PERIPHERAL NERVE DISORDERS IN PRIMARY CARE

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DEFINITION: PERIPHERAL NEUROPATHY

• “…a result of damage to your peripheral nerves, often causing weakness, numbness, and pain…” - Mayo Clinic

• “… conditions that result when nerves that carry messages to and from the brain and spinal cord from and to the rest of the body are damaged or diseased.” - WebMD

• “… damage to or disease affecting nerves, which may impair sensation, movement, gland or organ function, or other aspects of health, depending on the type of nerve affected.” - Wikipedia

• “Neuropathic disorders encompass diseases of the neuron cell body (neuronopathy) and their peripheral processes (peripheral neuropathy)” - AAN
OVERVIEW

- Over 100 types
- Poly-/mono-
  - Metabolic/Toxic/Inflammatory/Compressive/Hereditary
- 10% prevalence
- Structured evaluation is critical
  - Confirm peripheral - where?, time course?, nerve fiber types?, primary pathology?, other pertinent features?
“The life so short, the craft so long to learn”

–HIPPOCRATES
EVALUATION: CONFIRM
PERIPHERAL/LOCALIZATION

- Non-PNS considerations: assymetry, unusual sx patterns, DTRs, somatoform disorders
- Mimics: multiple sclerosis, cerebrovascular disease, cervical myelopathy, poliomyelitis related to WNV, polyradiculopathy, ALS, neuromuscular junction disease, myopathy
EVALUATION: TIME COURSE

• Acute
  • Vasculitic mononeuritis multiplex, idiopathic plexopathy, AIDP, acute toxin, paraneoplastic sensory neuropathy

• Chronic
  • Diabetic PN, CIDP, idiopathic, hereditary
EVALUATION: NERVE FIBER TYPES/SYMPOTOMS

- Sensory, Motor, Autonomic
- Sensory level/Vibration/Soft touch/Pin/Temp/Proprioception
- DTRs: consider age/prior CNS involvement
- Motor signs: atrophy/fasciculations/strength and gait
- Orthopedic signs: high arches/hammertoes/foot injuries
- Other/Autonomic: edema/rubor/hair pattern loss/orthostatic sx/s/sexual dysfunction/Sicca symptoms
EVALUATION: PRIMARY PATHOLOGY

• Demyelination vs Axonal
  • EMG/NCS
  • Nerve biopsy
EVALUATION: PERTINENT FEATURES

- Symptoms - worsening balance, falls, paresthesias, hyperalgesia, allodynia, problems dressing
- Medical history - prior dx, difficulty with sports, foot “trouble”
- Medication/exposure review - include vitamins and prior pertinent exposures i.e chemo/immunosuppression
- Family history - use of braces, ortho considerations
SIGNS/SYMPTOMS

• Motor nerve injury
  • atrophy, hypotonia, weakness, hyporeflexia, fasciculations, cramps

• Sensory nerve injury
  • Large Fiber - dec vibration/ temp/ proprioception; sensory ataxia/ paraesthesias
  • Small Fiber - dec pain/ temp; dysesthesias/ allodynia

• Autonomic nerve injury
  • Hypo-/ hypertension; urinary retention; hyper-/ anhydrosis; ED; vascular color changes; gastroparesis
# DDX of Sensory-Predominant Neuropathy

<table>
<thead>
<tr>
<th>Condition</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes Impaired Glucose Tolerance</td>
<td>5-15% 25-30%</td>
</tr>
<tr>
<td>Idiopathic</td>
<td>20-35%</td>
</tr>
<tr>
<td>Vit B12 Deficiency</td>
<td>1-5%</td>
</tr>
<tr>
<td>THIAMINE Deficiency</td>
<td>&lt;1 %</td>
</tr>
<tr>
<td>Vit B6 Def/Excess</td>
<td>&lt;1 %</td>
</tr>
<tr>
<td>Thyroid Disease</td>
<td>2%</td>
</tr>
<tr>
<td>INFLAMMATORY/RHEUMATOLOGIC</td>
<td>1%</td>
</tr>
<tr>
<td>Paraneoplastic</td>
<td>&lt;1 %</td>
</tr>
<tr>
<td>Drugs</td>
<td>&lt;1 %</td>
</tr>
</tbody>
</table>

AXONAL VS DEMYELINATING

<table>
<thead>
<tr>
<th>Nerve Type</th>
<th>Mechanism</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>primary axonal</td>
<td>Sens/Mot</td>
<td>metabolic</td>
</tr>
<tr>
<td></td>
<td>or</td>
<td>amyloidosis, porphyria, CTD</td>
</tr>
<tr>
<td>primary demyelinating</td>
<td>sens/mot</td>
<td>immune</td>
</tr>
<tr>
<td></td>
<td>or</td>
<td>AIDP, CIDP</td>
</tr>
<tr>
<td>mixed axonal/demyelinating</td>
<td>sens/mot</td>
<td>diabetes</td>
</tr>
<tr>
<td></td>
<td>or</td>
<td></td>
</tr>
</tbody>
</table>

Attal, N. “Neuropathic Pain: Mechanisms, Therapeutic Approach, and Interpretation of Clinical Trials.” Continuum, Feb 2012. p 166
METABOLIC PERIPHERAL POLY-NEUROPATHIES

- Diabetes, Diabetes, Diabetes...
- Microvascular injury involving small bv supplying vasa vasorum
- Prototypical stocking-glove, symmetric, sens loss/pain, rare distal weakness
- Axonal/demyelinating
- 25-40% idiopathic
DIABETIC PERIPHERAL NEUROPATHY

- Distal Predominantly Sens Polyneuropathy
- Small Fiber Peripheral Neuropathy: Pain!
- Autonomic Neuropathy
- Compressive Mononeuropathies
- Noncompressive focal/multifocal neuropathies
- Diabetic Amyotrophy
- MFMN/MM
- CN
- CIDP
TOXIC PERIPHERAL NEUROPATHIES

- Heavy metals** - (arsenic/thallium/lead - disproportionate weakness/mercury - cognitive/behavioral/cerebellar)

- Cardiovascular - (Amiodarone, also statins, enalapril, propafenone)

- Chemotherapeutics** - (Cisplatin, Taxol, Vinca alkaloids, Thalidomide, misonidazole)

- Antiretrovirals** - (Stavudine, Zalcitabine, Didanosine)

- Antibiotics - (Dapsone, Metronidazole, Nitrofurantoin)

- CNS agents - (NO, phenytoin, lithium)

- Ethanol

** Particularly Painful Causes
INFLAMMATORY/IMMUNE PERIPHERAL NEUROPATHY

• GBS ("mostly" AIDP - Miller Fisher - Paraparetic GBS)
  • antecedent illness (CMV/C. jejuni)
  • paresthesias distally, followed by weakness, spreading proximally, low back pain
  • Nadir reached in 2-4 weeks
  • prox and distal limb segments, demyelinating
  • Also AMAN, AMSAN

• CIDP: Classic, MADSaM, MMM - all demyelinating
  • Associated with lymphoma, Waldenstrom’s, POEMS, DM, HIV, SLE, malignancy, Nephrotic syndrome
INFLAMMATORY/IMMUNE PERIPHERAL NEUROPATHY

- Vasculitic Neuropathy
  - Primary:
    - Large: GCA
    - Medium: Polyarteritis nodosa
    - Small: Wegener granulomatosis, Churg-Strauss, microscopic polyangiitis
INFLAMMATORY/IMMUNE PERIPHERAL NEUROPATHY

• Vasculitic Neuropathy

• Secondary

  • CT disease: RA, Sjogren’s, SLE, Dermatomyositis

  • Inflammatory bowel disease

  • Sarcoidosis

  • Behcet disease

  • Malignancy
COMPRESSIVE PERIPHERAL NEUROPATHIES

- Median mononeuropathy at the wrist - between the carpal bones and the flexor retinaculum
  - Most common entrapment neuropathy of the UE
  - DDx: proximal median neuropathy, brachial plexopathy, C6-7 radiculopathy

- Ulnar Neuropathy at the elbow - between either the retroepicondylar groove or the humeroulnar arcade
  - DDx: lower trunk/medial cord brachial plexopathy; C8-T1 radiculopathy
HEREDITARY PERIPHERAL NEUROPATHIES: COMMON TYPES

- HMSN/CMT
  - Slowly progressive; weakness/distal mm atrophy; sens deficits/decreased DTRs
  - AD/AR/X-linked
- HNPP
  - Painless, recurrent, focal mononeuropathies with spont recovery
  - Painless brachial plexopathies in 25%
- HSAN
  - Rare; young pts
HEREDITARY PERIPHERAL NEUROPATHY: DIAGNOSIS/TX

- Family history
  - CMT families - <30% will seek medical attn for sx
- Electrodiagnostic studies/genetic assays
- No cure - supportive only
  - Tx, gait assist devices, genetic counseling
“All through my life, I have been tested. My will has been tested, my courage has been tested, my strength has been tested. Now my patience and endurance are being tested.”

–MUHAMMAD ALI
TESTING

• AAN practice parameter (Jan 2009)
  • *Blood glucose (consider GTT); *Vit B12 with metabolites (methylmalonic acid with and without homocysteine); electrolytes for renal/liver function; thyroid studies; *SPEP

• No genetic panels!

• Decompressive surgery for DM-PN is unproven
TESTING

• Other labs: ANA, RF, Lyme, RPR, HIV, antigliadin IgG/IgA and transglutaminase, urine/serum heavy metal screens, serum copper level, Vitamin E, Anti-mag antibodies, Anti-GM1/Anti-GQ1B, fat pad aspirate, paraneoplastic antibody panel, CSF studies

• EMG/NCS

• Skin biopsy

• QSART testing

• Nerve biopsy (vasculitis, amyloid, leprosy, sarcoidosis, leukodystrophies)
SMALL FIBER PN: EPIDERMAL NERVE FIBER DENSITY

Normal Image of Epidermal Nerve Fiber Density

Abnormal Image of Epidermal Nerve Fiber Density

https://www.therapath.com/
“The art of medicine consists of amusing the patient while nature cures the disease”

—VOLTAIRE
TREATMENT: MEDICATION MANAGEMENT FOR NEUROPATHIC PAIN

- TCAs: amitriptyline, nortriptyline
- SNRIs: duloxetine, venlafaxine
- AEDs: gabapentin, pregabalin, carbamazepine, lamotrigine
- Topical lidocaine, capsaicin, topical combinations from compounding pharmacies
- Opiates: tramadol, morphine, oxycodone, methadone
- Other: THC, botox, TENS
TREATMENT: SUPPORT

• Physical therapy/Occupational Therapy
• Psychologists
• Vocational Therapy/Driver testing and vehicle modifications
• Management of Neuropathic arthropathy/Foot and Wound Care
• Orthotics/AFOs/gait assist devices
• Pressure-relieving mattress/Bathtub benches/Handheld showers/raised toilet seats/grab bars
“Isn’t it a bit unnerving that doctors call what they do “practice”?"

–GEORGE CARLIN