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Diagnosis and Evaluation of Peripheral Neuropathies

February 21, 2013

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A PASSION FOR BETTER MEDICINE.™



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
- Carbamazepine (Tegretol)
 - 200-400mg daily
- Phenytoin (Dilantin)
 - 300-400mg at bedtime
- Lamotrigine (Lamictal), Mexiletine, Narcotics, Baclofen (Lioresal), Clonazepam (Klonopin), Tizanidine (Zanaflex), Tramadol (Ultram), Venlafaxine (Effexor)

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.
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- 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/mm³ 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