Neurology Internal Medicine
Boards Review

S. Andrew Josephson MD
Department of Neurology, UCSF
July 11, 2011

Case 1: A 32 year-old man reports difficulty walking. On exam he has weakness of only his bilateral proximal lower extremities with normal reflexes and sensory exam. What is the most likely localization?
A. Brain
B. Spinal Cord
C. Nerve
D. Muscle
E. Neuromuscular Junction (NMJ)

Localization in Clinical Neurology

- Commonly tested topic
- Approach
  - Step 1: UMN vs. LMN
  - Step 2: Breakdown of UMN or LMN

Upper Motor Neurons

Predictable Pyramidal Pattern of Weakness:
UE Distal Extensors and LE Distal (Dorsi)Flexors

Step 1: UMN vs. LMN

<table>
<thead>
<tr>
<th></th>
<th>UMN</th>
<th>LMN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pattern of weakness</td>
<td>Pyramidal</td>
<td>Variable</td>
</tr>
<tr>
<td>Function/Dexterity</td>
<td>Slow alternating movements</td>
<td>Variable</td>
</tr>
<tr>
<td>Tone</td>
<td>Increased</td>
<td>Decreased</td>
</tr>
<tr>
<td>Tendon Reflexes</td>
<td>Increased</td>
<td>Decreased, absent or normal</td>
</tr>
<tr>
<td>Other signs</td>
<td>Babinski sign, other CNS signs</td>
<td>Atrophy (except for NMJ disorders)</td>
</tr>
</tbody>
</table>

Step 2: UMN Breakdown

- Either:
  - 1. Brain (including brainstem)
  - 2. Spinal cord
- Pearls
  - A sensory level on the trunk = spinal cord
  - Bladder dysfunction = spinal cord
  - “Crossed signs” = brainstem
  - Facial weakness = brain (above the pons)
Step 2: LMN Breakdown

• Either:
  – 1. Anterior Horn Cell (AHC)
  – 2. Nerve
  – 3. Neuromuscular Junction (NMJ)
  – 4. Muscle

Step 2: LMN Breakdown Pearls

• Sensory Symptoms or Signs = Nerve
• Reflexes Decreased = Nerve (or AHC)
• Proximal Weakness = Muscle or NMJ
  – Fatigue or fluctuating weakness = NMJ
• Fasciculations = AHC (or Nerve)
• Combination of UMN and LMN signs = ALS

Case 2

• A 65 year-old man with a history of DM, HTN presents with 9 hours of L sided binocular visual loss
• Examination shows left-sided homonymous hemianopia and is otherwise unremarkable.
• The patient is on ASA 81mg daily

What treatment should you initiate?

A. IV t-PA
B. Heparin
C. Aspirin 325 mg
D. Plavix (clopidogrel)
E. Aggrenox (ER dipyridamole + ASA)

Intravenous t-PA

• Time of onset=last time seen normal
• Pivotal IV t-PA NINDS trial (0-3 hours***)
  – 30% increase in minimal or no disability at 90 days
  – Symptomatic hemorrhage risk increased 0.6 to 6.4%
• Ischemic stroke with significant disability
• No bleed on non-contrast head CT

Intravenous t-PA

• Important contraindications to remember
  – INR greater than 1.7
  – Platelets less than 100
  – Seizure at onset, low glucose
  – Recent surgery or hemorrhage
  – BP>185/100 sustained despite treatment
Shrinking Indications for Anticoagulation in Stroke

1. Atrial Fibrillation
2. Some other cardioembolic sources
   - Thrombus seen in heart
   - ?EF<35
   - ?PFO with associated Atrial Septal Aneurysm
3. Vertebral and carotid artery dissection
4. Rare hypercoagulable states: APLA

Antiplatelet Options

1. ASA
   - 50mg to 1.5g equal efficacy long-term
2. Aggrenox
   - 25mg ASA/200mg ER Dipyridamole
     • ESPS-2, ESPRIT (Lancet 5/06)
3. Clopidogrel (Plavix)
   • MATCH (Lancet 7/04), FASTER (Lan Neurol 11/07)
   • PRoFESS trial results announced 5/08

Aggrenox vs. Plavix

• Aggrenox
  - Headache in first 2 weeks: 30% discontinue
  - Perhaps not compatible with cardiac antiplatelet goals or with unstable angina
  - Cannot be crushed in FT
• Plavix
  - Concerns regarding use with ASA

Antiplatelet Options

• If on no antiplatelet medication
  - ASA or Plavix or Aggrenox
• If already on ASA
  - Switch to Aggrenox or Plavix

When to Fix the Carotid?

• NASCET in early 1990s
  - Benefit of endarterectomy in patients with symptoms ipsilateral to 70-99% stenosis
    • Comparison: best medical management at the time
• In stroke management don’t miss carotid disease or atrial fibrillation

Differential for Transient Focal Neurologic Deficit

• The Big Three
  - 1. TIA
  - 2. Seizure
  - 3. Complicated Migraine
Case 3

• A 67F is hospitalized with a community-acquired pneumonia. On Day#3 she is feeling much better awaiting discharge when her nurse finds her unresponsive with rhythmic shaking of all limbs.
  • PMHx: COPD
  • Meds: Ceftriaxone, NKDA
  • SH: 100pk yr hx tobacco, no hx EtOH
  • FH: No neurologic disease

Case 3

• You are called to the bedside and after 3 minutes, these movements have not stopped. Options for your next course of action are….
  A. Continue to wait for the spell to subside
  B. Administer IV Diazepam
  C. Administer IV Lorazepam
  D. Administer IV Fosphenytoin
  E. Administer IV Phenytoin

Case 3

• Following Lorazepam 2mg IV x 3 (2 minutes apart), the patient is still having these movements (now 7 minutes). What is your next course of action?

Status Epilepticus

• Changing definition and time window in 2010
• Incidence: 100,000 to 150,000 per year nationally
• Contributes to 55,000 deaths per year nationally
• 12 to 30 percent of epilepsy first presents as status
• Generalized convulsive status most dangerous

Status Epilepticus Algorithm:
Real World

1. Lorazepam 2mg IV q2 minutes up to 6mg
2. Fosphenytoin 18-20mg/kg (Dilantin Equivalents) IV
2a. Fosphenytoin additional 10mg/kg or Phenobarbital
3. General Anesthesia with continuous EEG
   a. IV Midazolam gtt
   b. IV Propofol gtt
Monotherapy for Seizures
• 70% of epilepsy can be managed with monotherapy, most on first drug tried
• Concept of Maximal Tolerated Dose (MTD)
• Rarely check levels
  – Assess compliance
  – Steady state level
  – Not practically available with newer AEDs

New Drugs: Clinical Pearls
• IV formulations: VPA, DPH, PHB, LVT
• Levels to Monitor: VPA, DPH, PHB, CBZ
• Lamotrigine (Lamictal)
  – Rash (1/1000) progressing to Stevens-Johnson
• Levetiracetam (Keppra)
  – No drug interactions (useful on HAART)
• Topiramate (Topamax)
  – Well tolerated?: weight loss and cognitive side effects

New Drugs: Clinical Pearls
• Oxcarbazepine (Trileptal)
  – Tegretol pro-drug
  – Hyponatremia
• Felbamate (Felbatol)
  – Aplastic Anemia with required registry
• Gabapentin (Neurontin)
  – Not a great AED

Case 4
• A 45 yo man presents with 2 days of progressive tingling and weakness of the lower extremities. He now is having trouble walking and rising from a chair.

Case 4
• Exam
  – MS, CN normal
  – Motor: normal tone throughout, normal power in upper ext., 4/5 throughout in the lower extremities
  – Sensory: decreased PP/Vib/temp patchy in lower extremities, Sensory level to PP at T4
  – Reflexes: 1 and symmetric throughout, toes neutral

What test should you next order?
A. MRI Brain
B. MRI Thoracic Spine
C. MRI Lumbar/Sacral Spine
D. Lumbar Puncture
E. Blood Cultures
Workup of Myelopathy

- First step: MRI with contrast
  - Pick appropriate level
  - Excludes structural disease
- Second Step: If MRI negative, usually proceed to lumbar puncture
  - Pleocytosis = autoimmune or infectious transverse myelitis
  - No Pleocytosis = metabolic, vascular, genetic

Case 5

A 44 man presents with bilateral numbness of the legs, urinary incontinence and spinal fluid with an elevated white blood cell count consisting of mainly lymphocytes. Upon his death, a pathological specimen of his spinal cord is shown. What is the etiology of his symptoms?

Case 6: 56F with bilateral numbness and weakness of the legs with macrocytic anemia

Case 7: A 66M presents with tremor. Which of the following findings makes the diagnosis of Parkinson’s Disease more likely than Essential Tremor?

A. Speed: 4-6 Hz
B. Tremor is primarily postural
C. Tremor relieved with alcohol
D. Symmetric Tremor
E. +FH of a similar tremor

Parkinson’s Treatment

1. Give L-Dopa
   - Levodopa/Carbidopa
2. Dopamine Receptor Agonists
   - Pramipexole, Ropinirole
3. Alter Dopamine/L-Dopa Metabolism
   - MAO-B Inhibitors: selegeline, rasagiline
   - COMT Inhibitors: entacapone
4. Decrease Cholinergic tone (rarely used)
5. Surgery: Deep Brain Stimulation (DBS)
**Parkinson’s Treatment Pearls**
- Only treat when function is impaired
- Start with L-dopa or a dopamine agonist
  - Agonists are best in those age <70 as they have cognitive side effects (hallucinations) in the elderly
- If L-dopa is “wearing off”, increase the frequency or add COMT inhibitor
- Reduce the dose if peak-dose dyskinesias are impairing function

**Wilson’s Disease**
- Consider in any young patient with a movement disorder
  - Especially with LFT abnormalities
  - Especially with psychiatric findings
- Diagnosis with low serum ceruloplasmin
- Usually treat with chelators such as penicillamine, trientine

**Migraine Therapy**
- Abortive Therapy
  - Begin with NSAIDs, ASA, acetaminophen
  - Triptains
    - Contraindicated with CAD
    - Caution with OCPs, especially in smokers age >35
    - Avoid if hx of complicated migraine
- Prophylactic therapy
  - Start if >4-6 spells per month
  - Multiple agents to choose from

**Obscure, but often asked ABIM fact:**
Name the disease below

**Case 8:** A 54M comes to the ED with the worst headache of his life. Which of the following findings would be most worrisome for SAH?
A. Extremely severe head pain
B. Photophobia
C. Pain reaching maximum intensity in seconds
D. Vomiting
E. No relief with high doses of opioids

**Cluster Headache**
- Males ages 20-50
- Unilateral, periorbital pain, often with autonomic symptoms
- Occur at the same time each day
- Occur in clusters over time
- EtOH can trigger
- Treatment: High flow O₂, Lithium, Prednisone, Triptans, Nasal Lidocaine
Trigeminal Neuralgia
• Electric shocks in trigeminal distribution
• No objective sensory deficits
• Unilateral
• Trigger sites for many patients
• Consider MRI to exclude brainstem lesion, especially in young
• Treatment: carbamazepine
• Refractory cases: surgical decompression

Temporal Arteritis
• Consider in any new HA over 50
• Consider in any new visual change over 50
  – Missed diagnosis leads to permanent visual loss
• Most helpful for diagnosis
  – Elevated ESR
  – Jaw claudication
• Begin steroids immediately, prior to Bx

Diagnosis of Multiple Sclerosis
• Lesions separated by time and space
• MRI clues
  – Involvement of corpus callosum
  – Some lesions with enhancement in acute period
• History of optic neuritis helpful
  – Visual Evoked Potentials (VEPs)
• Spinal Fluid
  – Oligoclonal bands, elevated IgG index
    • VERY non-specific for MS

Case 9
• A 40 yo man comes to the ED with increasing weakness and dyspnea. The patient states that he has a history of myasthenia gravis diagnosed at an OSH two weeks ago but “things are going downhill.” He is on Mestinon (pyridostigmine) 60mg PO q4hrs and Prednisone 60mg PO qd. MIF is –10, FVC 250cc

Myasthenic Crisis
• True crisis vs. cholinergic crisis
• Triggers
  – Infection, surgery, initial steroids
• Management
  – Usually stop all anti-cholinesterase meds
  – Pheresis or IVIg
  – ICU, intubation, DVT/PE prophylaxis
    • Follow MIF and FVC
  – Drugs to Avoid: NMJ blockers, aminoglycosides

Myasthenia Gravis: Key Points
• Two types of myasthenia
  – Young F>M
  – Old M=F
• Weakness fatigues with exercise and throughout the day
• Pure ocular form common (ptosis, diplopia)
• Diagnosis
  – Antibodies (90% in generalized myasthenia)
  – EMG with repetitive stimulation, single fiber EMG
Myasthenia Gravis: Key Points

- **Management**
  - Pyridostigmine (Mestinon)
  - Immunosuppression
    - Prednisone first then Imuran/CellCept/Cytoxan
  - What about the Thymus?

Case 10

- A 63yo man comes to the ED with 3 days of inability to walk. The patient reports a 2 week history of tingling in his hands and feet while also stating that he has been stumbling while walking for five days.

Case 10

- **Exam**
  - General exam nl with stable vitals
  - Mental status, cranial nerves normal
  - Motor exam with mild-moderate symmetric weakness prox>distal in the upper ext., distal>prox in the LEs
  - Sensory exam completely normal
  - Reflexes 2+ throughout except 0 ankles, plantar response flexor bilaterally

Guillain Barre Syndrome: Key Points

- Clinically must think in the setting of paresthesias and weakness
  - Normal sensory exam, weakness not always ascending
  - Areflexia the rule, but not early in the disease
  - High protein with no cells on LP the rule, but not early in the disease
- **EMG/NCS for diagnosis**
  - Axonal and Demyelinating forms
- Antecedent illness or infection only 30%
- Other Variants: Miller Fisher variant w/ GQ1bAbs

Guillain Barre Syndrome: Key Points

- What will kill the patient
  - Respiratory Failure: Intubate for less than 20cc/kg
  - Frequent MIF/FVC
  - ICU or stepdown care always
  - DVT/PE: SQ heparin
  - Autonomic instability: cardiac (telemetry), ileus
- **Treatment**
  - IVIg or Pheresis, NOT steroids
  - The earlier the better

### Mononeuritis Multiplex Differential

- **Inflammatory/Immune**
  - Vasculitis
  - Cryoglobulinemia
  - Sarcoid

- **Infectious**
  - Leprosy
  - Lyme
  - Hep C
  - CMV

- **Neoplastic**
  - Lymphoma
  - Carcinomatous meningitis

- **Others:** DM (rare), Waldenström’s, Amyloid

### Answers to Questions

- **Case 1 = D**
- **Case 2 = D or E**
- **Case 3 = C**
- **Case 4 = B**
- **Case 5 = Neurosyphilis**
- **Case 6 = B12 deficiency**
- **Case 7 = A**
- **Case 8 = C**