CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY

INTRODUCTION

- Chronic inflammatory demyelinating polyneuropathy is an acquired, immune-mediated neuropathy affecting peripheral nerves and nerve roots, characterized by a relapsing-remitting or progressive course over 8 weeks, glucocorticoid responsiveness, and electrodiagnostic or pathologic features of demyelination.
- In its classic form, CIDP manifests as a symmetric, motor-predominant neuropathy that results in both proximal and distal muscle weakness.
- Recognized variants include asymmetric and/or sensory-predominant forms.
- CIDP is important to recognize among the varied causes of polyneuropathy, as it is treatable with immunomodulatory therapies.

EPIDEMIOLOGY

- The reported prevalence of CIDP ranges from 0.7 to 10.3 cases per 100,000 people.
- There is a male predominance.
- CIDP primarily affects adults and the incidence rises with advancing age.

PATHOGENESIS

- Both the cellular and humoral components are involved in the pathogenesis.
- The characteristic pathologic features of CIDP include segmental demyelination and remyelination of peripheral nerves, and onion bulb formation.
- In approximately 10 percent of patients with a clinical diagnosis of CIDP, IgG4 subclass autoantibodies (neurofascin isoforms and contactin 1) against nodal and paranodal proteins have been identified, which are pathogenic.

CLINICAL FEATURES

1. Typical CIDP (symmetric sensorimotor)

2. Atypical CIDP variants –

- Asymmetric sensorimotor (multifocal)
- Sensory-predominant
- Distal and sensory-predominant
- Proximal (polyradiculopathy)
- Pure motor
- Neurofascin antibody-mediated
- Contactin 1 antibody-mediated

TYPICAL CIDP -

- Most common subtype.
- Symmetric sensorimotor polyneuropathy in which motor involvement exceeds sensory involvement.
- Symptoms are gradually progressive over the course of several months or longer.
- Weakness in a non-length-dependent pattern, affecting both proximal and distal muscles equally.
- Proximal muscle weakness - difficulty climbing or descending stairs, rising from a seated position, lifting objects overhead, trouble walking and report frequent falls.
- Distal muscle weakness - scuffing or tripping over the feet due to "foot drop," difficulty with fine motor tasks like buttoning, and difficulty opening doors or jars.
- Other motor symptoms - Cranial nerve and bulbar involvement and Tremors
- Sensory involvement and globally diminished or absent reflexes. Sensory impairment in CIDP is usually greater for vibration and position sense than for pain and temperature sense, reflecting the involvement of larger myelinated fibers.
- Unlike motor involvement, sensory involvement tends to be worse distally, with finger involvement frequently seen as early as toe and foot involvement.

ATYPICAL CIDP VARIANTS -

1. **Asymmetric sensorimotor (multifocal) —**

- The Lewis-Sumner syndrome AKA multifocal acquired demyelinating sensory and motor neuropathy (MADSAM).
- Patients present with a strikingly asymmetric, multifocal picture, indistinguishable from other forms of mononeuropathy multiplex, involving sensory and/or motor symptoms in individual nerve distributions.
- Some patients may have autonomic symptoms, neuropathic pain, and cranial nerve involvement

2. **Sensory-predominant** — Large fiber sensory dysfunction leading to balance problems, pain, paresthesia, and dysesthesias.

3. **Distal and sensory-predominant** — Distal acquired demyelinating symmetric neuropathy (DADS) refers to a distal and sensory-predominant variant of CIDP. Additional features in some patients include ataxia, neuropathic pain, cramps, fatigue, autonomic symptoms, and tremor. As in other variants of CIDP, reflexes are typically absent.

- DADS with monoclonal IgM and anti-myelin-associated glycoprotein (anti-MAG) antibodies is called monoclonal gammopathy of clinical significance (MGCS) is resistant to the standard immunomodulatory therapies for CIDP.

- DADS without monoclonal IgM responds to treatment with immunomodulatory therapies.

4. Proximal (polyradiculopathy) - AKA "chronic immune sensory polyradiculopathy" (CISP),

- Confined to sensory nerve roots.

- Presents with symmetric sensory ataxia with marked vibration and proprioceptive deficits, indicative of large fiber sensory dysfunction.

5. Pure motor - Involvement of motor nerves and sparing of sensory.

- Weakness tends to be relatively symmetric and may involve any part of the body, including motor cranial nerves
- This variant is rare.

6. Neurofascin antibody-mediated -

- Seen in younger patients
- Sensory ataxia and prominent tremor
- These patients do not typically respond to IVIG but can be responsive to B cell depletion therapy (e.g. rituximab)

7. Contactin 1 antibody-mediated –

- Severe and predominantly motor with early axonal involvement.
- Responsive to B cell depletion therapy (e.g., rituximab) and refractory to IVIG therapy.

DIFFERENTIAL DIAGNOSIS

- Acute inflammatory demyelinating polyneuropathy
- Subacute inflammatory demyelinating polyneuropathy
- Multifocal motor neuropathy
- Distal acquired demyelinating symmetric neuropathy (DADS) with monoclonal IgM gammopathy and anti-myelin-associated glycoprotein (anti-MAG).
- IgM-associated demyelinating neuropathies
- POEMS syndrome (osteosclerotic myeloma: Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal protein, Skin changes). (See "POEMS syndrome".)
- Demyelinating neuropathy associated with medications such as tumor necrosis factor-alpha blockers

DIAGNOSIS

- EMG
- Labs - glucose levels, calcium, creatinine, CBC, LFTs, Thyroid function studies, Vitamin B12, Hepatitis panel (for types B and C), HIV antibody, Serum protein electrophoresis (SPEP) and immunofixation, Serum free light chain (FLC) assay, or 24-hour urine protein electrophoresis (UPEP) and immunofixation
- Lumbar Puncture
- MRI with contrast
- Nerve biopsy
- Treatment trial

TREATMENT

- IVIG
- GLUCOCORTICOIDS
- PLEX