerous spontaneous potential (Table 1).*

Motor nerve conduction velocities were reduced bilaterally, in nerves median, ulnar and peroneal, all of them with values under 44 m/s.

Nerve	Left	Right
	Velocity	Velocity
Median	43.8 m/s	39.8 m/s
Ulnar	29.7 m/s	34.5 m/s
Peroneal	38.3 m/s	28.5 m/s

*Table 1.*

### *Nerve conduction velocities in Median, Ulnar and Peroneal nerves.*

Acute denervation was determined in the supinator muscles, first dorsal interosseous of the hand and left anterior tibialis. Polyphasic potentials were obtained in the left trapezius.

Increased insertional activity in all the muscles explored.

The recruitment patterns of the trapezius, supinator, first dorsal interosseous of the hand, gastrocnemius, tibialis, and left peroneal muscles are obtained with a reduced recruitment pattern in the right medial rump.

Neuro conduction: the median and ulnar right and left nerves, latency, amplitude and velocity values are obtained in normal values. Its F waves were obtained in a low percentage, but with latency within normal values.

Peroneal nerve: very low amplitude (0.89 mV in the left and 0.79 mV in the right). Latency and speeds in normal values. Its F waves were not possible to obtain.

Sural nerve: the left limb showed no potential.

Superficial peroneal nerve: right limb unresponsive

As for this patient, she showed progressive weakness and numbness, both of which indicate alterations in the peripheral nervous system (PNS), then the EMG confirmed the damage of the PNS.

Subsequent studies revealed further deterioration of nerve conduction velocities especially in the legs, with acute denervation in muscles innervated by right C3-C4 roots, bilateral C5-C6 and right L4-L5-S1, with severe degree of involvement and neuro conduction study showing multiple motor mononeuropathy with axonal involvement of the bilateral suprascapular, bilateral radial, right ulnar and fibula or bilateral nerves, with a moderate degree of involvement.

Because of the sensory motor deficits, and cytological protein dissociation in cerebrospinal fluid, the patient was diagnosed with chronic inflammatory demyelinating polyneuropathy. It is to note that this patient had evidence of involvement of the CNS (central nervous system), given the MRI hyperintense areas, nystagmus and cerebellar signs.

A 3-day course of 1000 mg intravenous methylprednisolone was administered followed by oral corticosteroid treatment, prednisone 60 mg daily, diminishing 20 mg every two weeks to reach 20 mg, and then continuation to 10 mg, associating at this point with azathioprine 100 mg daily.

The patient also started a program of physiotherapy to improve muscle strength, function and mobility, and minimize the shrinkage of muscles and tendons and distortions of the joints.

The numbness and weakness improved, and the patient could walk with the help of others; In a 6 months follow-up, the results showed there was still slight numbness of all limbs, and she could walk slowly, most of the time without help.

### **Discussion**

The diagnosis of CIDP can be made when patients fulfil a set of clinical, electrodiagnostic, and laboratory criteria<sup>1,25</sup>.

However, the diagnosis can be difficult, in part because of the extensive list of differential diagnoses that mimic CIDP<sup>8</sup>.

Poorly performed nerve conduction studies, misinterpretation of their findings, and non-adherence to electrodiagnostic criteria commonly lead to misdiagnosis<sup>18,29-31</sup>.

An incorrect diagnosis can also occur in patients reporting subjective improvement after treatment, or when minor elevation of the CSF protein concentration (probably not exceeding 1 g/L) is considered clinically relevant by the treating neurologist<sup>30-34</sup>.

As for this patient, she showed progressive weakness and numbness, both of which indicate alterations in the peripheral nervous system (PNS), confirmed for the EMG of the lower limbs, at the time she had clinical signs of alterations of the central nervous system, and lesions in the MRI that suggested demyelination.

The explanation of how CIDP can combine with central lesions, is still unclear. On the point of molecular biology: the myelin consists of inner and outer lipids and in-between myelin sheath.

Approximately 15% to 30% of myelin proteins are found in the CNS and the PNS. At least 2 common proteins which consist of the myelin have been found, resulting in similar autoimmune disorder in peripheral and central nerves in theory<sup>35</sup>.

When the blood-brain and blood-nerve barriers are damaged, the antibodies cross the damaged barrier, resulting in an immune reaction in peripheral and central nerves. So, if there appears immune-mediated inflammatory response, there is a certain molecular basis of the mutual lesion. But the specific mechanism remains unclear<sup>36</sup>.

## Conclusions

CIDP is a disabling immune-mediated polyradiculoneuropathy with a typical phenotype and atypical variants, that involves both demyelination and axonal degeneration, with the balance being determined by disease duration and severity<sup>37</sup>.

The task of correctly diagnosing CIDP is often not easy, as there are many differential diagnoses and possible mimics. However, an early and accurate diagnosis is important to initiate treatment and to prevent further nerve damage<sup>30-32</sup>.

On the other hand, the consequences of over diagnosis are not trivial. From a safety perspective, the risks assumed from immunotherapy exposure are obvious. The therapies we use to treat CIDP are not benign, nor are they (in most cases) cheap<sup>38</sup>.

This is the reason why we consider patients affected by CIDP require close follow up due to the neuronal demyelination along with axonal degeneration associated with the disease process, giving the opportunity to the medical team of adequating therapeutics and other medical interventions, according to the evolution of the symptoms, to prevent irreversible axonal degeneration.

## Conflict of Interest

None declared.

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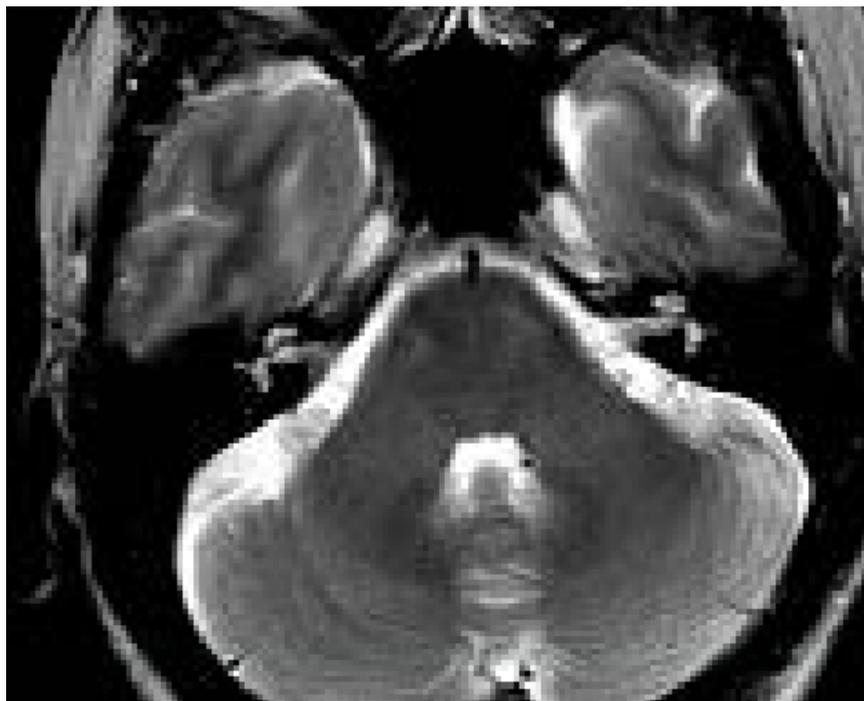
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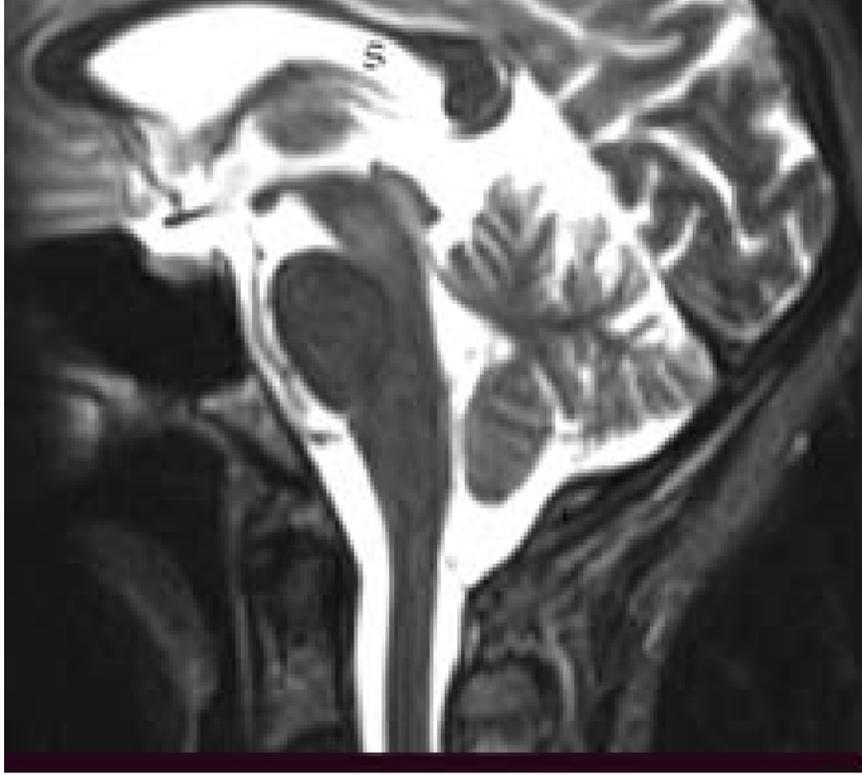
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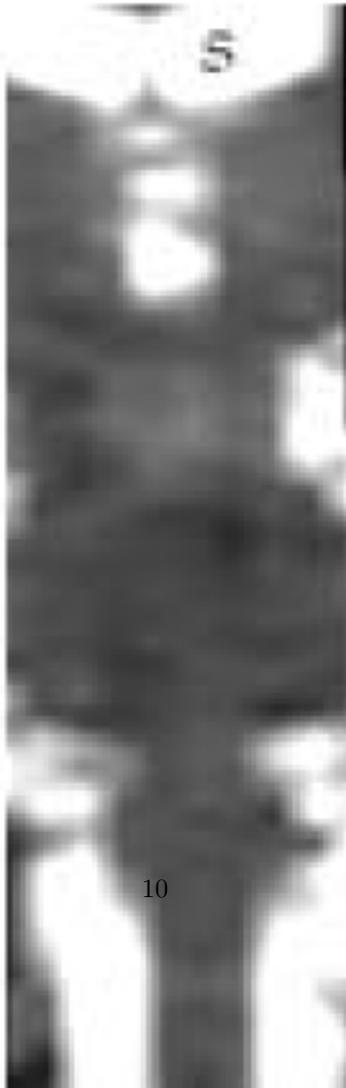
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<b>Nerve</b>	<b>Left</b>	<b>Right</b>
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