Initial Evaluation of Suspected Neuropathy

Saša Živković, MD PhD
Peripheral neuropathy

- Peripheral neuropathy is a general term indicating a disorder of the peripheral nervous system.

- Clinical presentations and etiology of neuropathies vary widely.

- Most common type
  - *Distal Symmetric Polyneuropathy*
Signs and symptoms of neuropathy

• Sensory loss
  – Different sensory modalities
    • light touch, pinprick, vibration, cold temperature, proprioception
  – May be described as "numbness"

• Paresthesias and neuropathic pain
  – Tingling, pins and needles, burning, aching, shock-like sensation

• Allodynia
  – Normal touch causing pain

• Weakness
  – Usually worse distally

• Hyporeflexia

• Dysautonomia
  – Orthostatic hypotension, abnormal sweating, urinary and intestinal dysfunction, arrhythmia
Neuropathy phenotypes
6 key questions

1. What systems are involved?
   • Motor, sensory, autonomic

2. What is the distribution of weakness?
   • Distal vs proximal; Focal/asymmetric vs symmetric

3. What is the nature of the sensory involvement?
   • Severe pain, severe proprioceptive loss

4. Is there evidence of upper motor neuron involvement?
   • Stroke, motor neuron disease, myelopathy

5. What is the temporal evolution?
   • Acute (days to 4 weeks), subacute (4-8 weeks), chronic (>8 weeks), preceding events/exposures

6. Is there evidence for a hereditary neuropathy
   • Family history, skeletal deformities

Differential diagnosis of “neuropathic” pain

• Polyneuropathy
• Spinal stenosis
  – Radiculopathy, myelopathy
• Musculoskeletal causes
  – Arthritis, plantar fasciitis
• Chronic pain syndromes
  – Complex regional pain syndrome, fibromyalgia
Epidemiology of neuropathy

• 2-8% of population has neuropathy
  – >8% after age of 55
• Diabetic neuropathy – 40-60% of diabetics
  – 10% of patients with IGT have neuropathy
• Guillain Barre syndrome – annually 1-4/100,000
• CIDP – yearly 0.2/100,000; prevalence 1-2/100,000
• CMT – prevalence 1:2500
• Vasculitic neuropathy – 35% of patients with PAN or GPA
• Paraproteinemic neuropathy – 10% of cryptogenic neuropathies
  – MGUS vs malignancies, most common with IgM
• Toxic neuropathy – alcohol (30%), chemotherapy (30-40%)
• Leprosy – 10,000,000 worldwide (Third World)
Etiology of Peripheral Neuropathy

Adults

- Inherited: 27%
- Acquired: 43%
- Inflammatory: 13%
- Undiagnosed: 17%

Children

- Inherited: 19%
- Acquired: 10%
- Inflammatory: 71%

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Basic battery of tests with initial evaluation of neuropathy

• **Laboratory testing**
  – B12/folate, HgbA1C, GTT or fasting glucose, immunoelectrophoresis, sed rate or CRP, CBC, CMP, TFTs

• **Consider EMG/NCS**
  – It may take 2-3 weeks for electrical changes to develop (wait at least 10-14 days)
  – !!! Exception: early changes in GBS may be present after Day 5

• **Consider lumbar puncture if Guillain-Barre syndrome is suspected**
Work-up of neuropathy

New diagnoses (N=71/458)

- Impaired glucose tolerance (6.1%)
- B12 deficiency (4.4%)
- Diabetes mellitus (1.7%)
- Thyroid dysfunction (1.7%)
- Alcohol abuse (0.4%)
- End-stage renal disease (0.4%)
- Paraproteinemia (0.2%)

*JAMA Neurology 2014; 71:1143-9.*
Red flags

- Rapidly progressive course
- Severe weakness
- Pain
- Ataxia
- Weight loss
- Other B signs (fever, night time sweating)
Neuropathy syndromes you don’t want to miss

- **Guillain Barre syndrome**
  - Ascending paralysis with paresthesias, areflexic, 70% with triggering events
- **Vasculitic neuropathy**
  - Usually asymmetric painful neuropathy with stepwise progression
  - More common as a part of systemic vasculitis, but also may present as single-organ vasculitis
- **Toxic neuropathy**
  - Typically slowly progressive with symmetric length-dependent involvement
  - Temporally associated with environmental toxins or neurotoxic medications, often gets better after offending agent is removed (e.g. alcohol, chemotherapy, antibiotics)
- **Paraproteinemic neuropathy**
  - Most common with MGUS, 25% will convert into malignancy over 25 years
Treatment of neuropathy

• Treatment of underlying cause of neuropathy
• Treatment of symptoms
  – Pain
  – Unsteadiness (!! Risk of falls)
  – Numbness – *very limited benefit of treatment*
• Assistance with ADLs
• Treatment of comorbidities
Quality measures for **Distal Symmetric Polyneuropathy** as recommended by American Academy of Neurology

- Documentation of neurologic symptoms and signs
- Consideration of electrodiagnostic studies within 6 months of initial evaluation
- Diabetes/prediabetes screening
- Screening for unhealthy alcohol use
- Query about pain and pain interference with function
- Query about falls

*Neurology 2014; 82:1745-8*
How compliant are we with basic neuropathy screening in DSP?

- 1,031 patients with new diagnosis of neuropathy in 1996-2007 Health and Retirement Study (HRS) Medicare claims

- Fasting glucose 23.4%; HgbA1c 43.2%; B12 32.6%; SPEP – 13.3%

- No previous diagnosis of diabetes
  - Fasting glucose 19%, HgbA1c 17%; B12 41%; SPEP 19%; GTT 1%


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References

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  ([http://smartmedicine.acponline.org/content.aspx?gbosid=63](http://smartmedicine.acponline.org/content.aspx?gbosid=63))

• *Arch Intern Med* 2012; 172:127-32.


• *Neurol Clin* 2013; 31:343-61.

• *Neurology* 2014; 82:1745-8
Signs of systemic disease associated with neuropathy

- Sicca - Sjogren’s
- Large tongue - Amyloid neuropathy
- Orange tonsils - Tangier disease
- Ichthyosis - Refsum disease
- Angiokeratoma - Fabry disease
- Xanthoma - Cerebrotendinous xanthomatosis
- Visceromegaly - POEMS
- Skin hyperpigmentation - POEMS
- Endocrinopathy - POEMS
- Lymphadenopathy - Paraproteinemic/paraneoplastic
- Purpuric rash - Vasculitis
- Abdominal pain, psychosis - Porphyria