Radiculopathy and Polyneuropathy

Jeffrey W. Ralph, MD
Jeffrey.Ralph@ucsf.edu
UCSF Department of Neurology

Radiculopathy
- Anatomy & Signs & Symptoms
- Diagnostics
- Conservative management vs. Surgical decompression

Polyneuropathy
- Categories and diagnostic approach
- Role of electrodiagnostic testing
- Utility of nerve biopsy

Objectives

Radiculopathy: Anatomy & Spondylosis
- Spondylosis means degeneration of the spine
  - A part of human life
  - Osteophytes extending from facet or uncovertebral joints
  - Degeneration of the disc
  - Ossification of the spinal ligaments
- Radiculopathy
  - Usual mechanism is herniation of nucleus pulposus, often in the context of other spondylitic changes

Radiculopathy, cont.
- C5/C6 neural foraminal stenosis → C6 root injured
- L4/L5 neural foraminal stenosis → L4 root injured
Symptoms and Signs
- Numbness and tingling and Common Referred Pain Sites (Often do not match up)
  - C7: Numb middle finger; pain in triceps and scapular pain
  - C8: Numb medial hand and forearm; pain at elbow and scapular pain
  - L4: Knee pain; Numbness in anterior shin
- Coughing or Sneezing exacerbates pain

Exam
- Spurling test (cervical radiculopathy)
- Straight leg raise (lumbosacral radiculopathy)
- Weakness: Myotome distribution
- Numbness: Dermatomal distribution
- Reflexes: Note: There is no reflex for L5

Less common causes of radiculopathy
- Vertebral metastasis
- Paget's disease
- Gout
- Tarlov cysts
  - Polyradiculopathy (strongly consider LP for CSF analysis)
  - Spondylosis
  - Carcinomatosis meningitis
  - Infections: Lyme, CMV
  - Diabetes
  - Radiation Injury
  - Arachnoiditis
  - Congenital anomalies

Case I
- 45 year-old man presents with a 2 week history of right buttock pain that radiates to the lateral right thigh and leg. He notices a slapping sound when he walks.

EXAM:
- Motor: Moderate weakness of right ankle dorsiflexion, eversion, inversion, and toe extension/flexion.
- Reflexes: Normal
- Sensory: Impaired sensation on dorsum of the right foot

Case I: Questions
Which is incorrect?
1. He is likely to improve no matter what I do.
2. Surgery usually leads to an initial exacerbation of radicular pain.
3. If the weakness progresses, surgical decompression is indicated.
4. An MRI scan of the lumbar spine is indicated.
**Imaging**

- Imaging is recommended for persistent (>2 weeks) symptoms
- An MRI scan is the modality of choice for radiculopathy; plain films provide only limited information
  - Main fault: Too sensitive
- CT imaging (+/- CT myelography) also helpful
  - Superior imaging of bony anatomy
  - Cannot determine cord injury
  - Sometimes is the only option (e.g., pacemaker)
- Imaging findings correlate poorly with prognosis


**EMG/NCS cont.**

- Findings
  - NCS: Normal sensory potentials despite sensory symptoms and signs
  - EMG: Denervation of muscles that share the same myotome
  - EMG: Denervation of the paraspinal muscles
- EMG/NCS are good but not great (limited sensitivity) tests for radiculopathy
  - Main fault: Not sensitive enough
  - Most useful when a patient has clear signs but distinguishing between radiculopathy or mononeuropathy clinically is difficult

**Non-invasive Interventions**

- Education/counseling
- Medications
  - NSAIDs
  - Oral steroids
  - Narcotics
  - Muscle relaxants
- Physical therapy
  - ROM
  - Traction
- Chiropractic manipulations
- Brace/corset
- Acupuncture
- TENS unit
- Magnets

May help, but poor evidence of efficacy
Epidural Steroid Injections

- Intraspinal injections have been performed for >50 years.
- Corticosteroid plus anesthetic usually injected
- Techniques and operator skill are important determinants of outcome
- Usually performed under fluoroscopic or CT guidance
- Multiple randomized studies have shown a benefit

<table>
<thead>
<tr>
<th>Author</th>
<th>Site</th>
<th>Design</th>
<th>Outcome</th>
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</thead>
<tbody>
<tr>
<td>Carette S</td>
<td>Lumbar</td>
<td>138 patients with herniated nucleus pulposis received methylprednisolone or isotonic saline</td>
<td>Significant improvement in pain scores in the patients receiving the steroid injections</td>
</tr>
<tr>
<td>Riew KD</td>
<td>Lumbar</td>
<td>55 patients with lumbar pain and radiographic confirmation requested operative management randomized to bupivacaine alone or bupivacaine with betamethasone</td>
<td>29 of 55 decided not to have surgery 9 of 27 in bupivacaine alone group decided NO operation 20 of 28 patient receiving bupivacaine plus betamethasone decided NO operation</td>
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Epidural Steroid Injections Cont.

- Rarely, complications occur even in the best of hands
- Myelopathy and stroke are rare complications
- Risk higher for cervical injections

Surgical Interventions: Randomized Trials

<table>
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<tr>
<th>Trial</th>
<th>Site</th>
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<tr>
<td>Persson, LC (1997)</td>
<td>Cervical</td>
<td>81 patients with clinical and radiographic evidence of radiculopathy; duration of sx &gt; 3mos.; randomized to surgery, physiotherapy, or collar</td>
<td>At 4 months, surgical pts had greater improvement in pain, strength, and sensation. At one year, no difference in pain or sensory sx, though surgical patients had better strength</td>
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<tr>
<td>Weber, H (1983)</td>
<td>Lumbar</td>
<td>126 patients with “uncertain indication” for surgery randomized to surgery vs. conservation management</td>
<td>At 1 year, surgery patients did better; At 4 years still better but not statistically significant</td>
</tr>
<tr>
<td>Spine Patient Outcomes Research Trial (SPORT) (2006)</td>
<td>Lumbar</td>
<td>Randomized comparison of medical (n=246) versus surgical (n=232) management (Many of the subjects flipped to the opposite treatment)</td>
<td>Surgical &gt; medical treatment for rapid improvement; Surgical=Medical treatment in long term; Patients tend to improve with either approach</td>
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SPORT Trial

- Non-operative care
- Operative management
- Attending CME course

Take Home Points from Surgical Literature:
- Surgical interventions may lead to rapid improvement in pain level
- Long term outcomes with surgery similar to non-operative care
- Poor standardization of non-operative management a problem across most studies
An Approach to Radiculopathy

- Physical Therapy
- NSAIIDs, Neuropathic Pain Agents, Possible muscle relaxant, Consider oral steroid course
- Consider Surgical Decompression
- Epidural Steroid Injections
- MRI and/or CT imaging & EMG/NCS

Time & Persistent Symptoms

Case I: Questions

- Which is incorrect?
  1. He is likely to improve no matter what I do.
  2. Surgical intervention leads to a poorer initial outcome in terms of pain.
  3. If the weakness progresses, surgical management is indicated.
  4. An MRI scan of the lumbar spine is indicated.

Objectives

- Radiculopathy
  - Anatomy & Signs & Symptoms
  - Diagnostics
  - Conservative management vs. Surgical decompression
- Polyneuropathy
  - Categories and diagnostic approach
  - Role of electrodiagnostic testing
  - Utility of nerve biopsy

Polyneuropathy

- Nerve Responses to Injury
  - Dying-back axonopathy
  - Multifocal axonopathy
  - Neuronopathy
- Diagnosis
  - Possible: Symptoms suggestive of polyneuropathy
  - Probable: Weakness and/or sensory deficits and/or reflex abnormalities
  - Definite: Confirmed with testing (usually NCS but other tests (skin biopsy) for small fiber and autonomic (QSART; heart rate variability) neuropathies
Numbness and weakness thought to be of peripheral origin

**TIME COURSE** (Table 1)
- Rapid: Guillain-Barre syndrome; Toxic (heavy metals); Severe nutritional
- Subacute: Inflammatory (CIDP/Vasculitis); Toxic; Nutritional
- Chronic: Metabolic/genetic

**EXPOSURES including DRUGS**

**FAMILY HISTORY**

Anyone else with weakness or numbness in the feet? Anyone else with high arches or hammertoes? Can your _____ stand on her heels and toes?

**WORK-UP**

**EXAMINATION**

**SYMMETRIC or MULTIFOCAL SENSORIMOTOR** (Tables 2 & 3)

**PURE SENSORY: LARGE** (Table 5) or **SMALL FIBER** (Table 6)

**Polyneuropathy cont.**

**EXAMINATION**

Diabetes Hereditary Sensory-Autonomic Neuropathy

**WORK-UP**

**SYMPTOMATIC or MULTIFOCAL SENSORIMOTOR** (Tables 2 & 3)

**MOTOR PREDOMINANT** (Table 4)

**PURE SENSORY: LARGE** (Table 5) or **SMALL FIBER** (Table 6)

**Uncommon (Potentially Worrisome) Polyneuropathy, Cont.**

**EMG/NCS**

If rapidly progressive, consider Mononeuritis Multiplex (incl. Vasculitic Neuropathy) Labs

Consider nerve biopsy

*A Note: There can be mild slowing of nerve conduction velocities in diabetes and uremia*

- **Axonal** (Usually Sensory > Motor Sx and Signs)
- **Demyelinating** (Usually Motor > Sensory Sx and Signs)
- Inflammatory (CIDP)
- Genetic (CMT)
- Toxic or Metabolic (less likely)

**CSF studies** UPEP/IFE 

DNA Analysis

If **negative**, consider **Tier II** Studies or Have Neurologist Do It; Definitely in <40 yo

NEXT SLIDE…

Welcome to the Neurology Clinic

If Negative, Idiopathic Polyneuropathy

Tier I Studies (Do on everyone): Fasting Glucose/HbA1c (or 2 hr. OGTT); B12; SPEP/IFE; EMG/NCS (esp. if cryptogenic)

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**Tier 1 Studies (Do on everyone):**

- Fasting Glucose/HbA1c (or 2 hr. OGTT)
- B12
- SPEP/IFE
- EMG/NCS (esp. if cryptogenic)

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Longstanding Neuropathy – Probable Genetic

Vasculitis

- If multifocal: Lyme disease; leprosy; diabetes; CIDP variant; vasculitis
- If subacute onset: CIDP
- If very chronic: Charcot Marie Tooth

Broad Differential

**Uncommon (Potentially Worrisome) Polyneuropathy, Cont.**

**EMG/NCS**

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If Negative, Idiopathic Polyneuropathy

Any other with weakness or numbness in the feet? Any other with high arches or hammertoes? Can your _____ stand on her heels and toes?
Nerve Biopsies
- Generally reserved for rapidly progressive and/or asymmetric axonal polyneuropathies.
- Diagnoses that may depend on nerve biopsies:
  - Vasculitic neuropathy
  - Leprosy (+ some other oddball infections)
  - Sarcoid
  - Amyloidosis
  - Neoplastic infiltration (neurolymphomatosis)
- Generally not ordered for demyelinating polyneuropathies (e.g., Charcot Marie Tooth or CIDP), which are diagnosed based on clinical presentation and EMG/NCS findings.
- Generally, only sensory nerves are biopsied.
- A good target: recently affected nerve and absent sensory nerve action potential for that nerve.

Utility of EMG/NCS
- Often not needed if cause of the neuropathy is known or if the neuropathy is indolent.
- Defines whether a neuropathy is present.
  - Remember: nerve conduction studies cannot detect pure small fiber sensory neuropathy.
- Defines whether the neuropathy is axonal or demyelinating.
- Can serve as a baseline and useful for assessing progression of neuropathy.
- Can identify a nerve to biopsy.
- DEFINITELY order an EMG/NCS for asymmetric or rapidly progressive neuropathies.

Case 1: Burning Feet
- 65 year-old venture capitalist presents with 6 months of burning sensations in both feet. The feet often appear pink. He does not notice any numbness or weakness.
- Exam: Feet appear mildly red. Muscle bulk and strength are normal. Reflexes are normal, even at the ankles. Light touch and vibration sensation are intact at the toes. Hyperalgesia to pinprick stimulation.

Burning Feet, II
Which is least likely?
1. Excessive alcohol consumption
2. Impaired glucose tolerance
3. HIV infection
4. Vitamin B6 intoxication
Diabetic Polyneuropathy

- About 50% of diabetics develop polyneuropathy (depends how neuropathy is defined)
- Pathophysiology
  - Metabolic: accumulation of glycosylation products + sorbitol, disruption of hexosaminase pathway, protein kinase C pathway disruption, oxidative stress
  - Microvascular injury: thickened blood vessels; vascular occlusions
  - HTN, Triglycerides, BMI and smoking independently associated with PN in type 1 DM (EURODIAB study)

Treatment of Diabetic Polyneuropathy

- Tight glycemic control helps
  - Type I DM: Diabetes Control & Complications Trial (1441 patients)
    - 3 or more insulin injections daily or basal insulin vs. 1-2 insulin injections
    - 60% reduction in neuropathy in the rigorous group
  - Type II DM: ACCORD Trial
    - 10,200 patients, mean 10 years, randomized to intensive goal ($\text{A1c} < 6$) vs. $\text{A1c} 7-8$
    - Trial stopped after median 3.7 because of increased mortality in intensive arm; hint of improved neuropathy in intensive arm
- Reduction of lipids and treatment of HTN → reduced risk of polyneuropathy in DMII patients (Steno-2 Trial)
- Alpha Lipoic Acid → 600 mg daily effective in randomized studies (SYDNEY II)

Impaired Glucose Tolerance

- Defined as a serum glucose value between 140-200 mg/dL 2 hours after a 75-g glucose load
- 138 patients with idiopathic neuropathy had OGTT (Smith AG, Singleton JR. Arch Intern Med 2004)
  - 45% had prediabetes
  - 16% with previously unrecognized diabetes
  - (15% prevalence of prediabetes in general population).
- 73 patients with neuropathy of unknown cause had OGTT (Sumner CJ et al, Neurology 2003)
  - 26 had IGT
  - 15 had DM
  - Most of the patients with IGT had a predominantly small fiber neuropathy
- IGTN Study (Smith 2006) Diet and exercise counseling improved status of polyneuropathy in pts with IGT

Idiopathic Distal Polyneuropathy: A Very Common Problem

- Don’t “go silent” when you reach this diagnosis. Even if no dx, neuropathic pain can be treated.
- Symptoms and signs stabilize after initial period of progression or progress very slowly
- Sometimes there is spontaneous improvement
- Significant impairment (using assistive device) rare
- Reassessment and repeating testing identifies a cause in 5-30% of cases
  - Causes include: EtOH, CMT, CIDP, Monoclonal gammopathy, malignancy, B12 deficiency
Neuropathic Pain

- Topicals—Lidocaine patch, capsaicin
- Opioids
- Antidepressants—TCA/SNRIs >> SSRIs
- Anticonvulsants—pregabalin and gabapentin, tramadol
- Marijuana (?)

General Strategy

- MONOTHERAPY → IF FAIL → then MONOTHERAPY
- from DIFFERENT CLASS → IF FAIL
- then COMBINATION THERAPY →
- IF FAIL → then INTERVENTIONAL APPROACHES

Case II

What is the diagnosis?

1. Arsenic poisoning
2. Chronic inflammatory demyelinating polyneuropathy
3. ALS
4. Statin-induced myopathy

CIDP: Symptoms

- Diffuse muscle weakness
- Numbness (“deadness”), tingling common, but pain (e.g., burning or stabbing) less so
- Occasional: facial weakness; double vision

Case II

- A 60 year-old attorney with hypercholesterolemia
- 5 year hx of difficulty climbing stairs
- 3 year hx of difficulty getting up from a chair
- 1 year hx of difficulty buttoning clothes
- Mild tingling in the toes

Exam: Moderate generalized weakness, worse in proximal > distal muscles; Global areflexia; Mildly impaired vibration sensation at the toes.

CIDP: Signs

- Papilledema in rare cases
- Diffuse weakness, usually distal > proximal
  - Little or no muscle atrophy
- Reflexes usually absent
- Vibration and position sensation impaired > temperature or pain sensation
  - Pseudoathetosis and gait ataxia
- Coarse action tremor

Clinical Course

- Chronic Progressive
- Relapsing-Remitting

Concurrent Illness and CIDP

- Monoclonal Gammopathy
  - Monoclonal gammopathy of undetermined significance
  - Malignant monoclonal gammopathies
    - Multiple Myeloma
    - Plasmacytoma
    - Malignant lymphoproliferative disease
    - Waldenstrom’s macroglobulinemia
    - Lymphoma
    - Chronic lymphocytic leukemia
- Infections
  - HIV
  - Hepatitis C
  - Inflammatory bowel disease
  - Malignoma
  - CNS demyelination
  - Nephrotic syndrome
  - Diabetes mellitus
  - Hereditary neuropathy
  - Thyrotoxicosis

Paraproteins & Neuropathy: Complex Interactions

LAB TESTS:
- CBC
- TSH
- HIV & Hepatitis C
- SPEP/IFE
- UPEP/IHE or SERUM LIGHT CHAIN ASSAY
- Fasting Glucose

MOST CASES ARE IDIOPATHIC
First-line Treatments for Idiopathic CIDP

- IVIG
- Plasma Exchange
- Steroids

Treating these patients is often very rewarding...

Summing Up....

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The End

Thank you