PERIPHERAL NEUROPATHY

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OBJECTIVES

- To understand the mechanism, screening, diagnosis, and treatment for peripheral neuropathy (PN)
- To establish an diagnostic approach to evaluating diabetic PN
- Prerequisites: None
- See also
  - Flames regarding other chronic complications of DM

BACKGROUND

- PN affects ~2.4% of the general population, and manifests differently in every patient
- In general, PN can be acquired or hereditary
- The most common cause of acquired PN is underlying diabetes mellitus
  - Generally seen in late stage in T1DM, but can be early in T2DM
- *Bonus pearl: the most common cause of hereditary PN is Charcot-Marie-Tooth*
- All patients with PN require further evaluation before it can be solely attributed to DM

BACKGROUND (CONT'D)

- PN is a functional or structural disorder of the peripheral nervous system (PNS)
- It may affect motor, sensory, or autonomic nerves (ANS)
  - Motor involvement may cause muscle atrophy, weakness, fasciculations
  - Sensory involvement may demonstrate difficulty with vibratory sense, proprioception, paresthesias, pain, and thermal sensation dysregulation
  - Changes in ANS may manifest as CV, GI, GU dysfunction

BACKGROUND (CONT'D)

- More specifically, damage to sensory nerves → loss of sensibility, lack of balance, pain, or tingling
  - Damage to large sensory nerves → impairs touch, vibratory sensation, muscle strength
  - Damage to small sensory fibers → impairs thermal sensation and pain
- Other common manifestation DM PN include:
  - Hypoglycemic unawareness
  - Diabetic diarrhea, constipation, or fecal incontinence
  - Bladder dysfunction
  - Sexual dysfunction

PATHOPHYSIOLOGY

- PN occurs due to axonal degeneration or demyelination. In most cases, this is distal and symmetric and depends on the length of the axon
  - Axonal degeneration occurs from direct injury/dysfunction to cell body
  - Demyelination occurs from Schwann cell dysfunction, myelin protein gene mutations, or direct damage to myelin sheaths

MANIFESTATIONS OF DIABETIC PN

- Sensory Motor Neuropathy – nerves with the longest axons are affected resulting in stocking and glove distribution paresthesias
  - Aka "Distal symmetric polyneuropathy"
- Autonomic Neuropathy – occurs in the late stage of long-term poorly-controlled diabetics resulting in sympathetic, parasympathetic, and enteric nerve damage
  - Vasomotor neuropathy – Can lead to hypotension by affecting splenic and peripheral vascular beds → syncope and dizziness by decreasing input to vascular neural beds
  - Sudomotor neuropathy – Can cause dysfunction of thermal regulatory mechanisms
  - Gastrointestinal autonomic neuropathy – Can cause paresis secondary to damage to splanchnic nerves
  - Bladder and sexual dysfunction

HISTORY & PHYSICAL

- Symptoms:
  - Numbness/tingling, burning, (stocking and glove sensory loss) leading to unsteady gait, foot dragging, GI/GU dysfunction
- Signs:
  - Broad based gait, foot drop, pt requires vision/vestibular sense to maintain balance
- Physical Exam Findings:
  - Monofilament testing – Hallmark of assessing loss of sensation
  - 128-hz tuning fork testing – Assesses vibratory sensation, proprioception, loss of sensation suggestion peripheral neuropathy
    - Usually performed at the medial malleolus, the great toe and the fifth toe
  - Observation/strength testing – Muscle atrophy, muscle weakness
  - Reflex hammer testing – Reduced for absent lower extremity reflexes

DIFFERENTIAL DIAGNOSIS

- Metabolic: DM, Hypothyroidism
- Infectious: HIV, Hep C, Lyme Disease
- Traumatic: Compression, Fracture
- Autoimmune: RA, Sjogren, Guillain-Barre (GBS), Chronic Inflammatory Demyelinating Polyneuropathy (CIDP), Celiac
- Nutritional Deficiencies
- Iatrogenic/Toxins: Chemotherapy, Metronidazole, Colchicine, Alcoholism
- Neoplastic: Multiple Myeloma, Amyloidosis, Neurofibromatosis
- Idiopathic

DIAGNOSIS

- PN due to DM is made in the setting of chronic or uncontrolled DM and based on exclusion of the aforementioned underlying causes
- Initial work-up should include:
  - Serum studies: CBC, CMP, HbA1c, ESR, B12, TSH, HIV, RPR, ANA, ANCA
- Secondary work-up:
  - Lumbar Puncture with CSF studies: total protein, lactate, glucose, protein electrophoresis, total cell count, cell analysis, and antibodies against borreliae, bacteria, and neurotropic viruses
  - Electromyography/nerve conduction (EMG/NCS)
    - Axonal peripheral neuropathy would demonstrate reduced amplitude in sensory or motor response
    - Demyelinating peripheral neuropathy which showed disproportionate slowing of conduction velocities

TREATMENT

- Goals of treatment: control underlying disease, improve symptoms
  - With a target goal A1c <7, and peak postprandial glucose levels less than 180 mg/dL
  - Annual foot exams, properly fitted footwear, avoid walking barefoot
- Symptomatic treatment can often be achieved with pharmacologic interventions, common treatments include:
  - First Line:
    - Gabapentin, Pregabalin
    - SNRI: Duloxetine
    - TCAs: Amitriptyline, Nortriptyline
    - Topiramate, Carbamazepine,
    - Lidocaine Patches, Capsaicin
  - Second Line:
    - SNRI: Venlafaxine
    - Tramadol (off-label)

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