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Diagnosis and Evaluation of Peripheral Neuropathies

February 21, 2013

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Overview

- Clinical pearls for neuropathy
- Anatomic patterns to look for
- Differential diagnosis
- Diagnostic testing
- Symptomatic treatment
Case 1

- 55yo male with 6-12 months of painful numbness in feet. Began in toes and now involves balls of feet. Worse when resting or sleeping. No weakness. No back pain.
- Exam reveals stocking like sensory loss in both feet to pin. Normal power. Normal arm and knee reflexes and absent ankle jerks.
History and Clinical Exam

Bilateral lower extremity pain/burning/numbness

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

2. What is the temporal evolution?
   - Acute, sub acute, chronic, progressive, relapsing

3. What is the distribution of weakness?
   - Distal, proximal, symmetric, asymmetric

4. What is the nature of sensory involvement?
   - Painful, burning, tingling, numb, ataxic
   - Rocks in my socks
   - Small fiber vs. large fiber
History and Clinical Exam

5. Could this be a hereditary neuropathy?
   - Slow progression, high arches, foot deformities

6. Could this be something else?
   - Hips, knees, and vascular disease

A thorough general exam is key.
Patterns of Neuropathic Disorders

- Symmetric *diffuse* weakness + sensory
- Symmetric *distal* weakness + sensory
- Asymmetric *distal* weakness + sensory
- Asymmetric *distal* weakness, no sensory
- Symmetric sensory loss, no weakness
- Autonomic symptoms and signs
Sensory Loss

Image(s) have been omitted
Pes Cavus (high arches)

Image(s) have been omitted
Diseases Associated with Peripheral Neuropathies

- Diabetes mellitus
- Chronic renal disease
- Carcinoma, paraneoplastic
- Plasma cell dyscrasias
- Post Gastric bypass
- Rheumatoid arthritis
- Sjogren’s syndrome
- Scleroderma
- Systemic lupus erythematosus
- Hypothyroidism
- Polyarteritis nodosa
- Cryoglobulinemia
- Amyloidosis
- Porphyria

- Chronic liver disease
- Herpes zoster, HIV, Lyme
- Diphtheria
- Vitamin B12, folate deficiency
- Malnutrition
- Sarcoidosis
- Lymphoma, myeloma
- Gout
- Polycythemia vera
- COPD
- Tropical spastic paraparasis
- Drugs, toxins, heavy metals
- MLD, Refsum’s disease
Patterns of “Neuropathy”

1. Polyneuropathy — Idiopathic, hereditary, immune mediated, metabolic, infectious, toxin, malignancy related

2. Focal Neuropathies — Vasculitic (mononeuropathy multiplex), carpal tunnel, ulnar neuropathy, Bells, peroneal neuropathy, HNPP

3. Motor Neuropathy / Neuronopathy - ALS, multifocal motor neuropathy
Small Fiber Predominant Carry Pain and Temperature

- **Infectious**
  - HIV

- **Hereditary**
  - Amyloid
  - Fabry’s (α-galactosidase)

- **Toxic**
  - Ciguatera
  - Alcohol
  - Rx meds – flagyl, Chemotx

- **Metabolic**
  - Diabetes
  - ESRD
Large Fiber Predominant Vibration and Joint Position

- **Toxic**
  - B6
  - Cisplatin

- **Deficiencies**
  - B12, E

- **Infectious**
  - Syphilis

- **Immune**
  - anti-MAG
  - Guillain Barre, MFS
  - CIDP

- **Hereditary**
  - ataxia telangiectasia
  - Fredreich’s / F+
Painful Neuropathies

- Toxic
  - alcohol
  - thalium
  - Chemotx- cisplatin, nitrofurantoin, taxol
  - thalidomide
- Idiopathic sensory

- Diabetes Mellitus
- Hereditary
  - Fabrys, Amyloid
  - porphyria
- Mononeuritis Multiplex
- HIV
Prescription Drugs causing Neuropathy

- Amiodarone
- Chemotherapy vincristine, cisplatin, taxol, thalidomide
- Metronidazole (flagyl)
- Linezolid
- Phenytoin (dilantin)

- Nitrofurantoin
- Isoniazid
- Dapsone
- Vitamin B6
Approach to Neuropathy
Why EMG/NCS?

Tests nerve function
Document presence and location of Neuropathy
Identify peripheral modalities involved -
  Sensory, Motor, Autonomic, Polyradiculopathy
Identify the predominant pathophysiology
  Axonal vs. Demyelination
    Uniform vs. Multifocal with conduction block
    Conduction slowing - hereditary?, acquired
    Radiation Plexopathy
Establish temporal profile and prognosis
Diagnostic Approach to Neuropathy
Which serum studies?

- **Primary**
  - CBC, CMP, ESR
  - FBS, Hemoglobin A1C
  - SPEP, IFE
  - B12, MMA, folate

- **Secondary**
  - TSH, ANA, RPR, RF, CPK, SS A/B, cryoglobulins, hepatitis, ANCA, Vit E, lyme, HIV, heavy metals, homocysteine, Anti-MAG, Anti-GM1, Genetic (CMT), paraneoplastic.
Approach to Neuropathy
When biopsy?

- Vasculitis
- Sarcoidosis
- Amyloidosis
- Tumor Infiltration
- ?CIDP, leprosy
When Skin Biopsy

- Can be done when no answers forthcoming and neuropathy affects small fibers
  - In most cases all studies are previously normal
  - Small punch biopsy of skin on thigh and ankle
  - Does not change treatment plan
Case 1

Idiopathic Sensory Polyneuropathy

- Represents approx 1/3 of neuropathy patients
- Diagnosis of exclusion - axonal pathology
- Distal symmetric pain, numbness and tingling without weakness
- Absent ankle reflexes
- Mean age 50-60
- Temp>pin>position
- Minimal distal weakness
Idiopathic Sensory Polyneuropathy

- 70% of patients reach a plateau
- Vast majority remain stable or progress slowly
- Generally a benign course with maintained strength and ambulation
- Symptomatic treatment
Diabetic Neuropathy

- 45-60% of all diabetics develop neuropathy
- May be presenting sign in up to 5% of patients
- Most common cause of non-traumatic amputations
- Distal sensory > motor polyneuropathy
  - small fibers affected initially - pain and temp
  - weakness and autonomic dysfunction as well
Diabetic Neuropathy
Variations

- Acute diabetic axonal polyneuropathy
  - worsening diabetes and weight loss, change in tx

- Diabetic Amyotrophy
  - severe thigh/back pain with weakness, atrophy
  - CIDP-like variant - some response to IVIG

- Cranial neuropathies - 3 and 6

- Focal compression neuropathies
Symptomatic Treatment for Painful Polyneuropathy

- Ulcer prevention, foot care
- Symptomatic Treatments
  - Snug, warm socks; braces, physical therapy
  - NSAID’s
  - FDA approved Rx
  - TCA’s, Anticonvulsants
  - Topical Creams
  - Narcotics
Symptomatic Treatment for Painful Polyneuropathy

- Duloxetine (Cymbalta) 60-120mg daily
- Pregabalin (Lyrica) 50-150mg three times daily
- Gabapentin (Neurontin) Start 300mg at HS, up to 900mg TID
Symptomatic Treatment for Painful Polyneuropathy

- Amitriptyline (Elavil), Nortriptyline (Pamelor)
  - Start 10-25mg HS, up to 150mg
  - 200-400mg daily
- Carbamazepine (Tegretol)
- Phenytoin (Dilantin)
- Lamotrigine (Lamictal), Mexiletine, Narcotics, Baclofen (Lioresal), Clonazepam (Klonopin), Tizanidine (Zanaflex), Tramadol (Ultram), Venlafaxine (Effexor)
- 300-400mg at bedtime
Other Symptom Treatments

- Capsaicin Cream
- Amitriptyline / Lidocaine cream
- Lidocaine patch
- Acupuncture
- Multiple other creams available
Case 2

- A 32 year old woman with 10 days of progressive weakness and numbness.
- Developed 2 weeks after several days of diarrhea and fever.
- Pins and needles in both feet and hands followed by progressive weakness of both arms and legs.
- Exam - mild proximal and distal weakness of all extremities, trace arm and absent leg reflexes and mild distal sensory loss.

- A 54 year old with a 12-24 hour history of rapidly progressive weakness and inability to ambulate. This began while golfing the previous afternoon.
- Exam reveals flaccid weakness of all four extremities and facial weakness. Areflexic throughout. Within 3 hours of admission he is intubated for respiratory failure.
Diagnostic Criteria for Guillain Barre Syndrome (GBS)

**Required**
- Progressive weakness in more than 1 limb
- Areflexia or hyporeflexia

**Supportive**
- Progression in less than 4-6 weeks
- Symmetric weakness
- Sensory symptoms/signs
- Autonomic dysfunction
- Cranial nerve involvement, VII
- Elevated CSF protein, cell count < 20
- Demyelination by nerve conduction studies
Features Casting Doubt in GBS

Marked asymmetry
Early bowel or bladder dysfunction
Sensory level
> 50 cells/mm$^3$ in CSF, polys
GBS - Etiology

- Most common cause of acute generalized weakness - mean age 40
- Mortality 5%
- 85% have a full functional recovery
- Usually preceded 1 to several weeks by systemic infection
  - Campylobacter, EBV, CMV, URI,
  - HIV seroconversion
GBS - Treatment

- Supportive Care - ICU, DVT prophylaxis
- FVC’s - intubation <15 - 20cc/kg
- Autonomic instability
- Plasma exchange
  - 200-250cc/kg total over 5 - 14 days
- Intravenous Immunoglobulin
  - 2g/kg total at 400 mg/kg/day
- Immediate dramatic improvement not the rule
- Steroids not helpful
Conclusions

- Good H&P and neurologic exam
- Look for patterns of weakness and sensory loss
- Differential diagnosis
- Routine vs. acute neuropathies
- How EMG/NCS helps?
- Primary and consider secondary blood work
- Treatments - not only symptomatic