Myelopathy and Myelitis

Stacey L. Clardy, MD PhD
Associate Professor of Neurology
Director, Autoimmune Neurology Fellowship
University of Utah & Salt Lake City VA
Stacey.Clardy@hsc.utah.edu

Twitter @StaceyLClardy

VA | U.S. Department of Veterans Affairs

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- Site investigator for the Alexion clinical trial for Eculizumab in Relapsing NMO patients.

***We WILL discuss off-label use of medications – because there are very few on label!**

(AQP4+ NMOSD now has 3 approved FDA Medications!)

What is Transverse Myelitis?

- Diagnostic criteria currently being revisited, but otherwise not since 2002
- Historically, definition vague, complicated by “transverse” requirement
- Transverse” first described in case in 1948
  - Referred to clinical finding of band-like area of altered sensation -- **not** extent of spinal cord involvement on imaging

Varied Definitions:

- Some requiring bowel/bladder involvement, or motor involvement
- Time limitation for symptom onset
- Some excluding vascular
- Some excluding complete or partial lesions

Suchett-Kaye, 1948; Kerr, 2010

Time to symptom nadir matters!

- Acute/hyperacute <12 hrs to nadir
  - Spinal cord infarct
- Time to nadir: 1-21 days
  - Inflammatory: Transverse myelitis, MS, NMOSD
- Progression over >21 days
  - Spondylosis
  - Tumor
  - Dural AVF
- Caution: Relapsing/Remitting
- Misdiagnosis of GBS still very common

Myelitis vs. Myelopathy

- What's in a name?
  - "itis" vs. "opathy"
  - Ideal Clinician approach: **Start at myelopathy, rule in/out myelitis**
  - Diagnostic implications -- ? etiology
  - Treatment implications
- Myelopathy is not always Myelitis
  - Vascular
- Myelitis not always Demyelinating
  - Acute Flaccid Paralysis

Myelopathy

- Clinical assessment matters!
  - CSF, MRI, spinal angio help
- CSF:
- Non-inflammatory (WBC normal; no OCB)
  - Infarct, Dural AVF, Spondylosis, tumor, B12
- Inflammatory (↑WBC; +/- OCB's)
  - MS, NMOSD, MOGAD, infectious, sarcoid
- Markedly ↑CSF protein; normal cell count
  - Spinal block (tumor/spondylosis); Guillain-Barre
- ↓Glucose
  - Meningomyelitis

Barreras et.al. Annals 2014

Clinical biomarkers differentiate myelitis from vascular and other causes of myelopathy

Paula Barreras, MD, Kathryn C. Fitzgerald, ScD, Maureen A. Mealy, RN, BSN, Jorge A. Jimenez, MD, Daniel Becker, MD, Scott D. Newsome, DO, Michael Levy, MD, PhD, Philippe Gailloud, MD, and Carlos A. Pardo, MD

Correspondence
Dr. Pardo
cpardov1@jhmi.edu

Neurology® 2018;90:e12-21. doi:10.1212/WNL.0000000000004765

457 patients referred to a myelopathy center with presumptive diagnosis of TM

Conclusions

The temporal profile of symptoms serves as a clinical biomarker in the differential diagnosis of TM. The establishment of a definite diagnosis in TM requires a critical analysis of the MRI and CSF characteristics to rule out non-inflammatory causes of myelopathy.

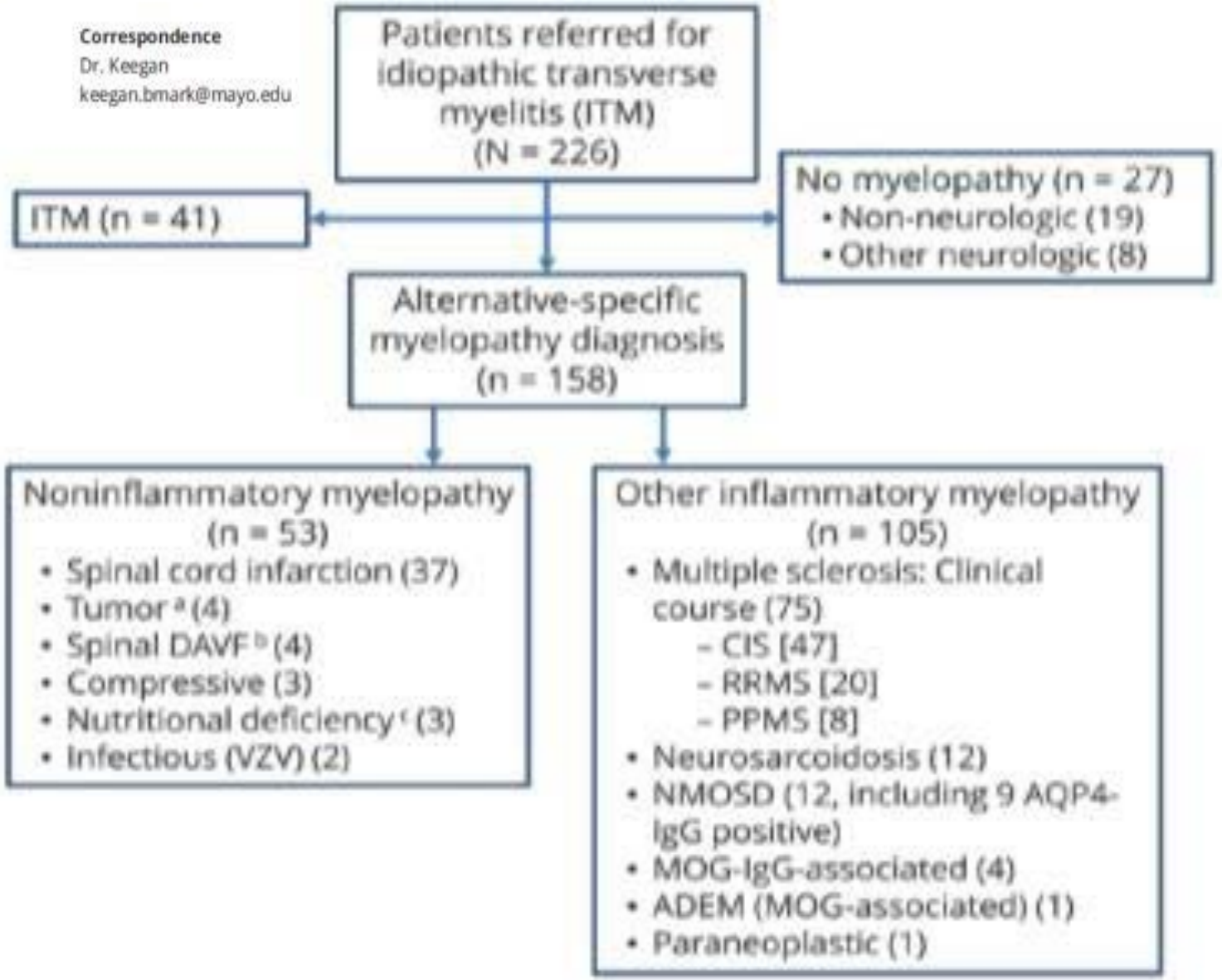
***Of all predictors, the temporal profile of symptoms contributed the most to the increased discriminatory power.**

Evaluation of idiopathic transverse myelitis revealing specific myelopathy diagnoses

Nicholas L. Zalewski, MD, Eoin P. Flanagan, MB, BCh, and B. Mark Keegan, MD

Neurology® 2018;90:e96-102. doi:10.1212/WNL.0000000000004796

Correspondence
Dr. Keegan
keegan.bmark@mayo.edu



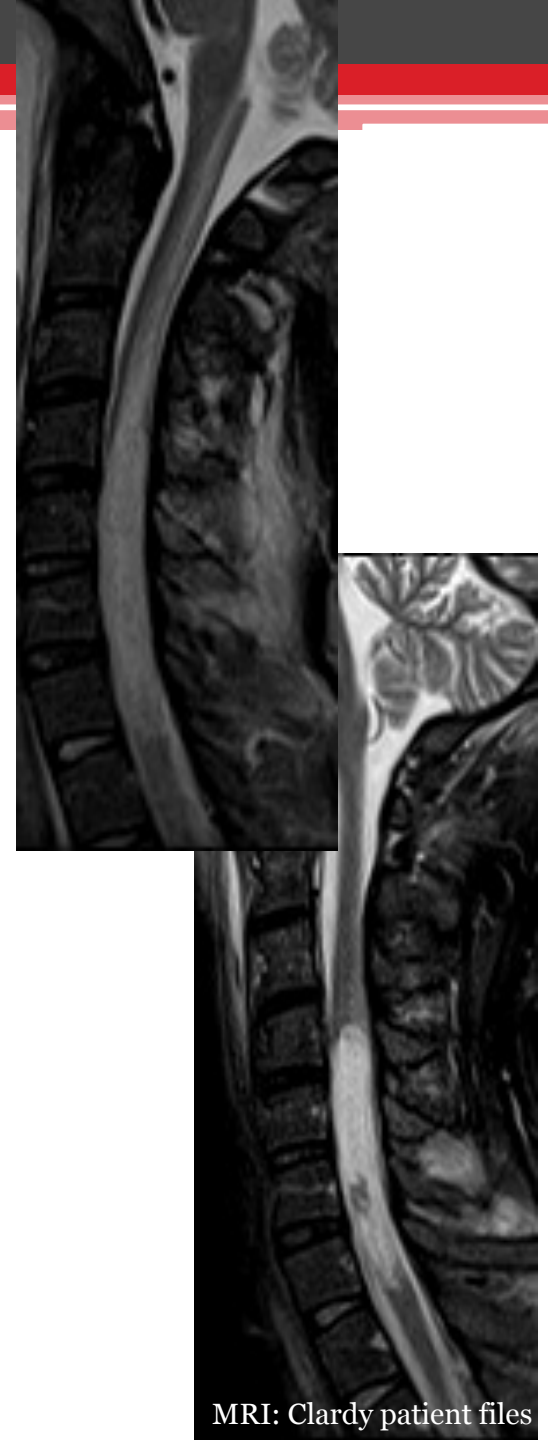
Functional loss = Clue to etiology

- Complete loss of spinal cord function
  - Acute compressive lesion, a necrotizing myelitis, or trauma
- Central cord lesion: autonomic dysfunction, spinothalamic deficits, pyramidal distribution weakness below level of lesion
  - Syrinx or possibly NMO
- Anterior spinal cord syndrome w/ acute flaccid weakness, spinothalamic dysfunction but preserved dorsal column function
  - Anterior spinal artery occlusion
- Isolated loss of vibration & joint position sense
  - Vitamin B12 /copper deficiency, nitrous oxide toxicity
- Isolated tract involvement other than dorsal columns
  - Possible paraneoplastic
- Brown-Sequard syndrome (hemicord): ipsilateral motor weakness, vibration & joint position sensory loss; contralateral pain & temperature loss
  - Often MS or Compressive

Jacob and Weinshenker, 2008; Kumar, 2010; Pittock et al., 2005; West et al. 2012

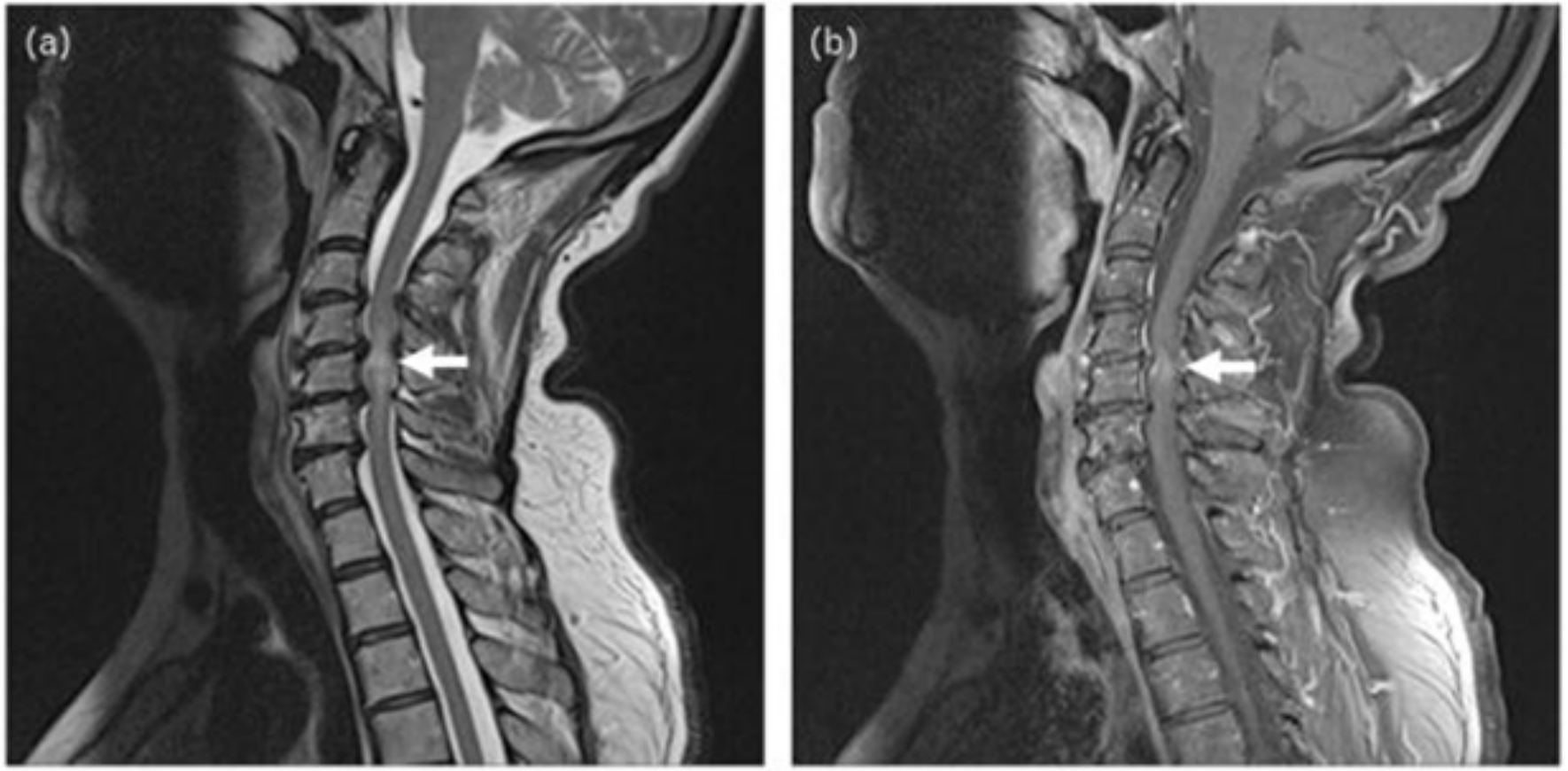
Myelopathy - Vascular

- Vascular
  - Vascular causes more common than appreciated
    - AVM/fistula, Venous thrombosis, Stroke
    - Many LETM
  - Hyperacute + Chronic presentations
  - Spinal angiogram likely underutilized*
  - Average time to diagnosis of Dural AVF in Mayo Clinic series: 2 years
  - Red Flags: Worsening symptoms with Plasma Exchange/Steroids



MRI: Clardy patient files

Myelopathy – Compressive

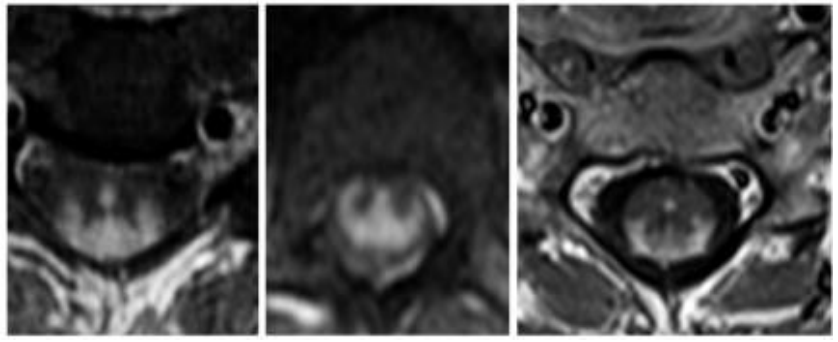


(a) T2 sagittal and (b) T1 postcontrast sagittal images demonstrate high signal & associated degenerative disk disease and 'pancake-like' enhancement at point of maximal stenosis (arrows).

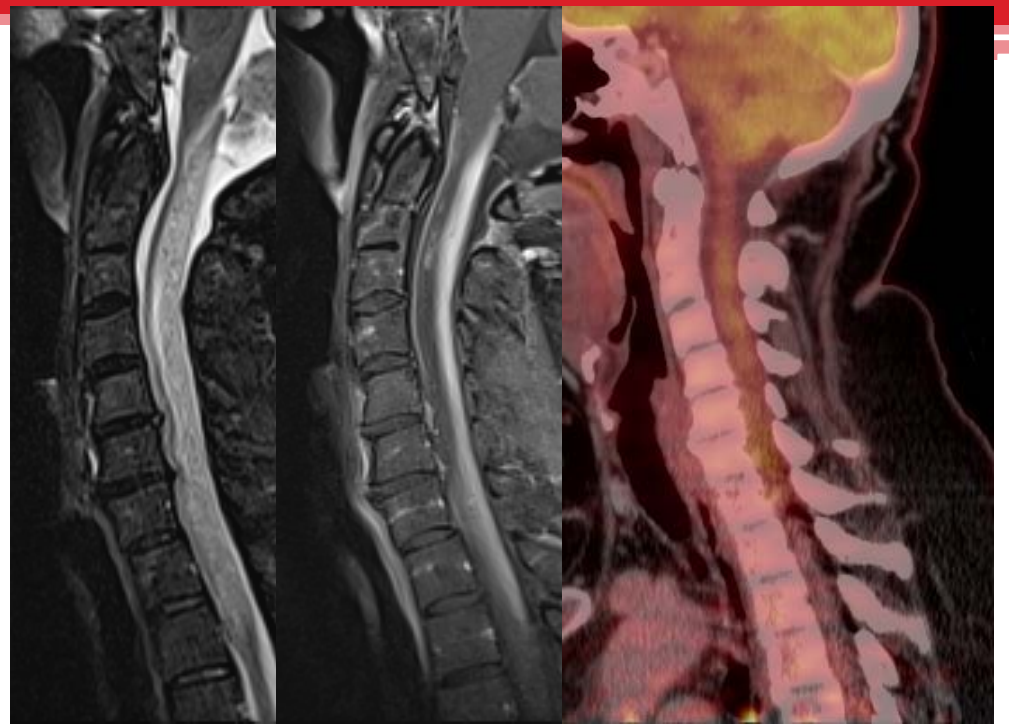
Tobin et.al. Curr Op Neurol 2014

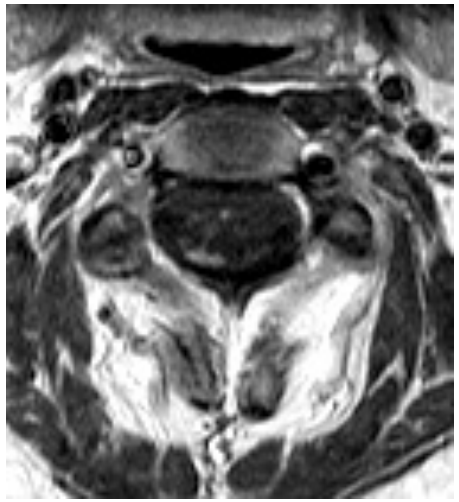
LETM

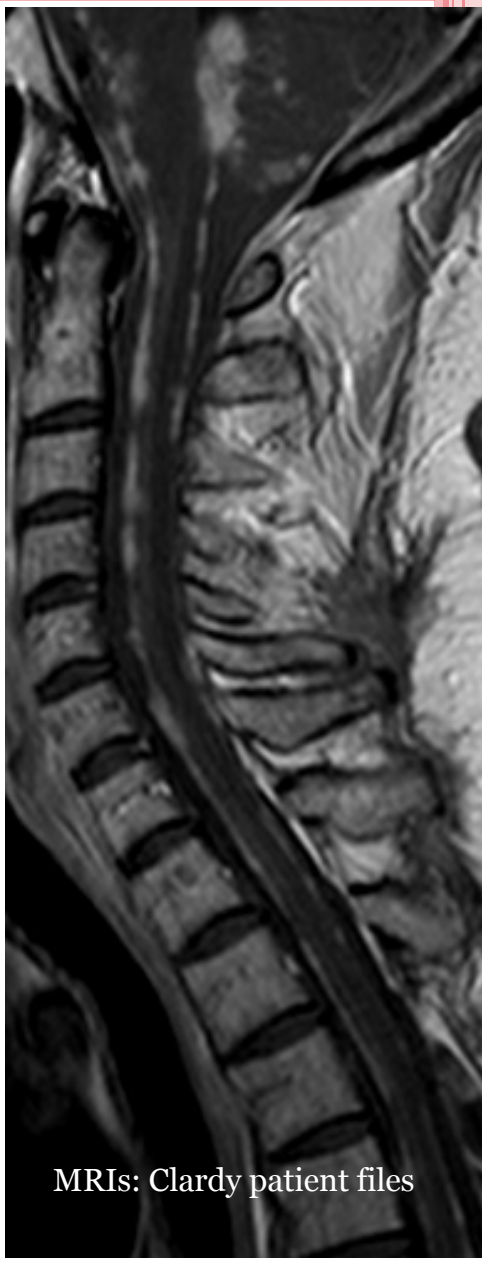
- **Sarcoidosis**
  - Many with posterior column
  - Many with isolated myelopathy
  - Contrast enhancement, persistent
  - Leptomeningeal enhancement (~50%)
  - Trident sign



Zawlewski et al Neurology 2016





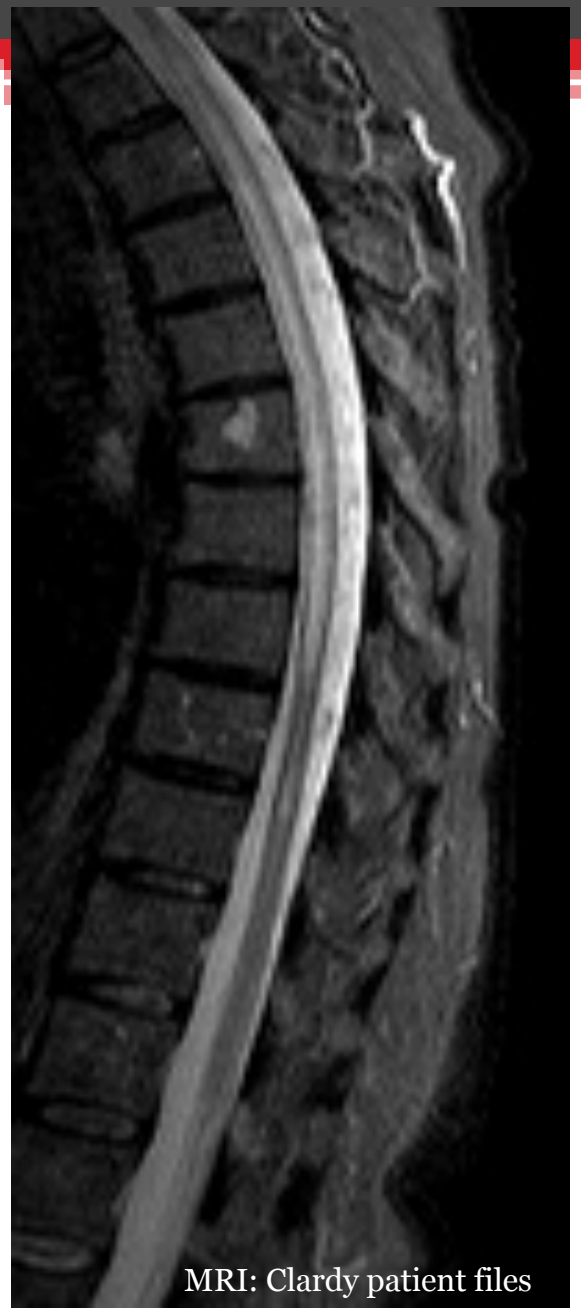


MRIs: Clardy patient files

Tobin et.al. Curr Op Neurol 2014

LETM

- NMOSD:
  - **More likely to involve ½ cross sectional area of cord**
  - Enhance and centrally located
  - Both central and peripheral in cord
  - T1 hypointense
  - Gray matter involvement
  - Mass effect



Pekcevik et.al. Mult Scler 2015; Tobin et.al. Curr Op Neurol 2014

NMO Diagnosis

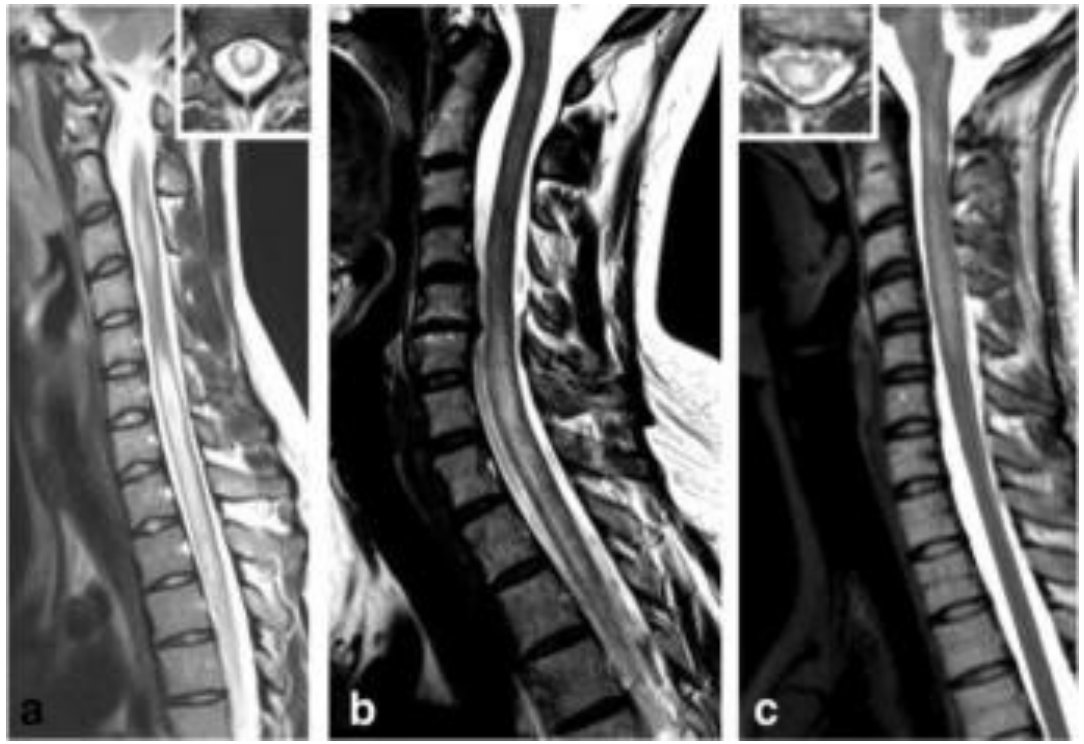
- NMO Spectrum disorders present with variable phenotypes
- Frequently misdiagnosed NMO patients:
  - Overlap syndromes –Sjogren's, Lupus, Myasthenia Gravis
  - Prolonged Nausea, Vomiting, or Hiccups
    - Area postrema lesions
  - Hydrocephalus
  - Narcolepsy/Anorexia
  - Brainstem Syndromes
  - Recurrent myalgias with hyperCKemia

Newer myelopathies on the block

- MOGAD
  - Monophasic or relapsing acute ON, myelitis, brainstem encephalitis, or encephalitis, or any combination of these syndromes
    - *Antibody Testing not 100%

- GFAP
  - May have tremor, optic disc edema
  - CSF most sensitive/specific
  - NMDA, AQP4 antibodies may coexist
  - Steroid-responsive

- Acute Flaccid Myelitis –
  - *stay tuned* (lecture later today)



Kitley, Vincent, Palace et al. JAMA Neurol 2014; Jarius et al. J Neuroinflamm 2016; Fang B et.al. JAMA Neurol. 2016.

Treatments – Evolving!

Initial/Acute

- IV methylprednisolone, Plasma exchange, IVIG …

Targeted:

- Neurosarcoidosis: High dose glucocorticoids initially, then Infliximab now favored regimen. *Need trials!*
- AQP4 NMOSD: Now 3 FDA approved treatments!
- MOGAD: Glucocorticoid, Rituximab … IVIG? *Need trials!*
- Multiple Sclerosis: 15+ FDA approved treatments
- Dural AV fistula: Surgical
- Spinal Cord Stroke: ? IV TPA (acutely only)
- Genetic/Mitochondrial: Important to diagnose to AVOID unnecessary immunotherapy
- Infectious: IVIG? Other? Depends on infection…
  - *Acute flaccid myelitis talk later today*

- **Aggressive Rehab for all, and symptomatic management, especially pain and spasticity management!!**

Summary

- Start at myelopathy
  - Don't delay treatment – However --
  - Index of suspicion required for vascular etiology
    - Suspect if worsening with steroids/PLEX
    - Can have "inflammatory" CSF findings, including bands
    - Skilled angiographer
- Rule in/out Myel**itis**
- Pay attention to Season and Geography – History is KEY
- Save CSF and Serum!! (prior to immunotherapy)

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Summary

Course of the illness as told by YOU (patient/caregiver) is *always* informative (acute/subacute/chronic/stuttering).

Must have a clinician Review the Imaging in **Detail** – axial and sagittal, and post-contrast imaging – many clues to the trained eye (contrast in IV important in diagnostic phase!)

LP rule for physicians (Advocate for yourself !):

If you are going to stick a needle in someone's back –

- Get extra CSF
- Always order oligoclonal bands
- Empiric treatment often warranted, but treatment will interfere with ability to achieve a diagnosis – so ALWAYS save pretreatment serum and CSF.

Thank you!

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Twitter @ StaceyLClardy
Stacey.Clardy@hsc.utah.edu

2020 RNDS

Sravanthi Vegunta, MD

Neuro-ophthalmology Fellow at
University of Utah Health

What is MOG Antibody Disease (MOGAD)?

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ALEXION

Genentech
A Member of the Roche Group

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