Acute Myelopathy: Focus on Transverse Myelitis

David N. Alexander M.D.
August 29, 2012
Las Vegas, NV
PVA
Track: Spinal Cord Injury: Clinical (ID: PVA2012-SCI)
Outline of today’s presentation

• Anatomy

• Extra-axial causes of acute myelopathy examples with imaging

• Causes of intrinsic acute myelopathy,
  • variation based on location and inclusion criteria

• Acute transverse myelitis (ATM): Sx/Signs , epidemiology, causes

• ATM mimics
Patient Presentations, cause external to cord

• A 65 yo man presents with a complaint of back pain.
• He had been hospitalized 2 months after a UTI and then subsequent TURP with finding of prostate cancer.
• He has been increasing his physical activity during his recovery, and thought he had strained his muscles.
• You find on exam some hyperreflexia in his legs.
73 yo aerospace engineer
Back pain, then IR aspiration, antibiotics
2 mo, new paraparesis

PMHx
Afib, prostate ca 2002, lipids, fall 2 y prior with t12 and other fractures
RX

Pott’s Puffy Tumor
Mycobacterium Tuberculosis

- Irrigation debridement of epidural t12 abscess
- Sp posterior fusion from t9 to L2
- Rifampin, isoniazid, pyrazinamide, ethambutol
Causes of Myelopathy Vary by location

• South Africa
  – 100 consecutive admissions myelopathy
  – TB, particularly HIV+
  – HIV- were older with neoplasms and degenerative spondylosis

• India
  – Spinal TB most common cause of NTSCI-30%
  – Then ATM 20%, and
  – primary spinal cord tumors 10%
Acute myelopathy

- *Not traumatic, compressive, extra-medullary*
- Intra-axial, intramedullary
- Acute or subacute onset
- Motor, Sensory, Autonomic (bladder, bowel, sexuality)
Case: Pregnant Lawyer

• 33 y.o. employment lawyer, pregnant, at term, fell at home because of leg weakness and had fecal incontinence
• Tingling in Ambulance
• Weak in ER, 4 cm dilated in labor
• How would you manage?
• DDx?
Acute Myelopathy, 79 cases

- MS: 43%
- Systemic Disease: 17%
- infarct: 14%
- Unknown: 16%
- Radiation: 4%
- Para Infectious: 6%
- Acute Myelopathy: 47%
Diagnostic Criteria for TM:
TM Consortium Working Group

Sensory, motor, or autonomic dysfunction attributable to the spinal cord
Bilateral signs and/or symptoms
Clearly defined sensory level
Inflammation defined by CSF pleocytosis or elevated IgG index or gadolinium enhancement
Progression to nadir between 4 hours and 21 days
Acute Evaluation

• Recognizing that it is a myelopathy
• Clinical manifestations of myelopathy
  – Urinary retention
• Determine Cause
Emergent Evaluation

Presentation with non-traumatic acute Spinal Cord Dysfunction

Time course and nature and extent of deficits,
Prior infection, such as URI,
Hx systemic inflammatory disease
Risk factors for stroke,
Prior history of cancer, MS, radiation exposure, or optic neuritis.
Immunosuppressed?.

MRI with gadolinium of spine, appropriate level
Dx Criteria for TM

- Bilateral
- Sensory level
- Sx to nadir: 4 hour to 21 days
- Spinal Cord inflammation:
  - pleocytosis or ↑IgG index, or
  - MRI gad+ spinal cord lesion
- Not compressive, post radiation, neoplastic, vascular
Acute Transverse Myelitis (ATM)

1. Idiopathic (Post-infectious, para-infectious)

2. Acquired demyelinating disease

3. Systemic Disease
Acute Transverse Myelitis (ATM)

1. **Idiopathic (Post-infectious, para-infectious)**
   - associated with an antecedent or precedent viral illness with a
   - presumed secondary or post-infectious development of autoantibodies attacking the spinal cord

2. Acquired Demyelinating Disease

3. Systemic Disease
Epidemiology of idiopathic or post-infectious TM

- Bimodal peak, 10-19 then 30-39.
- 1.3 to 8 cases per million
- 24.6 cases per million if included acquired demyelinating disease
- Path: lymphocytes and monocytes in spinal cord with demyelination, axonal injury and astrocyte and microglial activation.
- Molecular mimicry
Adaptive Immune Response
ATM Case, mild

- 43 yo man LE weakness, tingling in feet, 4 day hx with slight progression, unsteady on feet
- Bronchitis, ED, for cough starting 11 day PTA
- No B/B dysfunction, No PMHx
- 4/5 weakness, hypereflexia knees, T6 sensory level, back pain.
- MRI negative
- Is this ATM?
Diagnostic Criteria for TM

- Sensory, motor, or autonomic dysfunction attributable to the spinal cord
- Bilateral signs and/or symptoms
- Clearly defined sensory level
- Inflammation defined by CSF pleocytosis or elevated IgG index or gadolinium enhancement
- Progression to nadir between 4 hours and 21 days
CSF tests

**NEGATIVE**
- ALBUMIN, CSF
- GLUCOSE, CSF
- IGG INDEX
- CSF APPEARANCE
- VZV IgG AB, CSF
- BACTERIAL CULTURE CSF
- OLIGOCLONAL BANDS

**POSITIVE**
- CELL COUNT & DIFF, CSF --- 8
  WBC, primarily lymphocytes
- CNS IGG SYNTHESIS RATE -- elevated
- PROTEIN, CSF — 86
Blood tests Performed

- ALBUMIN INDEX
- ALKALINE PHOSPHATASE
- ALT (SGPT)
- ANGIOTENSIN CONVERTING ENZYME
- ANTINUCLEAR AB
- APTT
- AST (SGOT)
- BETA-2-GLYCOPROTEIN
- BILIRUBIN, CONJ
- BILIRUBIN, TOTAL
- CARDIOLIPIN IGA
- CARDIOLIPIN IGG
- CARDIOLIPIN IGM
- CBC & PLATELET CT
- CBC & PLT & DIFF
- CK, TOTAL
- COMPREHENSIVE METABOLIC PANEL
- CORRECTED APTT
- CREATININE
- DIL. RUSSELL VIPER VENOM TIME
- DRUGS OF ABUSE SCREEN, URINE
- DRVVT INTERPRETATION
- ELECTROLYTE PANEL
- ELECTROLYTES, WHOLE BLOOD
- GLOMERULAR FILTRATION RATE EST
- GRAM STAIN
- HEPATIC FUNCTION PANEL
- HEPATIC FUNCTION PANEL
- HIV1/HIV2 ANTIBODY SCREEN
- HSV TYPE 1 & 2 BY PCR
- HTLV I-II DNA QUAL, RT-PCR
- HTLV I/II AB, REFLEX CONFIRM
- IGG SYNTHESIS RATE PROFILE
- IGG SYNTHESIS, BLOOD SPECIMEN
- IONIZED CALCIUM
- LYME DISEASE AB TOTAL
- LYME DISEASE, WESTERN BLOT
- MAGNESIUM
- Mycoplasma pneumoniae, IGG/IGM
- Neuromyelitis optica (NMO)
- NORMAL APTT
- OLIGOCLONAL BANDS IN CSF & SERUM
- PATIENT APTT
- PHOSPHORUS
- PROTHROMBIN TIME PANEL
- RPR
- UREA NITROGEN
- URINALYSIS, ROUTINE
- VITAMIN B12
- VZV AB IMMUNE STATUS
Blood Tests Positive

- **MYCOPLASMA PNEUMONIAE IGG** 2.24 U/L
  - Reference interval: Mycoplasma pneumoniae Ab, IgG
  - 0.09 U/L or less .......... Negative
  - 0.10 - 0.32 U/L .......... Equivocal
  - 0.33 U/L or greater ......... Positive

- **MYCOPLASMA PNEUMONIAE IGM** @ 2.83 U/L ≤0.76
  - Reference interval: Mycoplasma pneumoniae Ab, IgM
  - 0.76 U/L or less .......... Negative:
  - 0.77 - 0.95 U/L .......... Low Positive:
  - 0.96 U/L or greater ...... Positive: Highly significant
  - Amount of M. pneumoniae-specific IgM antibody detected

**DRUGS OF ABUSE SCREEN, URINE**
- **CANNABINOIDS** @ Positive 50
ATM Case, mild

DX:

• Post-infectious ATM related to mycoplasma pneumonia bacterial bronchitis.
ATM case, severe

• 38 yo woman pharmacy technician with R UE ad RLE numbness, then L sided weakness over hours, with chest pressure and back pain, incontinence, then L sided involvement.
• MRI R>L, C5 to T2-3, initially without enhancement, subsequently enhancing. CSF initially negative.
• Rx with IV solumedrol, plasma exchange, mitoxantrone, without improvement.
Vaccines

• **Adverse Effects of Vaccines: Evidence and Causality**
• IOM, 2011, review epidemiologic evidence, mechanistic evidence, and provide opinions on causation
• Transverse Myelitis, evidence inadequate or insufficient to attribute causality
  – including MMR, Varicella, Hep A&B, DPT, Meningococcus, influenza
Acute Transverse Myelitis (ATM)

1. Idiopathic (Post-infectious, para-infectious)

2. **Acquired Demyelinating Disease**
   - Multiple sclerosis
   - Neuromyelitis Optica

1. Systemic Disease
Tract specific
Lateral corticospinal tract
MRI clues

• 1-2 vertebral levels: MS
• Partial, assymmetric, periphery (not central) WM tracts: MS
• >3 vertebral levels, LETM (Longitudinally Extensive Transverse Myelitis): NMO
Acute Transverse Myelitis (ATM)

1. Idiopathic (Post-infectious, para-infectious)
2. Acquired Demyelinating Disease (MS, NMO)
3. Systemic Disease
   - SLE
   - Sjogren’s
   - Sarcoid
   - Connective tissue diseases
TM associated with auto immune disease

• SLE, systemic lupus erythematosus
• Sjogren’s syndrome
• Sarcoidosis

• Mixed connective tissue disease
• Antiphospholipid antibody syndrome
• Behcets
• cryoglobulinemia
Further Work-up

• CSF: cells, protein, IgG
  – Pleocytosis indicates inflammation
  – Confirmatory, supplemental lab tests for systemic disease
    • ANA, SSA, SSB, ACE,

• MRI Brain or more spinal levels

• CBC, CMP
Treatment

• Specific disease

• For TM
  – Methylprednisolone (Solu-Medrol) 1 gram IV daily x 5d
  – No RCT, based on MS,
  – PLEX for not responders.
  – ↓ Edema, ↓ cytokine
  – Cyclophosphamide for SLE, Sjogrens

• Long term immunomodulatory or immunosuppressive Rx for demyelinating disease
Treatment

- DVT prophylaxis
- Analgesics
- Baclofen
- Rx neurogenic bladder and bowel
Pregnant Lawyer

- ER
- Hx Familial Mediterranean Fever
- Brain MRI
- SVD
- MRI T/LS cord
## Moderate Paraparesis

<table>
<thead>
<tr>
<th>Right</th>
<th>Left</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>5</td>
<td>C5 - Elbow flexors (biceps, brachialis)</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td>C6 - Wrist extensors (extensor carpi radialis longus and brevis)</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td>C7 - Elbow extensors (triceps)</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td>C8 - Finger flexors (flexor digitorum profundus) to the middle finger</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td>T1 - Small finger abductors (abductor digiti minimi)</td>
</tr>
<tr>
<td>4</td>
<td>3-</td>
<td>L2 - Hip flexors (iliopsoas)</td>
</tr>
<tr>
<td>4-</td>
<td>4</td>
<td>L3 - Knee extensors (quadriiceps)</td>
</tr>
<tr>
<td>3+</td>
<td>3</td>
<td>L4 - Ankle dorsiflexors (tibialis anterior)</td>
</tr>
<tr>
<td>3</td>
<td>3-</td>
<td>L5 - Long toe extensors (extensor hallucis longus)</td>
</tr>
<tr>
<td>4</td>
<td>4</td>
<td>SI - Ankle plantar-flexors (gastrocnemius, soleus)</td>
</tr>
</tbody>
</table>
# Sensory Examination

<table>
<thead>
<tr>
<th></th>
<th>Right</th>
<th>Left</th>
</tr>
</thead>
<tbody>
<tr>
<td>T6</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>T7</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>T8</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>T9</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>T10</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>T11</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>T12</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>L.1</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>L.2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>L.3</td>
<td>1→2</td>
<td>2</td>
</tr>
<tr>
<td>L.4</td>
<td>1→2</td>
<td>2</td>
</tr>
<tr>
<td>L.5</td>
<td>1→1</td>
<td>2</td>
</tr>
<tr>
<td>S1</td>
<td>1→2</td>
<td>2</td>
</tr>
<tr>
<td>S2</td>
<td>1→2</td>
<td>2</td>
</tr>
<tr>
<td>S3</td>
<td>1→1</td>
<td>1→1</td>
</tr>
<tr>
<td>S4-S5</td>
<td>0→1</td>
<td>0→1</td>
</tr>
</tbody>
</table>
Workup showed a normal or negative studies including the following

- MRA of the brain, MRV of the brain, MRI C-spine, CT angiogram in the abdomen and pelvis, Echo
- Negative HIV, RPR, lupus, anticoagulant screening, anticardiolipin antibodies, beta-2 glycoproteins, homocysteine, ANA, double-stranded DNA, SSA, SSB, C4 level. Protein S is normal.
- She has had a total cholesterol of 216, LDL of 103, C3 slightly elevated, anti thrombin III slightly elevated, Factor II activity slightly elevated and protein C minimally elevated. Pending tests include ANCA, rheumatoid factor, Factor V Leiden, hepatitis C.
- CSF protein was also normal.
- Pending FMF genetic study. (MEFV gene)
Treatment

- Prednisone and ASA
- heparin for DVT prophylaxis
- colchicine.
- She is also on iron, prenatal vitamins and vitamin C.
Infarction of cord

- Venous hypertension, localized leading to venous infarction, reduced perfusion
- Arterial
  - Thoracic cord
  - Aortic manipulation
  - Hypotension
  - Artery of Adamkiewicz
  - AVMs, AV Fistulas
Differential Diagnosis Mimics

- venous or arterial infarction
- GBS
Differential diagnosis: Mimics GBS

• Guillain-Barré Syndrome or acute demyelinating inflammatory polyradiculoneuropathy (AIDP)

• Transverse myelitis must be differentiated acutely from the most common paralytic acquired illness in the United States:
Differential Diagnosis Mimics

- venous or arterial infarction
- GBS
- Infectious myelitis
  - Treponema pallidum
  - HIV vacuolar myelopathy
  - Polio, West Nile virus
  - VZV, HSV, CMV
- bacterial
Differential Diagnosis Mimics

- venous or arterial infarction
- GBS
- Infectious
- Hypokalemia
- B12, nitrous oxide,
- Copper deficiency (Zinc)
- Neoplasia
- hereditary
Other Myelopathies, usually subacute to chronic

• Neoplasia
  – ependymoma, astrocytoma, hemangioblastoma
  – Paraneoplastic, SP Radiation

• Hereditary
  – Spastin gene (HSP), Frataxin gene (Friederichs ataxia)
Gliosarcoma brain and spine
Other Myelopathies, usually subacute to chronic

• Neoplasia
  – ependymoma, astrocytoma, hemangioblastoma
  – Paraneoplastic, SP Radiation

• Hereditary
  – Spastin gene (HSP), Frataxin gene (Friederichs ataxia)
### Diagnostic Criteria for Transverse Myelitis

**Table 1. Diagnostic Criteria for Transverse Myelitis.***

- Bilateral (not necessarily symmetric) sensorimotor and autonomic spinal cord dysfunction
- Clearly defined sensory level
- Progression to nadir of clinical deficits between 4 hours and 21 days after symptom onset
- Demonstration of spinal cord inflammation: cerebrospinal fluid pleocytosis or elevated IgG index, † or MRI revealing a gadolinium-enhancing cord lesion
- Exclusion of compressive, postradiation, neoplastic, and vascular causes

*Clinical events that are consistent with transverse myelitis but that are not associated with cerebrospinal fluid abnormalities or abnormalities detected on MRI and that have no identifiable underlying cause are categorized as possible idiopathic transverse myelitis.

† The IgG index is a measure of intrathecal synthesis of immunoglobulin and is calculated with the use of the following formula: (CSF IgG ÷ serum IgG) ÷ (CSF albumin ÷ serum albumin), where CSF denotes cerebrospinal fluid.

Abnormal MRI of cord

• Axial anatomy: complete/central or partial with specific tract involvement
• Sagittal longitudinal anatomy: 1 vertebral segment, 3 or more vertebral segments
• Gadolinium enhancement? Inflammation
• Normal Cord? Confirm suspected level, consider early involvement, consider alternatives: GBS
Transverse Myelitis

• Inflammatory
  – MS, NMO
  – Systemic
  – Post or para-infectious
  – Idiopathic
  – infection

• Non inflammatory
  – infarction
  – Radiation myelitis
Summary

• Acute myelopathy: recognize it
• MRI a key study
• Acute transverse myelitis: many causes, Big 3: primary demyelinating, systemic, idiopathic/post-infectious.
• Rx steroids:
Questions and Comments

• Contact information:
  • David N. Alexander, M.D.,
  • Director of Neurological Rehabilitation and Research Unit,
  • Professor, UCLA Dept of Neurology
  • alexdn@ucla.edu