UT Southwestern
O'Donnell Brain Institute

Moving Beyond 'Transverse Myelitis': Inflammatory Myelopathies and their mimics

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Learning Goals and Objectives

- Review new proposed nomenclature for inflammatory myelopathies.
- Review important causes of disease-associated myelitis and their MRI features.
- Review mimics of myelitis and identify red flags for mimics.

A critical look at the term ‘Transverse Myelitis’

Transverse myelitis is not a well-defined medical term.

Two meanings:
- Inflammatory myelopathy syndrome (similar to optic neuritis or myositis).
- Shorthand for ‘idiopathic transverse myelitis’.

- Semantically incorrect: myelitis involves all anatomic dimensions, rarely across the entire transverse plane.

- Potential for premature closure: assumption that diagnosis is idiopathic early in the diagnostic process.



Zalewski et al. Neurology 2018.

Murphy et al. Journal Neurol Sci 2022.

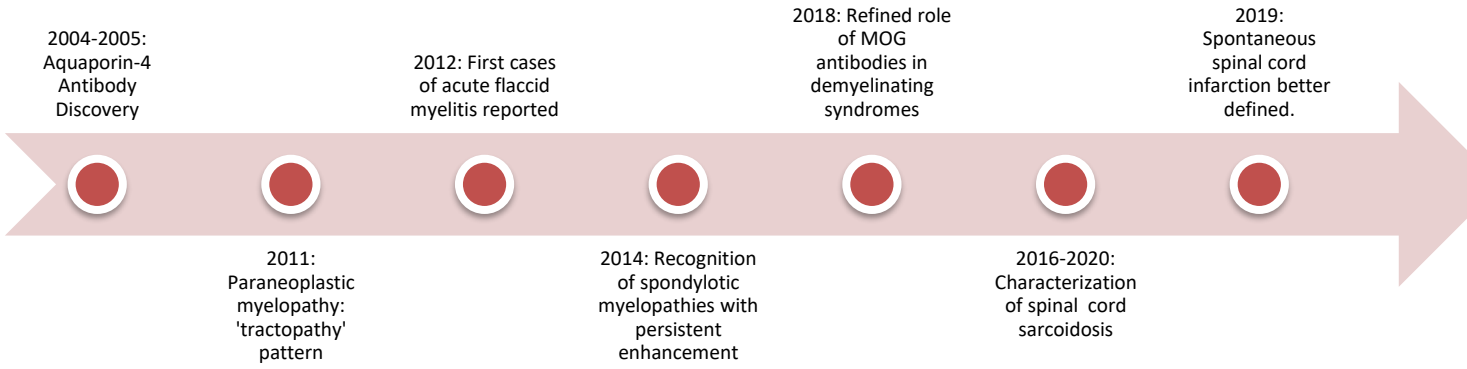
The most recent acute transverse myelitis criteria were published in 2002

Several problems with current standing criteria:

- Many important, newly recognized causes not discussed.
- Current criteria exclude important causes (e.g., AFM).
- Mimics of myelitis are better characterized.

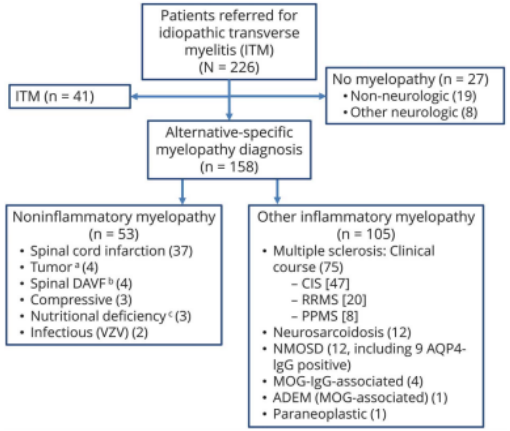
Table 1 *Criteria for idiopathic acute transverse myelitis*

Inclusion criteria	Exclusion criteria
Development of sensory, motor, or autonomic dysfunction attributable to the spinal cord	History of previous radiation to the spine within the last 10 y
Bilateral signs and/or symptoms (though not necessarily symmetric)	Clear arterial distribution clinical deficit consistent with thrombosis of the anterior spinal artery
Clearly defined sensory level	Abnormal flow voids on the surface of the spinal cord c/w AVM
Exclusion of extra-axial compressive etiology by neuroimaging (MRI or myelography; CT of spine not adequate)	Serologic or clinical evidence of connective tissue disease (sarcoidosis, Behçet's disease, Sjögren's syndrome, SLE, mixed connective tissue disorder, etc.)*
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 lumbar puncture evaluation between 2 and 7 d following symptom onset meet criteria	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)*
Progression to nadir between 4 h and 21 d following the onset of symptoms (if patient awakens with symptoms, symptoms must become more pronounced from point of awakening)	Brain MRI abnormalities suggestive of MS*
	History of clinically apparent optic neuritis*

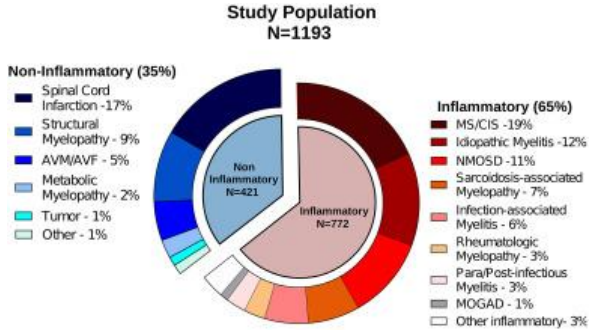


Transverse Myelitis Consortium Working Group. Neurology 2002.

The result of outdated criteria: many people with 'transverse myelitis' are misdiagnosed

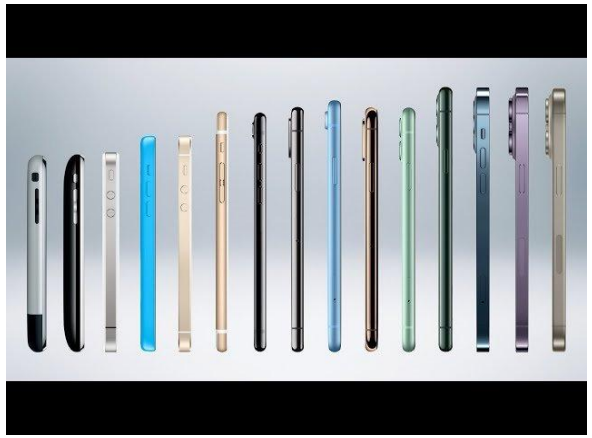


Zalewski et al. Neurology 2018.



Murphy et al. Journal Neurol Sci 2022.





Retiring ‘transverse myelitis’

Current revision to the 2002 diagnostic criteria is ongoing.

One highly agreed upon change: replace transverse myelitis with ‘myelitis’.

Rationale:

- A fresh start: encourage updated review of the myriad of myelopathy/myelitis causes.
- Find the appropriate adjective: avoid premature closure of diagnosis, encourage deeper work-up.
- Improve provider-patient communication: Discussion about ongoing work-up to avoid confusion.

Transverse Myelitis

How do we define ‘myelitis’ and identify the correct cause

It all starts with identifying a myelopathy.

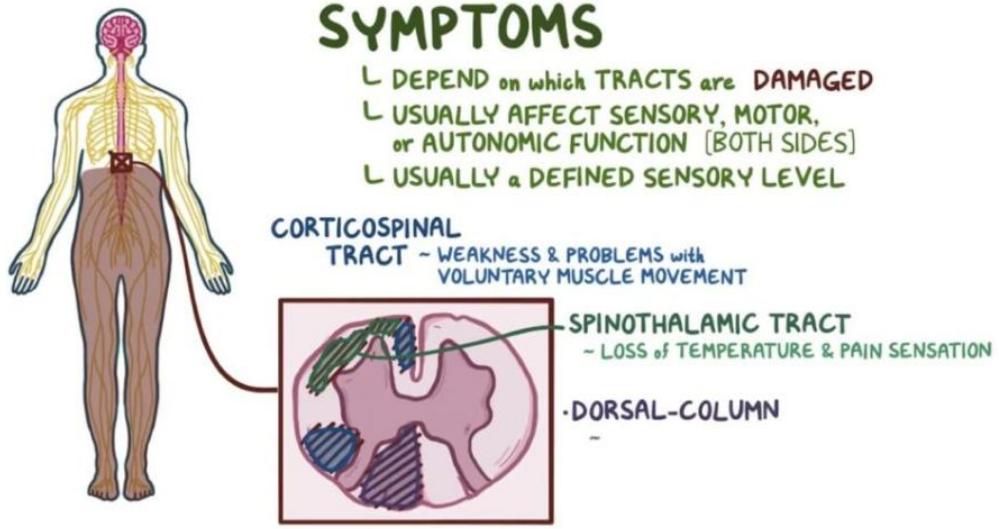
Domains of myelopathy signs and symptoms:

- Motor dysfunction: Weakness in one or more limbs, tonic spasms
- Sensory dysfunction: sensory level, Lhermitte’s sign, or sensory deficits referable to the spinothalamic tracts or dorsal columns
- Autonomic dysfunction: acute urinary, bowel or sexual dysfunction

Other exam findings: gait impairment, reflex changes.

Myelopathies often have features from multiple domains, but NOT always (e.g., acute flaccid myelitis).

Features may rarely be strictly unilateral (2002 criteria required bilateral features).

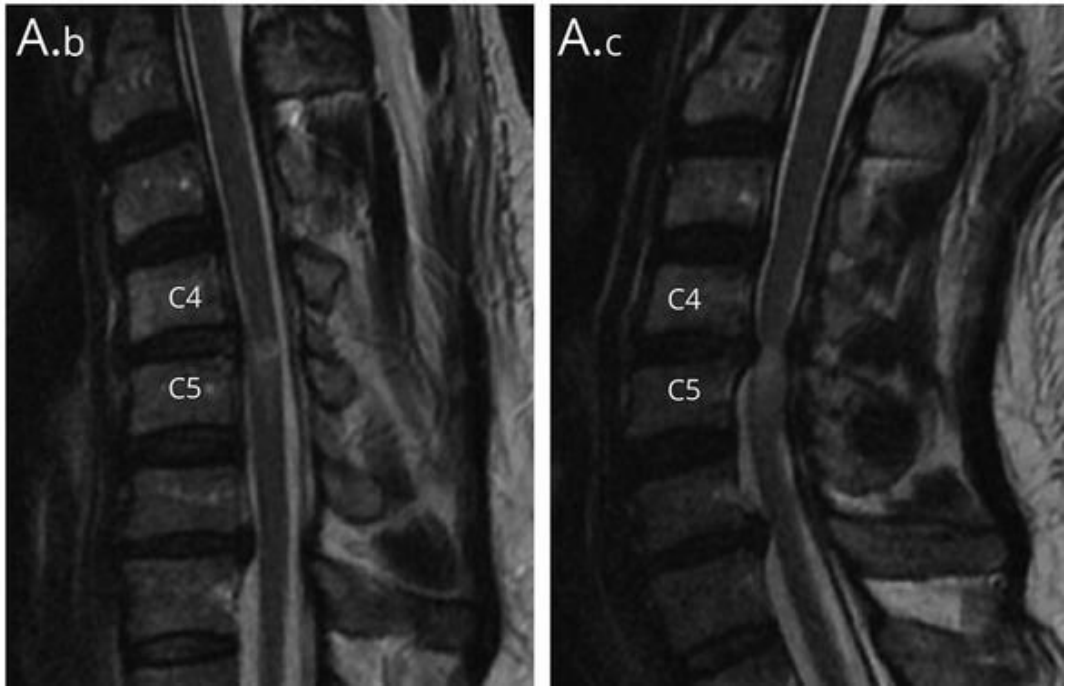


Once a myelopathy is recognized, imaging is critical to diagnosis.

Recommended that an MRI of the spinal cord is obtained as soon as possible.

Rationale:

- Rule out compressive myelopathy: common cause that requires surgical evaluation.
- If compressive is suspected but not obvious, flexion-extension imaging can be helpful.



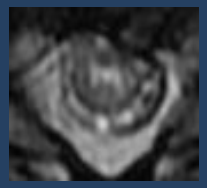
Substantial information can be gained from imaging review

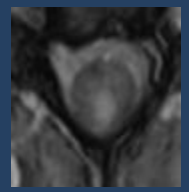
Craniocaudal Extension

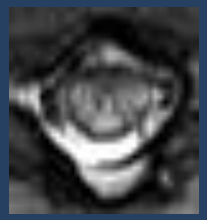


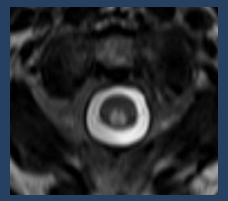
Longitudinally extensive vs. short lesion

Involvement in axial plane



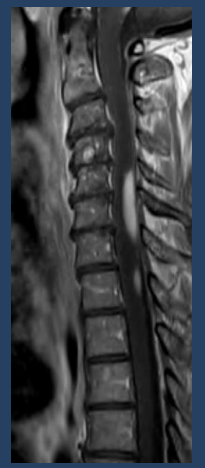






Central vs. peripheral
Specific Tracts involved?

Contrast enhancement:
Presence + Pattern

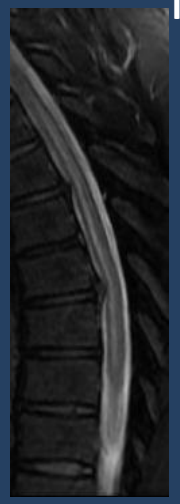


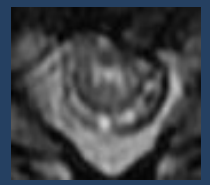


Patchy or homogenous?
Ring?
Duration of enhancement?

Common MRI patterns and their differential

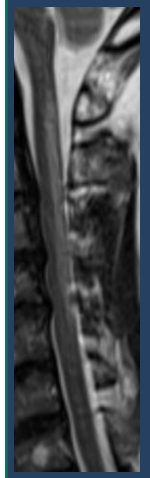
Prominent Gray matter involvement

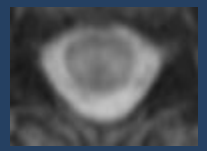


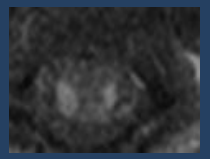


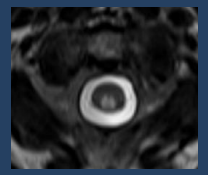
- Spinal cord infarction
- MOG Antibody Disease
- Acute Flaccid Myelitis (Enterovirus)
  Flaviruses (WNV)

‘ Tractopathy’ pattern





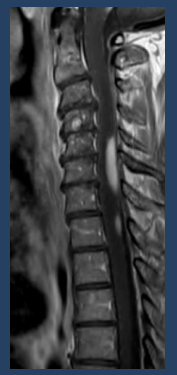




- Metabolic Myelopathies (Nutritional)
- Paraneoplastic
- Genetic/Mitochondrial Myeloapathies

Chronic Enhancement







- Spondylosis
- Sarcoidosis
- Malignancies
- Dural AV Fistula

Next review history and exam in detail

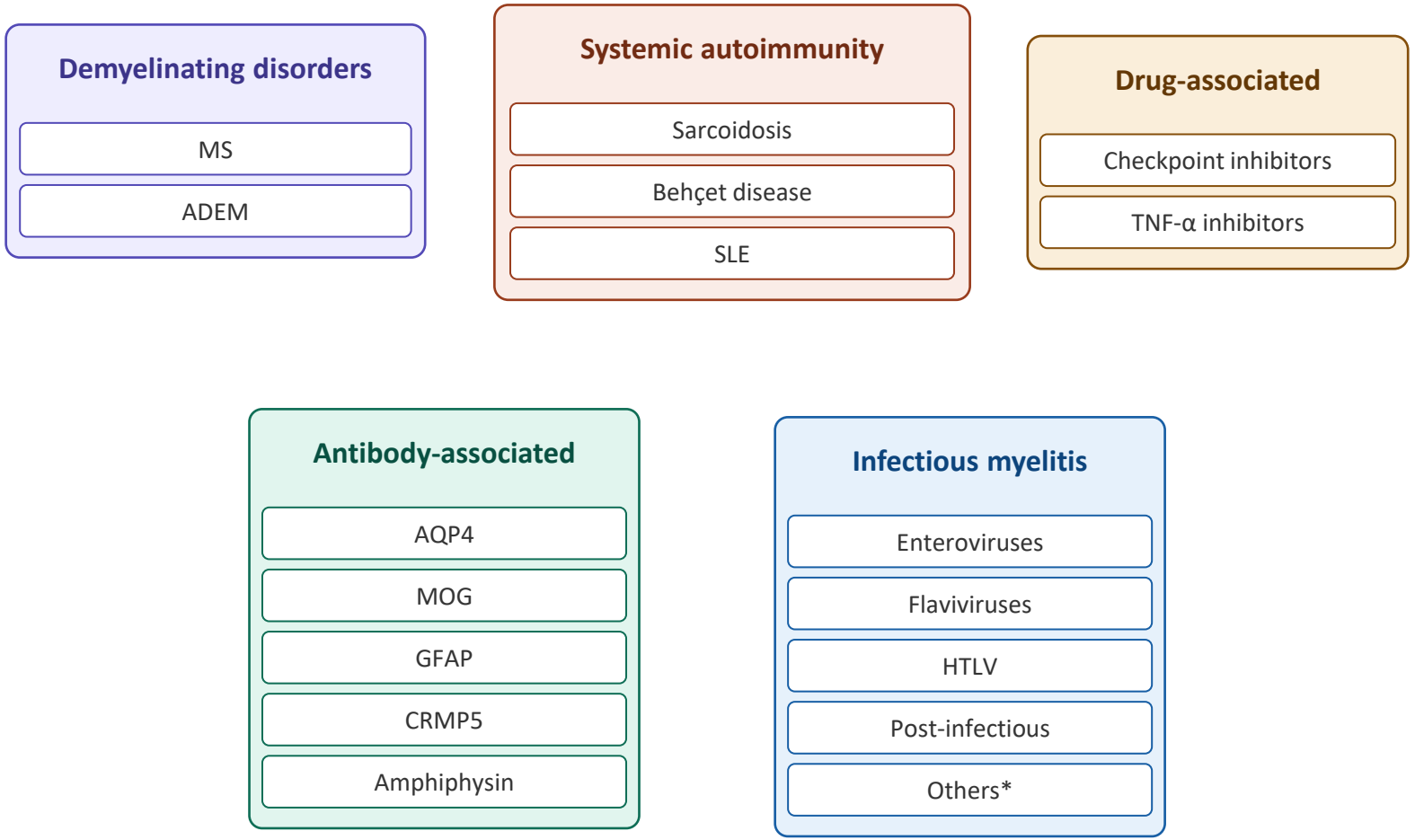
Other important details:

- Domains involved.
- Severity of deficits.
- Relapsing vs. progressive course.
- Presence of sensory level.

Time-to-nadir is one of the most important details in classifying myelopathies.

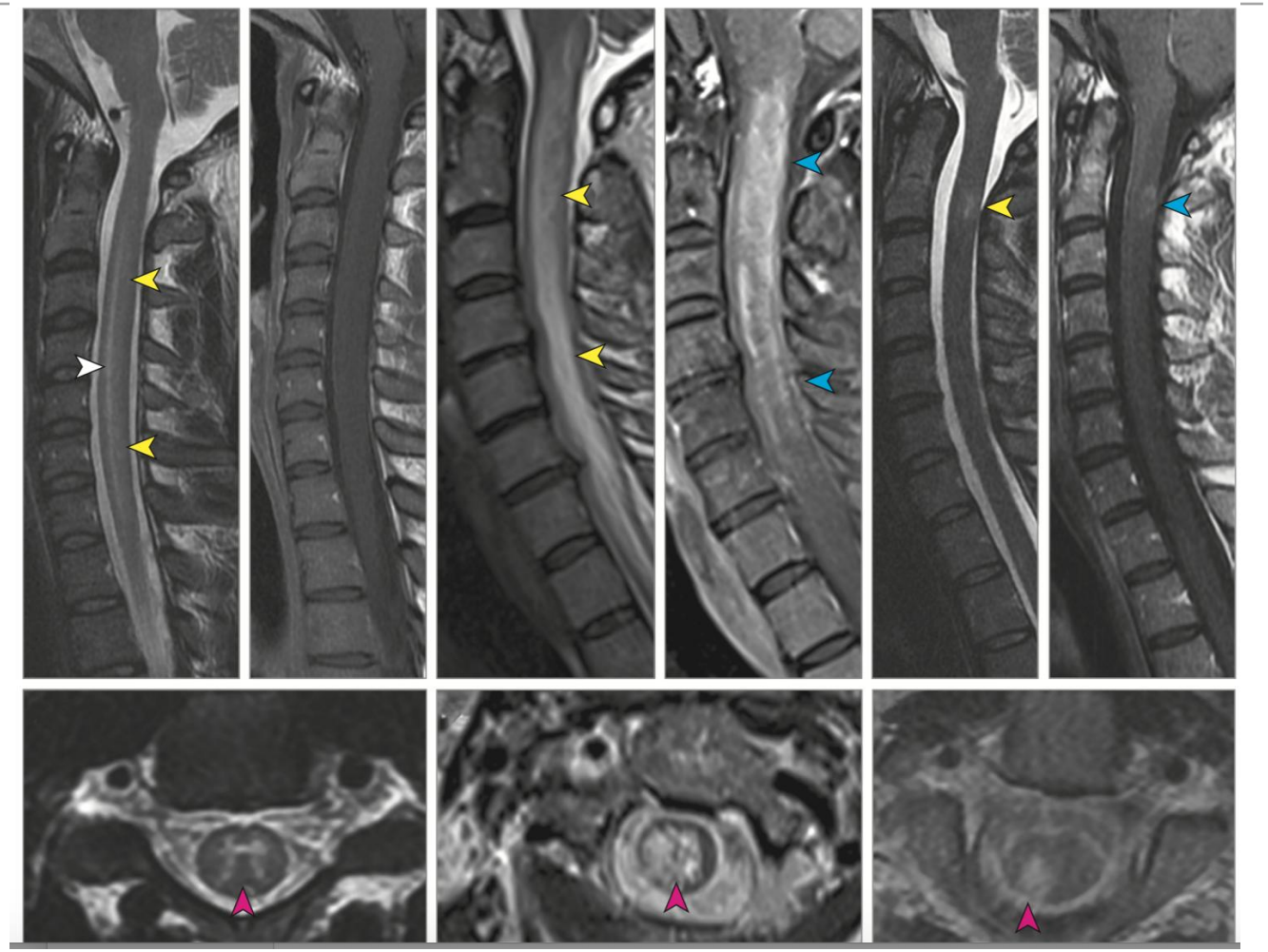
Hyperacute (0-12 hrs)	Acute-Subacute (12 hrs -90 days)	Chronic (90 or more days)
Spinal cord infarction Functional neurological disorder Rare myelitis presentation	Typical myelitis	Spondylotic myelopathy AV fistula/malformation Spinal Cord Malignancy Metabolic Myelopathy Genetic Myelopathy Rare Myelitis Presentation[+]
Compression		

Myelitis should be considered in patients with abnormal imaging and acute-subacute timeline



MOG Antibody Disease

- Frequently involves lower thoracic, conus medullaris.
- Imaging features
  - Gray matter involvement common.
  - Often longitudinally extensive (can skip)
  - Contrast enhancement rare.
  - Can initially have normal imaging (~10%, often abnormal on short repeat).
- Lower percentage with motor disability at follow-up, bowel/bladder/sexual dysfunction common.

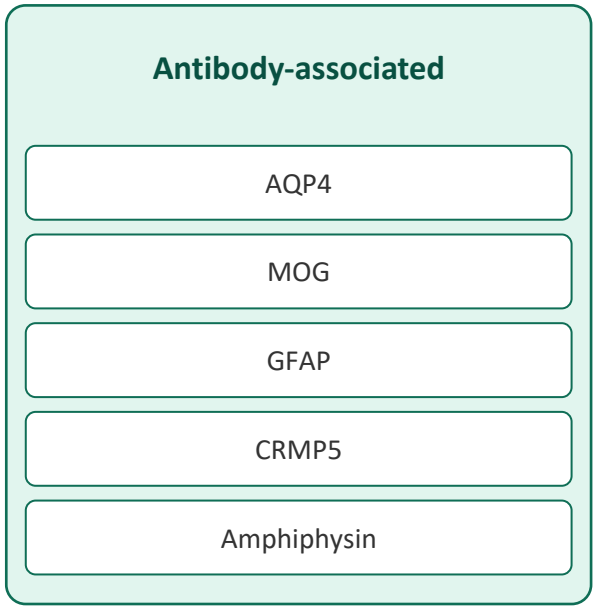


Antibody-Associated Myelitis

- There are antibodies associated with myelitis beyond aquaporin-4 and MOG.
- Commercial labs now offer a ‘myelopathy panel’ containing relevant antibodies.

Consider testing broadly when:

- Longitudinally extensive lesion, unexplained.
- Tract involvement
- History of cancer

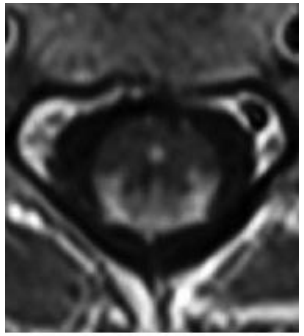


Neurosarcoidosis

- Often subacute myelopathy.
- Imaging features:
  - –Often longitudinally extensive
  - –Vivid, meningeal/subpial enhancement.
  - –'Trident' sign
  - –Enhancement often present for months.
- A biopsy should be pursued when possible to confirm sarcoidosis.



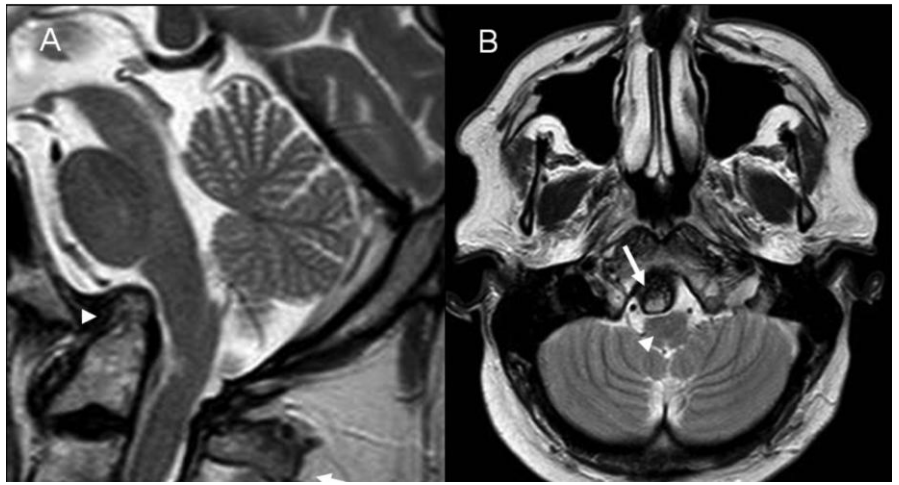


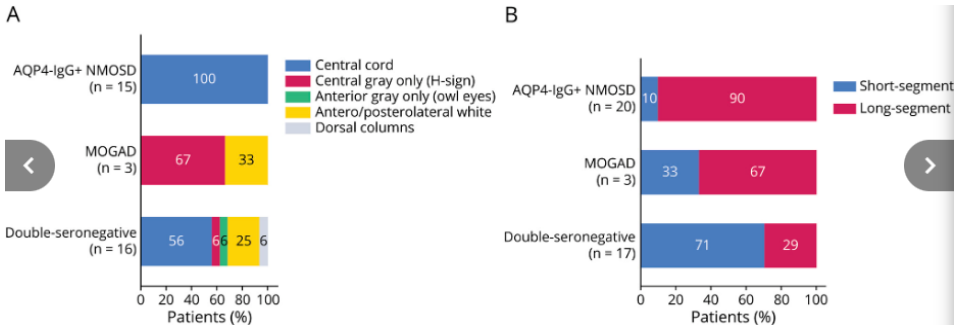


Myelitis Associated with systemic autoimmunity

Literature still suggests inflammatory myelopathy may occur in patients with rheumatologic disorders without evidence of a well-characterized neurologic inflammatory disorder.

Important to exclude disease-associated myelitis (e.g., AQP4+ autoimmunity common overlap with SLE/Sjogren's) and consider mimics (e.g., atlantoaxial dislocation in RA).





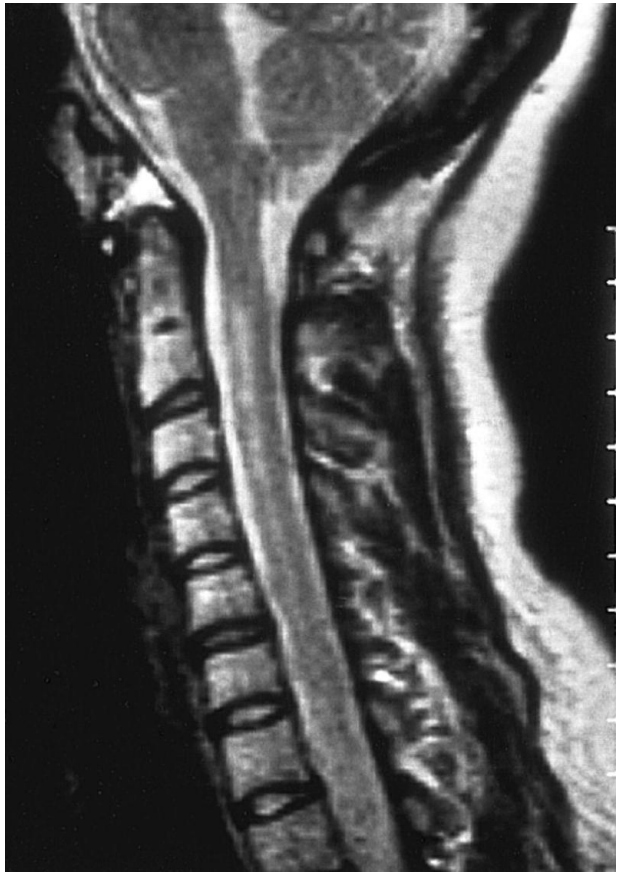
Renna et al. Journal Rheumatology. 2013
Krett et al. Neurology Neuroimm Neuroinflamm. 2024.

Mimics of myelitis are common (one-third of cases diagnosed as ‘transverse myelitis’)

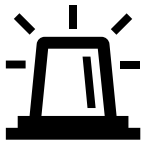
Feature	Possible etiologies	Inflammatory etiologies
Time-to-nadir of severe deficits less than 12 hours from onset	Spinal cord infarction, spinal cord hemorrhage, acute compressive myelopathy, functional neurologic disorder	AFM, AQP4+ NMOSD
Chronic course (Time-to-nadir greater than 90 days)	Spondylotic myelopathy, metabolic myelopathies(e.g. vitamin B12 deficiency), arteriovenous malformations, malignancy, genetic disorders, stiff person spectrum disorder, neurodegenerative disorders (e.g., ALS)	Sarcoidosis, paraneoplastic
‘Step-wise’ progression: chronic progressive course with discrete episodes of subacute worsening or claudication	Arteriovenous malformations (Dural arteriovenous fistula)	
Persistent enhancing lesions > 3 months from initial spinal cord MRI	Dural arteriovenous fistula, arteriovenous malformations, spinal cord tumors, post compressive myelopathy	Sarcoidosis, paraneoplastic
Normal imaging of spinal cord or isolated nerve root enhancement	Guillain Barre syndrome, cauda equina syndrome,	AFM, MOGAD, tropical spastic paraparesis, stiff person syndrome

Spontaneous Spinal cord Infarction

- Epidemiologic studies challenging, estimated to represent 5-8% of myelopathies.
- Mechanisms:
  - Procedure related (aneurysm repair) (up to 33% can experience ischemia)—either intraoperatively, or delayed (up to 48 hours later)
  - Embolic (fibrocartilagnous, cardioembolic)
  - Aortic/Subclavian/Vertebral Dissection
  - Vasculitis (infectious or inflammatory)



Spinal cord Infarction Symptoms



Neck of back pain (localizing to level of infarct) common (~33%)



Asymmetric or unilateral involvement common



Lower thoracic region commonly affected



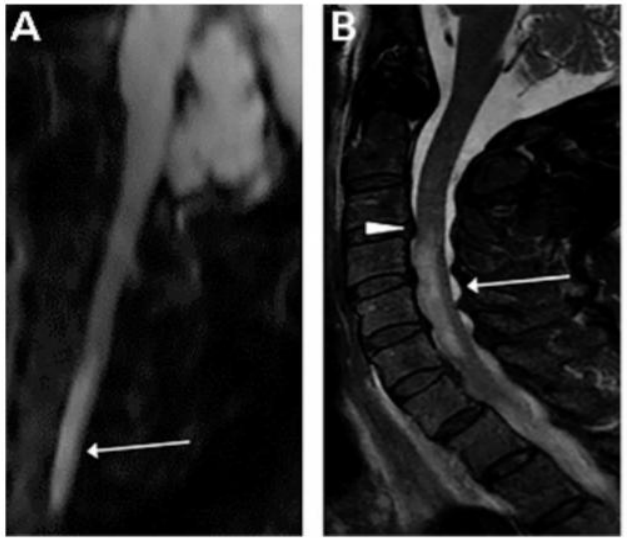
Anterior spinal artery regions most commonly recognized



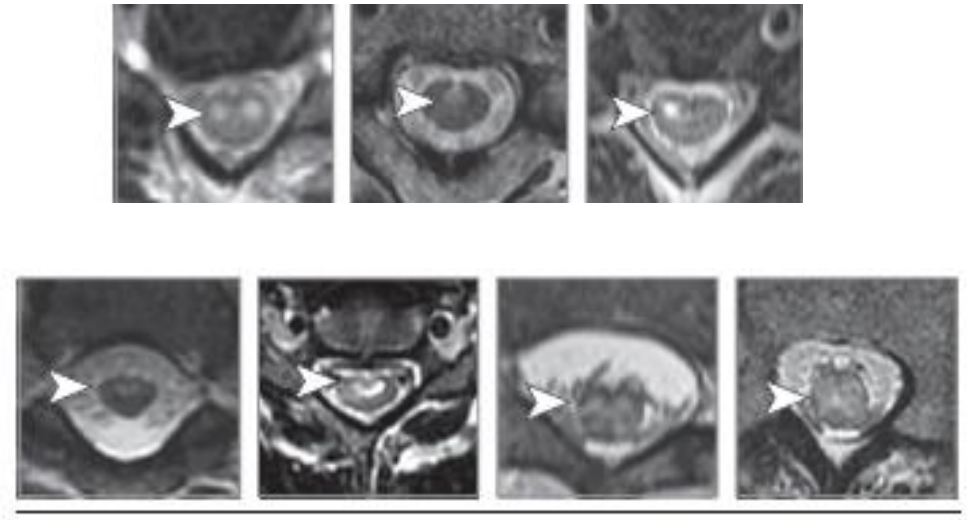
Time-to-nadir is often < 12 hrs.
Stuttering symptoms common

Spinal Cord Infarction, Imaging

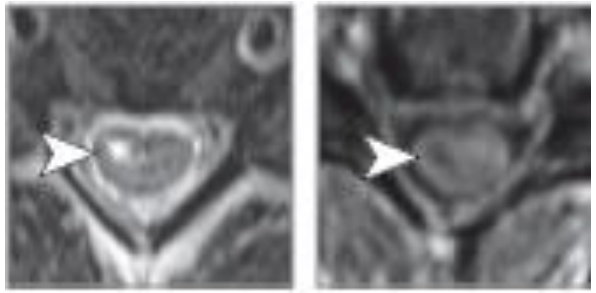
- Think of cerebral stokes.
- First changes on DWI (though this modality can be insensitive due to artifact, small infarcts)→ then T2 change (hours-->days)→ enhancement.
- Axial images will typically show gray matter involvement/anterior cord involvement.







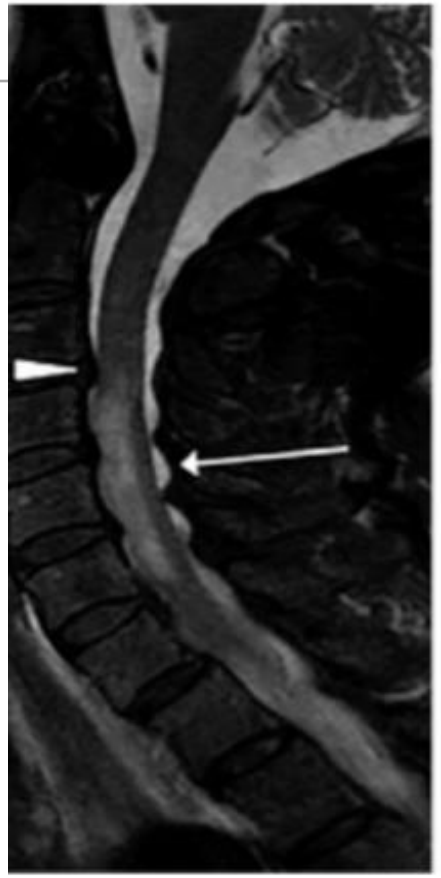
Spinal Cord Infarction, Other Imaging Features



Myelomalacia



Bone infarction



Disc herniation at site of infarction

(supportive of FCE)

Dural AV Fistulas

- Direct connection between radiculomedullary artery and vein→ venous engorgement→ venous hypertension and infarction.

- Frequently present with a chronic progressive myelopathy, frequently misdiagnosed with inflammatory.



Dural AV Fistula Clinical Features

- Often occur in males in 7th decade or later in life.
- Typically start at conus medullaris and spread rostrally.
  - Early bowel/bladder involvement, then gradually worsening sensorimotor symptoms.
  - Mixed UMN/LMN symptoms, often asymmetric.
- Often has features of claudication:
  - Worsening of symptoms with activity, Valvasava that improves with rest.
- Symptoms may worsen (at least temporarily) with IV steroid administration



Now

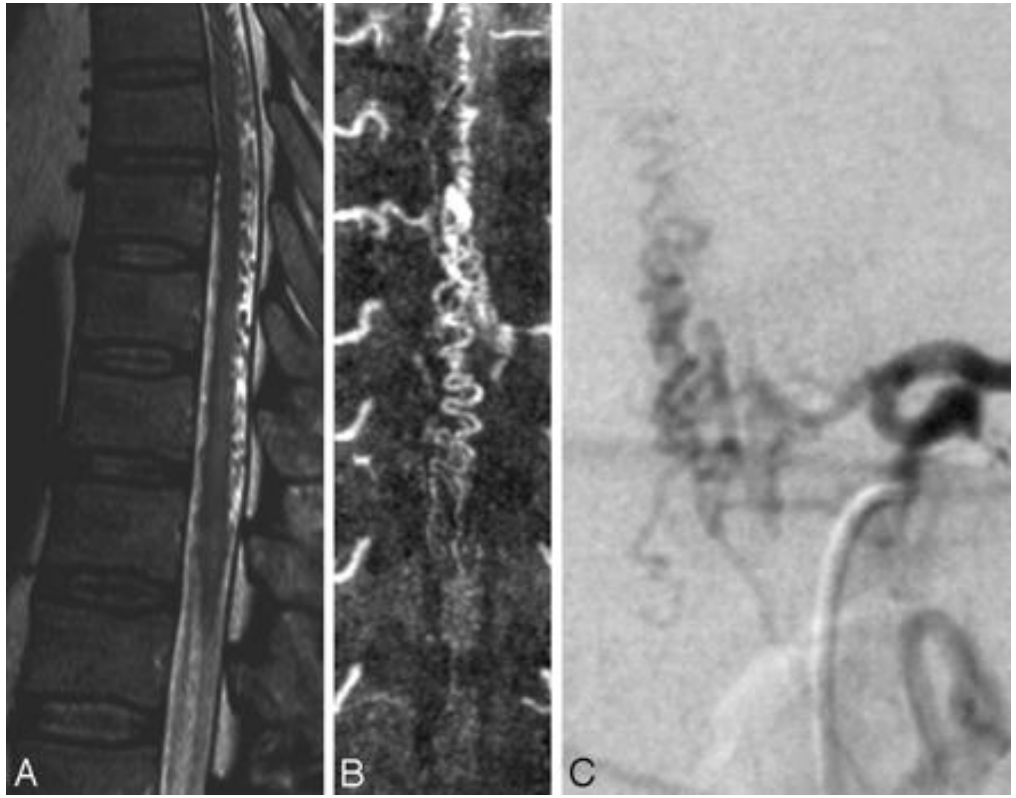
Imaging Features

- At the time of detection, frequently a longitudinally extensive lesion.
- Frequently with central/holocord involvement on axial slides.
- May lack contrast enhancement or have patchy enhancement that is chronically present.
  - 'Missing piece' sign: may be present
- Flow voids: T2 hypotensities around cord, may be present



Management of dAVF

- dural AV Fistulas are treatable!
- Angiography required to confirm diagnosis.
  - –CTA vs. MRA spine may show abnormality. May be normal in low flow fistulas.
  - –Catheter angiography: gold standard and allow for intervention at time of identification.



Spondylotic myelopathies may have a typical enhancement pattern, that lasts for years.

Clues for compressive myelopathy:

Spindle shape lesion at maximal site of compression on sagittal imaging.

‘Pancake’ like enhancement, at the level of the highest compression.

Enhancement can last for years, often leading others to question diagnosis.



Thank you!





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