Multiple Sclerosis

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ARS Question

A 21 y.o. female presents with infrequent tingling and pain that migrates around her body for 10 minutes at a time. There are no permanent symptoms. The exam is normal.

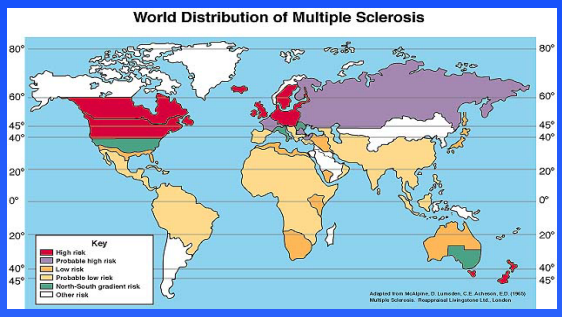
How would you proceed?

A. Stroke work-up
B. MS work-up
C. Neuropathy work-up
D. Other work-up
E. Reassurance and symptom management

Multiple Sclerosis

- Primarily CNS demyelinating disease
- Axonal loss is also present
- Females/white > males/non-white
- Sex 2-3:1 = F:M
- More common with distance from equator
- Prevalence 5-250/100,000 population

Map



MS: Genetics

- Risk to 1st degree relative ~3%
  - » Parents
  - » Sibling
  - » Child (mostly female)
- Monozygotic twins 26%

MS: Immunopathogenesis

- Viral theory
- Auto-immune theory
  - » Epitope spreading
- Combination theory
  - » Exposure early in life
  - » Loss of self antigen tolerance

MS: Pathology

- Four types of pathology recognized
- Each patient has only one type
- MS is probably not a single disease

MS: Types

- Relapsing-remitting MS (RRMS)
  - » 60-80%
  - » Secondary progressive
- Primary progressive MS (PPMS)
  - » 20-30%
  - » Older, cervical disease

MS: Clinical

- Optic neuritis
  - » Blurry, color desaturation
  - » Painful eye movement
- Weakness, spasticity
- Sensory
- Ataxia, tremor
- Cognitive
- Lhermitte's sign
- Fatigue
- Heat and exercise intolerance
- Bladder
- Sexual dysfunction

Optic Neuritis

RRMS: Clinical

- Exacerbations over hours to days
  - » > 24 hrs.
- Resolution over days to months
- 2 events separated in time and space
  - » Time: one month
  - » Space: clinical or paraclinical (MRI, CSF, EPs)
- No other explanation

Progression to MS in 5 yrs

Syndrome	N	Normal MRI (%)	Abnormal MRI (%)
Optic neuritis	44	1/16(6)	23/28(82)
Brainstem	17	0/5(0)	8/12(67)
Myelopathy	28	1/11(9)	10/17(65)
All	89	6%	72%

PPMS: Clinical

- Chronic symptoms > 6 months
- No other explanation
- Testing positive

ARS Question

A 23 y.o. woman has loss of vision in the right eye for 2 days. One year ago she had numbness in her left arm for 3 weeks but did not see a doctor.

What is the best test to confirm a diagnosis of MS?

A. Visual evoked potentials
B. CSF for oligoclonal bands
C. No test is needed
D. Head MRI

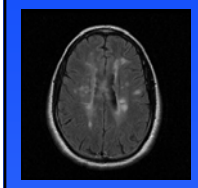
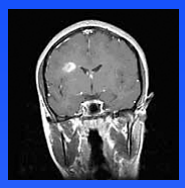
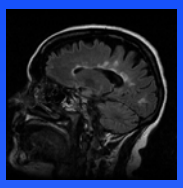
MS: Testing

- MRI
- CSF (Oligoclonal bands)
- Evoked potentials

MRI

- 90-95% sensitive at first presentation
- Visual detection of plaques
  - » Demyelination
  - » Gliosis
  - » Inflammation
- Location
  - » Periventricular
  - » Corpus callosum
  - » Cerebellum
  - » Brain stem
- Acute lesions enhance (Gd+)

MRI

Axial flair | Coronal T1 with Gad | Sagittal flair

Diagnostic Criteria: MRI

Table 1. New diagnostic criteria for MRI determination of dissemination in space

(After Barkhof et al and Tintore et al)

Three out of four of the following:

- One Gd+ lesion or 9 T2 hyperintense lesions
- One infratentorial lesion
- One juxtacortical lesion
- Three periventricular lesions

(one spinal cord lesion = one brain lesion)

Table 2. New diagnostic criteria for MRI determination of dissemination in time

- Gadolinium-enhancing lesion demonstrated in a scan done at least 3 months following onset of a clinical attack at a site different from attack, or
- In the absence of gadolinium-enhancing lesions at the 3 month scan, follow-up scan after an additional 3 months showing a gadolinium-enhancing lesion or new T2 lesion.

CSF

- Detects immune changes inside the blood-brain barrier
- Oligoclonal bands
  - » Sensitivity
    - – 85-90% RRMS
    - – 60% PPMS
  - » Specificity 60%
- Elevated IgG index
- Normal glucose
- Protein <100
- Cells <50

Evoked Potentials

- Detects conduction slowing through CNS
  - » Demyelination
- Type : Sensitivity
  - » Visual : 70%
  - » Tibial : 70%
  - » Median : 60%

Diagnostic Criteria

New MS Diagnostic Criteria

Clinical Attacks	Objective Lesions	Additional Requirements to Make Diagnosis
2 or more	2 or more	• None; clinical evidence will suffice (add'l evidence desirable but must be consistent w/MS)
2 or more	1	• Dissemination in *space* by MRI ***or*** positive CSF and 2 or more MRI lesions consistent w/MS ***or*** further clinical attack involving different site
1	2 or more	• Dissemination in *time* by MRI ***or*** 2nd attack
1 mono-symptomatic	1	• Dissemination in *space* by MRI ***or*** positive CSF and 2 or more MRI lesions consistent w/MS AND • Dissemination in *time* by MRI ***or*** 2nd attack
0	1	• Positive CSF AND • Dissemination in *space* by MRI evidence of 9 or more T2 brain lesions ***or*** 2 or more cord lesions ***or*** 4-8 brain and 1 cord lesion ***or*** positive VEP with 4-8 MRI lesions ***or*** positive VEP with less than 4 brain lesions plus 1 cord lesion AND • Dissemination in *time* by MRI ***or*** continued progression for one year

(Source: National MS Society)

ARS Question

The same 23 y.o. woman has MS confirmed by MRI. Her vision loss has become severe in the past few days.

How should we treat her?

A. Oral prednisone 60mg/d x 10 days
B. IV methylprednisolone 1000mg IV qd x 3-5
C. Betaseron SQ qod
D. Both A and C
E. Both B and C
F. None of the above

MS: Treatment

- Symptomatic
- Acute
  - » Methylprednisolone 1000mg IV qd x 3-5
- Chronic (Disease modifying drugs)
  - » Interferon beta-1b (Betaseron)
  - » Interferon beta-1a (Avonex)
  - » Interferon beta-1a (Rebif)
  - » Glatiramir acetate (Copaxone)
- Mitoxantrone (SPMS)

MS: Treatment

- Depression
  - » SSRIs
  - » Wellbutrin
  - » Others
- Spasticity
  - » Baclofen (PO, IT)
  - » Tizanidine
  - » Benzos
- Fatigue
  - » Amantidine
  - » Pemoline
  - » Modafinil
- Bladder
  - » Anticholinergic
  - » Catheter
- PT/OT