A 3-step Method to Diagnose Multiple Sclerosis

*Diagnosing and Misdiagnosing MS: An Ongoing Challenge*

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Editorial

• MS and Related Disorders

Book

• *Common Pitfalls in MS and CNS Demyelinating Disease*
Outline: 3-Step Diagnosis of MS

1. Classical Clinical Features of MS
   • Pitfalls!!

2. Neurological Examination
   • Normal, Consistent with MS, Consistent with OND

3. Investigations
   • MRI: Brain, Cervical, Thoracic Spine
   • Cerebrospinal Fluid (CSF)
   • Evoked Potentials
   • MS Mimickers: serology, other investigations
3-Step MS Diagnosis

1. Classical Clinical Features of MS

2. Neurological Exam:
   Normal, MS, OND

3. MS Investigations:
   MRI; CSF; EP; rule out mimickers
Classical Clinical Features of MS

- Monocular visual loss
- Pain
- **Progression**: hours-days
- **Resolution**: weeks-months

Optic neuritis
Optic Neuritis Pitfalls

- Mild, painless, transient (seconds to minutes) visual blurring
- No observed visual deficit or RAPD
- Normal VER

Classical Clinical Features of MS

- Diplopia
  - **Binocular**: i.e. close one eye resolve
  - Painless
  - Hours-days

Brazis and Lee Mayo Clinic Proceedings 1999
**Diplopia Pitfalls**

- Mild, transient “looking and then looking back”
- Seconds in duration
- Monocular only

**Classical Clinical Features of MS**

**Trigeminal Neuralgia**
- Lancinating, shock-like, intermittent, very severe facial pain
- Unilateral
- May be first symptom of MS
Trigeminal Neuralgia Pitfalls

Trigeminal Neuralgia

- Dull, aching, burning, pulling or squeezing
- Constant, or longer duration (minutes, hours, days)
- Bilateral

Classical Clinical Features of MS

Sensory myelopathy

- Progressive sensory level
- With or without paraquadriplegia
- Hands and feet simultaneously
Sensory Pitfalls

Sensory Myelopathy

• Mild, transient

• No clear pattern i.e.
  • Myelopathy (sensory level)
  • Brainstem (alternating loss)
  • Cortical (face, arm, leg)

Classical Clinical Features of MS

Neurogenic Bladder

• Urgency and urge-related incontinence

• Hesitancy; re-emptying

• Recurrent UTIs
**Neurogenic Bladder Pitfalls**

**Bladder symptoms**

- Urinary frequency only
- Anatomical: prior pregnancies, bladder procedures

**Classical Clinical Features of MS**

**Gait Impairment**

- Functional Impairment: # of blocks
- Stairs, bathtub, falls
- Not “just” fatigue or deconditioning
**Gait Impairment Pitfalls**

- Symptom of fatigue or deconditioning
- Functional limitations eg. distance, stairs, bathtub, falls

**Fatigue Pitfalls**

- Exceedingly common and highly non-specific
- May be associated with depression
- Often accompanies high temperatures
Memory Concerns Pitfalls

- May be associated with depression
- Non-specific, but often mild with MS so difficult to discount
- Need objective evidence to use as a reliable feature

Classical Clinical MS Symptoms
Neurological Examination

• Normal
• Consistent with MS
• Consistent with “other neurological disease”

Neurological Examination Consistent with MS

• Mental status: memory, often mild
• Optic neuropathy: visual field, color, acuity, afferent pupillary defect
• EOM: internuclear ophthalmoplegia
• Cerebellum: dysarthria, limb, gait ataxia
• Spinal Cord: sensory level, upper motor neuron para-quadriparesis, extensor plantars
• Gait: spastic, ataxic
Neurological Examination Consistent with Other Neurological Disease

• **Mental Status**: Impaired consciousness, severe dementia

• **Cranial nerve**: Fatigable ptosis, pupillary involving extraocular movement impairment, early dysphagia

• **Brainstem**: Palatal myoclonus, opsoclonus

• **Motor**: Fasciculations, lower motor neuron

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MS Investigations

• **MRI**: Brain, cervical, thoracic spinal cord

• **CSF**: IgG index, OCB

• **Evoked potentials**: VER

• **Other investigations**: MS mimickers
Brain MRI Periventricular Lesions

Brain MRI “Dawson Fingers”
Non-specific White Matter lesions

Brain MRI - Pitfalls

MRI Brain- non-specific T2 white matter changes

- Migraine, cigarette smoking, hypertension, aging
- Over calling by neuroradiologists?MS, ?vasculitis
MRI Cervical, Thoracic Spine

- Small, ovoid lesions
- <3 vertebral segments
- Axial imaging helpful

Spinal Cord MRI Pitfalls

- Scanner quality modest, lumbar spine not needed
- Underutilized reference for non-specific MRI brain abnormalities
- Cord lesions don’t occur with vascular risk factors
CSF Examination

1. Elevated CSF oligoclonal bands
   • Vs serum OCB

2. Elevated IgG index

3-Step MS Diagnosis

1. Classical Clinical Features of MS

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   MRI; CSF; EP; rule out mimickers
A woman with numbness, and prior visual loss: possible multiple sclerosis

• 41-yr-old woman shaving legs: right leg and thigh sensation gone; anterior and posterior

• Sensory loss progressed over days to foot, buttocks, genitalia and lower back on the right

• Spontaneous improvement over 3 weeks

• 5 yrs ago: left eye blurriness with ocular pain resolved spontaneously over 3 weeks

• No diplopia, dysarthria, hearing loss; no prior episodes of visual or sensory impairment.

• Ambulation normal walks and bikes miles

A woman with numbness, and prior visual loss: possible multiple sclerosis

• Neurological examination: mental status normal, visual acuity and color vision were normal bilaterally.

• Motor exam: normal

• Reflexes: normal, flexor plantars

• Sensory exam: decreased right sensation to T5 preserved vibratory, joint position sense.

• Gait: normal
A woman with numbness, and prior visual loss: possible multiple sclerosis

- **Brain MRI**: radially oriented increased T2 signal cerebral hemispheres, cerebellum and pons with Gad enhancing lesions, suggestive of MS
- **Cervical spine MRI**: normal
- **Thoracic spine MRI**: short segment T2 signal abnormality at T4.
- **CSF**: elevated oligoclonal bands and IgG index, normal
- **Visual evoked potential**: slowing on left

**MRI Brain FLAIR, T1 with Gad**
3 Step Assessment

1. Classical Clinical MS Features
   • Sensory myelopathy
   • Monocular visual loss

2. Neurological Examination
   • Consistent with MS-sensory level

3. Investigations
   • Brain MRI c/w MS
   • Spinal cord MRI c/w MS
   • CSF c/w MS
   • VER c/w MS

• Diagnosis: Relapsing remitting multiple sclerosis

• Tip: Satisfies all 3 steps.
A woman with diffuse pain and abnormal brain MRI scan. It is MS?

- 44-year-old woman evaluation of possible MS
- Hx migraine headaches without aura
- Severe HA, worse with activity, photophobia, phonophobia and nausea and vomiting
- Multiple foot surgeries, complex regional pain syndrome
- Non-specific memory concerns. Able to prepare meals, shop independently, drives w/o difficulty

A woman with diffuse pain and abnormal brain MRI scan. It is MS?

- **Neurological Examination:** Normal apart from pain associated with complex regional pain syndrome (CRPS)
MRI Brain

MRI Cervical, Thoracic Spine

• Normal
CSF

• Negative for elevated OCB or IgG index

3 Step Assessment

1. Classical Clinical MS Features
   • None

2. Neurological Examination
   • Normal

3. MS Investigations
   • Brain MRI inconsistent with MS
   • Spinal cord MRI normal
   • CSF inconsistent with MS
   • Evoked potentials normal
3 Step Assessment

• Diagnosis: Migraine HA, CRPS

• Tip: Satisfies none of the 3 steps.

A man with intermittent, steroid responsive brainstem symptoms

• 37 year-old man, 2 yr. intermittent facial tingling

• 6 mos. prior painless, horizontal, binocular diplopia with gait ataxia worsening over mos.

• Brain MRI, Cervical Spin MRI: gad-enhancing lesions in pons and spinal cord;

• CSF: elevated OCB

• IV methylprednisolone with improvement; no syx one yr
A man with intermittent, steroid responsive brainstem symptoms

• **Neurological examination:** Worsened gait ataxia, dysarthria and diplopia

• **MRI:** Enlarging areas of Gd-enhancement in brainstem; similar cervical, thoracic cord lesions

• **Pontine biopsy:** chronic inflammatory changes no infection, neoplasm, MS, sarcoidosis, lymphomatoid granulomatosis, histiocytosis
A man with intermittent, steroid responsive brainstem symptoms

- Intermittent therapy with IV methylprednisolone clinical and radiological improvement

- Deterioration reliably followed discontinuation

- Chronic therapy with prednisone and methotrexate
3 Step Assessment

1. Classical Clinical MS Features
   • Intermittent brainstem symptoms; steroid responsiveness

2. Neurological Examination
   • Consistent with MS

3. MS Investigations
   • Brain MRI inconsistent with MS
   • Spinal Cord MRI inconsistent with MS
   • CSF consistent with MS
   • Biopsy inconsistent with MS

Chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids (CLIPPERS)

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Urgent admission for MS

- 46-year-old woman, remote hx of bacterial meningitis in 1990s
- Burning pins, needles, initially in feet but over 2 months spread up legs to midback and fingertips, with saddle anesthesia.
- Urinary incontinence with loss of voiding sensation and severe constipation
- Weakness left leg, catches her toe, needs to lift her leg into a car with her arms, spontaneous clonus lower extremities

Urgent admission for MS

- Intermittent **monocular double vision** with stress, with eye swelling and drainage
- **Cognitive**: “forgetting store names stores she might go to”
- “No prior neurologic syndrome suggestive of multiple sclerosis, such as optic neuritis, INO, hemibody syndromes, or prior episodes of myelitis”
- Rx: methylprednisolone without improvement
Urgent admission for MS

- **Neurological Examination:** Bilateral upper motor neuron impairment left more than right with spastic gait
- Hyperreflexic, sustained clonus left, bilateral extensor plantar responses
- Sensory level T6
- Use of walker…now wheelchair

MRI Brain Thoracic Spine
MRI Cervical Spine

CSF

• Negative OCB and IgG index
3 Step Assessment

1. Classical Clinical MS Features  
   • Subacute myelopathy

2. Neurological Examination  
   • Consistent with MS- myelopathy

3. MS Investigations  
   • Brain MRI inconsistent with MS  
   • Spinal cord MRI inconsistent with MS, consistent with compressive cause  
   • CSF inconsistent with MS
Summary

3-Step Diagnosis of MS
1. Classical Clinical Features of MS
2. Neurological Examination
   • Normal, MS, OND
3. MS Investigations
   • MRI: brain, cervical, thoracic spinal cord
   • CSF: OCB, IgG index
   • EP: VER
   • MS Mimickers: other investigations
Thank you!