Immune Mediated Neuropathies

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AIDP and CIDP

- Acute inflammatory demyelinating polyneuropathy (AIDP) or Guillain Barré Syndrome
- Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP)

Guillain-Barré Syndrome (GBS)

- Monophasic, acute inflammatory demyelinating polyneuropathy
- Variants include axonal or mixed axonal/demyelinating pathology
  - acute motor axonal neuropathy (AMAN)
  - acute motor sensory axonal neuropathy (AMSN)
  - acute autonomic neuropathy (AAN)
  - Miller-Fisher syndrome
    - ophthalmoplegia
    - ataxia
    - areflexia

GBS: Clinical Features

- AIDP and AMSN present in similar fashion
  - begins with rapidly progressive ascending paralysis
    - proximal muscles are often affected more than distal muscles
    - weakness progresses over 7 to 21 days
    - mean duration from onset to maximal weakness is 12 days

GBS: Clinical Features

- Annual incidence of 1-2/100,000
- Occurs at any age
- Onset
  - 70% of cases follows a respiratory or gastrointestinal infection (campylobacter jejuni) by 5 days to 3 weeks
  - other precipitating factors:
    - HIV
    - immunization
    - pregnancy
    - Hodgkin’s disease
    - surgery

- associated with cranial nerve and respiratory muscle weakness
  - intubation occurs in 20% of patients
  - loss of deep tendon reflexes
  - distal paresthesias and sensory loss
  - papilledema, autonomic disturbances and SIADH are seen in some patients
- AMAN
  - pronounced distal weakness with sparing of cranial nerves
Diagnosing GBS
- Quadriplegia without facial weakness is unusual with GBS
- A hanging jaw suggests a diagnosis of myasthenia gravis
- Weakness of muscle supplied by upper cervical roots and orofaryngeal dysfunction is highly associated with subsequent respiratory distress
- Early urinary retention occurs and can mimic spinal cord disease
- Presence of deep tendon reflexes throughout is not consistent with GBS

GBS: Diagnostic Workup
- Electrodiagnostic studies
  - nerve conduction studies show loss of “F” wave latency response and reduced conduction velocity (myelin damage)
  - reduced motor fiber amplitudes reflect secondary axonal damage and imply a worse prognosis for recovery

GBS: Diagnostic Workup
- LP
  - CSF reveals cytoalbuminologic dissociation
    - elevated protein with normal WBC count
  - elevated CSF protein may not be evident until 2 weeks into the disease process
  - mild lymphocytic or monocytic pleocytosis is sometimes seen and should raise suspicion for an infectious polyradiculopathy (HIV, CMV or Lyme disease) or polio
- Anti-GM1 and anti-GQ1b antibodies
- CMV titers

GBS: Treatment
- Patients with signs of respiratory muscle weakness should be admitted to an ICU for observation until it is clear that the illness has stabilized
- Respiratory parameters for elective intubation
  - VC <20 ml/kg
  - Plmax <30 cm H2O or PEmax <40 cm H2O
  - >30% reduction in VC from baseline

GBS: Treatment
- Plasmapheresis
  - if initiated within 10 days of the onset of symptoms, can speed the onset of recovery
  - a total of 5 treatments is performed every 1 to 2 days with a total of 2 to 4L of plasma exchanged for 5% albumin during each treatment

GBS: Treatment
- Intravenous immune globulin (IVIG)
  - 0.4 gm/kg/day for 5 consecutive days
  - rebound deterioration after completing a course of IVIG can sometimes occur
  - there is no proven benefit of combining IVIG and plasmapheresis treatments
GBS: Treatment

- **Pain management**
  - pain can be severe and may result from meningeal inflammation or neuropathic mechanism
- **Dysautonomia**
  - most frequent cardiovascular manifestation is sustained hypertension and tachycardia
  - beta-blockers
    - propranolol or labetolol
- **Rehabilitation**

GBS: Poor Prognosis

- **Advance age**
- **Very low distal motor amplitudes**
- **Rapidly progressive weakness occurring over the first week**
- **Respiratory failure requiring intubation**

Chronic Acquired Demyelinating Polyneuropathy (CADP)

- Autoimmune disease that targets the myelin sheaths of peripheral nerves
- **Diagnosis difficult:**
  - clinical heterogeneity of the disease
  - multifocality
  - predilection for proximal nerve segments

CADP

- 54% of patients have features that do not conform to the typical presentation:
  - predominantly distal features
  - pure sensory neuropathy
  - marked asymmetries
  - associated CNS demyelinating disease
  - predominant cranial nerve involvement

CADP: Phenotypic Pattern

Distinguish demyelinating polyneuropathies by the phenotypic pattern: that is, what are the examination features?

Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP)

- Separate from GBS or AIDP on basis of chronic relapsing course, enlargement of nerves and responsiveness to steroids
CIDP: Prevalence
- Underestimated due to underreporting, differences in diagnostic criteria and the uncertainty in making the diagnosis
- 1 to 7.7 per 100,000
- 2,000 to 15,000 cases in the US
- 5% of all neuropathies, 10 million cases of neuropathy in US then approximately 500,000
- 40% achieve lasting remission
- 60% could have active disease at any given time

CIDP: Clinical Manifestation
- Insidious onset and evolves slowly
- Clinical course (at least 2 months)
  - steadily progressive
  - stepwise progressive
  - chronic monophasic
  - recurrent

CIDP: Clinical Manifestation
- Motor and sensory (numbness, paresthesias and dysesthesias of the hands and feet) involvement
- Hyporeflexia or areflexia
- Polyradicular
- Symmetric
- Proximal and distal muscles
- Cranial and respiratory muscles were sometimes also involved

CIDP: Pathology
- Segmental demyelination and remyelination
- Thinned myelin sheaths in proportion to axon caliber
- Onion bulb formation
- Sural nerve may be unaffected in polyradicular and preferential involvement of motor fibers

CIDP: Pathology
- Mononuclear cell infiltrates may also be seen in the endoneurium
  - more prominent in the proximal nerve trunks or spinal roots
  - typically spars or absent in sural nerve biopsies.
- Require electron microscopy and teased fiber analysis
  - not available to most practicing neurologists

CIDP: Diagnostic Workup
- Electrodiagnostic study
  - multifocal conduction block
  - prolonged distal latencies
  - nerve conduction velocity slowing to less than 80% of normal
  - loss of late responses
  - abnormal temporal dispersion of the compound muscle action potential
- LP
  - CSF reveals cytoalbuminologic dissociation
- Biopsy
**Diagnostic Criteria for CIDP**

<table>
<thead>
<tr>
<th>Clinical</th>
<th>Pathology of axonal involvement</th>
<th>Motor sensory dysfunction involving more than six limbs</th>
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</thead>
<tbody>
<tr>
<td>At least 3 weeks of axonal involvement</td>
<td>Referral to neurologist</td>
<td>At least 1 week</td>
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<tr>
<td>Partial or complete axonal loss in peripheral nerves</td>
<td>Disturbance in deep tendon reflexes</td>
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</tr>
<tr>
<td>Elbow, knee, ankle</td>
<td>EMG shows axonal loss</td>
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**CIDP: Treatment**

- **Corticosteroids**
  - Oral
    - 1 mg/kg daily of prednisone
    - titrate dose according to clinical response
  - IV methylprednisolone
    - 1 gm IV q day times 3-5 days

- **Antimetabolites**
  - Azathioprine
    - 1.5-3 mg/kg/day
  - Mycophenolate mofetil
    - 1-1.5 gm PO BID

- **Alkylating agents**
  - Cyclophosphamide

- **Immunophilins**
  - Cyclosporin
    - 2.5-5.0 mg/kg/day divided into 2 doses PO

- **Intravenous immune globulin**
- **Plasmapheresis**

**CIDP: Prognosis**

- Patients with discrete relapses have a better prognosis than those with a progressive course
- In one study, 73% were said to have made a good recovery but the long term outcome in this disease has been generally poor with decades of disability and treatment dependence
- 10% of cases, the disease burns out after many years and treatment can be withdrawn

**Neuropathy Comparison**
## Variants of CADP

- **Temporal variants**
  - SjDP

- **Distribution variants**
  - MMN
  - MADSAM neuropathy
  - DADS neuropathy

- **Concurrent illness variants**
  - MGUS
  - diabetes mellitus
  - HIV infection
  - lymphoma
  - osteosclerotic Myeloma
    - POEMS syndrome
    - Crow-Fukase syndrome
    - Castleman’s disease

- **Possible variants**
  - chronic active hepatitis
  - inflammatory bowel disease
  - connective tissue disease
  - bone marrow and organ transplants
  - central nervous system demyelination
  - nephrotic syndrome
  - hereditary neuropathy
  - thyrotoxicosis
  - axonal
  - pure sensory