Spinal movement disorders in TM, NMOSD, and MOGAD

Hesham Abboud, MD, PhD
Assistant Professor of Neurology
Case Western Reserve University School of Medicine
Director, Multiple Sclerosis and Neuroimmunology Program
Staff Neurologist, Movement disorders Center
University Hospitals Cleveland Medical Center

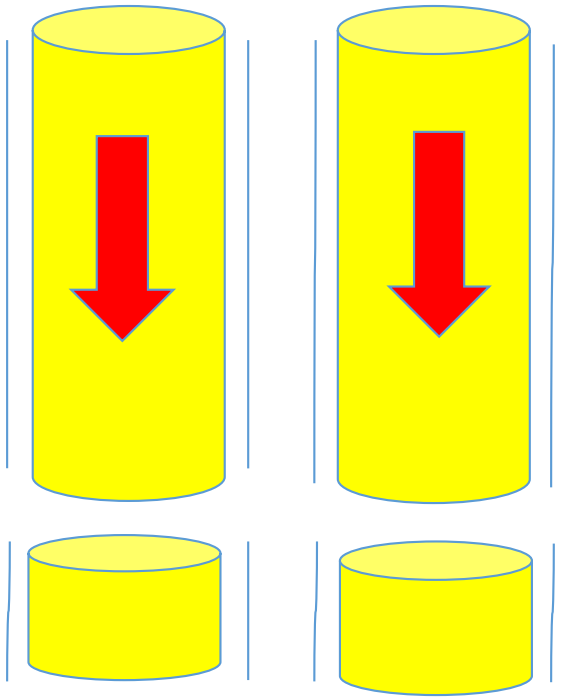
Background

- Historically, movement disorders were thought to be uncommon in MS and related diseases.
- Basal ganglia involvement is rare and so are traditional movement disorders.
- A prospective study of movement disorders in MS and NMOSD showed that spinal movement disorders (SMDs) are the most frequent demyelination-related movement disorders.[1]
- Comparative studies suggest that tonic spasms are more prevalent in NMOSD compared to MS.[2]
- In a previous retrospective study, the prevalence of SMDs in NMOSD patients was 43%.[3]
- In a large retrospective study from China the prevalence of painful tonic spasms was 43%.[4]
- However, there has been no prospective studies evaluating spinal movement disorders in NMOSD nor in MOGAD or idiopathic transverse myelitis (TM).

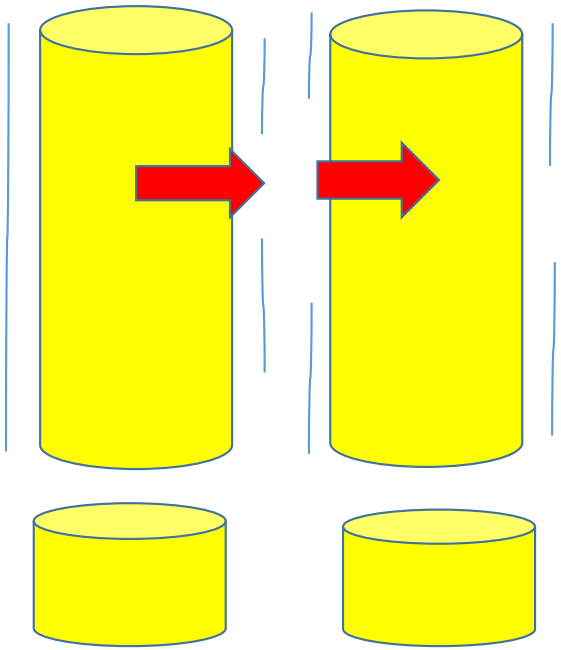
(1) Abboud H, et al. (2018) Neurol Clin Pract
(2) Kim SM, et al. (2012) Arch Neurol
(3) Abboud H, et al. (2016) Movmnt Disords Clncl Practice
(4) Li QY, et al. (2020) Mult Scler Relat Disord

Pathogenesis: Ephaptic transmission

- Vertical synaptic transmission via myelinated fibers



- Transversely spreading ephaptic transmission in demyelinated fibers.



Spinal movement disorders subtypes

SMD	Definition
Flexor tonic spasm	Paroxysmal sustained increase in muscle tone resulting in visible tonic posturing of the affected body part (often the whole limb or part of the limb) in flexion secondary to spinal cord pathology
Extensor tonic spasm	Paroxysmal sustained increase in muscle tone resulting in visible tonic posturing of the affected body part (often the whole limb or part of the limb) in extension secondary to spinal cord pathology
Isometric tonic spasm	Paroxysmal sustained increase in muscle tone that can be felt by the patient and palpated by the examiner, but does not result in visible change in posture (e.g., abdominal wall muscles) secondary to spinal cord pathology.
Unspecified tonic spasm	A tonic spasm not meeting criteria for other spinal movement disorders or not specified in documentation secondary to spinal cord pathology
Paroxysmal focal dystonia	Paroxysmal involuntary sustained muscle contraction of antagonistic muscle groups resulting in abnormal posture (other than simple flexion or extension) secondary to spinal cord pathology
Nonparoxysmal focal dystonia	Persistent (nonparoxysmal) sustained muscle contraction of antagonistic muscle groups resulting in a fixed abnormal posture secondary to spinal cord pathology
Focal/Segmental spinal myoclonus	Sudden, brief (nonsustained), shock-like focal muscle contraction of one or more adjacent body parts secondary to spinal cord pathology
Propriospinal myoclonus	Sudden, brief, shock-like, arrhythmic jerks of the trunk, hips, and knees (sparing the head) often in flexion secondary to spinal cord pathology
Tremors of spinal origin	Postural and/or action tremors occurring after spinal cord pathological event in absence of brain/brainstem/cerebellar lesions and personal or family history of essential tremors
Spontaneous clonus	Spontaneous (noninduced) involuntary, rhythmic muscle contractions and relaxations associated with spasticity secondary to spinal cord pathology. It commonly involves the ankle or the wrist and appears in certain positions or with certain movements.

Abboud H, Fernandez HH, Mealy MA, Levy M. Spinal Movement Disorders in Neuromyelitis Optica: An Under-recognized Phenomenon. Mov Disord Clin Pract. 2016.

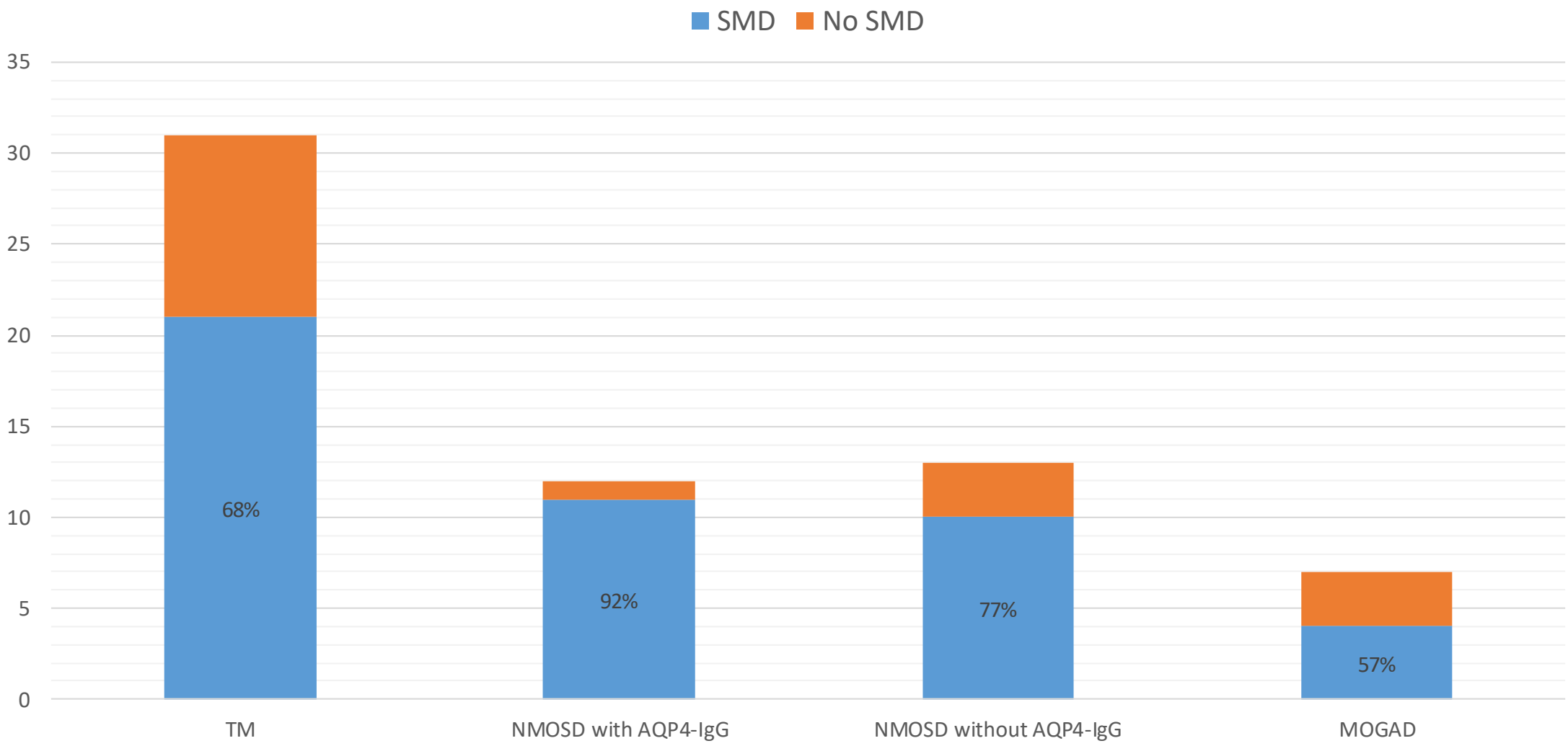
Study design

- Patients referred for evaluation of NMOSD, MOGAD, or idiopathic TM were evaluated by a neurologist trained in both neuroimmunology and movement disorders.
- All patients answered a movement disorders survey and underwent a movement disorder-focused exam.
- Movement disorders were compared among patients with NMOSD with AQP4-IgG, NMOSD without AQP4-IgG, MOGAD, and ITM.
- Patients with and without movement disorders were also compared to identify predictors of spinal movement disorders.

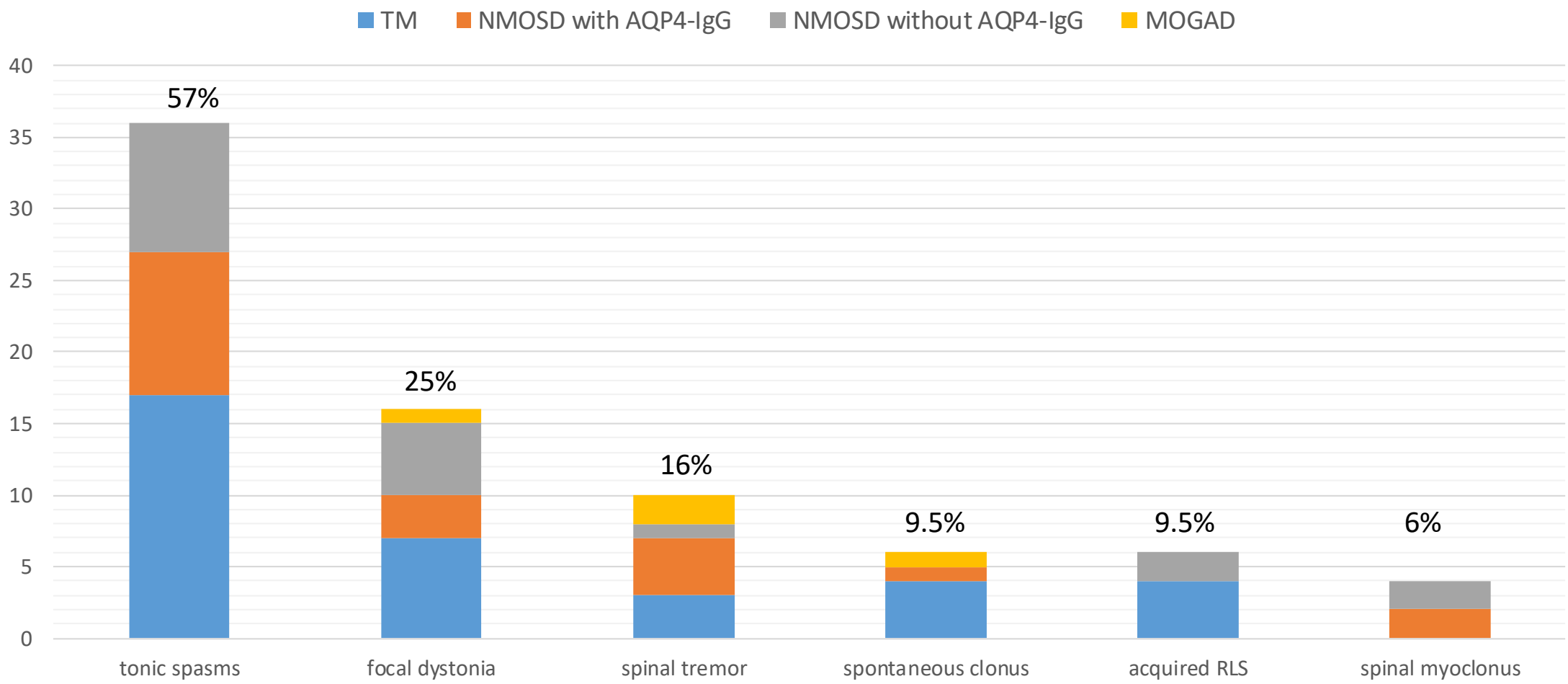
Results

- Eighty patients were evaluated from 2017 to 2021.
- Seventeen NMOSD/MOGAD patients without cord lesions were excluded.
- The remaining 63 patients were analyzed (71% females, average age 48+/-14 years).
- Of the total, 49% had idiopathic TM, 21% had NMOSD without AQP4-IgG, 19% had NMOSD with AQP4-IgG, and 11% had MOGAD.
- Movement disorders were present in 73% of all patients and were most frequent in NMOSD with AQP4-IgG (92%) and least frequent in MOGAD (57%).
- SMDs were the first symptom of the disease in 11% of cases.

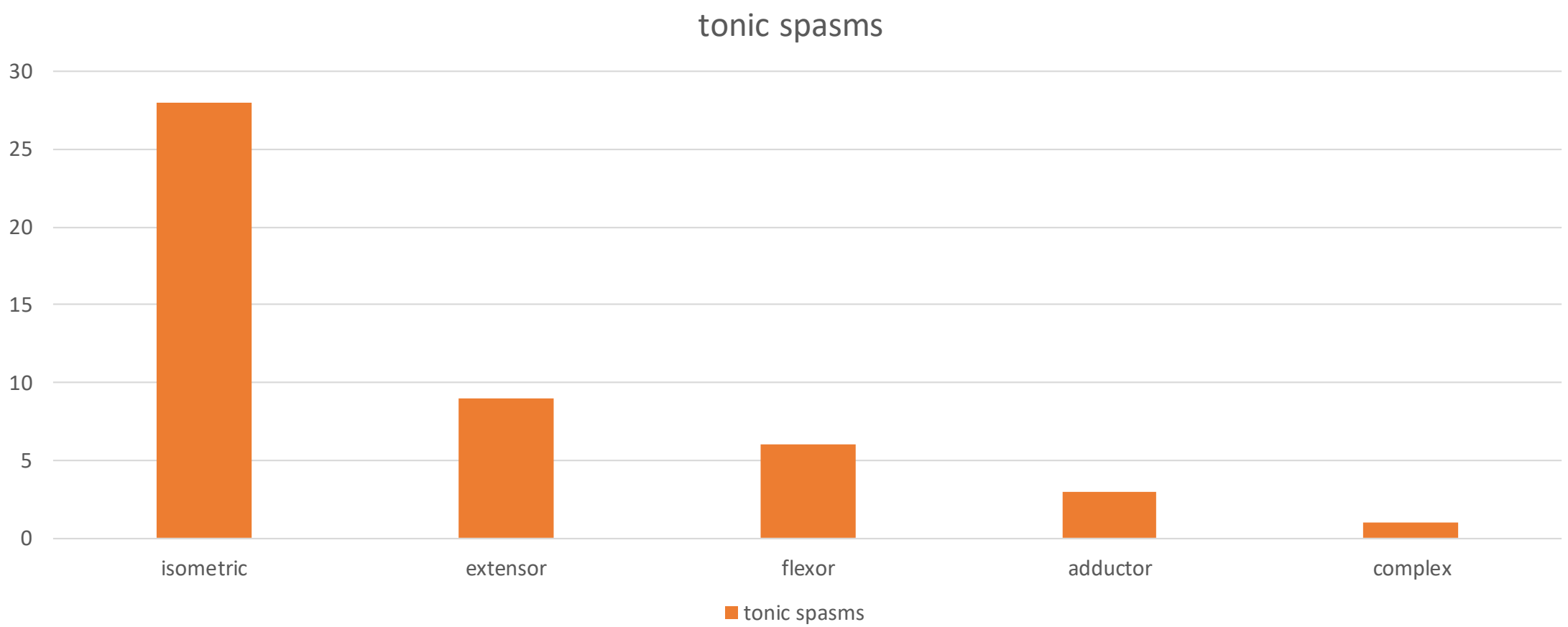
Prevalence of SMDs per disease category



Frequency of SMD subtypes



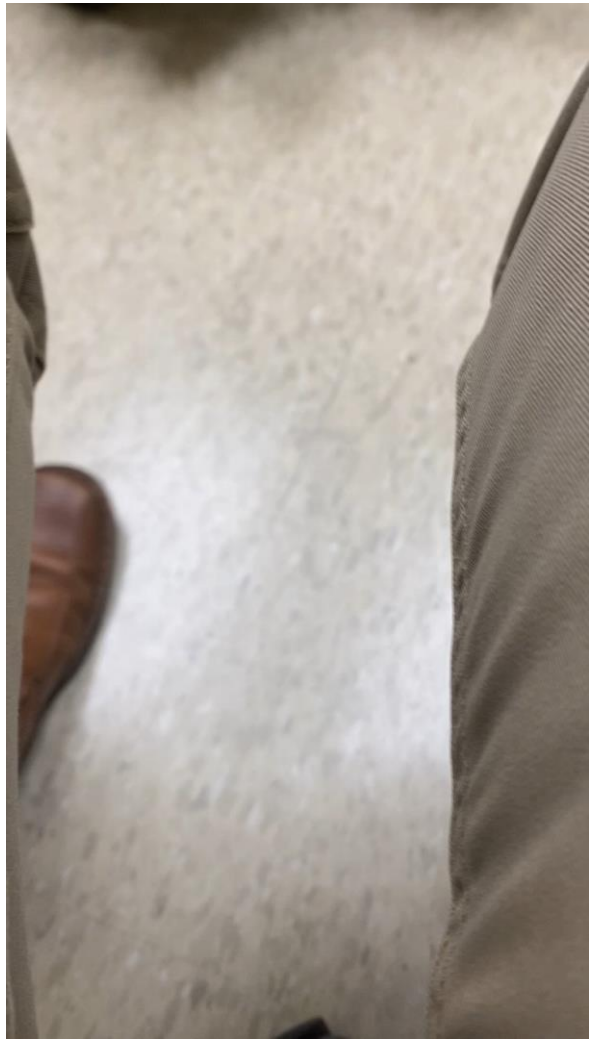
Frequency of tonic spasms subtypes



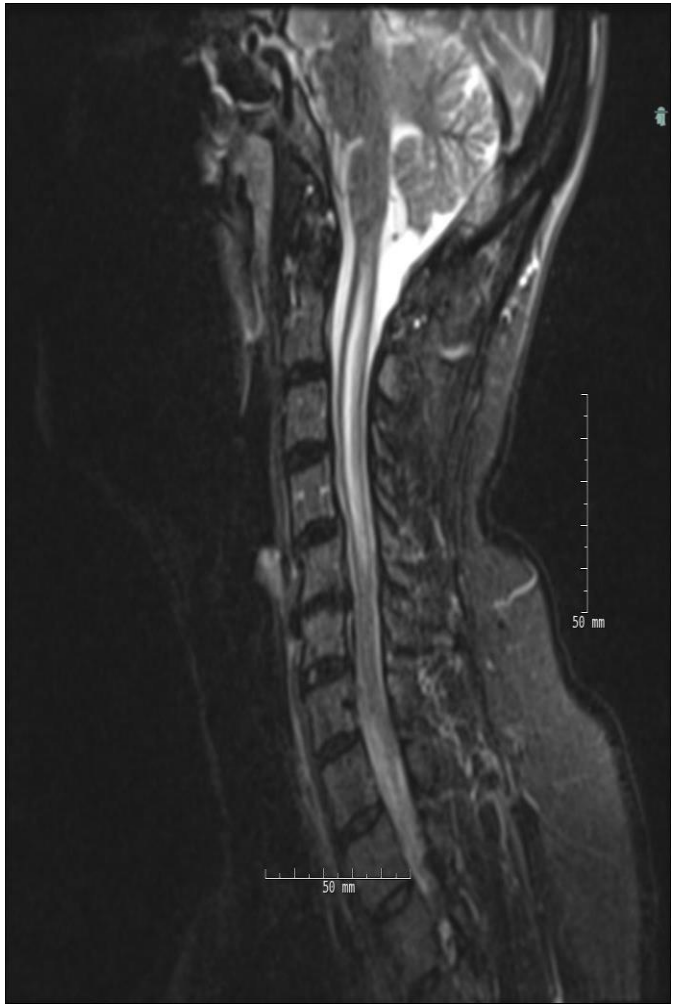
Statistical analysis

- NMOSD with AQP4-IgG patients were more likely to have any tonic spasms (P=0.003), isometric tonic spasms (P=0.013), spinal myoclonus (P=0.04), and painful SMDs (P=0.02).
- Compared to those without SMDs, patients with SMDs had longer disease duration, were more likely to have a relapsing course, were more likely to be AQP4-IgG positive, and more likely to be white.
- Multivariate analysis showed that white race and AQP4-IgG sero-positivity are independent predictors of spinal movement disorders in patients with myelitis.
- Patients with SMDs were more likely to have LETM (57%) than those without SMDs (24%) but detailed radiological analysis is still ongoing.

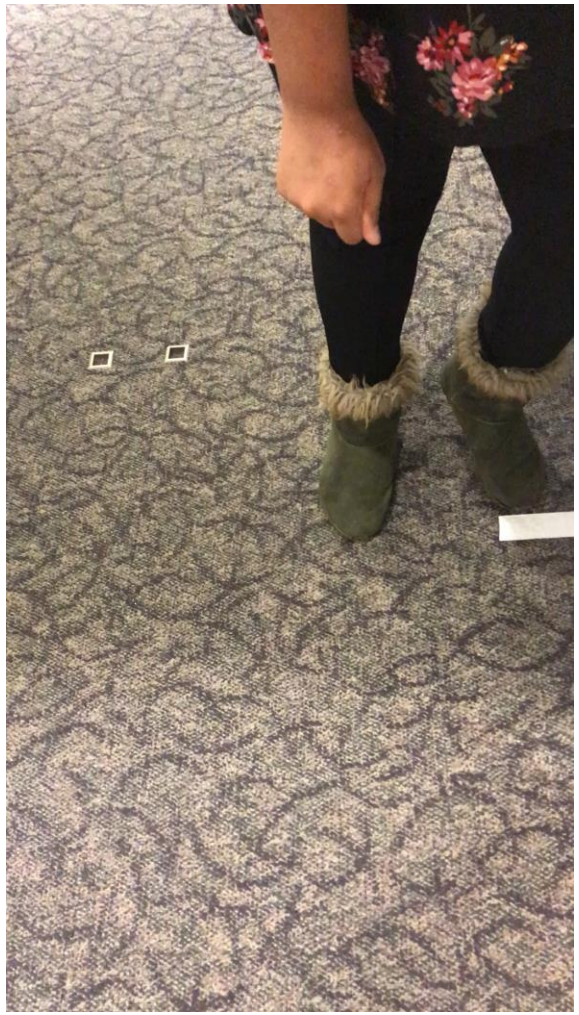
67 yo female with lower thoracic LETM and continuous hip adductor spasms

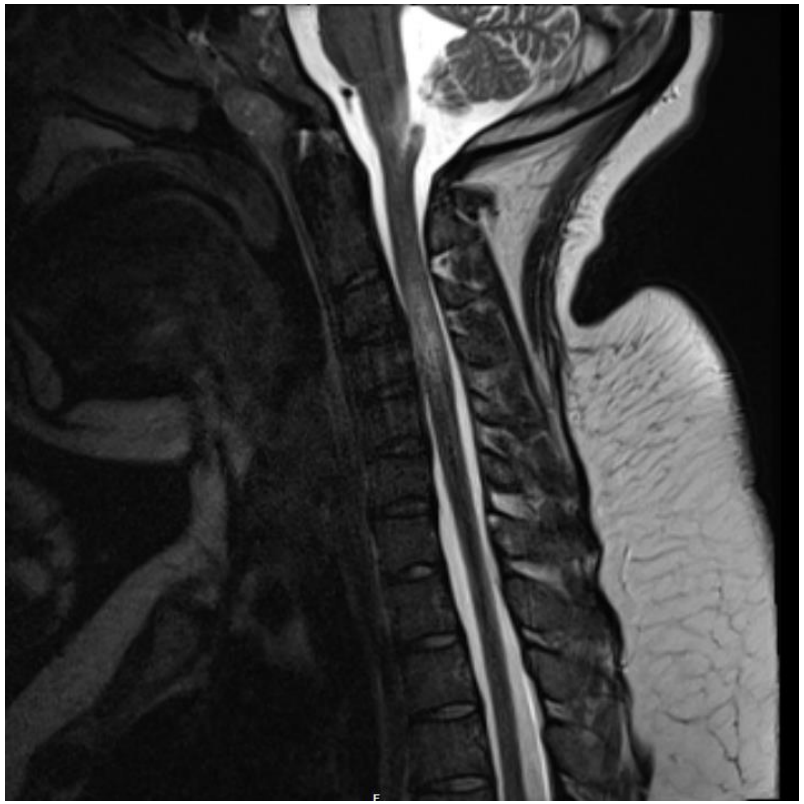


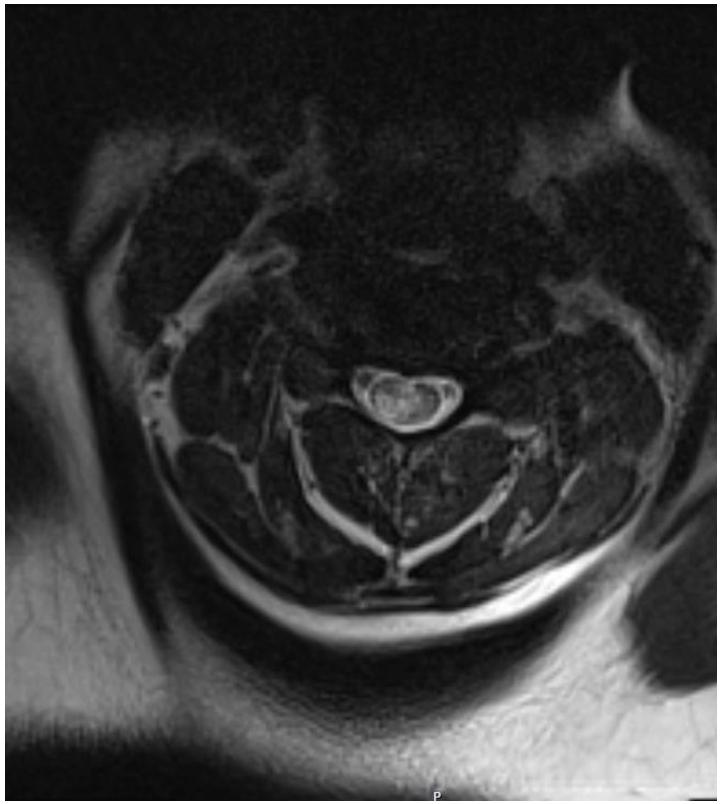
Flexor tonic spasm in NMOSD with AQP4-IgG



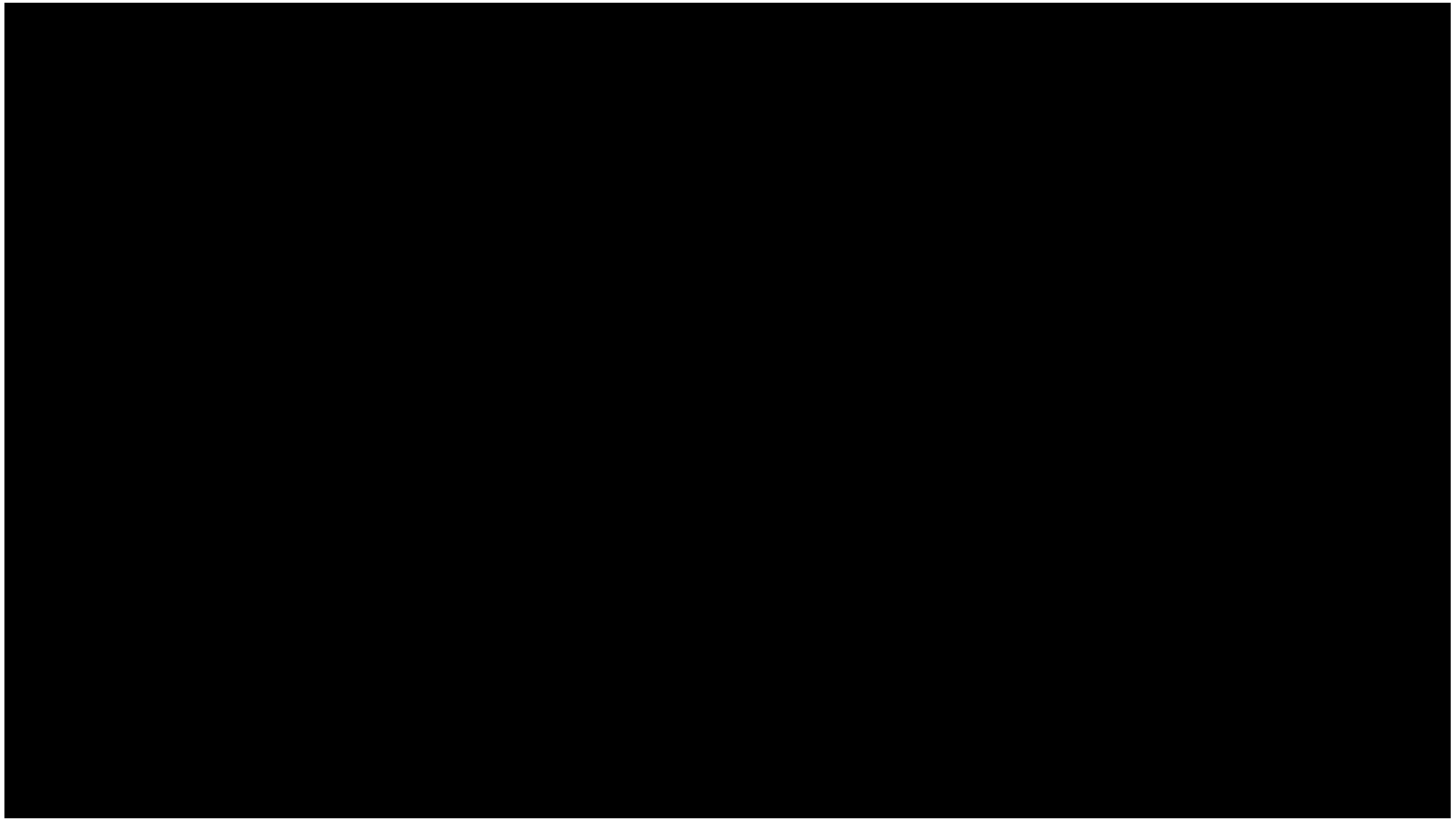
31 YO female with NMOSD with AQP4-IgG and paroxysmal focal dystonia of the right hand

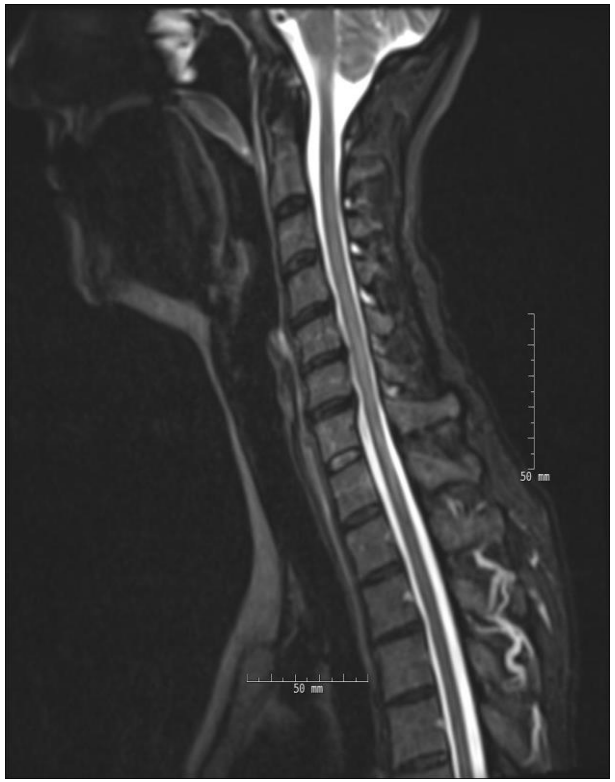




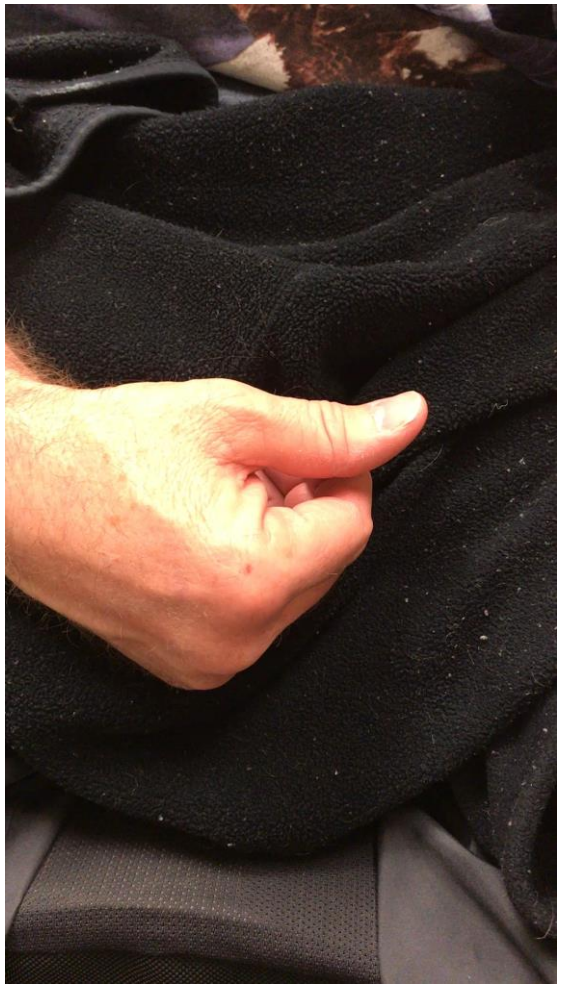


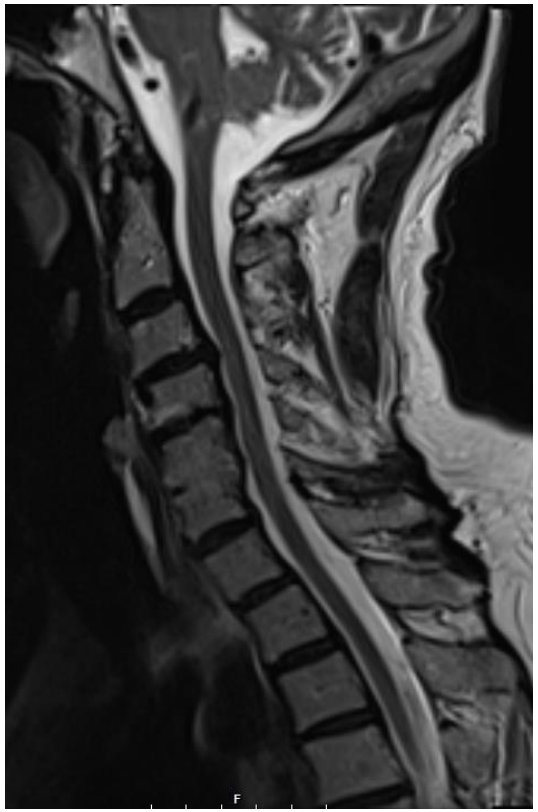
Paroxysmal focal dystonia in NMOSD

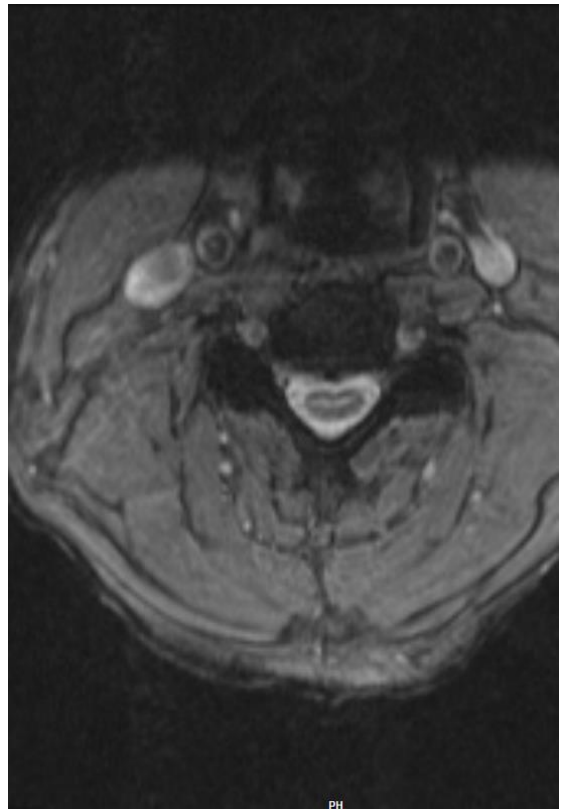




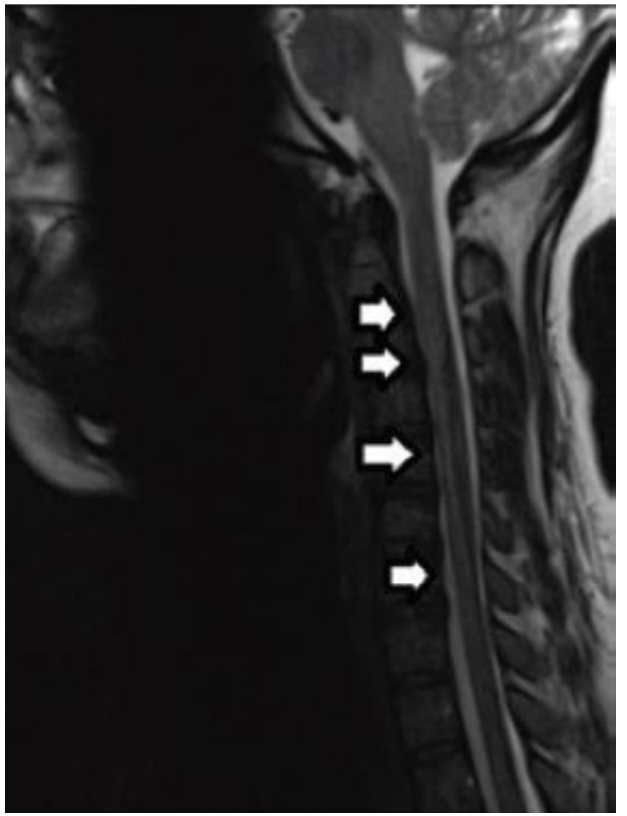
A 65 yo man with NMOSD without AQP4-IgG and spinal postural tremor







A 37 YO female with MOGAD and irregular postural/action tremor (spinal and brainstem)



Spontaneous hip clonus in a patient with GFAP-IgG encephalomyelitis

Focal spinal myoclonus in a patient with SCI

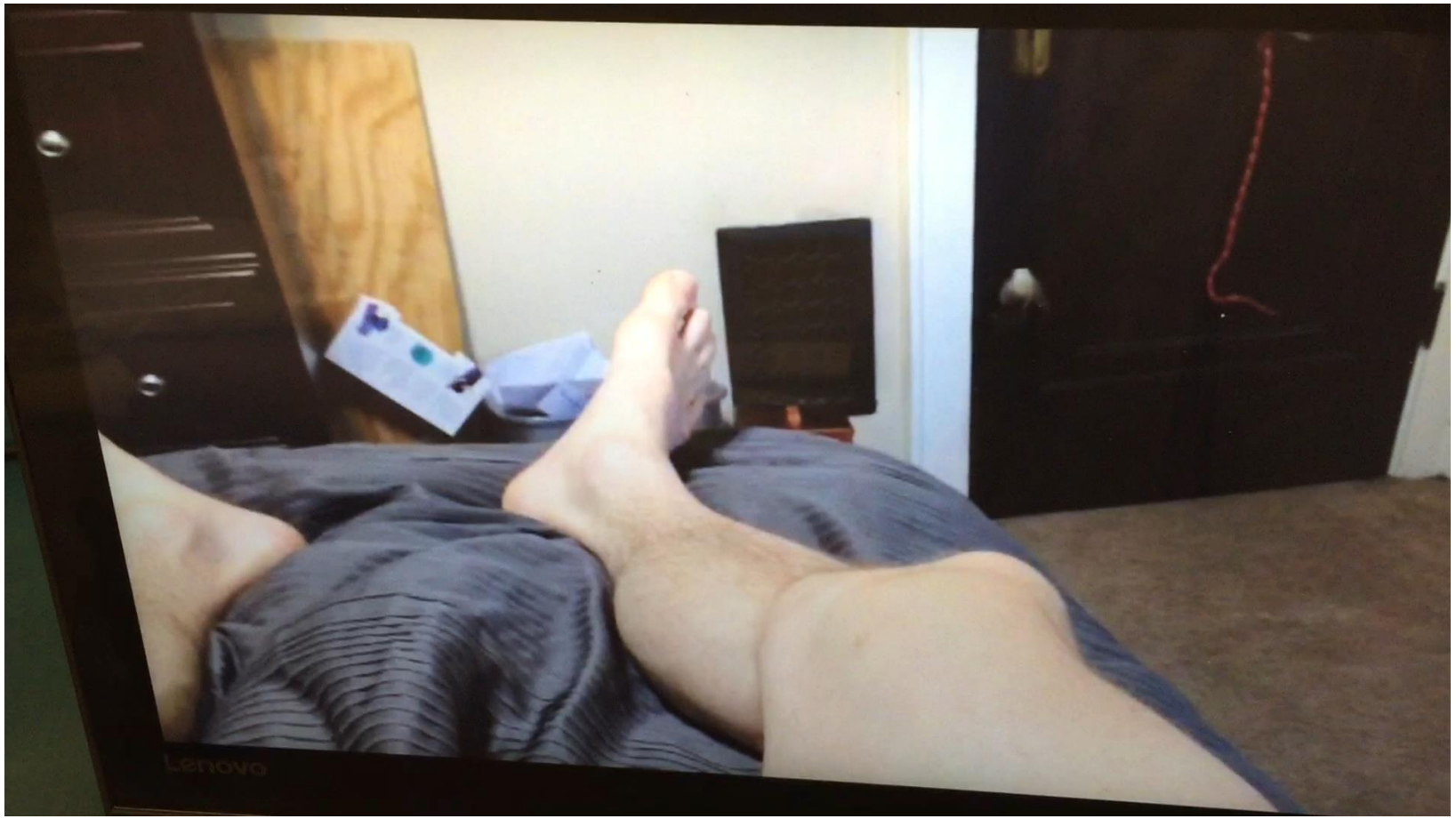


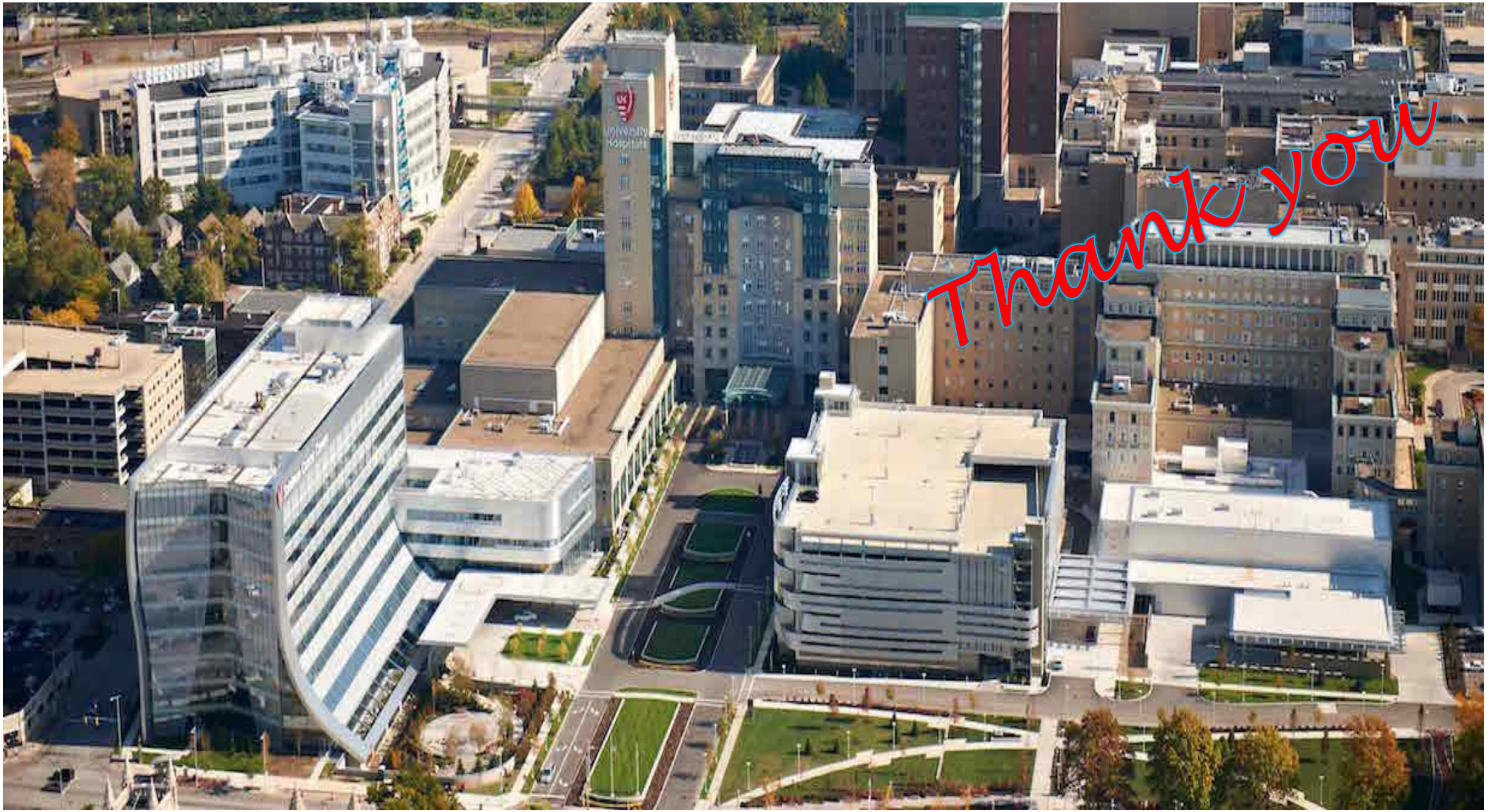
Table 1 Pharmacological options for symptomatic therapy in NMOSD

Symptomatic therapy	Indications	Common daily dosage	Side effects	Class of evidence*
Anti-convulsants				
Gabapentin	-Neuropathic pain -Tonic spasms	300–3600 mg	Dizziness, drowsiness, fatigue, falls	Class 1 for SCI-related neuropathic pain [1]
Pregabalin	-Neuropathic pain -Tonic spasms	50–300 mg	Dizziness, drowsiness, fatigue, falls	Class 1 for SCI-related neuropathic pain [2]
Carbamazepine	-Tonic spasms -Neuropathic pain	100–1200 mg	Dizziness, drowsiness, nausea, vomiting, ataxia, hyponatremia, agranulocytosis, skin rash	Class 4 for NMOSD-related tonic spasms [3]
Oxcarbazepine	-Tonic spasms -Neuropathic pain	150–1200 mg	Dizziness, drowsiness, nausea, vomiting, ataxia, hyponatremia, agranulocytosis, skin rash	Class 4 for NMOSD-related tonic spasms Class 1 for SCI-related neuropathic pain [4]
Levetiracetam	-Neuropathic pain	250–1000 mg	Irritability, agitation, drowsiness	Class 1 for MS-related neuropathic pain [5]
Muscle relaxants				
Oral baclofen	-Spasticity -Tonic spasms	5–80 mg	Sedation, dizziness, drowsiness, nausea, vomiting, urine retention	Class 2 for MS-related spasticity Class 3 for MS-related tonic spasms [6]
Intrathecal baclofen	-Spasticity -Tonic spasms	100–2000 mcg	Muscle weakness, risk of baclofen withdrawal syndrome, sedation	Class 1 for MS-related spasticity and tonic spasms [6]
Tizanidine	-Spasticity -Tonic spasms	2–36 mg	Sedation, dizziness, drowsiness, nausea, livery injury	Class 1 for MS-related spasticity [6]
Dantrolene	-Spasticity	25–400 mg	Weakness, hepatotoxicity	Class 3 for MS-related spasticity [6]
Botulinum toxin injections	-Focal spasticity or dystonia -Overactive bladder -Tonic spasms -Neuropathic pain	50–300 units	Depend on the site of injection and may include: focal weakness, dysphagia, dry mouth, urinary retention, rarely generalized weakness	Class 1 for MS-related spasticity [6] Class 1 for SCI-related neuropathic pain [7]

Abboud H, Salazar-Camelo A, George N, Planchon SM, Matiello M, Mealy MA, Goodman A; On-behalf of the Guthy-Jackson Foundation NMO International Clinical Consortium. Symptomatic and restorative therapies in neuromyelitis optica spectrum disorders. J Neurol. 2022 Apr

Conclusion

- When prospectively evaluated, spinal movement disorders are highly prevalent in patients with LETM.
- White race and AQP4-IgG sero-positivity are predictors of spinal movement disorders.
- Tonic spams, focal dystonia, and spinal tremor are among the most common SMDs in patients with NMOSD, TM, and MOGAD.
- This is different from MS where acquired RLS is the most common SMD, likely due to the predominant sensory involvement.
- Patients with NMOSD are more likely to have painful movement disorders, tonic spasms, and spinal myoclonus compared to patients with idiopathic TM and MOGAD.
- Symptomatic research should explore the best therapeutic approaches to SMDs in myelitis patients.


Thank you