Multiple Sclerosis

HIHIM 409

Patterns of MS

- Relapsing - remitting
  - Attacks with complete/incomplete recovery
  - Stable between attacks
- Secondary - progressive
  - Initially relapsing-remitting
  - Then progression +/- attacks
- Progressive - relapsing
  - Initial gradual detioriation
  - Subsequent episodes
- Primary progressive
  - Gradual decline
  - No attacks

Clinical Manifestations

- Demographic
  - Female
    - Women make up to 70%-75% MS patients
  - Young age
    - Onset before age 16: 5% of cases
    - Peak onset post puberty, early 20`s
      - Relapsing MS 28-30 years
- Symptoms
  - Recent onset
  - Frequently progressive
    - Coming on over 1-several days
    - Very acute symptoms possible

The MS Event

- Attack/relapse/exacerbation
  - Acute episode of CNS dysfunction
  - Lasting at least 24 hours
  - In absence of fever or metabolic derangement
  - All events within 30 days are unitary

MS Symptoms

Deficit reported	Presenting %	During course %
Visual/oculomotor	49	100
Paresis	42	88
Paresthesias	41	87
Incoordination	23	82
Genitourinary/bowel	10	63
Cerebral	4	39

Source: Whitaker JN, Mitchell GW 1997

Clinical Manifestations

- Motor
  - Weakness, spasticity, ataxia
  - Rarely radicular
    - lesion ant. horn, root entry zone
    - painful
    - atrophy
- Somatosensory
  - 1st sx. in 43% patients
    - Includes visual
  - Any anatomic distribution
  - Any combination
    - Loss pain, temp, light touch, vbn, position
  - Positive sx. common
    - Paresthesiae, hyperpathia, allodynia, dysesthesias

Nonspecific Associated Features That Suggest MS

- Excessive unexplained fatigue
- Temperature sensitivity
  - Hot, humid weather
- Relatively recent symptoms
- History of Lhermitte's sign
- History of bandlike sensation around the waist
- Uhthoff's phenomenon
  - eg, blurry vision with exercise or heat exposure

Clinical Manifestations

- Fatigue
  - One of the most important causes of disability
  - Several sources
    - Handicap fatigue
      - Increased effort to perform routine tasks
    - Secondary fatigue
      - Depression, sleep disturbances, medication side-effects, other conditions
    - Systemic fatigue
      - Chronic lack of energy, tirdness, malaise
      - Etiology unknown

Clinical Manifestations

- Cognitive Disturbances
  - Common, frequently overlooked
    - Estimated 50-75%
  - Most common
    - Impaired attention, slow info processing, short term memory loss, reduced visuospatial skills, impaired executive function
  - Impaired driving skills
  - Important impact QoL, ADL
  - Can occur independent
    - of disease course
    - other manifestations

MRI in MS

- Brain lesions
  - Character
    - Large $\geq$ 3 mm
    - Ovoid
    - Oriented perpendicular to ventricles
    - Enhancing
      - Open-ring enhancement
      - Multifocal homogeneous
  - Location
    - Multiple white matter
    - Brainstem, infratentorial
    - Juxtacortical
    - Corpus callosum
      - Pointing away
      - Moth eaten
      - Callosal atrophy

Evoked Potentials

- Visual evoked potentials
  - Not auditory or somatosensory
  - May point to subclinical involvement of optic nerve
    - Quality control issues

Principal Differential Diagnosis of Multiple Sclerosis

- Infection
  - Lyme, Syphilis, Progressive Multifocal Leukoencephalopathy, HIV, HTLV-1
- Inflammatory
  - SLE, Sjogren syndrome, vasculitis, Sarcoidosis, Bechet's disease
- Metabolic
  - B12 deficiency, lysosomal disorders, adrenoleukodystrophy, mitochondrial disorders, other genetic diseases
- Neoplastic
  - CNS lymphoma
- Spine disease
  - Vascular malformations, degenerative spine disease

Cerebrospinal Fluid

- Useful, not diagnostic
  - Other conditions
    - Chronic CNS infections, viral syndromes, neuropathies
- Immunoglobulin abnormalities
  - Production of immunoglobulin
    - By plasma or B cells in CNS
  - Oligoclonal bands of immunoglobulin (IgG) (OCB)
    - In CSF, not serum
    - Isoelectric focusing technique
  - Elevated IgG index
    - Ratio of IgG/protein in serum and CSF
    - index = $\frac{\text{(csf IgG/csf albumin)}}{\text{(serum IgG/serum albumin)}}$

Cerebrospinal Fluid

- First event - chance of progression to MS
  - In 3 years
    - OCB +ve: 25%
    - OCB -ve: 9%
- CIS:clinically isolated syndrome
  - 62.5% cases +ve OCB
- Clinically definite MS
  - 90% +OCB

MRI in MS

- Spinal cord lesions
  - Character
    - Asymptomatic lesions
    - Focal T2/proton density hyperintense lesions
    - Diffuse proton density abnormalities
    - Atrophy
    - Asymmetric involvement
      - Multiple scattered lesions
    - Edema with acute plaques
      - Often enhancing
  - Location
    - Cervical and thoracic
      - Especially midcervical
    - Peripheral
    - Less than 2 vertebral segments
    - Less than 50% cross-sectional area
    - Lateral, dorsal cord

Paroxysmal Symptoms in MS

- Trigeminal neuralgia (and others)
- Tonic "seizures"
- Paroxysmal dysarthria
- Hemifacial spasm
- Paroxysmal itching
- Abrupt loss of muscle tone
- Paroxysmal aphasia
- Paroxysmal kinesogenic choreoathetosis
- Lhermitte's sign

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Clinical Manifestations

- Visual symptoms, afferent
  - Almost any pattern, related to location
  - Optic neuritis
    - Central scotoma
      - Mild: color desaturation
      - Severe: blindness
        - Vast majority have excellent return by 6 months
    - Frequent pain
      - Worse on eye movement

Optic Neuritis
Risk of Subsequent MS

- Higher Risk
  - Young adult (~~20-40 years~~)
  - Venous sheathing
  - Recurrent optic neuritis
  - Female sex
  - History of minor neurologic symptoms
  - Brain MRI lesions
  - CSF oligoclonal bands or intrathecal IgG production
- Lower Risk
  - Age < 10
  - Macular star/exudates
  - Retinal or disc hemorrhage
  - Severe disc edema
  - No brain MRI lesions
  - Normal CSF

Clinical Manifestations

- Visual symptoms, efferent
  - Any eye movement abnormality
  - INO
    - Internuclear ophthalmoplegia
      - Adductor weakness
      - Abduction nystagmus
      - In young adult strongly suggests MS
  - Nystagmus
    - Many types

Clinical Manifestations

- Other Brain Stem Structures
  - Facial weakness
  - Vertigo
  - Loss of hearing, taste
  - Dysarthria, dysphagia
    - Bulbar muscles
      - Weakness, ataxia, spasticity

Clinical Manifestations

- Psychiatric Disturbances
  - Depression
    - Also up to 75% of patients
    - Major depression less frequent
    - Suicide: 15% of adult MS deaths
      - Risk factors
        - Living alone
        - FH mental illness
        - Reporting social isolation
        - PH major depression, anxiety, alcohol abuse
  - Emotional incontinence
    - Frontal lobe involvement

Clinical Manifestations

- Bladder dysfunction; the importance of urodynamic studies
  - Failure to store: detruser hyperactivity
    - Urgency, frequency, nocturia
  - Failure to empty
    - Detruser-sphincter dyssynergia
    - Poor detruser contraction
      - Hesitancy, increased residual vol., retention
  - Both
    - Combined
      - detruser hyperactivity
      - detruser-sphincter dyssynergia
  - Incontinence
    - Detruser hyperactivity or
    - Overflow
    - Symptoms may not be accurate indicator of urodynamic pathology

Clinical Manifestations

- Bowel dysfunction
  - Constipation
    - Can be aggrevated by
      - fluid restriction
      - Anticholinergic medications
  - Urgency and incontinence
- Sexual dysfunction
  - Erectile dysfunction
  - Women: loss of libido, anorgasmia
  - Both sexes
    - Loss of perineal sensation
    - Neuropathic pain
    - Spasticity
    - Incontinence
    - Depression, fatigue

Pain Syndromes in MS

- Primary pain
  - Neuralgic
    - Trigeminal neuralgia
    - Other neuralgias
  - Dysesthetic pain
    - Most often burning (legs)
    - Other dysesthesias
  - Radicular pain
  - Tonic seizures
  - Spasticity
    - Flexor spasms
    - Extensor spasms
- Secondary pain
  - Low back pain
  - Osteoporosis with fractures

Neurologic Syndromes Likely for MS

- Optic neuritis
  - Unilateral eye involvement
  - Retrobulbar rather than papillitis
  - Eye pain
  - Partial vision loss, with at least some recovery
  - No retinal exudates, disc hemorrhages, macular star
- 10 years follow-up: 38% develop MS
  - MRI other lesions: risk 56%
  - MRI normal: risk 22%
- 20 years follow-up: 70% develop MS

Neurologic Syndromes Likely for MS

- Transverse Myelitis
  - Incomplete
  - Sensory > motor
  - Associated
    - Lhermitte's sign
    - Bandlike abdominal or chest pressure
- Internuclear Ophthalmoplegia
- Trigeminal Neuralgia
- Hemifacial Spasm

Neurologic Syndromes Likely for MS

- Paroxysmal symptoms
  - Last seconds to minutes
  - Occur multiple times daily
- Tonic spasms
- Dysarthria, ataxia
- Hemiparesis, hypesthesia

- Polysymptomatic Syndrome Without Mental Status Changes

Clues to a Misdiagnosis; MS

- Historical
  - No dissemination
  - Onset < 10 yrs. or > 55 yrs.
  - Genetic red flags
    - +ve FH
      - However about 20% of MS patients have FH
    - Early-age onset
    - Unexplained non-CNS disease
  - Progressive course starting before age 35
  - Localized disease

Clues to a Misdiagnosis; MS

- Examination
  - Prominent
    - fever, headache, uveitis, pain
  - Abrupt
    - hemiparesis, hearing loss
  - No
    - optic nerve/ocular involvement
    - bowel/bladder involvement
  - Progressive myelopathy
    - Without bowel/bladder involvement
  - Impaired level of consciousness
  - Nonscotomatous visual field defects
  - Grey matter features
    - Early dementia, aphasia
    - Fasciculations
    - Extrapyramidal features

Clues to a Misdiagnosis; MS

- MRI
  - Brain
    - Normal
    - Small lesions < 3 mm.
    - Subcortical location (internal capsule)
    - Prominent infratentorial involvement
    - Prominent grey matter involvement (basal ganglia)
    - Symmetric, confluent hemispheric white matter involvement
    - Hydrocephalus
    - Severe cerebellar/brain stem atrophy
    - No callosal/periventricular lesions

Clues to a Misdiagnosis; MS

- MRI
  - Spinal cord
    - Large lesion, multiple segments (>2)
    - Severe swelling
    - Full thickness lesions
    - Leptomenengial enhancement
    - T1 hypointense lesions

Clues to a Misdiagnosis; MS

- CSF
  - Normal
  - Disappearance of oligoclonal bands
    - Normalization of IgG index
  - Cell count > 50 wbc/cubic mm.
  - Protein > 100 mg/dl

MS Diagnosis; 1 Final Slide

- Manifestations due to CNS
  - Slowing or failure of transmission
  - Mostly damage of white matter tracts
  - Recent appreciation of axonal/grey matter involvement
- Diagnosis based on clinical and laboratory evidence of
  - Dissemination in time
  - Dissemination in space
  - Recent appreciation of role of MRI in assisting diagnosis
- In-office pattern recognition
  - Appropriate demographic
  - Appropriate clinical event