The Internist’s Approach to Neuropathy

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RELEVANT DECLARATIONS

• Financial disclosures: None

• Unlabeled Use of Products disclosure: This presentation will mention medications that are very commonly used in peripheral neuropathy that are not FDA – labeled
Why talk about neuropathy?

- Prevalence in general population about 2.4%
- 8% in those above age 55
- About 8% of patients with type 2 diabetes at the time of diagnosis
- Depending on definition 30-60% in long disease duration.
- Impairment of life quality
- Late complications (cardiac autonomic neuropathy, Charcot Neurorthopathy) are predictors of mortality
Case 1 - History

• 66 year-old man with 14 months of a sensation of “cotton” under his toes and ball of feet. He has some paresthesias and pins and needles sensation, as well as some numbness.

• He denies subjective weakness.

• He has no back pain

• He was diagnosed with type 2 diabetes 3 years ago, in addition to his several year history of hyperlipidemia, hypertension and obesity
What is the most likely diagnosis?

- A) Plantar fasciitis
- B) Onychomycosis
- C) Diabetic peripheral neuropathy
- D) Amyotrophic lateral sclerosis
- E) Guillain-Barré syndrome
Stepwise evaluation of neuropathic symptoms

• Spatial Distribution
• Involved nerve fibers
• What is the tempo
• Risk factors based on personal and family history
What is the likely spatial distribution described in Case 1?

- A) Mononeuropathy
- B) Mononeuropathy Multiplex
- C) Radiculopathy
- D) Distal symmetric polyneuropathy
- E) Sensory neuronopathy
• Primarily sensory complaints
• Motor symptoms occur late
• Slowly progressive

Neuropathy – Other Anatomic Patterns

• Mononeuropathies
Neuropathy – Other Anatomic Patterns

- Mononeuropathies
- Mononeuropathy multiplex

Neuropathy – Other Anatomic Patterns

- Mononeuropathies
- Mononeuropathy multiplex
- Neuronopathy

- Other causes of neuropathic symptoms
  - Radiculopathies
  - Brain and spinal cord lesions

Case

• 55 year old woman with 2-years of dry mouth, dry eyes, joint pains, swollen parotid glands presents with 4 months of severe burning in her feet, thighs and abdomen. She can not tolerate the sheets touching her feet when in bed. She wears loose clothing because tight clothing irritates her.

• On examination she has entirely normal strength, muscle bulk, normal vibration and reflexes. Her gait is unremarkable.

• Her EMG and nerve conduction studies are normal.
Where is the lesion?

• A) Motor neurons
• B) Small sensory fibers
• C) Large sensory fibers
• D) Multiple nerve roots
• E) This presentation is not due to neuropathy
Skin biopsy

Signs and symptoms based on fiber type

• Small sensory fibers
  • Symptoms: Burning, allodynia, hyperesthesia, numbness
  • Signs: Decreased pinprick, abnormal temperature sensation

• Large sensory fibers
  • Symptoms: Numbness, paresthesias, poor balance/falls
  • Signs: Loss of vibration and joint position, decreased distal reflexes, abnormal light pressure (monofilament), ataxia, pseudoathetosis
Signs and symptoms based on fiber type

• Autonomic fibers (same diameter as the small sensory fibers)
  • Symptoms: Orthostatic lightheadedness, bladder dysfunction, constipation, erectile dysfunction, early satiety
  • Signs: Resting tachycardia, orthostatic hypotension, hair loss, pale skin, cold or hyperemic feet

• Motor fibers
  • Symptoms: Weakness, cramps
  • Signs: Atrophy, weakness, fasciculations, cramps
What is the typical velocity speed of an upper extremity motor nerve in NCS?

- A) 20 m/s
- B) 50 m/s
- C) 80 m/s
- D) 100 m/s
- E) 200 m/s
Useful examination in 2 minutes

• Motor examination
  • Remove the shoes and socks
    • Is there atrophy?
    • Weakness in small hand or foot muscles
    • Functional weakness

• Sensory examination
  • Tuning fork or monofilament, joint position
  • Pinprick or temperature
  • Romberg sign

• Reflexes

• Gait!
Examination pictures/video
Back to our diabetic man- Examination

• He has normal strength and bulk
• Diminished vibration at the toes, preserved at the ankles
• Mild dullness to pinprick distal to his ankles
• Normal reflexes except depressed ankle jerks.
• His gait is normal.
Case

• 70 year-old woman with 20 years of diabetes presents with 1.5 years of intolerable paresthesias in her feet and distal legs. She has been feeling off balance and had a few falls. Her hands feel like “sand paper”. She must turn the lights on to be able to walk to the bathroom in the middle of the night. Legs feel stiff and sometimes she has painful spasms as if “the whole leg cramps up in a straight position.”

• On examination, she has normal strength in her arms but mild hip flexion weakness. She can’t walk on her heels.

• She has absent vibration at her toes and ankles, and impaired joint position

• Reflexes are 3+ throughout. Her gait is mildly wide based.
What is the best next step

• A) Start symptomatic treatment for diabetic neuropathy. No need for additional workup

• B) Perform additional simple neuropathy workup (Routine labs, B12, Protein electrophoresis)

• C) Perform neuropathy workup and obtain an MRI of her lumbar spine

• D) MRI of the cervical spine and blood work for myeloneuropathy

• E) MRI of the lumbar spine alone
When to refer to a neurologist

• Acute/subacute onset
• Severe symptoms
• Rapidly progressive symptoms
• Non-length dependent presentation
• Focal or multifocal symptoms
• Severe dysautonomia
• Motor predominance
Distribution of Causes of Neuropathy

- Diabetic polyneuropathy: 32%
- Cryptogenic axonal polyneuropathy: 5%
- Toxic polyneuropathy: 4%
- Immune-mediated polyneuropathy: 3%
- Hereditary polyneuropathy: 2%
- Polyneuropathy with systemic disease: 14%
- Metabolic polyneuropathy: 9%
- Polyneuropathy with vitamin B<sub>12</sub> deficiency: 5%
- Idiopathic small fiber neuropathy: 9%

Nora A. Visser et al. Neurology 2015;84:259-264
Figure 2 Age-stratified incidence of polyneuropathy (A) and percentage of incident patients of the etiologic subgroups of polyneuropathy compared with all polyneuropathies (B) • Incidence per 100,000 person-years.
Initial workup

- Hemoglobin A1C / Fasting glucose/ Oral glucose tolerance test
- Serum immunofixation electrophoresis
- Vitamin B12 (Methylmalonic acid for vitamin B12 levels 200-400)
- CBC
- Metabolic Panel
- +/- TSH
- Review of medical and family history!
Management

• Symptomatic treatment
• Treatment of underlying disorder
• Fall prevention
• Foot ulcer prevention
<table>
<thead>
<tr>
<th>Name</th>
<th>Instructions for Starting</th>
<th>Goal Dose</th>
<th>Maximum Dose</th>
<th>Good for Patients with:</th>
<th>Consider Alternatives if:</th>
<th>Common Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gabapentin</td>
<td>100 mg TID or 300 mg at bedtime</td>
<td>300 mg TID</td>
<td>3600 mg/d</td>
<td>Seizure disorder</td>
<td>Renal insufficiency</td>
<td>Dizziness, sedation, gait disturbance, confusion, peripheral edema</td>
</tr>
<tr>
<td>Pregabalin</td>
<td>75 mg BID</td>
<td>150 mg BID</td>
<td>600 mg/d</td>
<td>Seizure disorder</td>
<td>Renal insufficiency</td>
<td>Dizziness, sedation, gait disturbance, confusion, peripheral edema</td>
</tr>
<tr>
<td>Amitriptyline/ Nortriptyline</td>
<td>10-25 mg at bedtime</td>
<td>50-100 mg at bedtime</td>
<td>150 mg/d</td>
<td>Insomnia Migraine</td>
<td>Cardiac disease, arrhythmia, other serotonergic medications</td>
<td>Dry mouth (more common with amitriptyline), sedation, dizziness, confusion, QT-prolongation, orthostatic hypotension</td>
</tr>
<tr>
<td>Duloxetine</td>
<td>30 mg/d</td>
<td>60 mg/d (daily or split BID)</td>
<td>120 mg/d</td>
<td>Depression, anxiety, fibromyalgia</td>
<td>Hepatic failure, other serotonergic medications, anticoagulants</td>
<td>Nausea, dyspepsia, constipation, sedation, dry mouth, dizziness, hyperhidrosis, sexual dysfunction</td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>37.5 mg/d (XR)</td>
<td>150 mg/d (XR)</td>
<td>225 mg/d</td>
<td>Depression, anxiety</td>
<td>Uncontrolled hypertension, other serotonergic medications</td>
<td>Nausea, dyspepsia, sedation, dizziness, nervousness, insomnia, hypertension, sexual dysfunction</td>
</tr>
</tbody>
</table>

BID = 2 times per day; TID = 3 times per day; XR = extended release.

Wrapping it up