Transverse Myelitis

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Diagnostic Criteria of TM

- Acute or subacute motor, sensory or autonomic dysfunction
- Segmental distribution of sensory impairment
- No sc compression
- Exclusion of other causes
- < 4 wks from onset to peak
    - Berman et al., 1981

Differential Diagnosis of TM

- Trauma
- MS
- Spondylosis
- Tumors
- Paraneoplastic
- B12
- Intoxication
- Hemorrhage
- Ischemia
- AVM/AVF
- Vasculitis

TM Demographics

- Incidence: 4.6 per million, per year
- 1400 new cases in U.S. per year

- Prevalence: 34,000 people in the U.S. at any given time with morbidity from TM

Viral Etiologies

- Picornaviruses
  - Coxackie
  - Echo
  - Hep A
- Togaviruses
  - Arboviruses
  - Tick-borne
  - Rubella
- Retroviruses
  - HIV-1
  - HTLV-1
- Orthomyxoviruses
  - Measles
  - Mumps
- Bunyaviruses
  - California encephalitis

Viral Etiologies (cont.)

- Arenaviruses
  - LCMV
- Rhabdoviruses
  - Rabies
- Hepatitis B, C

- Herpes viruses
  - HSV-1
  - HSV-2
  - VZV
  - CMV
  - HHV-6

Clinical Classification of TM

- 45% parainfectious
- 21% MS
- 12% ischemic/vascular
- 21% idiopathic

- Retrospective analyses of 33 cases
  - Jeffery et al., 1993

Recurrence of TM

- MS 60%
- Idiopathic 15%
- Postinfectious 12%
- Ischemia 5%
  - Jeffery et al., 1993

Presenting Symptom in TM

- Pain 12/25
- Weakness 9/25
- Urinary dysfxn 3/25
- Sensory 1/25
- 25 children
  - Paine and Byers, 1953

- Pain 33/82
- Weakness 25/82
- Urinary dysfxn 33/82
- Sensory 64/82
  - Ropper and Poskanzer, 1978
  - Christensen et al., 1990

Antecedent Illness in TM

- 11/31 Misra et al., 1988
- 25/31 Al Deeb, 1997 (Saudi Arabia)
- 19/52 Ropper and Poskanzer, 1978
- 12/34 Lipton and Teasdall, 1973 (JHH)
- 20/67 Altrocchi, 1963

Progression of Symptoms of TM

- Onset to maximum
  - poor: mean 4.6 d
    - (0.3-17)
  - fair-good: 7.3 d
    - (0.8-19)

- Christensen et al., 1990

- <24 hrs- 45%
- 1-3 d- 10%
- 4-7 d- 9%
- >7 d- 36%

- Altrocchi, 1963, N=67

Association of TM with trauma

- Many people believe that mild-moderate trauma is associated with the development of TM
- 10% of cases in some series (Altrocchi, 1963).
- Often mild trauma/sprain

Pathology of TM

- Widely variable from demyelination to necrosis
- infarction-2/8
- non-specific necrosis-2/8
- meningomyelitis-1/8
- intramedullary capillary telangiectasias with hemorrhage-1/8
  - Lipton and Teasdall, 1973

Prognostic Variables in TM

- Good
  - retained reflexes
  - retained post. Column
- Poor
  - back pain
  - spinal shock
  - abnormal SEP
  - denervation on EMG
    - Kalita et al., 1998

- Non-predictive
  - age
  - sex
  - race
  - ant. Illness
  - rapidity of progression
  - level
  - CSF findings

Outcome from TM

- Good- 1/3
- fair- 1/3
- poor/death- 1/3
  - Berman et al., 1981 (N=48)
  - Christensen et al., 1990 (N=30)
  - Ropper and Poskanzer, 1978 (N=48)

Mortality of TM

- 5/34- Lipton and Teasdall, 1973 (JHH)
- 3/62- Berman et al., 1981
- 2/30- Christensen et al., 1990
- 1/31- Al Deeb et al., 1997

- total around 5%

TM and MS

- Rarely see spinal shock, back pain or large segmental involvement
- See spasticity early
- With partial TM: 42% (Miller et. al., 1989) or 80% (Ford et al., 1992) will develop MS

TM and MS (cont)

- OCB in 60%
- + CNS PVWML= PPV of 93%
- MR of C/T spine: lesions peripherally located, < 2 vertebral levels and occupy < 1/2 the cord diameter

TM and Vascular Malformations

- Dural AVF
- onset >40, <70
- males:females 4:1
- symptoms: PAIN, progressive weakness, saddle numbness, claudication, urinary sx.
- Postural relationship
- fluctuating or slowly progressive course

TM and AVF (cont.)

- PE: Spinal bruit or cutaneous angioma occasionally
- More prominent with Valsalva
- MRI: Enlarged cord, subtle gad of dorsal surface
- Myelography is procedure of choice

TM and AVF (cont.)

- Etiology: Increased venous pressure and vascular congestion
- Natural hx: 91% non-ambulatory by 3 yrs.
- Rx: Limited laminectomy nidus removal or vein ligation
- Gait improvement in 5 of 7 previously wheelchair-bound patients

TM and ID

- Oligoarticular arthritis - ?
- ECM-Lyme
- Palatal petechiae - ?
- Copper colored rash with amp - ?
- Lymphadenopathy/hepatosplenomegaly - ?
- Pharyngitis/myringitis - ?
- Hepatic renal dysfunction - ?

TM Treatment

- Steroids (? SCI protocol)
  - < 3 hrs: Solumedrol 30 mg/kg bolus then 5.4 mg/kg per hr x 23 hrs
  - 3-8 hrs: Same bolus with 48 hr infusion

TM Treatment (cont.)

- Solumedrol 1 gm qd x 3 d
- Open label, children
- Median time to independent ambulation 23 d vs. 97 d
- Proportion with full recovery: 80% vs. 10%
  - Sebire et al., 1997
  - Lahat et al., 1998

TM and SLE

- CNS lupus in 24-51% of SLE pts
- TM in 1-4% of SLE pts
- 20% of CNS lupus get TM
  - Neuwelt et al., 1995

TM and SLE (cont.)

- CSF abnormal in 63%
- MRI abnormal in 56%
- 10% lupus nephritis
- 40% ds DNA Ab
- No increase in ACL or LAC
  - Mok et al., 1997 (China)

TM and SLE (cont.)

- Improved outcome with IV-CYC
- Retrospective review
- IV-CYC: 500 mg/m2 per month up to 1000 mg/m2
- Dose-adjustment: WBC nadir of 3-4K
  - Neuwelt et al., 1995

Management of TM

- Avoid autonomic dysreflexia
- An emergency!
- Seen with lesions above T6
- Sx: Severe HA, spots in front of eyes, blurred vision, slow HR, goosebumps, sweating, flushing above lesion
- BP up to 280/140

Mechanism of Autonomic Dysreflexia

- Impaired descending fiber input to T6-T10 for alpha adrenergic vasodilation
- Hence vasoconstriction, HTN and vagal tone

Causes of Autonomic Dysreflexia

- pain signals
- full bladder
- infection
- stool impaction
- tests
- pressure sores
- hot and cold temp
- sunburn
- tight clothes
- menstrual cramps
- labor
- stomach ulcer
- some drugs

Treatment of Autonomic Dysreflexia

- Sit up!
- Find and remove the cause
  - Catheterization
  - Remove tight clothing
  - Bowel disimpaction
- Nitroglycerine ointment
- Nifedipine 10 mg sl

Bladder Dysfunction in TM

- Usually areflexic, atonic at first
- Resolves to hyperreflexic bladder with/without dyssynergia
- W/U: UA, C and S, BUN/Cr, IVP/retrograde cystometrogram
- Urodynamics a must, but not acutely

Management of Bladder Dysfunction

- IC: For volumes which don’t result in increased intravesicular pressure
- Indwelling catheter
- Suprapubic catheterization
- Crede Valsalva

Management of Bladder Dysfunction (cont.)

- Hyperreflexic bladder:
  - Anticholinergic
    - Oxybutinin 5mg tid/qid
    - Propantheline 15-30mg tid/qid
    - Imipramine 25mg tid
- DESD
  - Neuromuscular inhibition
  - IC and anticholinergics
  - Sphincterotomy

DESD in TM

- Dis-coordination between bladder and external sphincter
- Results in bladder wall changes, loss of compliance and high pressure voiding

Potential future therapies

- Novantrone (mitoxantrone)
  - novel medicine utilized for MS: decreases number of attacks and delay in disability progression in SPMS
  - Reduced deterioration in EDSS from 44% (placebo) to 17% (12 mg/m2 dose)
  - SE: nausea, alopecia, transient neutropenia,

Potential future therapies

- 4-Aminopyridine (fampridine)
  - potassium channel blocker, which diminishes the “leak” of ions in demyelinated areas
  - increases conduction of demyelinated neurons
  - iv or po
  - dose related seizures and chemical hepatitis
  - narrow therapeutic window
  - 27% vs 2% subjective improvement in MS patients (blinded)

Potential future therapies

- M1 monoclonal antibodies
  - accelerate remyelination in three animal models: viral, autoimmune and chemically induced
- IN-1 monoclonal antibodies
  - stimulates neurite outgrowth and overcomes the inhibition of CNS myelin
- Neurotrophins
  - NT-3, BDNF, GDNF

Potential Future Therapies

- Polyketides
  - Rapamycin/FK506 analogs
  - immunosuppressant and stimulant of neurite outgrowth (separable activities)
- Neuroimmunophilin ligands

Johns Hopkins Transverse Myelopathy Center (JHTMC)

- A unique multi-disciplinary center dedicated to the diagnosis and treatment of patients with transverse myelitis

JHTMC-MISSION STATEMENT

- Patient Care
  - Ensure the appropriate diagnosis and work-up of TM patients
  - Maximize function with existing technology
  - Minimize chance of ongoing damage
  - Develop new therapies
- Research (New Discoveries)
- Teaching

JHTMC-Patient Care Highlights

- Multi-disciplinary approach
- Hopkins experts
- Best technology
- Newest treatments
- Support- access to care/help with insurance/patient groups
- Education- PCP/community/home
- Long term care

JHTMC-Research Highlights

- Large cohort of patients: epidemiology/outcomes
- Develop/evaluate new technology
  - novel imaging strategies
  - prognostic variables
- Develop/evaluate new therapies
  - immune mediators/cytokine treatment
  - animal models for TM
  - neuronal stem cell therapies

JHTMC-Research (cont)

- Encourage pharmaceutical involvement in therapeutic trials

JHTMC-Education

- Patient
- Family/friends/caregivers
- Students
- Physicians/PCP
- Unique programs
- Access to materials

JHTMC-Unique Clinical Features

- Diagnostic studies
  - novel neuro-imaging strategies
  - novel CSF disease markers
  - infectious/inflammatory work up
  - MS evaluation
  - Electro-diagnostic studies

JHTMC-Unique Clinical Features (cont)

- Spasticity/Gait evaluation and treatment
  - Quantitative upper and lower limb spasticity evaluation
  - Functional gait/stability assessment
  - Intrathecal therapies for spasticity
  - Expert splinting/mobilization strategies

JHTMC- Unique Clinical Features (cont)

- Pain management
- Functioning in society
- Psychiatry evaluation tailored specifically to patients with TM
- Sexual function determination

JHTMC-Unique Clinical Features (cont)

- Expert evaluation of bladder dysfunction
- Urodynamics testing performed
- Determination of optimal therapy to maximize continence and minimize damage to the urinary tract
- Avoidance of UTIs