



MRI Predictors of Recurrence and Outcome after Acute Transverse Myelitis of Unidentified Etiology

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4/20/2021

Learning Objectives

By the end of this journal club, participants will be able to...

1. Understand a potential presentation of transverse myelitis
2. Recognize the key features of transverse myelitis on imaging
3. Understand the diagnostic criteria for transverse myelitis
4. Predict risk of idiopathic transverse myelitis recurrence based on MRI findings

Module Outline

- I. Case
- II. Background
- III. Article Overview
- IV. Clinical Questions
- V. Key Points

Case presentation

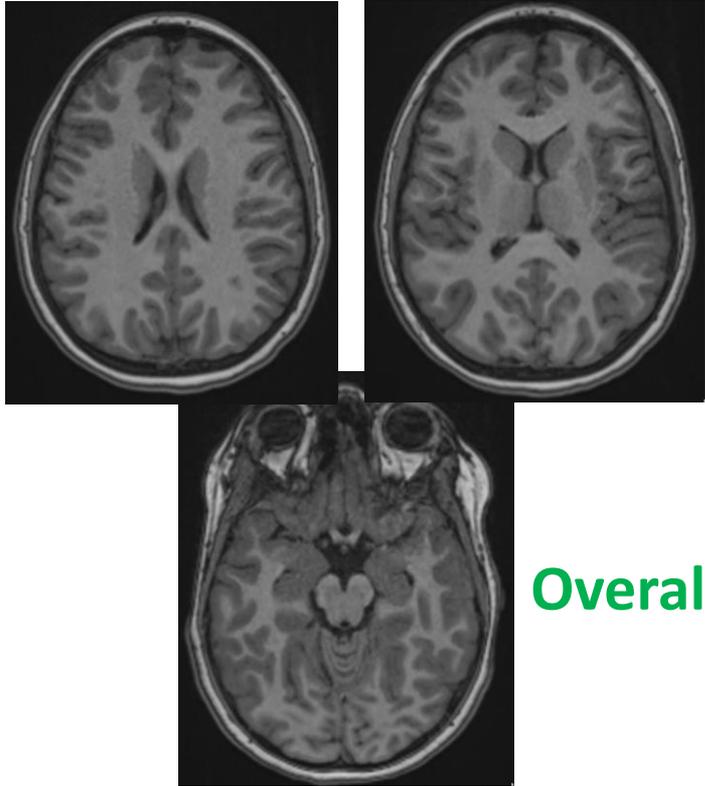
11yoF picking flowers around 12pm and noticed pain between her shoulder blades. Within 2-3 hours, she noticed weakness in her legs and truncal instability with a wobbly walk. She lacked fine motor movements in the hands at this time. She has been unable to urinate since before the pain began. She has no sick contacts, no recent illness, no other symptoms. Her mental status is intact, no changes in hearing/vision, no seizures. She has a typical adolescent diet but no honey. There is no relevant family history.

- Physical exam: CN II-XII intact, areflexive, 0/5 strength in LEs, severe truncal weakness and instability, 5/5 strength in flexion in UEs, 3/5 in extension. Unable to differentiate between sharp and dull touch diffusely.
- Labs: CMP, CRP, Tox Screen, COVID-19, enterovirus negative. CBC notable for WBC 12.6.



Initial Imaging: Brain, Cervical, Thoracic, and Lumbar MR w/out Contrast

T1-Weighted Brain MR Images
Axial plane

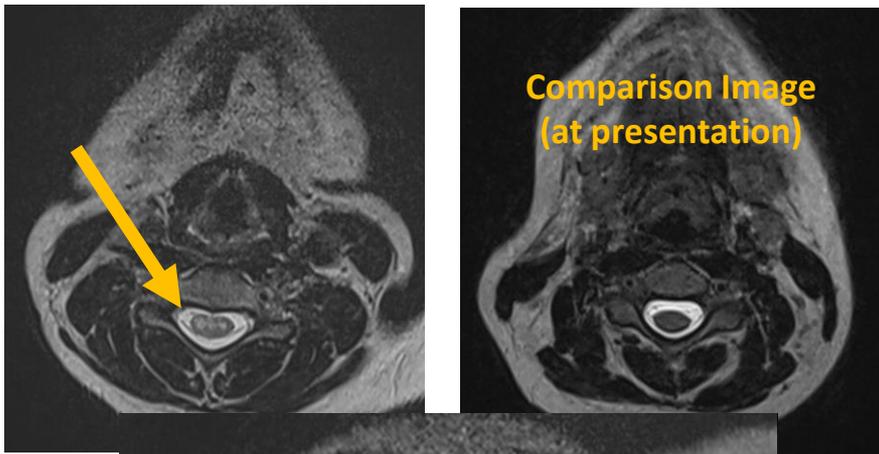


T1-Weighted Cervical,
Thoracic, and Lumbar
Spine MR Images
Sagittal Plane

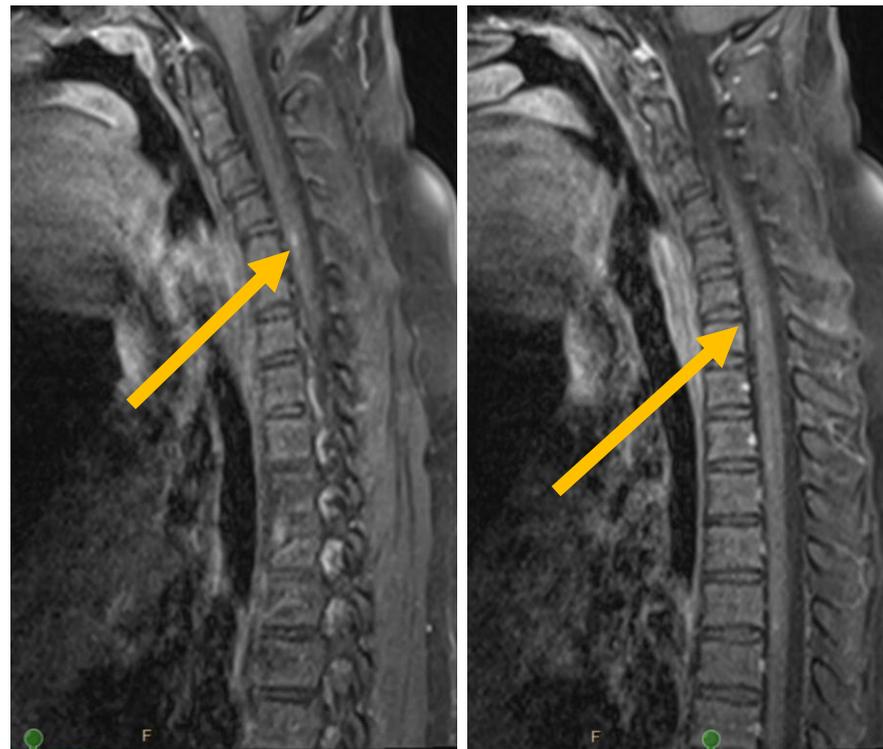


Overall unremarkable!

Repeat Imaging: Cervical and Thoracic MR w/ and w/out Contrast



T2-Weighted Axial MR Images of Cervical Spine
(~48hrs after presentation)



Post-Contrast T1-Weighted Sagittal MR
Images of Cervical and Thoracic Spine

Clinical Question

In acute transverse myelitis of uncertain etiology, are there any MRI findings that can predict risk of recurrence?

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Transverse Myelitis

- Acquired neuro-immune disorder of the spinal cord—rare!
- Peak onset between 10-19 and 30-39 years old
- Rapid onset of sensory changes, weakness, bowel/bladder dysfunction
- Can be idiopathic, post-infection or on a spectrum of neuro-inflammatory and/or autoimmune disorders
- Treated with high dose steroids +/- plasma exchange (PLEX)
- Recovery is slow; months to years—a third or more have permanent deficits

Diagnostic criteria for transverse myelitis

- Sensory, motor or autonomic dysfunction attributable to the spinal cord
- Bilateral signs and/or symptoms
- Clearly defined sensory level
- No evidence of compressive cord lesion
- Inflammation defined by cerebrospinal fluid pleocytosis **or** elevated IgG index **or** gadolinium enhancement
- Progression to nadir between four hours and 21 days

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(Not all necessarily required, but a good framework for diagnosing)

Module Outline

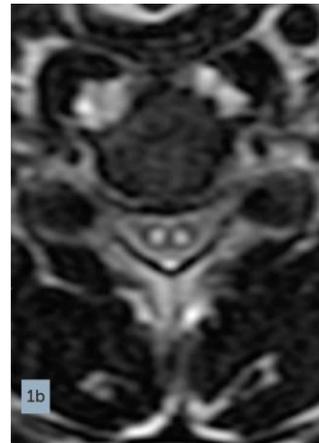
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Article Specifics

- **Purpose:** To identify MR imaging findings in transverse myelitis of unidentified origin that predict relapse and/or poor outcomes
- **Journal:** American Journal of Neuroradiology
- **Study Type:** Retrospective review of spine MR images
- **Number of Cases:** 77 patients and their accompanying scans included in final data analysis
- **Data:** Considered demographics, serologies, relapse rates, disability at 1 year or greater (1 to 14 years after 1st episode), and spinal cord MR imaging studies prior to start of treatment
 - Kurtzke Expanded Disability Status Scale (EDSS)
 - Relapse: New/return of symptoms with report of new lesion or changes on neuro exam
 - Scan time: Mean 10 days after symptoms started (range 1-30 days)

Materials and Methods

- Reports dictated at Johns Hopkins Hospital from Jan 1, 2005 - Jan 1, 2017
- Keywords “myelitis” and “myelopathy”
- Compared with clinical information to identify cases
- Standardized imaging protocols for spine MR
- Reviewed by two Neuroradiologists (blinded to clinical outcome)
- Analyzed all variables and demographics for associations
 - Logistic regression of variables performed to correlate specific factors with risk
- T2 hyperintensities: Extent, distribution, brainstem extension, location, cord expansion, contrast enhancement and T1 signal
 - Longitudinal lesions spanned 3 or more vertebral levels (others “short-segment” lesions)
 - Determined involvement of white matter, gray matter, or both
 - Looked for bright spotty lesions and owl’s eye sign



Study Cohort

- Inclusion Criteria:
 - Met diagnostic criteria for acute transverse myelitis set forth by Transverse Myelitis Consortium Working Group (2002)
 - No specific etiology found by 3 months after onset
 - MR obtained within 1-month after symptoms began
- Excluded those with technically inadequate scans or imaging findings of vascular myelopathy or compressive etiology
 - Further excluded those with an EDSS that was not able to be calculated and insufficient follow-up (<1 year)

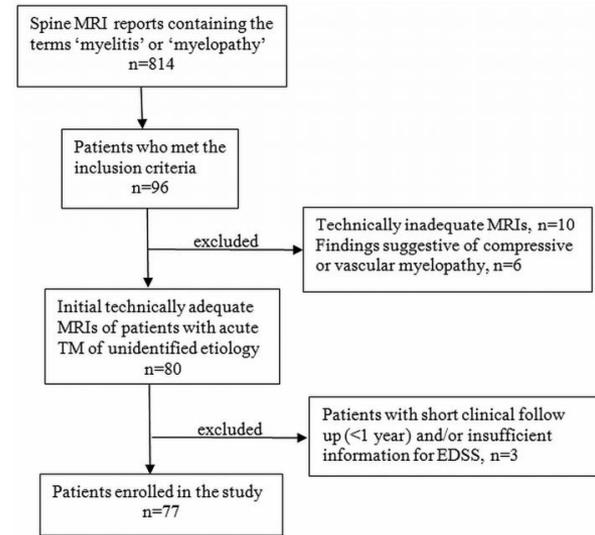


FIG1. Flow chart of patients who met the inclusion/exclusion criteria for the study population.

Study Cohort (Con't)

Table 2: The clinical characteristics of 77 patients who presented with acute transverse myelitis

Characteristics	Monophasic (n = 50)	Recurrent (n = 27)	P Values
Age at initial manifestation (mean) (yr)	34.2 ± 20.6	40.4 ± 18.5	.196
Female (n) (%)	25 (50%)	21 (77.8%)	.033
Ethnicity			.020
African American (n) (%)	10 (20%)	10 (37%)	
Caucasian (n) (%)	38 (76%)	12 (44.4%)	
Asian American (n) (%)	1 (2%)	3 (11%)	
Hispanic (n) (%)	1 (2%)	2 (7.4%)	
Seropositivity for anti-AQP4 Ab	1 (2%)	8 (29.6%)	.003
Mean follow-up time (yr)	2.4 ± 1.7	3.8 ± 3.8	.023
Mean EDSS score	4.2 ± 2.1	3.3 ± 1.8	.064
Patients with follow-up spine MRIs (n) (%)	16 (32%)	27 (100%)	<.001
Use of immunosuppressive/immunomodulatory treatment (n) (%)	9 (18%)	18 (66.7%)	<.001

Note:—AQP4 Ab indicates aquaporin 4 antibody.

Results

- 35% developed recurrent disease (27/77)
- Three main predictors of recurrence
 1. Cord swelling (expansion), Odds Ratio 5.30
 2. Contrast enhancement, Odds Ratio 5.05
 3. Bright spotty lesions (BSLs), Odds Ratio 3.63
- Disability scores did not significantly correlate with imaging variables
- Mean time to relapse 17.3 months, 77% of those who relapsed did so within 1 year
 - 66% of those with relapse had multiple episodes
- Age did not play a role in relapse but gender and African American race did
- Only one-third of those with relapse were still considered idiopathic at mean follow-up time of 45.2 months

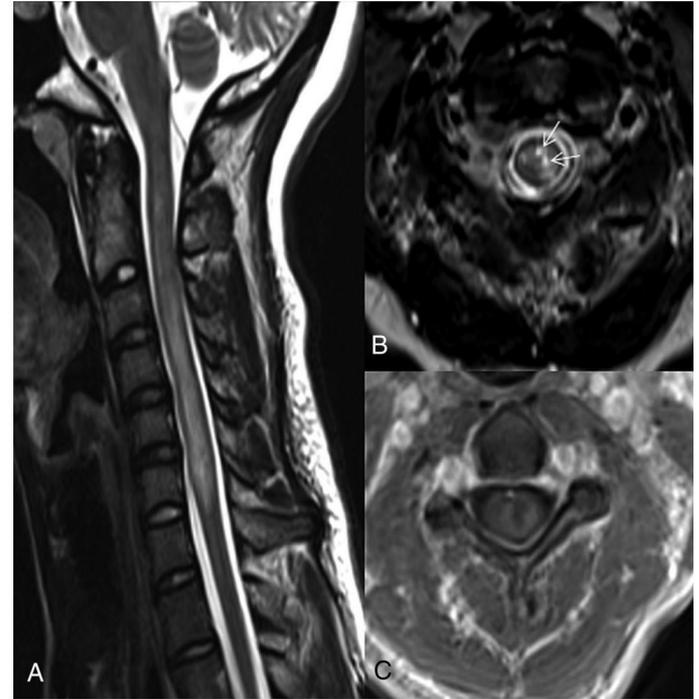


FIG 3. Spine MR images of a 29-year-old female patient with recurrent transverse myelitis. The sagittal T2-weighted image (A) shows a longitudinally extensive, expansile hyperintense lesion at the cervical spine. The axial T2-weighted (B) and postcontrast T1-weighted (C) images show gray and white matter involvement with bright spotty lesions (arrows in B) and ring enhancement of the lesion. The patient was diagnosed with NMOSD later at follow-up.

Results (Con't)

Table 3: The frequencies of spinal MRI findings and associations with monophasic/relapsing disease

MRI Findings	Monophasic Disease (n = 50) (n) (%)	Recurrent Disease (n = 27) (n) (%)	P Value	Unadjusted OR (95% CI)
LETM (n = 42) (54.5%)				3 (1.30–10.14)
Multifocal lesions (n = 16) (22.5%)				6 (0.44–4.21)
Distribution				
Cervical (n = 21) (27.3%)				
Cervicothoracic (n = 14) (18.2%)				
Thoracic (n = 35) (45.5%)				
Holocord (n = 7) (9.1%)				
Brain stem extension (n = 5) (6.5%)				
Location				
Gray matter (n = 3) (3.9%)				
Gray + white matter (n = 65) (84.4%)				
White matter (n = 9) (11.7%)				
>1/2 of the cord area (n = 55) (71.4%)	5 (10%)	4 (14.8%)		
Cord expansion (n = 48) (62.3%)	33 (66%)	22 (81.5%)	.242	2.26 (0.73–7.04)
T1 hypointensity (n = 23) (30.3%)	26 (52%)	22 (81.5%)	.021 ^a	4.06 (1.32–12.42)
BSLs (n = 27) (35.1%)	11/49 (22.4%)	12 (44.4%)	.089	2.76 (1.01–7.61)
Owl's eyes sign (n = 2) (2.6%)	12 (24%)	15 (55.6%)	.012 ^a	3.95 (1.45–10.74)
Enhancement (n = 48) (62.3%)	2 (4%)	0	.539	0.58 (0.06–5.88)
brain involvement (n = 11) (21%)	26 (52%)	22/26 (84.6%)	.011 ^a	5.07 (1.52–16.87)
	11/43 (25.6%)	6/20 (30%)	.950	1.24 (0.38–4.04)

Table 4: Adjusted ORs for associations of imaging variables/age

Variable	Adjusted ORs	P Value	95% CI
Cord expansion	5.30	.018	1.33–21.11
BSLs	3.63	.040	1.06–12.43
Enhancement	5.05	.023	1.25–20.34
Age	1.03	.084	0.99–1.061
Constant	0.01	.00	

^a Significant.

Discussion

- Identify potentially relapsing disease early to guide treatment and follow-up
- Demographics of relapse similar in previous reports (NMOSD overlap?)
- Those with longer sections of spinal cord involved also more likely to have recurrence—another finding in line with past research
- Cord expansion associated with NMOSD in the past, but in this study, associated with idiopathic disease instead
 - Many with BSLs later diagnosed with NMOSD, but still several “idiopathic”
 - Brain findings also correlated with NMOSD rather than unknown etiology
- First study to show contrast enhancement of any kind associated with relapse
- Relapsing disease may have worse clinical outcomes with longer follow-up times

Where does our patient fall in?

But wait... (Limitations)

- Different strength magnets used (1.5T and 3T) from various manufacturers
 - Also included transferred in images from outside hospitals
- Varying follow-up periods
 - Shorter than several other studies with contrasting results
 - Unable to rule out future relapse in currently monophasic cases
- Relatively small sample size (77 total cases included)
- No consideration of preventive therapy and its effects on relapse
- One patient did not have post-contrast imaging

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Clinical Questions Now

- What is the best preventive treatment option in our patient's situation?
- How do we find the balance of too little versus too much immunosuppression?
- What are other potential causes of “idiopathic” transverse myelitis and how can we best test for them?
- What is the optimal timing and regimen for physical therapy/occupational therapy (acute, intensive rehab) and for how long in order to reap maximal benefit?

UNC Top Three (Key Points)

1. Acute transverse myelitis can be idiopathic or the first presentation of another underlying neuroinflammatory condition.
2. Diagnosis is based on clinical presentation, history, physical exam, labs, and imaging findings—ALWAYS use physical exam to guide imaging decisions!
3. MR predictors of recurrent idiopathic transverse myelitis may include cord expansion, contrast enhancement, and bright, spotty cord lesions on T2-weighted images.

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