Distinguishing Typical and Atypical CIDP From Other Demyelinating Neuropathies

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Pattern Recognition of Neuropathic Disorders

- Symmetric proximal and distal weakness with sensory loss and decreased reflexes
  - Consider GBS/CIDP
  - But what if there is progressive weakness that is asymmetric…or only in arms…or only distal
    - These too can be acquired demyelinating neuropathies that may be responsive to therapy

Clinical Features to Differentiate Typical CIDP and Atypical Variants vs Other Demyelinating Polyneuropathies

<table>
<thead>
<tr>
<th>Features</th>
<th>CIDP&lt;sup&gt;1,2&lt;/sup&gt;</th>
<th>A-CIDP (variant)&lt;sup&gt;1-4&lt;/sup&gt;</th>
<th>DADS no MAG (variant)</th>
<th>MADSAM (variant)&lt;sup&gt;1&lt;/sup&gt;</th>
<th>MMN&lt;sup&gt;1&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weakness</td>
<td>• Symmetric</td>
<td>• Symmetric</td>
<td>• Symmetric</td>
<td>• Asymmetric</td>
<td>• Asymmetric</td>
</tr>
<tr>
<td></td>
<td>• Proximal + distal</td>
<td>• Distal &gt; proximal</td>
<td>• Distal only</td>
<td>• Distal &gt; proximal</td>
<td>• Distal &gt; proximal</td>
</tr>
<tr>
<td></td>
<td>• ≥8 weeks from</td>
<td>• ≤4-8 weeks from onset to</td>
<td>• Mild or none</td>
<td>• Upper limbs &gt; lower limbs</td>
<td>• Upper limbs &gt; lower limbs</td>
</tr>
<tr>
<td></td>
<td>onset to nadir</td>
<td>nadir</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensory deficits</td>
<td>• Yes</td>
<td>• Yes</td>
<td>• Yes</td>
<td>• Yes</td>
<td>• No</td>
</tr>
<tr>
<td></td>
<td>• Symmetric</td>
<td>• Symmetric</td>
<td>• Symmetric</td>
<td>• Multifocal</td>
<td></td>
</tr>
<tr>
<td>Reflexes</td>
<td>• Reduced or absent</td>
<td>• Reduced or absent</td>
<td>• Reduced or absent</td>
<td>• Reduced or absent</td>
<td>• Reduced or absent</td>
</tr>
<tr>
<td></td>
<td>symmetrically</td>
<td>symmetrically</td>
<td>symmetrically</td>
<td>(multifocal or diffuse)</td>
<td>(multifocal or diffuse)</td>
</tr>
</tbody>
</table>

A-CIDP = acute-onset chronic inflammatory demyelinating polyneuropathy; DADS no MAG, distal acquired demyelinating symmetrical neuropathy without myelin-associated glycoprotein; MADSAM = multifocal acquired demyelinating sensory and motor neuropathy; MMN = multifocal motor neuropathy.

Electrophysiologic Findings to Differentiate Typical CIDP and Atypical Variants vs Other Demyelinating Polyneuropathies

<table>
<thead>
<tr>
<th>Findings</th>
<th>CIDP(^1)</th>
<th>A-CIDP (variant)(^1,2)</th>
<th>DADS no MAG (variant)</th>
<th>MADSAM (variant)(^1)</th>
<th>MMN(^1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal CMAPs: demyelinating features</td>
<td>• Usually symmetric</td>
<td>• Usually symmetric</td>
<td>• Usually symmetric</td>
<td>• Asymmetric (multifocal)</td>
<td>• Asymmetric (multifocal)</td>
</tr>
<tr>
<td>Conduction block</td>
<td>• Frequent</td>
<td>• Frequent</td>
<td>• Uncommon</td>
<td>• Frequent</td>
<td>• Frequent</td>
</tr>
<tr>
<td>Abnormal SNAPs</td>
<td>• Usually symmetric</td>
<td>• Usually symmetric</td>
<td>• Usually symmetric</td>
<td>• Asymmetric (multifocal)</td>
<td>• SNAPs are normal</td>
</tr>
</tbody>
</table>

A-CIDP = acute-onset chronic inflammatory demyelinating polyneuropathy; DADS no MAG, distal acquired demyelinating symmetrical neuropathy without myelin-associated glycoprotein; MADSAM = multifocal acquired demyelinating sensory and motor neuropathy; MMN = multifocal motor neuropathy.

Pattern Recognition of Neuropathic Disorders

• Asymmetric Distal Weakness Without Sensory Loss

Consider:
A. With upper neuron findings consider
   1. Motor neuron disease/ALS
   2. If only LMN disease → PLS
B. Without upper motor neuron findings consider
   1. Progressive muscular atrophy
      a. Brachial amyotrophic diplegia (BAD)
      b. Leg amyotrophic diplegia (LAD)
   2. Multifocal motor neuropathy
Distal Acquired Demyelinating Symmetrical Neuropathy (DADS) no MAG (Variant of CIDP)

- Subacute
- Not truly length dependent
- Conduction block, slowing in motor nerves, but without motor signs
- Areflexia
- Responsive to first-line therapies

Distinguishing Typical CIDP and DADS no MAG (Variant of CIDP) from MAG Neuropathy

- Predominant sensory loss
- Ataxia is often out of proportion to small fiber symptoms
- Tremor is a common associated symptom
- Weakness is distal at ankles and toes if at all
- IgM monoclonal protein
- 50% of patients will have anti-MAG antibodies

MADSAM (Variant of CIDP)

- Motor and Sensory: MADSAM
  - MADSAM = multifocal acquired demyelinating sensory and motor neuropathy
  - Also called Lewis-Sumner syndrome

MADSAM (Variant of CIDP), cont.

- Sensory and motor
- Hands
- Individual nerves
- Stepwise

MADSAM (Variant of CIDP), cont.

- Focal conduction abnormalities
- CSF elevated in 82% vs MMN in 9%
- Responds to first-line treatment

Distinguishing MADSAM (Variant of CIDP) From Multifocal Motor Neuropathy

- Motor only
- Main differential is ALS
- Usually hands
- Stepwise
  - NOT PROGRESSIVE
Laboratory Evaluation of Multifocal Motor Neuropathy

- Focal conduction block
- CSF usually normal
- 50% with IgM GM1 Ab

EFNS/PNS Guidelines for CIDP: We Must Use Clinical and Electrodiagnostic Criteria

**Inclusion Criteria**

**Typical CIDP**
- Chronically progressive, stepwise, or recurrent symmetric proximal and distal weakness and sensory dysfunction of all extremities
- ≥2 months duration
- Cranial nerves may be affected
- Tendon reflexes absent/reduced in all extremities

**Atypical CIDP**
- One of the following, but otherwise as in typical (tendon reflexes may be normal in unaffected limbs):
  - Predominantly distal
  - Asymmetric
  - Focal
  - Pure motor
  - Pure sensory

**Exclusion Criteria**

**Infection, drug/toxin exposure**

**Hereditary demyelinating neuropathy**

**Prominent sphincter disturbance**

**Diagnosis of MMN**
- IgM monoclonal gammopathy with high-titer antibodies to MAG
- Other causes of demyelinating neuropathy