Acquired Neuropathies

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Acquired Inflammatory Diseases of Nerve

- Acute Inflammatory Demyelinating Polyneuropathy
  - AMSAN (acute motor-sensory axonal n.)
  - AMAN (acute motor axonal n.)
  - MFS (Miller Fisher syndrome)

- Chronic Inflammatory Demyelinating Polyneuropathy
  - DADS (distal acquired demyelinating polyradiculoneuropathy)
  - MADSAM (multifocal acquired demyelinating sensory and motor polyradiculoneuropathy)
  - MMN (multifocal motor neuropathy)
AIDP
Guillain-Barré Syndrome

- History precedent illness 60-70%
  - C. jejuni 32%
  - CMV 13%
  - EBV 10%
  - M. pneumoniae 5%
  - Also reported in relation to HIV, Hep A,B,C, influenza

- Autoimmune conditions
  - SLE, lymphoma, GVHD, organ rejection

- Physical insults
  - Surgery
  - Immunizations
  - ?trauma
AIDP
History

- Rapid onset (hours)
- Paresthesias that ascend from feet to hands (large > small fiber loss)
- Flank/back pain 50%
- Weakness
  - variable, from mild distal weakness to severe, vent-dependent
  - 56%: onset in legs
  - 12%: onset in arms
  - 32%: onset in both (Ropper et al, 97)
Strength
- Proximal and distal weakness
- Symmetric

Sensation
- Large > small fiber

DTRs
- Absent

Cranial nerves
- Ophthalmoplegia, ptosis: 5-15%

Autonomic instability
- Cardiac arrhythmias
- Labile BP

Respiratory failure: 30%
Now what?
Lab features

- Week 1
  - Normal CSF (30%)
  - Normal NCS/EMG
  - MRI may show nerve root enhancement

- Week 2+
  - CSF albuminologic dissociation (80%)
  - NCS/EMG
    - Max abnormal 3-8 weeks after onset

- CSF pleocytosis (>10-50 lymphs)
  - Lyme disease, HIV, sarcoidosis
  - Viral hepatitis, EBV, CMV if LFTs ↑
Electrophysiologic features  
NCS

- **Earliest abnormalities:**
  - Prolonged DL (NAGBSSG) (Albers et al, ’85)
  - Prolonged/absent F-responses (reflecting early involvement of nerve roots) (NAGBSSG)
  - ↓ CMAP amplitudes (50% 1 week after onset) (Albers et al, ’85)

- **3-8 weeks after onset:**
  - NCV slowing into demyelinating range
    - <80% if amplitudes relatively preserved
    - <70% if not
  - abnormal temporal dispersion
  - conduction block
  - absent F-waves
Uniform slowing

Non-uniform slowing

Abnormal temporal dispersion
Some conduction "fail" electrically because the myelin integrity is insufficient, even though the axon is intact.
Electrophysiologic features

NCS

- Latest abnormalities:
  - Nadir at 1 mo, with improvement over 1 yr
- Correlation with clinical severity
  - Generally none
  - CMAP amplitudes <10-20% normal > poor prognosis
- SNAPs
  - UEs involvement > LE (distinguishes from most sensory neuropathies)
Earliest abnormality:
- Reduced recruitment

Week 2-4
- ↑ abnormal spontaneous activity, p-waves, fibrillation potentials
- Myokymia!
AIDP
Treatment

- PE (200-250ml/kg qod over 10-14 d)
  - NA trial; French trial (↓ time to vent independence, unaided walking, improvement @ 1 mo)
- IVIG (2g/kg over 2-5 d)
  - Dutch IVIG trial; PE Sandoglobulin trial (no difference in efficacy from PE; no added benefit of both)
- ?s
  - Children
  - Mild disease in adults
  - >2 weeks of disease
- Steroids
  - Dutch GBS group: no efficacy
- Others
  - No benefit of IFNβ1a
AIDP
Hospital Care

- Regularly monitor pulmonary function (vital capacity, respiration frequency)
  - initially every 2–4 h
  - in stable phase every 6–12 h

- Regularly check for autonomic dysfunction (blood pressure, heart rate, pupils, ileus)
  - initially continuous monitor heart rate (ECG),
  - Pulse, blood pressure q2–4 h
  - in stable phase every 6–12 h

- Check for swallowing dysfunction

- Recognise and treat pain
  - acute nociceptive pain (try to avoid opioids)
  - chronic neuropathic pain (antiepileptic drugs or antidepressants)

- Prevent and treat infections and pulmonary embolism

- Prevent cornea ulceration due to facial weakness

- Prevent decubitus and contractures
AIDP Course

- Nadir: 2-4 weeks
  - 50%: nadir by 2 weeks
  - 80%: nadir by 3 weeks
  - 90%: nadir by 4 weeks
- Progression > 8 weeks excludes GBS
- Progression 4-8 weeks
  - Subacute IDP
AIDP Prognosis

- 15-50% patients: no residua
- 50-85% patients: some residua even up to 7 years after illness
- 5-10%: severe residua, including fatigue, motor & sensory
- 5% mortality rate
  - Respiratory complications; PE; cardiac arrhythmias; sepsis
- Poor prognostic factors:
  - Age > 50 y
  - Abrupt onset
  - Vent dependence
  - CMAP<10-20% normal
AIDP Variants

AMSAN: Acute Motor & Sensory Axonal Neuropathy

- Clinical features:
  - Indistinguishable from AIDP

- Lab features:
  - Indistinguishable from AIDP

- Electrophysiology:
  - Early: Indistinguishable from AIDP (low amp CMAPs)
  - >1 week: markedly ↓ CMAP/SNAP amps with normal/near normal CVs, DLs

- Treatment:
  - PE/IVIG
**AIDP Variants**

**MFS: Miller Fisher Variant**
(continuum with Bickerstaff encephalitis)

- **Clinical features:**
  - Ataxia, areflexia, ophthalmoparesis
  - Other CN deficits also occur
    - Facial weakness, dysphagia, facial paresthesias

- **Lab features:**
  - CSF cytoalbuminologic dissociation (59%)
  - **antiGQ1b** (85%)

- **Electrophysiology:**
  - Markedly ↓ SNAP amps with normal/near normal CVs, DLs
  - CMAPs usu. normal

**Treatment:**
- Natural history is good recovery
- IVIG?
- Little evidence for PE
AIDP Variants

AMAN: Acute Motor Axonal Neuropathy
Chinese paralytic syndrome

- Clinical features:
  - D>P weakness
  - CN deficits, RF more common (30%)
  - NO SENSORY INVOLVEMENT
  - Occasionally, ↑ DTRs
  - Looks like polio!

- Lab features:
  - Indistinguishable from AIDP

- Electrophysiology:
  - markedly ↓ CMAP amps with normal/near normal CVs, DLs
  - SNAPs normal

- Pathology:
  - Distal conduction block
  - Widespread axonal degeneration

- Treatment:
  - PE/IVIG
  - IVIG treated patients may recover faster but no difference in long term outcome
Chronic Inflammatory Demyelinating Polyradiculoneuropathy
CIDP

- Distinguished from AIDP by the presence of a relapsing-remitting course (MS of the PN)

- Variants
  - DADS (distal acquired demyelinating polyradiculoneuropathy)
  - MADSAM (multifocal acquired demyelinating sensory and motor polyradiculoneuropathy)
  - MMN (multifocal motor neuropathy)
  - MAMA (multifocal acquired motor axonopathy)
  - CISP (chronic immune sensory polyradiculopathy)
CIDP
Clinical features

- Progressive for > 2 mos.
- MS-like courses
  - Chronic monophasic (15%)
  - Chronic relapsing (34%)
  - Stepwise progressive (34%)
  - Steady progressive (15%)
- Risk factors
  - Male
  - Pregnancy
  - Infection
CIDP
Conditions associated with CIDP

- **Infectious**
  - HIV
- **Inflammatory**
  - SLE
  - IBD
  - Post-transplant (GVHD)
- **Metabolic**
  - DM
- **MGUS**
- **Paraneoplastic**
  - POEMS
  - Lymphoma
  - Waldenstroms macroglobulinemia (DADS)
  - Lung, pancreas, colon CA
  - melanoma
- **Toxic**
  - Cyclosporine
  - Tacrolimus
  - TNA blockers
Like, relapsing AIDP

Strength
- Symmetric, proximal and distal weakness

Sensation
- Subjective numbness: 68-80%
- Painful paresthesias 15-50%
- Sensory ataxia with gait imbalance
- SENSORY SIGNS > WEAKNESS, think ANTI-MAG

DTRs
- Areflexia, hyporeflexia

Cranial nerves
- Facial weakness, ophthalmoplegia, dysarthria, dysphagia
- NECK EXTENSOR WEAKNESS (think POEMS)
CIDP
Lab features

- **CSF**
  - 80-95% ↑ protein
    - 10% slightly ↑ lymphs (5/mm³)
  - Very high protein
    - POEMS
    - Cancer
  - ↑ cells in CSF
    - HIV
    - Sarcoidosis
    - Lyme disease
    - Lymphomatous, leukemic infiltration of nerve roots
  - 65% ↑ oligoclonal bands

- **Blood work**
  - 25% have a monoclonal gammopathy (IgA, IgG, IgM)

- **Imaging**
  - Hypertrophy/enhancement of nerve roots and PN

- **NCS/EMG**
  - <2/3 CIDP patients fulfill EPS criteria
CIDP
Electrophysiologic evaluation

- MNCV <70% LLN
- DML prolonged 125-150% ULN
- Absent F waves
- Abnormal temporal dispersion (>9ms between proximal and distal site)
  - Helps with differentiation from axonal and MN disorders, but not necessarily from hereditary forms
- Conduction block
  - Complete
  - Partial: >50% reduction in amplitude of CMAP from distal to proximal site of stimulation
CIDP Pathology

- Sural nerve biopsy

Onion bulbs (demyel/remyel)

Hypertrophy of nerve roots (Schwann cell proliferation)

Endoneurial/perineurial edema
CIDP

Treatment

- **Corticosteroids**
  - Pulse, or
  - 1.5 m/kg qd X 2 wks, then 100 mg qod until improvement or plateau (4-6 mos)
  - Taper 5 mg q2-3 wks

- **PE**
  - Transient effect, requires repeated exchanges
  - 200-250 mL/kg qod 5-6X
  - Better than steroids in uncontrolled DM, HIV
  - Better than IVIG in CRI or severe atherosclerotic cardiovascular disease
  - May be a better choice for a diagnostic-therapeutic trial as the response is faster

- **IVIG**
  - 2g/kg qmonth X 3 mos.
  - IgA deficiency
  - HA, myalgias, flu-like reactions, hyperviscosity

- **Other options**
  - AZT, Cyclosporine, Methotrexate, Cyclophosphamide, Mycophenolate
CIDP Variants

DADS

- **Clinical features:**
  - Distal sensory loss with mild or no distal weakness

- **Lab features:**
  - 67% have monoclonal protein (IgM>others)
  - antiMAG in 67% IgM DADs

- **Electrophysiology:**
  - Indistinguishable from CIDP
  - Less conduction block

- **Treatment:**
  - Steroids/PE/IVIG/cyclophosphamide
    - Response is better in idopathic DADS
    - Response is poor in IgM DADS
CIDP Variants
Multifocal motor neuropathy

- **Clinical features:**
  - Asymmetric
  - Distal > proximal, arms > legs
  - NO SENSORY INVOLVEMENT
  - 2 or more nerves (mononeuritis multiplex)

- **Lab features:**
  - CSF usually normal
  - Antiganglioside antibodies (GM1)
  - No nerve hypertrophy

- **Electrophysiology:**
  - Hallmark of disease is motor conduction block

- **Treatment:**
  - IVIG/cyclophosphamide/(rituximab/interferon beta)
CIDP Variants

MADSAM (MMN + SL)

- **Clinical features:**
  - Asymmetric
  - Distal > proximal, arms > legs
  - SENSORY INVOLVEMENT
  - Chronic sensorimotor mononeuritis multiplex

- **Lab features:**
  - ↑ CSF protein (60-80%)

- **Electrophysiology:**
  - CIDP features in distribution of single nerves
  - Looks like MMN with low amplitude or absent SNAPs

- **Treatment:**
  - IVIG/steroids
  - ?PE/cyclophosphamide/cyclosporine/AZT
How do you approach diagnosis of a neuropathy?
Anatomic approach

- Muscle
  - NMJ
  - Nerve processes (see patterns)
- 1 Nerve
  - (mononeuritis)
- Plexus
- Root
- MN

Anatomic approach: The diagram illustrates the anatomic approach involving various components of the nervous system, including muscle, NMJ, nerve processes, plexus, root, and MN, with a focus on mononeuritis.
Motor neuron

- Upper motor neuron
  - Primary lateral sclerosis
  - Hereditary spastic paraparesis

- Lower motor neuron
  - Progressive muscular atrophy
  - Spinal muscular atrophy
  - Kennedy’s disease
  - Monomelic amyotrophy
  - Polio/Post-polio syndrome
  - Motor neuronopathy (paraneoplastic; hereditary)

- Both
  - ALS
Root

- Compressive
  - HNP
  - OA
- Infectious
  - Herpes zoster
- Cancer
  - Meningeal carcinomatosis/lymphomatosis
Plexus

- Neoplastic
- Diabetic
- Familial
- HNPP-associated
- Idiopathic
Mononeuritis multiplex

- **Infectious**
  - Lyme
  - HIV
  - Leprosy
  - Hepatitis C

- **Inflammatory**
  - Vasculitis
  - Sarcoid
  - Cryoglobulinemia

- **Hereditary**
  - HNPP

- **Systemic disease**
  - Diabetes
  - Waldenstrom’s macroglobulinemia

- **Demyelinating**
  - Multifocal motor neuropathy
  - (CIDP)
Pattern Approach to acquired neuropathies

- Systems (M; S; both)
- Distribution (P; D; both)
- Symmetry (A; S)
- Autonomic involvement
- Pain
- Associated symptoms or “aha” clues
Patterns that lead to a differential: Systems

- **Motor only (Weakness)**
  - MND
  - Muscle
  - NMJ
  - Paraneoplastic motor neuropathy
  - Multifocal motor neuropathy

- **Autonomic**
  - DM
  - Amyloidosis
  - AIDP
  - Vincristine
  - Porphyria
  - HIV
  - Idiopathic
Patterns that lead to a differential: Systems, Distributions, Symmetry

- Symmetric, proximal + distal weakness, M+S
  - AIDP
  - CIDP

- Symmetric, distal weakness, M+S
  - Metabolic (DM, amyloidosis, renal/liver disease, vitamin deficiencies)
  - Drugs/toxins (Chemo, HMs, meds)
  - Hereditary (amyloidosis, CMT)

- Asymmetric, distal weakness, M+S
  - Single
    - Compressive mononeuropathy
    - Radiculopathy
  - Multiple
    - Vasculitis
    - HNPP
    - Infectious
      - Lyme, leprosy, HIV
    - MADSAM
Patterns that lead to a differential: Systems, Distributions, Symmetry

- Asymmetric, proximal + distal weakness, M+S
  - Polyradiculopathy
  - Plexopathy
  - Mononeuritis multiplex

- Sensory only (Numbness)
  - Sensory neuropathy
    - CSPN
    - metabolic (DM, amyloidosis, renal/liver disease, vitamin deficiencies)
  - Ganglionopathy
    - Paraneoplastic
    - Cisplatinum
    - B6 toxicity
    - HIV
    - Sjogren’s syndrome
    - Idiopathic
Young children see 9 dolphins