Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP) Joel Steinberg

Definition: Slowly evolving ascending symmetric weakness of the limbs over at least eight weeks, often accompanied by paresthesias, usually in a recurring pattern, often with spontaneous improvement, that reflects inflammation-mediated damage of peripheral nerve myelin.

- Additional features include areflexia and elevated spinal fluid protein.

Causes: Generally accepted to be an autoimmune disorder, wherein the body's immune system, macrophages as well as likely humoral factors, attacks peripheral nerve myelin.

- Triggers of attacks are unknown.

Scope of the Problem:

- Incidence as high as 1.5 new cases per 100,000 population identified annually.
- CIDP often runs a protracted course, over years.
- Thus its prevalence, the number of cases present at any one time, may run about 9/100,000.
- If left untreated, permanent nerve damage and disability may evolve; early diagnosis is thus important.

Differential Diagnosis:

<u>Other likely autoimmune peripheral neuropathies</u> - Multifocal (i.e., asymmetric) acquired demyelinating sensory and motor neuropathy (Lewis-Sumner syndrome)
<u>Compression neuropathies</u> - Spinal stenosis
<u>Spinal cord nerve tract pathology</u> - Amyotrophic lateral sclerosis
<u>Autoimmune neuromuscular junction disorders</u> - Myasthenia gravis
<u>Multisystem disorders via deranged plasma cells</u> - POEMS syndrome (a.k.a., Takatsuki syndrome, osteoclerotic myeloma), consisting of polyradiculoneuropathy, organomegaly, endocrinopathy, monoclonal plasma cell disorder, skin changes
<u>Hereditary peripheral neuropathies</u> - Charcot-Marie-Tooth syndrome, affecting principally the arms and legs

Diagnosis

History:

- Typical patient presents with slowly progressive weakness of their legs, extending over at least 8 weeks, leading to difficulty arising from a chair, walking and climbing stairs.
- Weakness of arms leads to difficulty using utensils and gripping objects.
- Sensory involvement also common, with loss of feeling and distal paresthesias, of the feet and hands.

PE:

- Limb weakness, with, e.g., difficulty arising, climbing onto an exam table, and a waddling gait.
- Deep tendon reflexes of weak limbs are diminished or absent.
- Some abnormal peripheral nerve issues commonly seen in acute demyelinating inflammatory polyneuropathy (AIDP or Guillain-Barré syndrome) are rare in CIDP, such as cranial nerve and autonomic nervous system involvement and breathing problems.

Lab:

- Electrodiagnostic criteria, i.e., nerve conduction velocity-electromyography findings to support a diagnosis of definite or probable CIDP have been established by the European Federation of Neurological Societies and Peripheral Nerve Society. See end.
- Spinal fluid protein usually elevated without a concomitant elevation in cells.
- When the diagnosis is questionable a nerve biopsy, read by a pathologist familiar with neuropathology, may be helpful.

Imaging:

- Occasionally an MRI of the spine will demonstrate enlarged nerve root or plexus.
- CT of the head can rule out CNS involvement.

Treatment

General guidelines: Early diagnosis and initiation of treatment likely help preserve nerve function.

1. Medications and Blood Derived Products

Most patients respond to at least one of three immunologic system interventions:

1)	High dose immunoglobulins. Traditionally given intravenously (a.k.a., IVIG) or delivered by the subcutaneous (SC) route. The IVIG brand, Gamunex® and the SC formulation, Hizentra® have FDA approval for treatment of CIDP. Most other IVIG brands are considered interchangeable. Treatments are typically given as a course over 5 days and eventually repeated if weakness recurs.
2)	Plasma exchange (a.k.a., plasmapheresis), i.e., removal of the liquid portion of blood (and its replacement with a solution substitute). As with IVIG, treatments are typically given over 5 days and repeated if weakness recurs.
3)	Corticosteroids. Ease of administration and low cost make corticosteroids an attractive first line therapy choice, but untoward side effects may limit its use.

   - Should patients respond poorly to the 3 first line treatment choices, various immunosuppressive drugs can be tried. All are off-label uses, i.e., not FDA approved.
   - These include: rituximab (Rituxan®), cyclophosphamide, cyclosporine, azathioprine (Imuran®), mycophenolate mofetil (Cellcept®)

2. Physical Therapy
   - Adjunctive physical and occupational therapy will often help the patient improve function such as mobility and other activities of daily living.
3. Natural History of CIDP
   - Many CIDP cases slowly dissipate or burn out, enabling a decrease in the frequency of
   - treatment dosing.
4. Supportive Care
   - Medical and lay literature, including patient support available through the GBS/CIDP Foundation International at www.gbs-cidp.org.

Clinical Pearl:

If left untreated, CIDP can lead to permanent nerve damage and disability.
Hence, unexplained weakness with difficulty walking warrants prompt evaluation, usually a nerve conduction velocity study to look for slowed conduction and other indicators of peripheral nerve demyelination.

Addendum:

Electrodiagnostic Criteria for CIDP (abbreviated version; see original publication for details)

(1) Definite: at least one of the following [a]
(a) Motor distal latency prolongation ‡50% above ULN in two nerves, or
(b) Reduction of motor conduction velocity ‡30% below LLN in two nerves, or
(c) Prolongation of F-wave latency ‡30% above ULN in two nerves, or
(d) Absence of F-waves in two nerves, or
(e) Partial motor conduction block, or
(f) Abnormal temporal dispersion (>30% duration increase between the proximal and distal negative peak CMAP), or
(g) Distal compound muscle action potential (CMAP) duration increase in ‡1 nerve

(2) Probable
‡30% amplitude reduction of the CMAP's proximal negative peak relative to distal peak

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ULN, upper limit of normal values; LLN, lower limit of normal values. [a] Any nerve meeting any of the criteria (a–g).

PYK Van den Bergh et al.; 2010; EFNS and Peripheral Nerve Society European Journal of Neurology 17, 356–363.