TRANSVERSE MYELITIS: A CLINICAL OVERVIEW

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DISCLOSURES

- I have no industry relationships to disclose.
- I will not discuss off-label use.
OBJECTIVES: TRANSVERSE MYELITIS

- Review the pathophysiology
- Identify approaches and challenges of diagnosis
- Discuss the treatment options
- Discuss the role of rehabilitation
WHAT IS TRANSVERSE MYELITIS?

- neurological disorder caused by inflammation across both sides of one level, or segment, of the spinal cord.

- *myelitis* = inflammation of the spinal cord

- *transverse* simply describes the position of the inflammation, that is, across the width of the spinal cord.

- Attacks of inflammation can damage or destroy myelin, the fatty insulating substance that covers nerve cell fibers.

- This damage causes nervous system scars that interrupt communications between the nerves in the spinal cord and the rest of the body.
### Terminology

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
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<tbody>
<tr>
<td>Myelopathy</td>
<td>CNS dysfunction due to anything</td>
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<tr>
<td>Transverse Myelopathy</td>
<td>Clinical finding suggesting problem at spinal cord level</td>
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<tr>
<td>Transverse Myelitis</td>
<td>When transverse myelopathy is due to ‘itis’</td>
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“Acute Myelitis” cases recognized far back as 1882. However, the term Transverse Myelitis (TM) was first coined in 1948 by Dr Suchett-Kaye, an English neurologist. He uses this to describe a case of rapidly progressive paraparesis with a thoracic sensory level, occurring as a postinfectious complication of pneumonia.

TM is a rare with an incidence of between 1 and 8 new cases per million people per year.
TM occurs in adults and children, in both genders, and in all races.

No familial predisposition is apparent.

A peak in incidence rates (the number of new cases per year) appears to occur between 10 and 19 years and 30 and 39 years.

Although only a few studies have examined incidence rates, it is estimated that about 1,400 new cases of transverse myelitis are diagnosed each year in the United States, and approximately 33,000 Americans have some type of disability resulting from the disorder.
Researches still uncertain of exact causes.

Process of inflammation that causes extensive damage to nerve fibers of spinal cord

cord may result from viral infections or abnormal immune reactions.

Transverse myelitis also may occur as a complication of syphilis, measles, Lyme disease, and some vaccinations, including those for chickenpox and rabies. Cases in which a cause cannot be identified are called idiopathic.

Post infectious (30-60%)– varicella zoster, herpes simplex, CMV, EBV, influenza, HIV, hepatitis, rubella, bacterial pneumonia, etc.
Autoimmune based: the immune system, which normally protects the body from foreign organisms, mistakenly attacks the body’s own tissue, causing inflammation and, in some cases, damage to myelin within the spinal cord.

Associated with other autoimmune disease SLE, sarcoid, or Sjogren’s

In some people, transverse myelitis may represent the first symptom of an underlying demyelinating disease of the central nervous system such as multiple sclerosis (MS) or neuromyelitis optica (NMO).
## PATHOGENESIS

<table>
<thead>
<tr>
<th>Disease</th>
<th>Examples</th>
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<tbody>
<tr>
<td>Bacterial Infections</td>
<td>Mycoplasma pneumoniae, Lyme borreliosis, syphilis (tabes dorsalis), tuberculosis</td>
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<tr>
<td>Viral Infections</td>
<td>herpes simplex, herpes zoster, cytomegalovirus, Epstein-Barr virus, enteroviruses (poliomyelitis, Coxsackie virus, echovirus), human T-cell, leukemia virus, human immunodeficiency virus, influenza, rabies</td>
</tr>
<tr>
<td>Post-Vaccination</td>
<td>Rabies, cowpox</td>
</tr>
<tr>
<td>Autoimmune diseases</td>
<td>SLE, Sjogren’s syndrome, sarcoidosis</td>
</tr>
<tr>
<td>Multiple Sclerosis</td>
<td></td>
</tr>
<tr>
<td>Paraneoplastic syndromes</td>
<td></td>
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<tr>
<td>Vascular</td>
<td>Thrombosis of spinal arteries, vasculitis secondary to heroin abuse, spinal AVM</td>
</tr>
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</table>
CLINICAL PRESENTATION

- Loss in spinal cord function over several hours to several weeks
- Sudden onset neck or back pain, weakness, sensory abnormalities
- Progress to paralysis, urinary retention, loss of bowel control
The segment of the spinal cord at which the damage occurs determines which parts of the body are affected. Damage at one segment will affect function at that segment and segments below it.

Nerves in the cervical (neck) region control signals to the neck, arms, hands, and muscles of breathing (the diaphragm).

Nerves in the thoracic (upper back) region relay signals to the torso and some parts of the arms.

Nerves at the lumbar (mid-back) level control signals to the hips and legs.

Finally, sacral nerves, located within the lowest segment of the spinal cord, relay signals to the groin, toes, and some parts of the legs.

Thoracic spinal cord most typically involved in adults, cervical spinal cord in children
CLINICAL PRESENTATION

- 50% will lose all movement in legs
- Nearly all have some degree of bladder dysfunction
- 80-94% have numbness, paresthesias, or band-like dysesthesias
- Autonomic symptoms may include: urgency, incontinence, difficulty or inability to void, incomplete evacuation of bowel and/or bladder, sexual dysfunction
- 80% of patients reach clinical nadir within 10 days of symptom onset
Some patients recover from transverse myelitis with minor or no residual problems.

Others suffer permanent impairments that affect their ability to perform ordinary tasks of daily living.

Most patients will have only one episode of transverse myelitis.

A small percentage (10-20%) may have a recurrence.
Differential Diagnosis

- Compression of spinal cord caused by trauma such as vertebral fractures
- Epidural or subdural hematoma,
- Epidural and/or paraspinal abscess complicating disc space infection
- Disc herniation,
- Intra- and extramedullary tumor,
- **Multiple Sclerosis (MS)**
- Infection
- Guillain-Barre syndrome
- Neuromyelitis optica
- Acute Disseminated Encephalomyelitis
TRANSVERSE MYELITIS VS MULTIPLE SCLEROSIS

- TM can be the presenting feature of MS
- Patients ultimately diagnosed with MS are more likely to have:
  - asymmetric clinical findings
  - predominant sensory symptoms with relative motor sparing
  - MRI findings extending over fewer than two spinal segments
  - cortical involvement abnormal brain MRI
  - oligoclonal bands
IMAGING

STIR  T2WI  T1+Gd
**DIAGNOSTIC CRITERIA**

**Inclusion criteria**

1. Development of sensory, motor or autonomic dysfunction attributable to the spinal cord.
2. Bilateral signs or symptoms (although not necessarily symmetric).
3. Clearly-defined sensory level.
4. Exclusion of extra-axial compressive etiology by neuroimaging (MRI or myelography; CT of spine not adequate).
5. Inflammation within the spinal cord demonstrated by CSF pleocytosis or elevated IgG index or gadolinium enhancement. If none of the inflammatory criteria is met at symptom onset, repeat MRI and LP evaluation between 2 and 7 days after symptom onset meets criteria.
6. Progression to nadir between 4 h and 21 days after the onset of symptoms (if patient awakens with symptoms, symptoms must become more pronounced from point of awakening).

**Exclusion criteria**

1. History of previous radiation to the spine within the past 10 years.
2. Clear arterial distribution clinical deficit consistent with thrombosis of the anterior spinal artery.
3. Abnormal flow voids on the surface of the spinal cord consistent with AVM.
4. Serological or clinical evidence of connective tissue disease (sarcoidosis, Behcet’s disease, Sjogren’s syndrome, SLE, mixed connective tissue disorder, etc.)
5. CNS manifestations of syphilis, Lyme disease, HIV, HTLV-1, mycoplasma, other viral infection (e.g. HSV-1, HSV-2, VZV, EBV, CMV, HHV-6, enteroviruses).
   (a) Brain MRI abnormalities suggestive of MS
   (b) History of clinically apparent optic neuritis

AVM, Arteriovenous malformation; CMV, cytomegalovirus; CNS, central nervous system; CSF, cerebrospinal fluid; CT, computed tomography; EBV, Epstein–Barr virus; HHV, human herpesvirus; HSV, herpes simplex virus; HTLV, human T cell leukemia virus; LP, lumbar puncture; MRI, magnetic resonance imaging; MS, multiple sclerosis; SLE, systemic lupus erythematosus. *Do not exclude disease-associated acute transverse myelitis.*
DIAGNOSIS

Presentation: Neurologic dysfunction consistent with a spinal cord injury at a specific level

- History and physical examination
  - Confirm acute myelopathy
  - Elicit time course and extent of deficits
  - Determine signs, symptoms or prior history suggesting infection, systemic inflammatory disease, vascular/ischemia, neoplasm, multiple sclerosis, radiation exposure, neuromyelitis optica, or trauma
  - Determine if recent history of vaccination or systemic illness

First priority: Rule out compressive etiology

- Gadolinium enhanced MRI of the spinal cord within 4 hours

Sufficient to cause compression myelopathy?

Yes

- Structural abnormality (spondylolisthesis) or spinal mass

- Yes

  - Urgent surgical evaluation
  - Consider intravenous methylprednisolone

- No

  - Second priority: Define presence/absence of spinal cord inflammation

    - Lumbar puncture

Consider non-inflammatory causes of myelopathy

- Ischemia-arterial, venous, watershed or arteriovenous malformation
- Radiation
- Epidural lipomatosis
- Fibrocartilaginous embolism
Consider early inflammatory myelopathy, false negative CSF (repeat LP in 2-7 days)

- No

CSF pleocytosis or gadolinium enhancement or elevated IgG index

- Yes

  - Third priority: Define extent of demyelination

    - Check brain MRI with gadolinium and visual evoked potential

- No

Brain/Brain and optic tract

- Site of demyelination

  - Yes

    - Demyelination?

      - Yes

        - Optic nerve/tract: Acute transverse myelitis (ATM): idiopathic or disease-associated (use standard criteria to distinguish and initiate appropriate treatment)

      - No

  - No

Possible diagnosis

- Multiple sclerosis
- ADEM
- Disease-associated ATM

Possible neuromyelitis optica (Devic's disease)
TREATMENT

- Treatments are designed to reduce spinal cord inflammation and manage and alleviate symptoms.
- Mainstays include:
  - corticosteroids: no randomized trials
  - plasmapheresis: moderate to severe cases, or those who do not respond to steroids after 3-5 days
  - Pulse dose IV cyclophosphamide
  - CSF filtration therapy: spinal fluid is filtered for inflammatory factors (not available in US)
- For severe, refractory cases: 2 year course of azothioprine, methotrexate, mycophenolate, or oral cyclophosphamide
PROGNOSIS

- Most will have monophasic disease
- Up to 20% will have recurrent inflammatory episodes within the spinal cord
- Significant recovery is unlikely if no improvement by 3 months
GOALS OF REHABILITATION

- Maximizing physical independence, capabilities, and potential
- Interdisciplinary team model approach used
- Includes physician, therapists, nurses, psychologists, case managers, respiratory therapists, speech, and orthotists, family members
GOALS OF REHABILITATION

PHYSICAL THERAPY
- Stretching program – prevent contractures
- Strengthening
- Transfers
- Gait training
- Wheelchair training
- Durable medical equipment

OCCUPATIONAL THERAPY
- Grooming
- Eating
- Dressing
- Bathing
- Toileting
- Adaptive equipment
GOALS OF REHABILITATION

- Prevention pressure ulcers
- Bladder management
- Bowel management
- Spasticity
- Pain control
- Autonomic dysreflexia
- Orthostatic hypotension