XIX Curso Nacional de NEURORRADIOLOGÍA

Radiología Raquimedular

20 y 21 de abril de 2023 • MADRID

Sede: CINESA. Calle de Fuencarral, 136

S.E.N.R Sociedad Española de Neurorradiología

"Procesos inflamatorios-desmielinizantes medulares"

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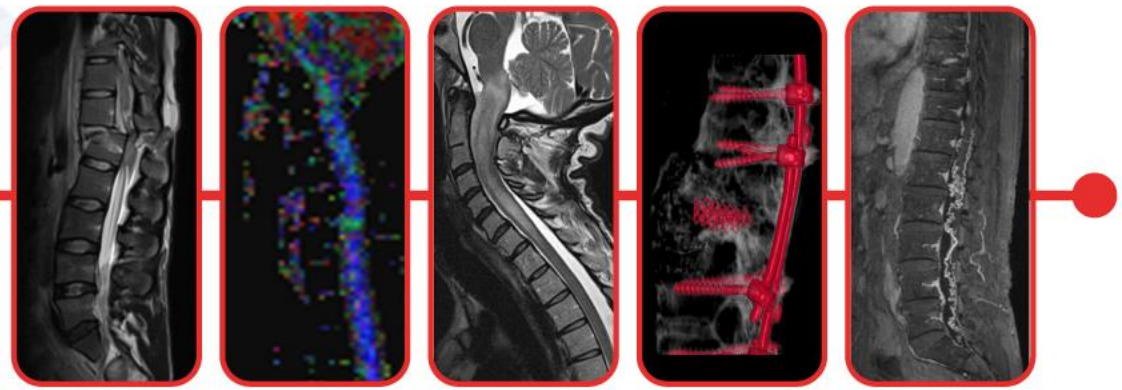

Disclosures

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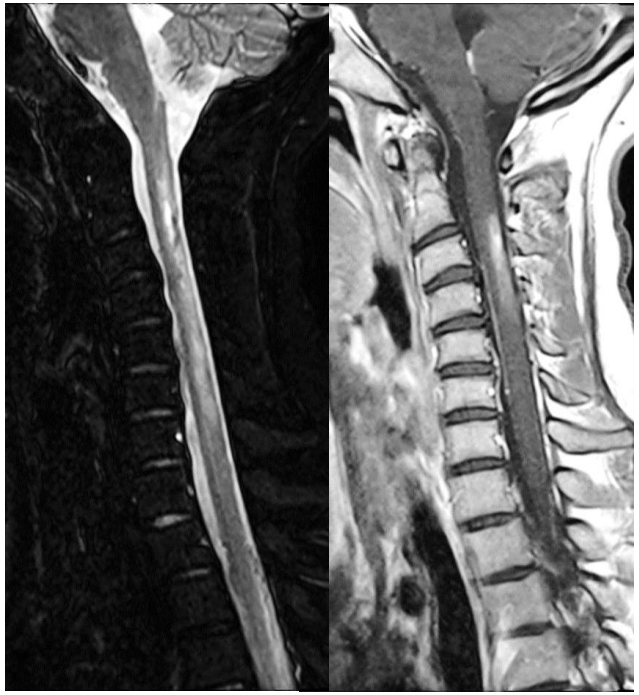
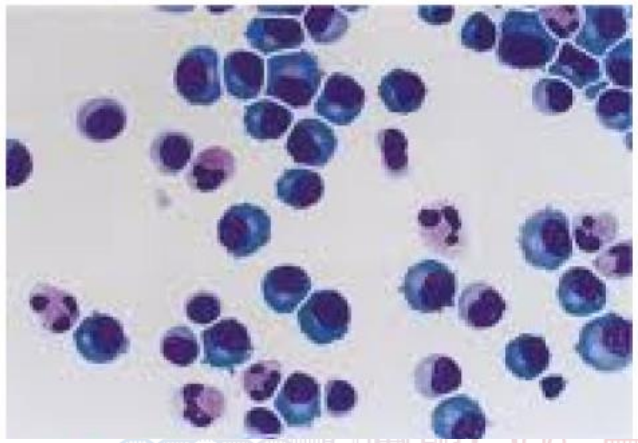
A. Rovira serves/ed on scientific advisory boards for Novartis, Sanofi-Genzyme, Biogen IDEC, OLEA Medical, Synthetic MR, TensorMedical, Icometrix and Bayer, has received speaker honoraria from Bayer, Sanofi-Genzyme, Bracco, Merck-Serono, Teva Pharmaceutical Industries Ltd, Novartis, Roche and Biogen Idec.

Transverse myelitis

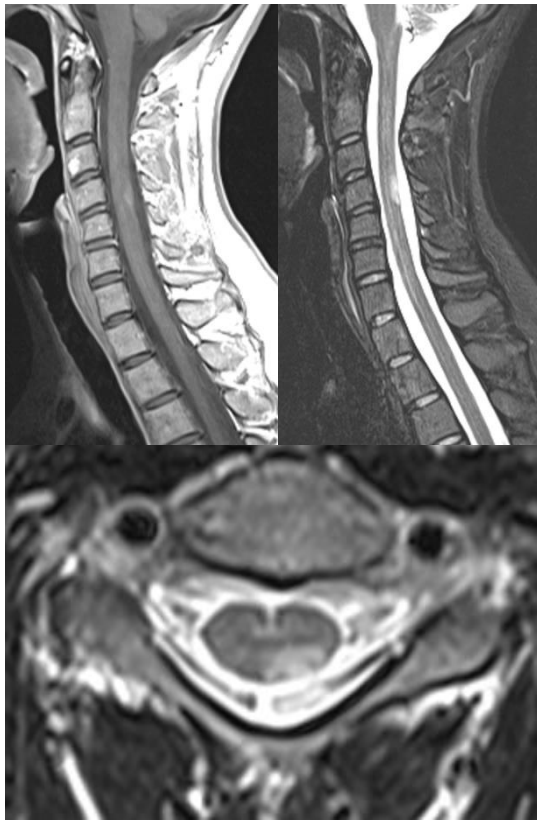
- Transverse myelitis (TM), is an **inflammatory lesion** of the spinal cord
- Acute/subacute course
- Occurs in 1 (severe) to 8 (mild) cases/ million per year (24 if MS included)
- Usually accompanied by MRI signal abnormality in the spinal cord, CSF pleocytosis, or both





Frohman et al. NEJM 2010; Scott et al. Neurology 2011

Transverse myelitis: etiology

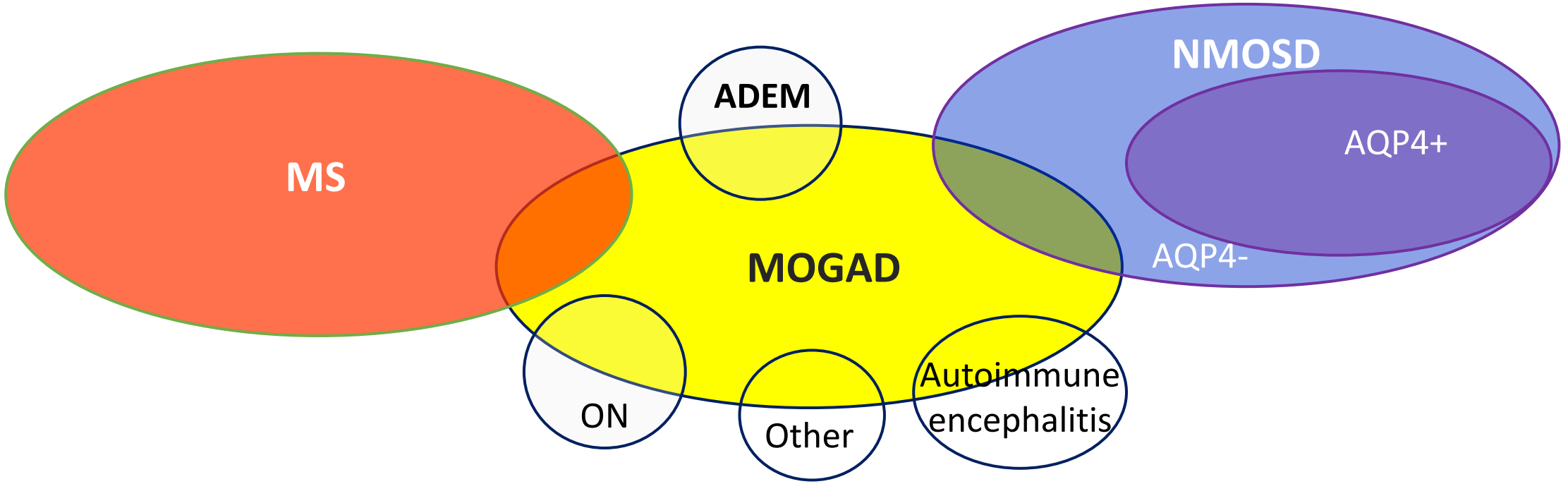


- Demyelination: **Multiple sclerosis,** ADEM, AQP4+NMOSD, MOGAD
- Primary angiitis
- Infectious: herpes zoster, simplex
- Systemic autoimmune diseases: SLE, Behçet, Sjögren, sarcoidosis
- Idiopathic: 15-36%

No demographic, family, and geographical data can predict the etiology with enough accuracy

Diagnosis based on imaging (MRI), clinical and lab findings

Inflammatory demyelinating diseases: new classification

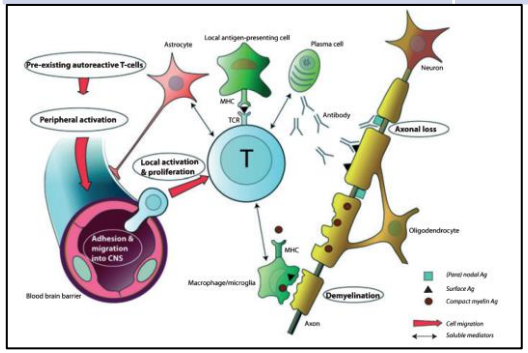


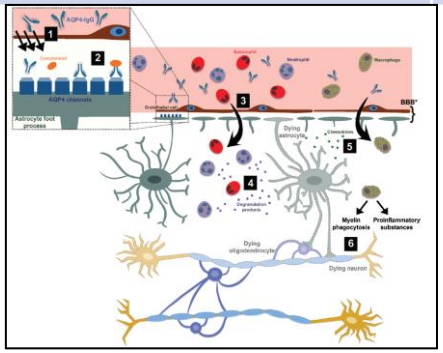
Integration of clinical, lab, and MRI data

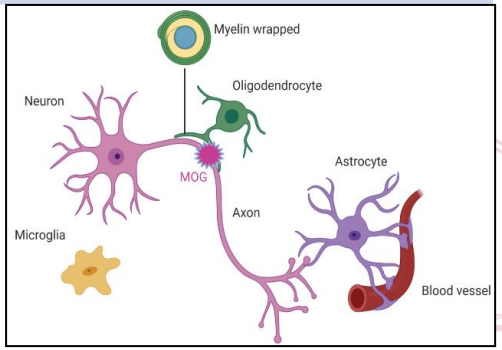
Narayan et al. Mult Scler Rel Dis 2018

Autoimmune inflammatory demyelinating diseases

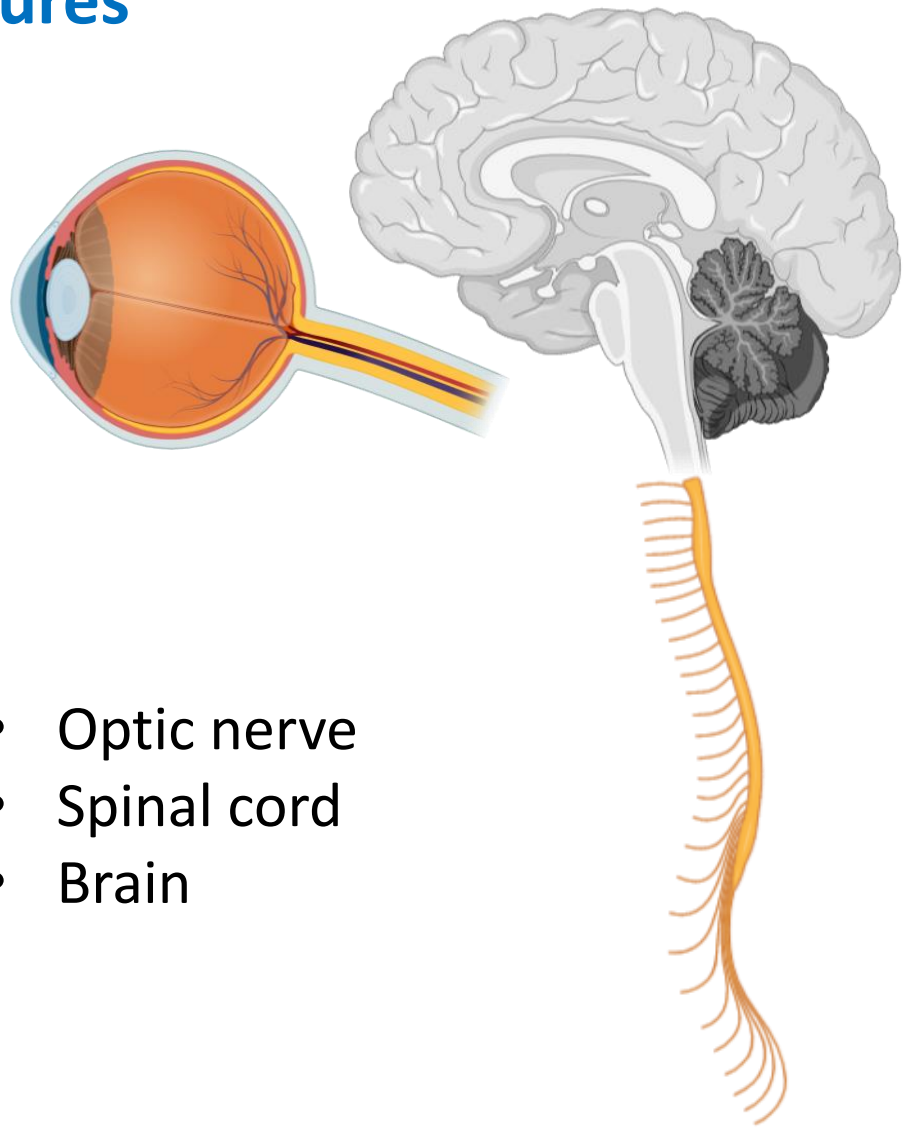
	Multiple sclerosis	AQP4 Ab	MOGAD
Target	**Myelin**	**Astrocyte**	**Myelin**
Female sex %	60-70	80-90	Slight predominance in women
Age at onset (years)	20-40	Around 40	Early to mid-30s
Disease course	Relapsing	Relapsing	Monophasic or relapsing
Attack severity	Usually mild	Usually severe	Mild-severe
CSF oligoclonal bands	Usually +	Usually -	Usually -
First-line preventative treatment	Immunomodulators	Immunosupressors	Immunosupressors



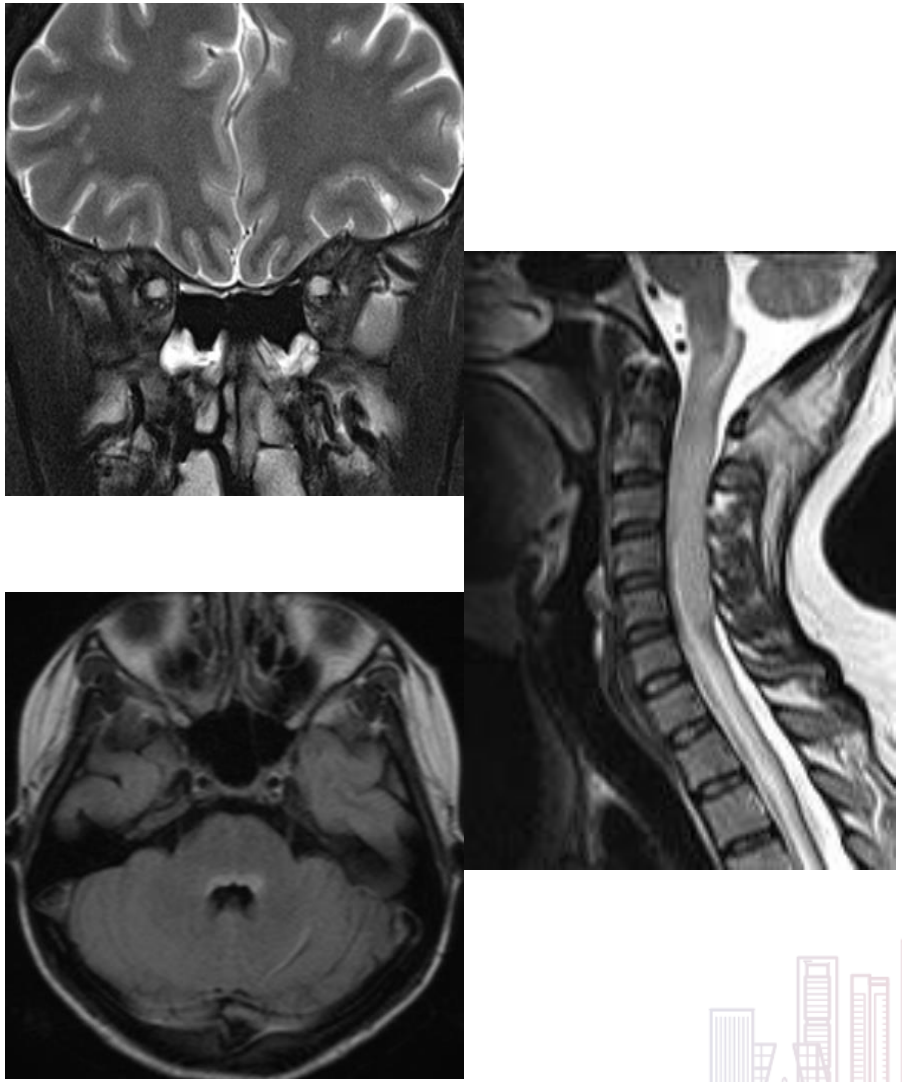




MRI features

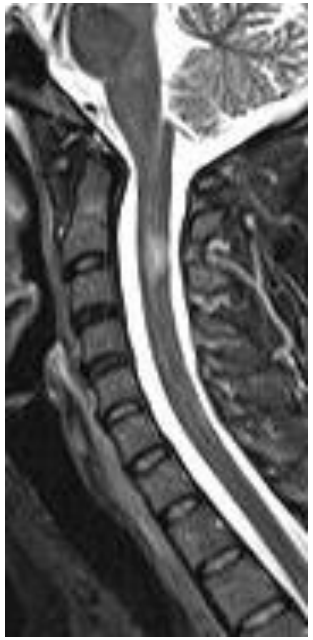


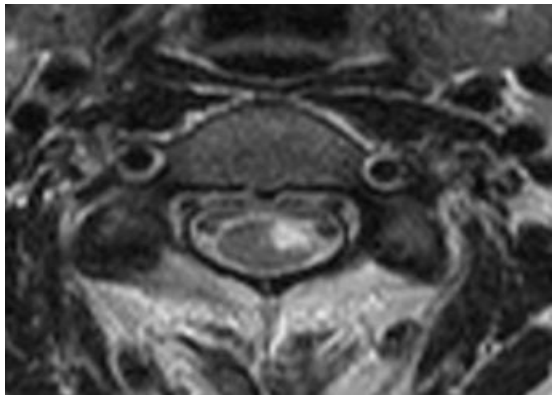
- Optic nerve
- Spinal cord
- Brain



Typical MR imaging findings: spinal cord

- ✓No cord swelling (unless active)
- ✓Unequivocal hyperintense T2; focal lesions
- ✓≥3mm in size; <2 vertebral segments long
- ✓Peripheral location, cigar shaped
- ✓Occupying only part of cord cross-section (less than 50%)
- ✓Enhancement uncommon (symptomatic)
- ✓Cervical > thoracic





Bot et al. Neurology. 2004; 62:226-33; Weier et al. Mult Scler 2012;18:1560-9; Gass et al. Lancet Neurol 2015;14:443-54

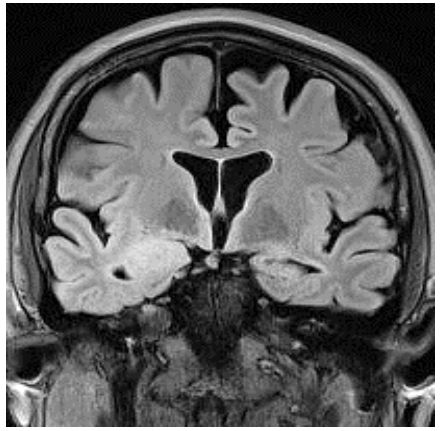
Prevalence of spinal cord lesions in Multiple Sclerosis

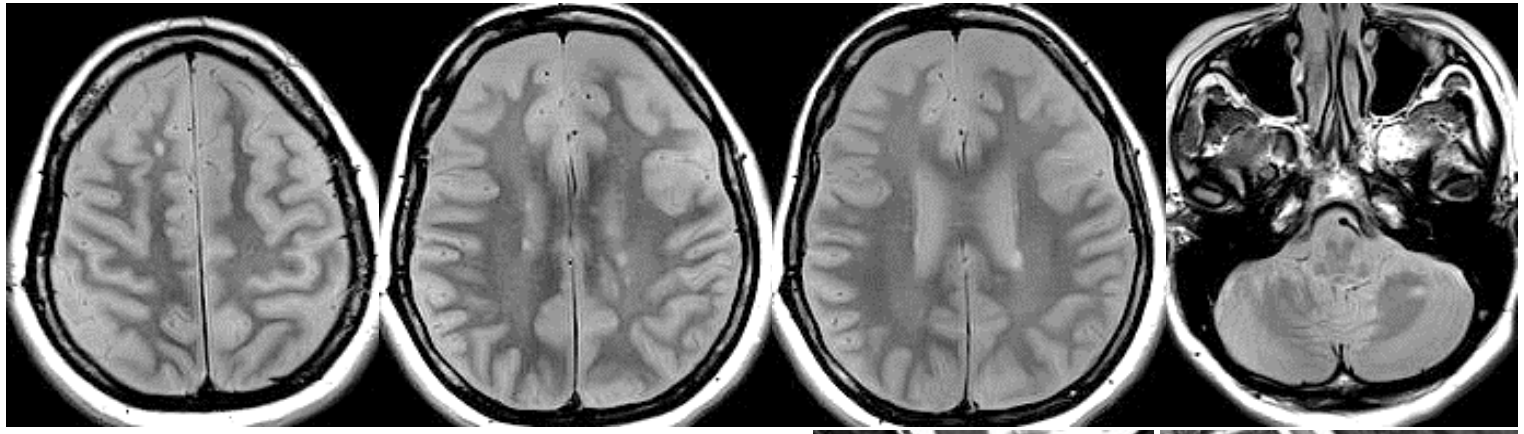
- Spinal cord lesions in **30%** of subjects with RIS
  - *84% progressed to CIS or PPMS (median time 1.6 years)*
  - *OR of clinical progression: 75.3*
- Subclinical lesions in **27-53%** of patients with CIS
- Spinal cord lesions **83%** of patients with early relapsing MS
- Spinal cord lesions in **74-92%** of patients with MS and in **6%** of patients with non-MS white matter diseases

O'Riordan et al. J Neurol Neurosurg Psychiatry. 1998; Dalton et al. J Neurol Neurosurg Psychiatry; Nijeholt et al. Brain 1998; Bot et al. Neurology 2004; Okuda et al. Neurology 2011

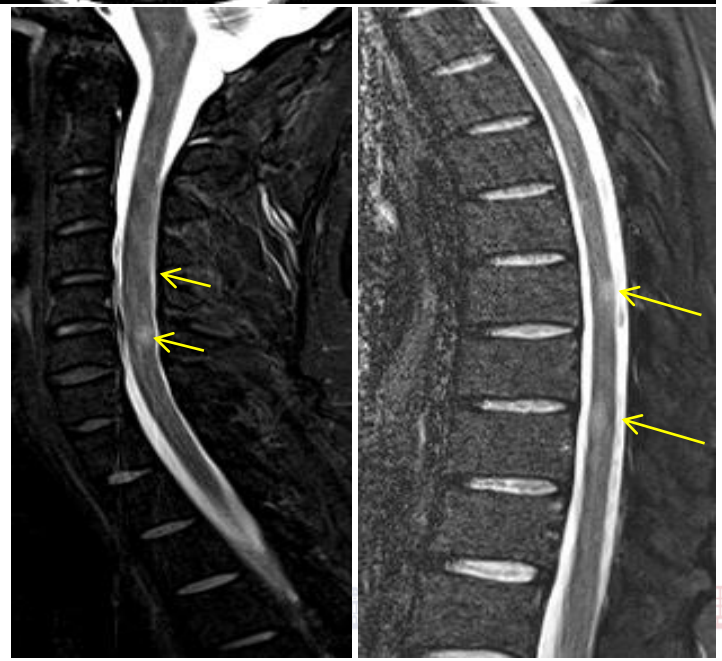
Radiological Isolated Syndrome RIS)

Male, 43 yo





TLE

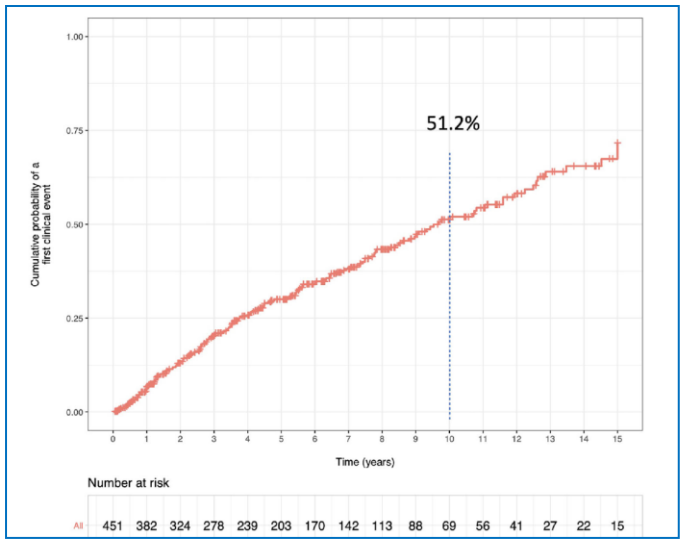


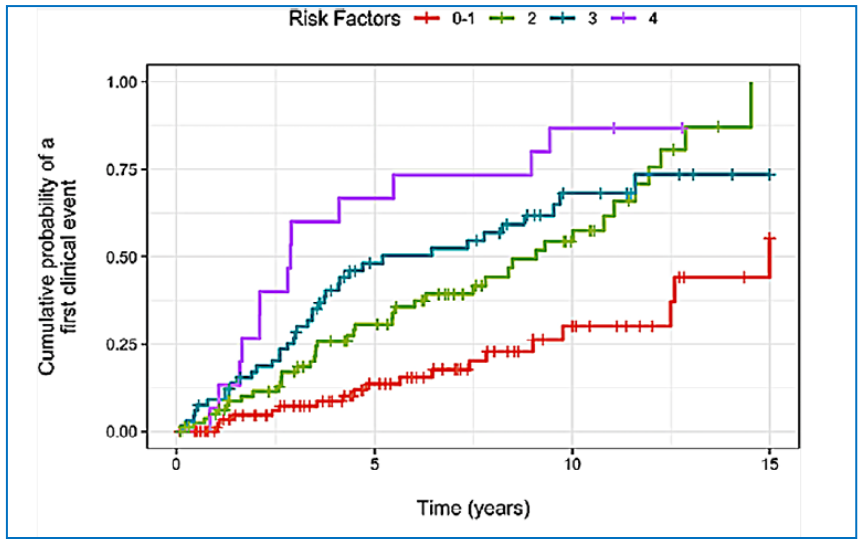
- Radiological isolated syndrome (RIS)
- High probability of MS in 5-10 years

Radiologically Isolated Syndrome (RIS): 10-year risk estimate

21 individual databases from 5 different countries

- Follow-up data available in 277 of 451 RIS subjects (86% female). Median follow-up 6.7 years
- Cumulative probability of a first clinical event at 10 years was **51.2%**.
- **Age, positive cerebrospinal fluid for oligoclonal bands, infratentorial lesions on MRI, and spinal cord lesions**, baseline independent predictors associated with a subsequent clinical event.
- Presence of **gadolinium-enhanced lesions during follow-up** associated with the risk of a seminal event

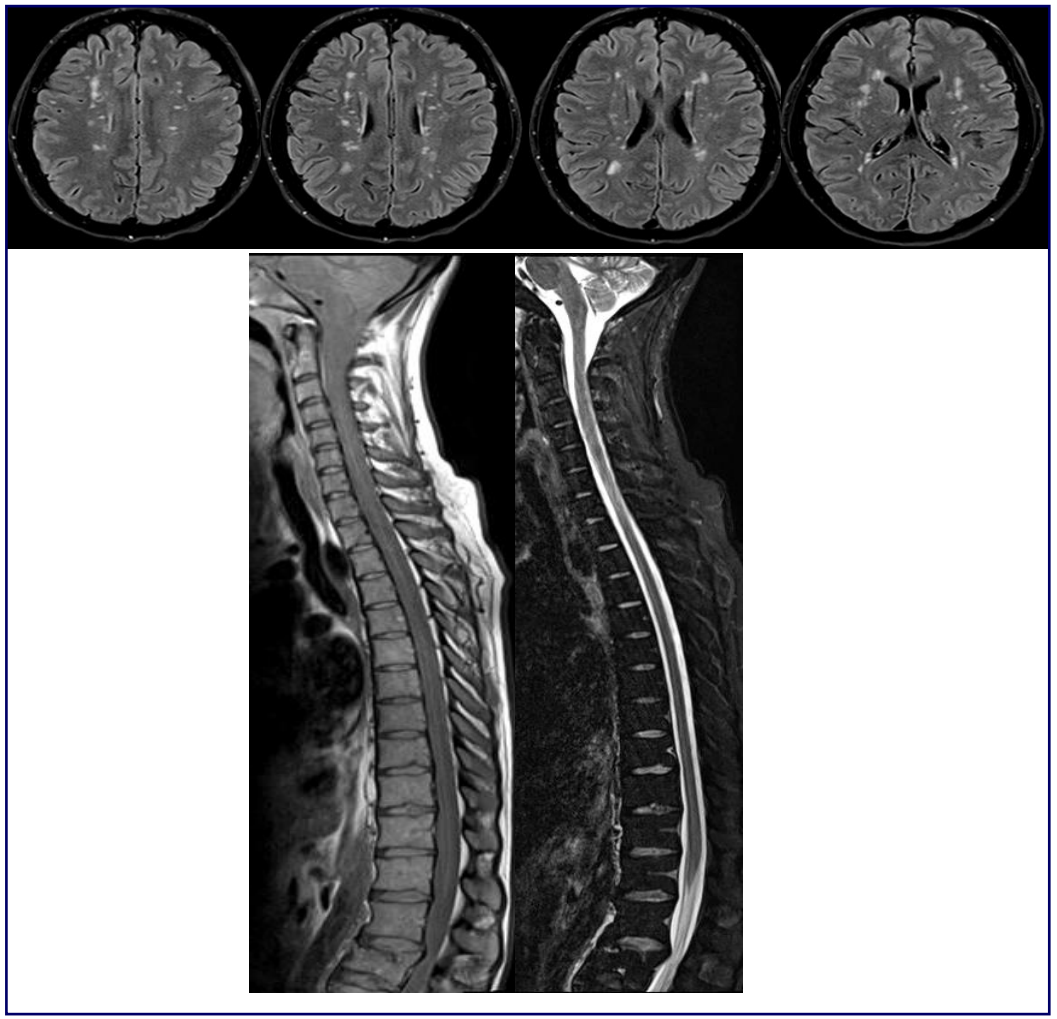


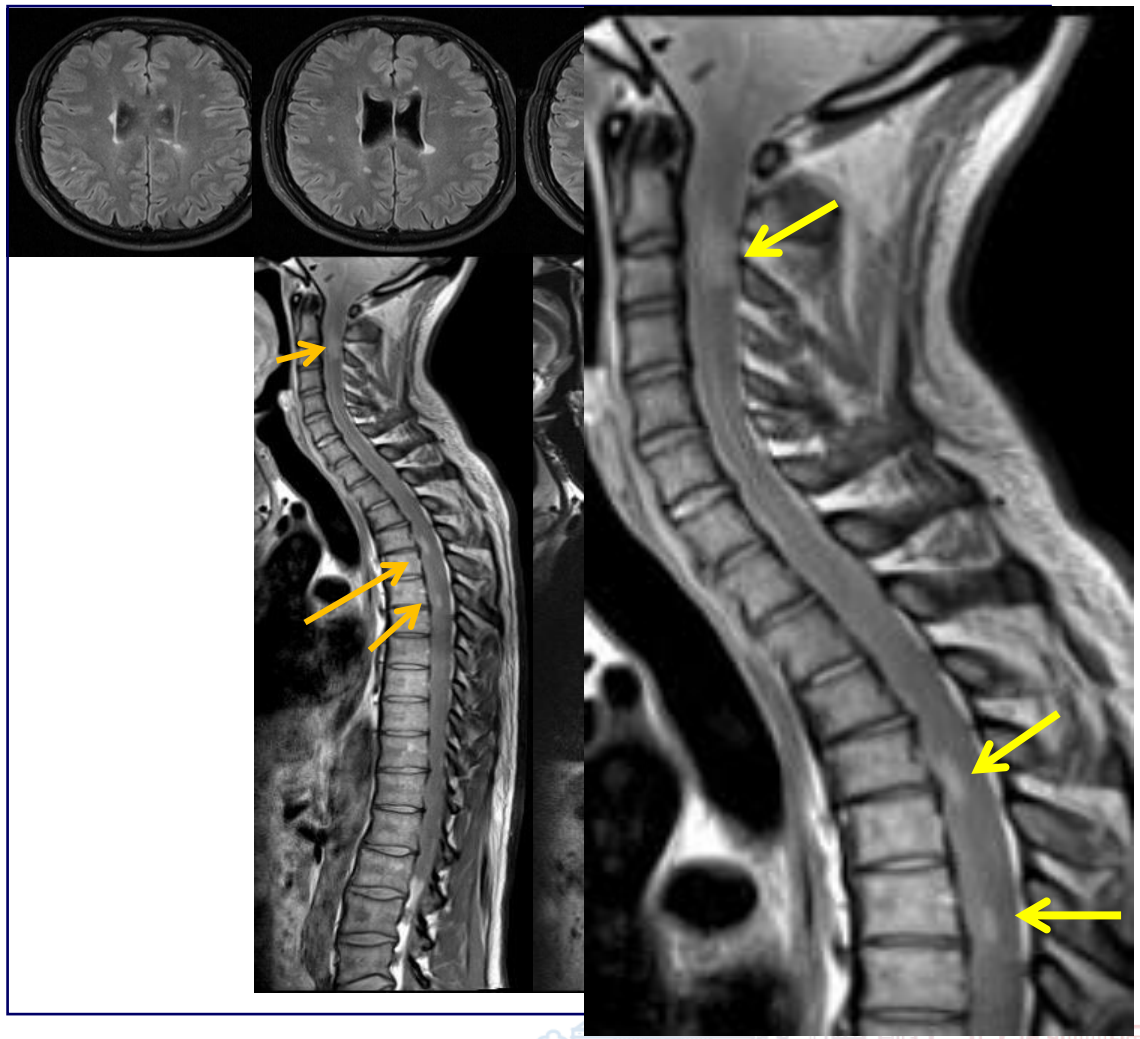


Baseline MRI characteristics	
Presence of ≥3 periventricular lesions, n (%)	440 (98.7)
Missing, n (%)	5 (1.1)
Presence of infratentorial lesions, n (%)	137 (30.4)
Missing, n (%)	5 (1.1)
Presence of juxtacortical lesions, n (%)	400 (90.1)
Missing, n (%)	7 (1.6)
Presence of spinal cord lesions lesions, n (%)	135 (35.2)
Missing, n (%)	65 (14)
Presence of gadolinium-enhancing lesions, n (%)	108 (28.3)
Missing, n (%)	70 (16)

Lebrun-Frenay et al. Ann Neurol 2020

Brain MRI with equivocal findings

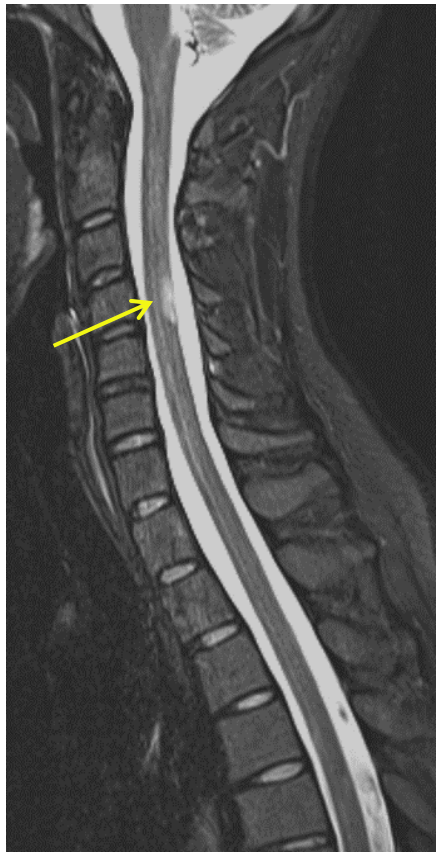




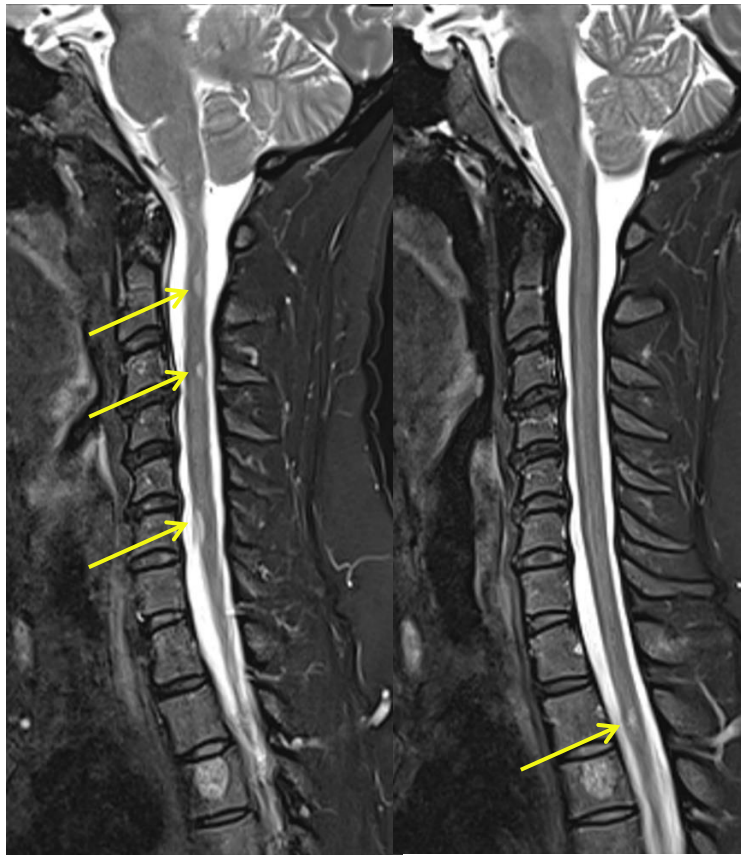
Rovira et al. Nat Rev Neurol 2015;11:471-82.

Lesion patterns in spinal cord MRI

Typical MRI patterns

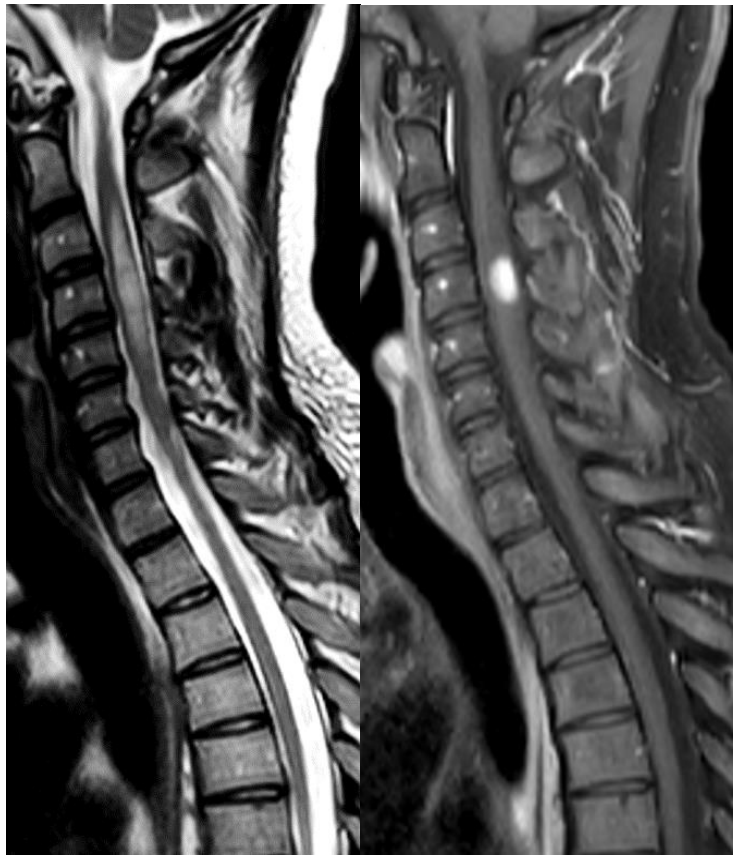


unifocal

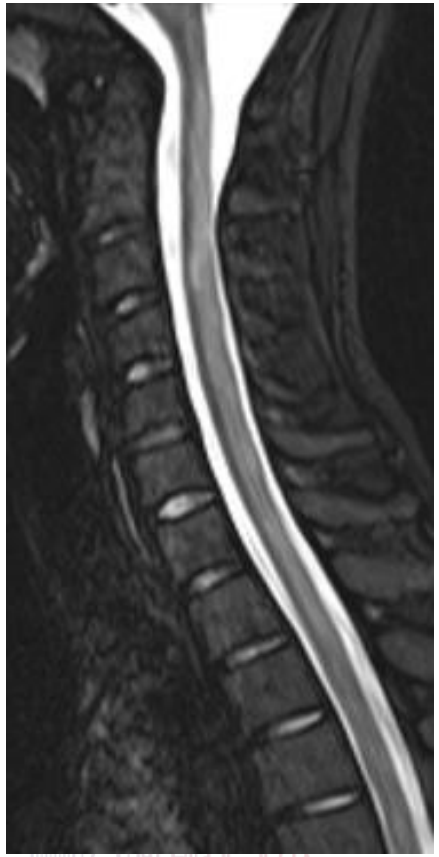


multifocal

Atypical MRI patterns

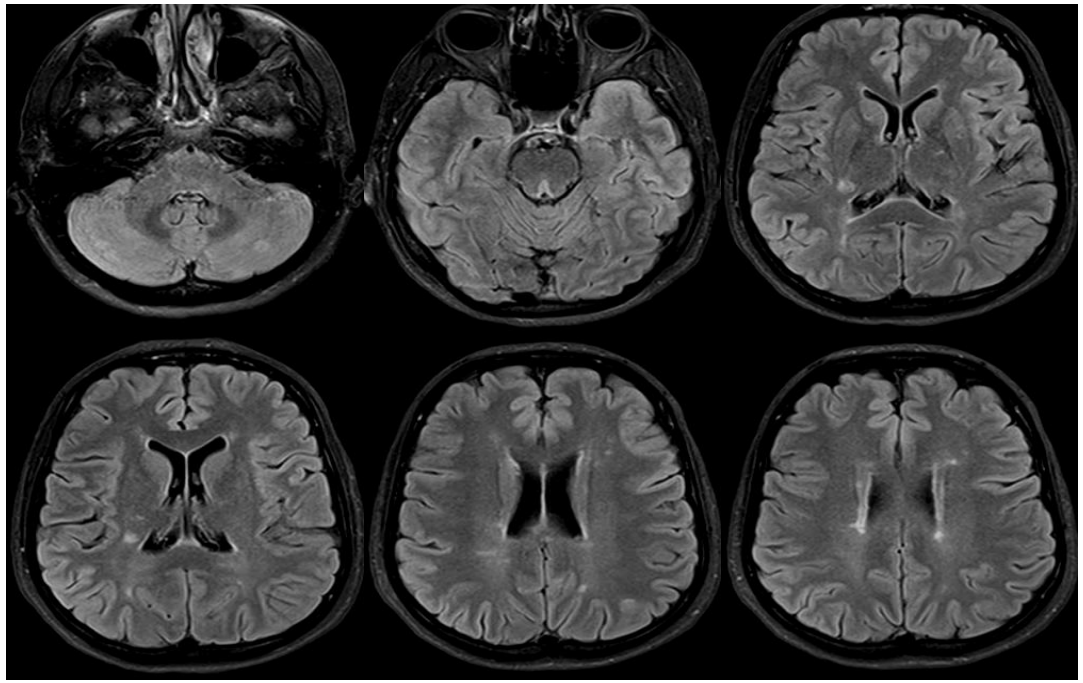


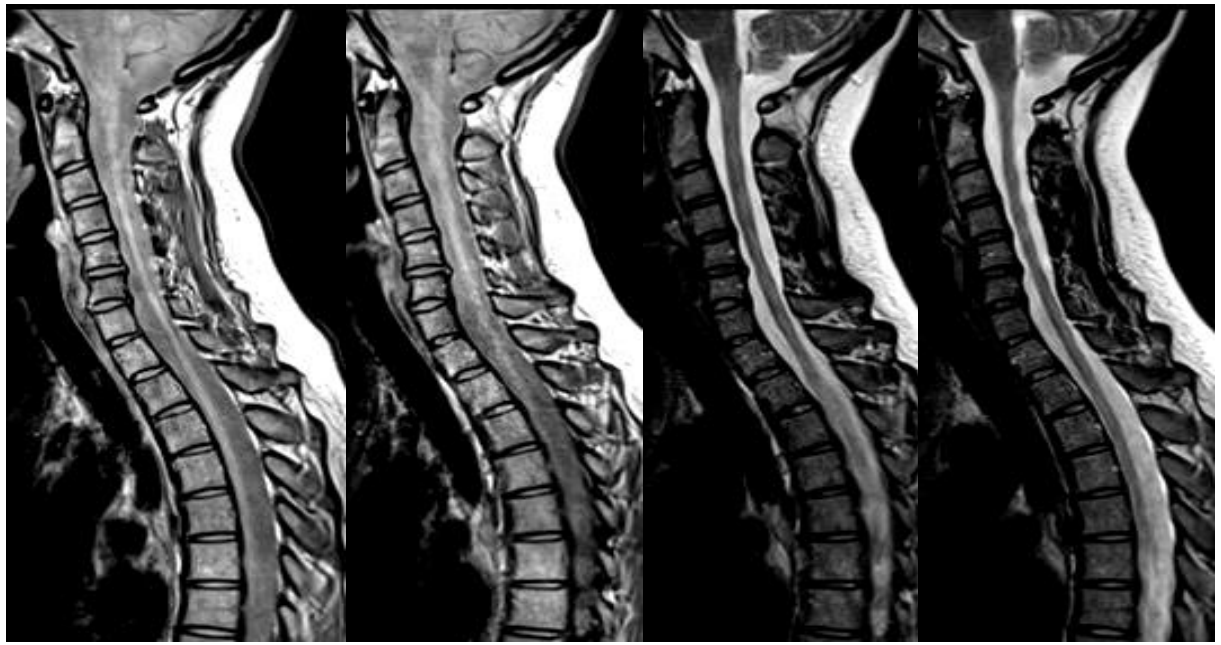
tumefactive



diffuse

Diffuse pattern in spinal cord MRI





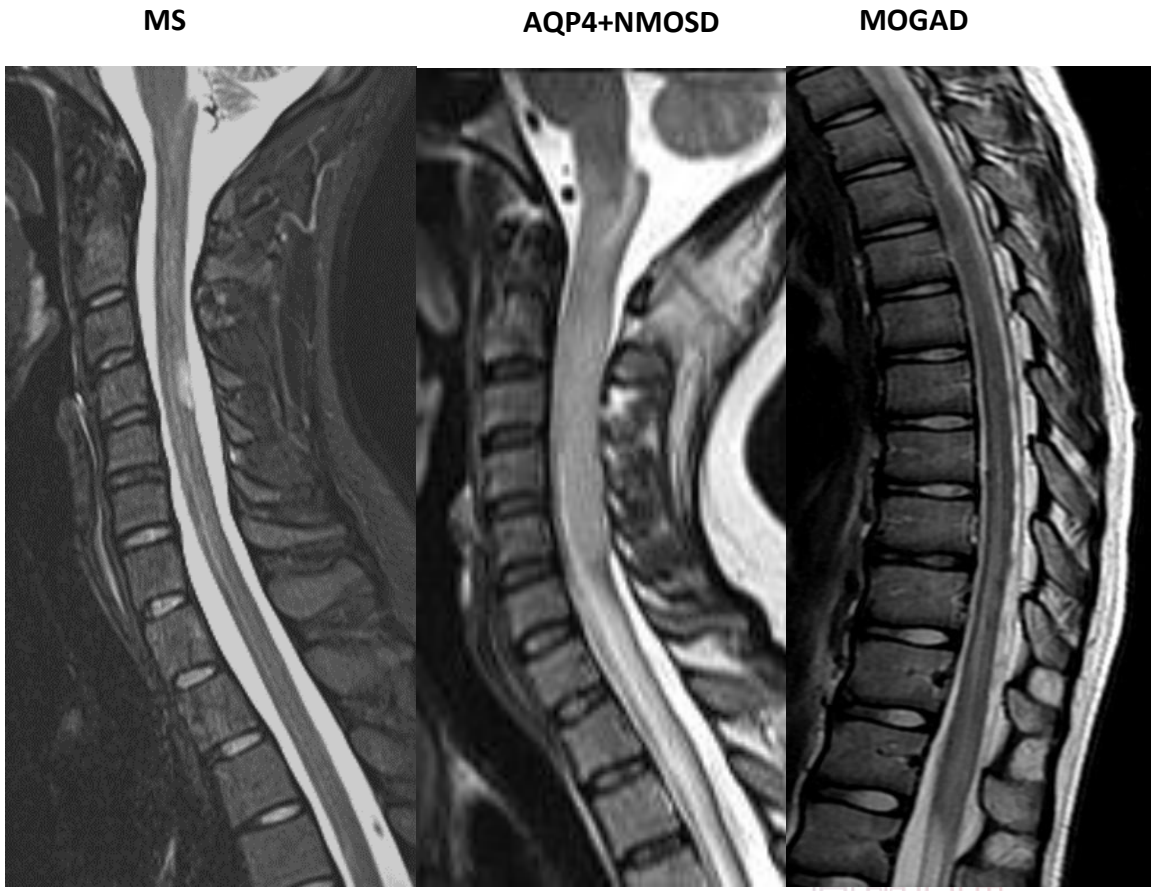
	RR	SP	PP
Spinal cord			
T_2 focal lesion load	2.25 (0–6.5)	2.0 (0–9)	2.4 (0–13)
T_1 focal lesion load	0	0	0
No. of patients with enhancing lesions (%)	0	2 (6%)	0
No. of segments showing diffuse abnormalities (%)	0 (0–19)	0 (0–19)	15 (0–19)§
No. of patients with diffuse abnormalities (%)	6 (21%)	10 (31%)	19 (61%)¶
CSA (mm^2)	77.5 (49–91.5)‡	67 (53–96)	72 (57.5–96)

Lycklama et al. Brain 1998

Spinal cord MRI features: MS, AQP4+, Anti-MOG

Characteristics MRI spine	MOG-IgG	AQP4 IgG	MS
Longitudinal extensive T2 lesion(s)	**Frequent**	**Very frequent**	**Very rare (pediatric)**
Short T2 lesion (s)	**Frequent**	**Infrequent**	**Very frequent**
Grey matter restricted (axial H shape, sagittal line)	Frequent (30-50%)	Infrequent (8%)	Not seen
Marginal (dorsal, lateral)	Rare	Rare	Very frequent (wedge-shaped)
Conus involvement	**25%**	**Rare**	**Rare**
Multiple lesions	Frequent	Rare	Frequent
Enhancement	Infrequent	Frequent (lens shape)	Frequent (nodular/ring)

Modified from Dubey et al. JAMA Neurol 2018



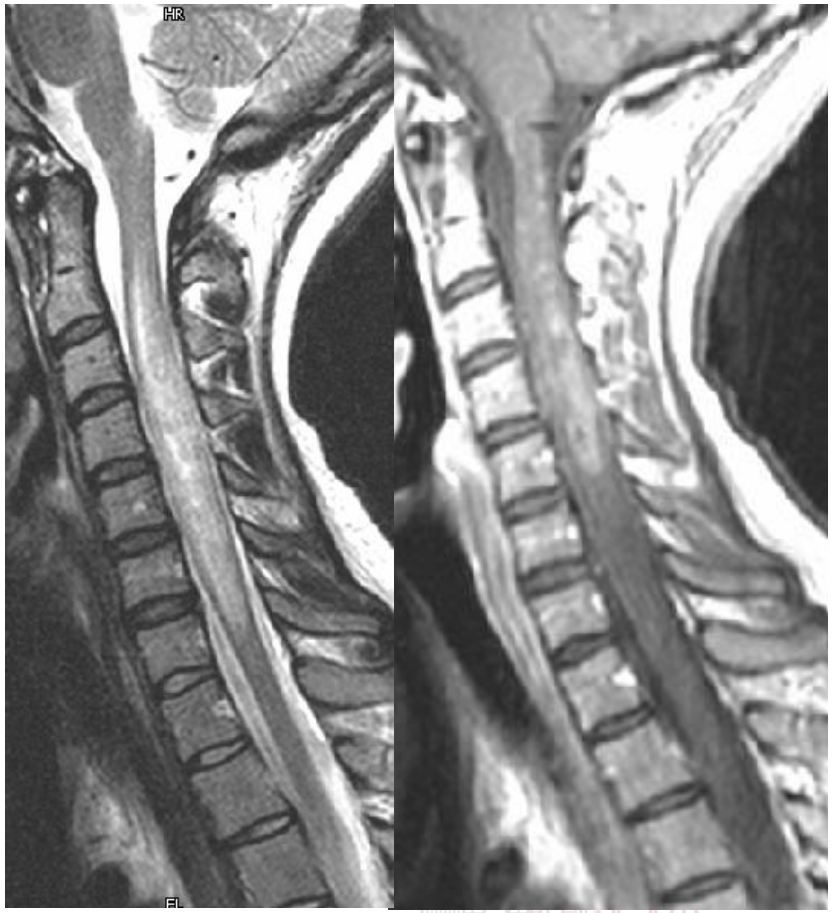
NMOSD, Neuromielitis optica spectrum disorder; MOG, Myelin oligodendrocyte glycoprotein; MS, multiple sclerosis; AQP4, aquaporin 4

Longitudinally extensive transverse myelitis (LETM)

Represents 2-10% of transverse myelitis

Diferential diagnosis

- **NMOSD (including MOGAD)**
- Myelitis associated with systemic autoimmunity (Behçet, Sjögren/SLE)
- Infectious: HIV, HTLV, herpes, TB…
- Post-infectious myelitis (including ADEM)
- Neurosarcoidosis
- Progressive MS with confluence of lesions /diffuse pattern
- Neoplastic and Paraneoplastic myelitis, GFAP antibodies
- Vascular causes (spinal cord infarction, dural AVF)
- Cervical spondylotic myelopathy
- Metabolic: B12, copper deficiency



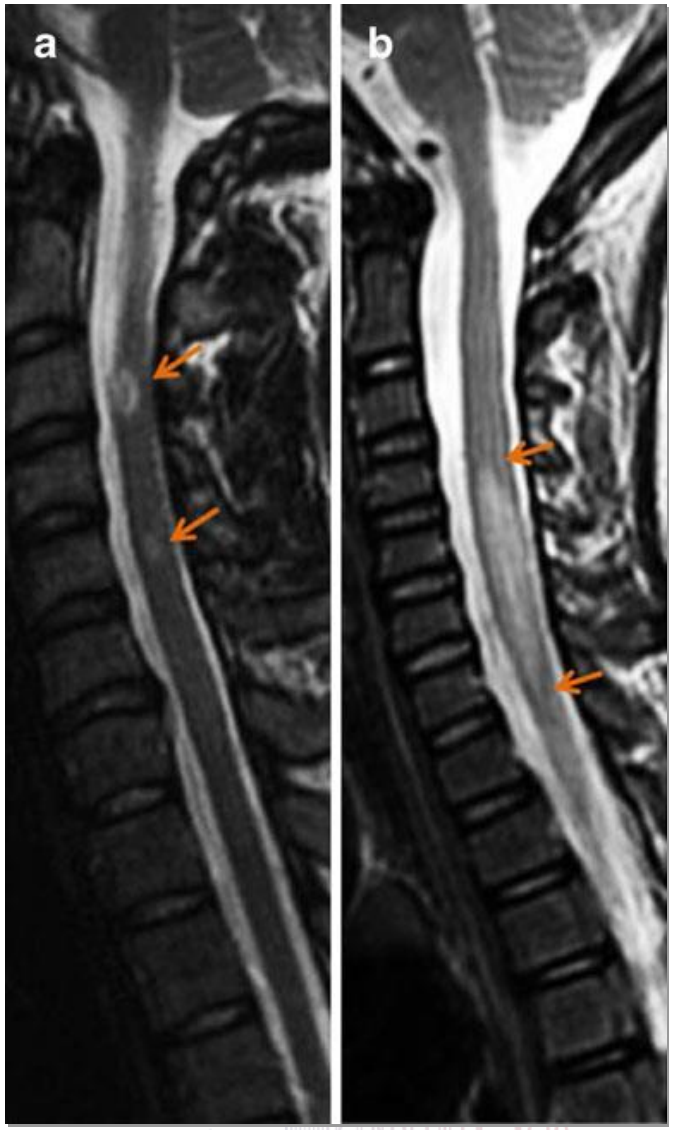
NMOSD AQP4 +

Kitley et al. Mult Scler J 2012; Trebst et al. Nat Rev Neurol 2011; Barnet et al. AJNR 2014

Spinal cord MRI in pediatric MS

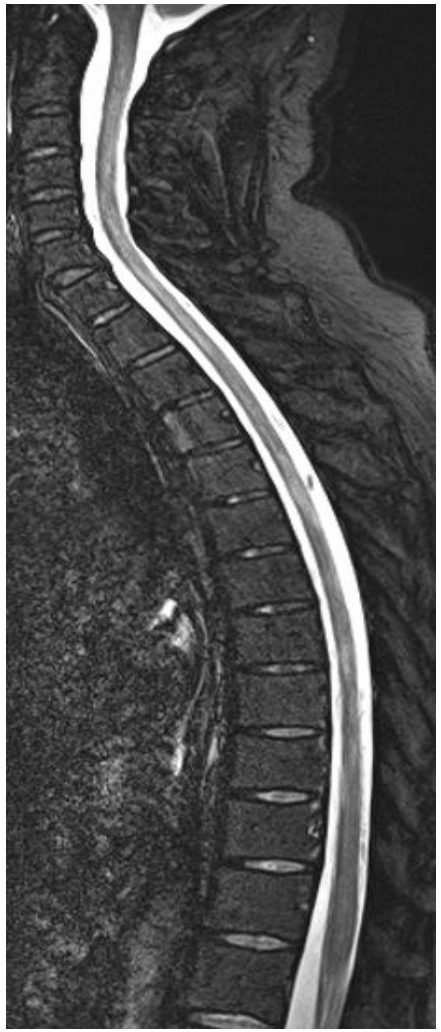
36 children (age, 14.3±3.3) with RRMS
MOG Ab not tested!!

	Summary statistics
Number of lesions per patient, median (IQR, range)	1 (1, 1–6)
Number of children with, *n* (%)	
Focal lesions	23 (64)
Longitudinally extensive lesions	3 (8)
Both	3 (8)
Number of children with lesions in each region, *n* (%)	
Cervical	11 (31)
Thoracic	9 (25)
Cervical and thoracic	9 (25)
Lumbar	0
Number of children with gadolinium enhancing lesions, *n* (%)[a]	5 (31)
Number of lesions detected in 36 children, *n* (%)	60 (100)
Number of focal lesions, *n* (%)	54 (90)
Number of longitudinally extensive lesions, *n* (%)	6 (10)

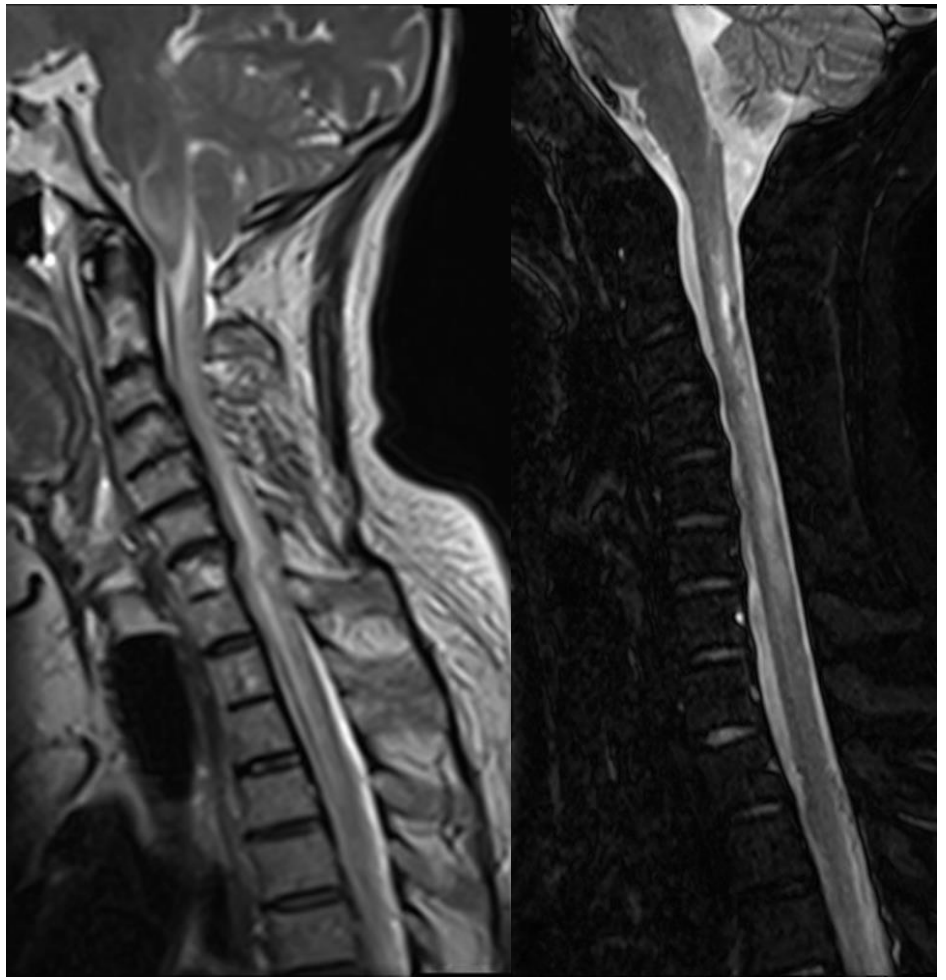


Verhey LM et al. *Neuroradiology* 2010, 52: 1153-62

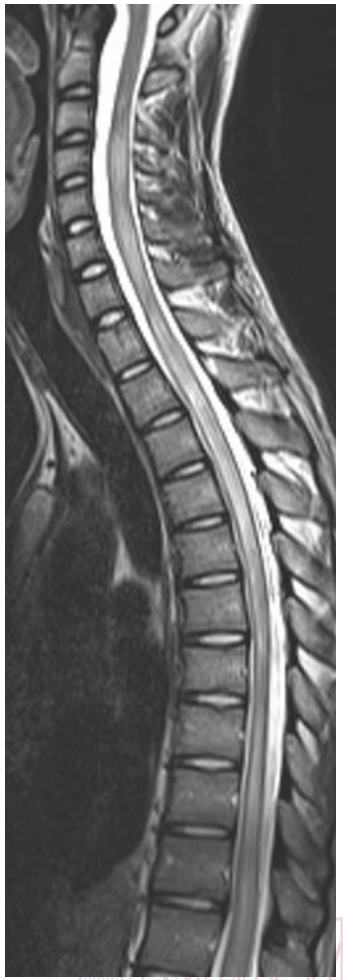
Diffuse pattern in spinal cord MRI



MS



AQP4 + NMOSD



MOGAD

Spinal cord MRI features: MS, AQP4, Anti-MOG

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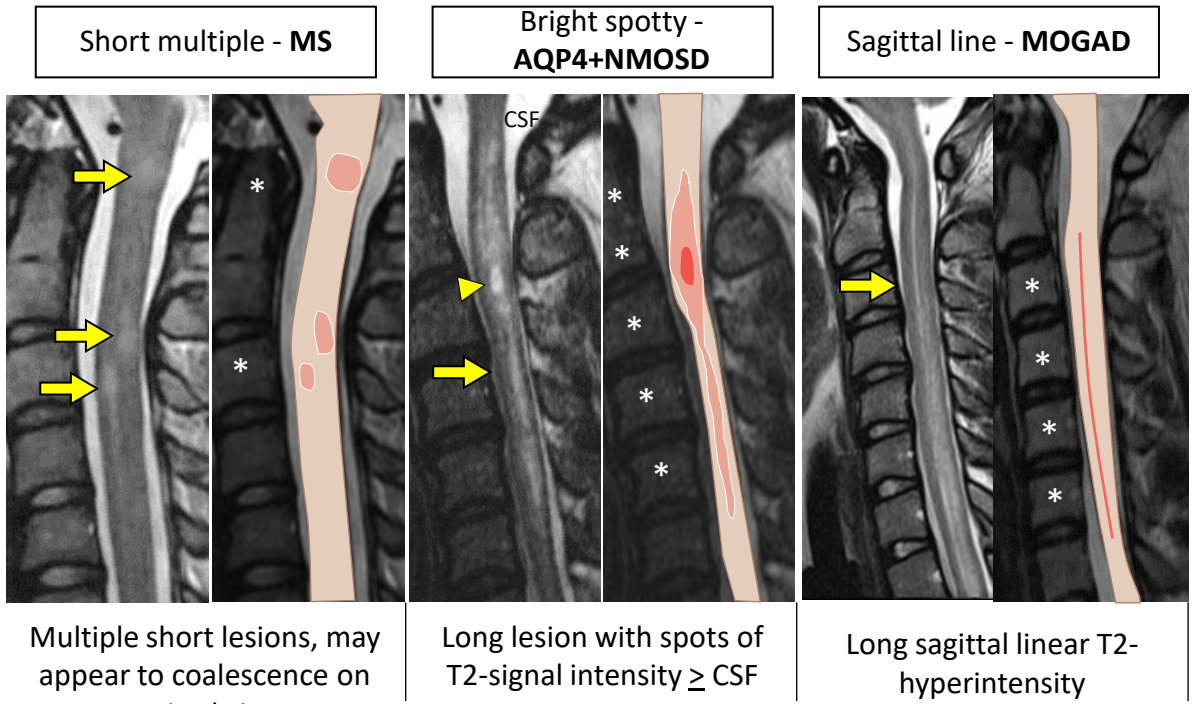
Courtesy of L. Cacciaguerra (Milan)



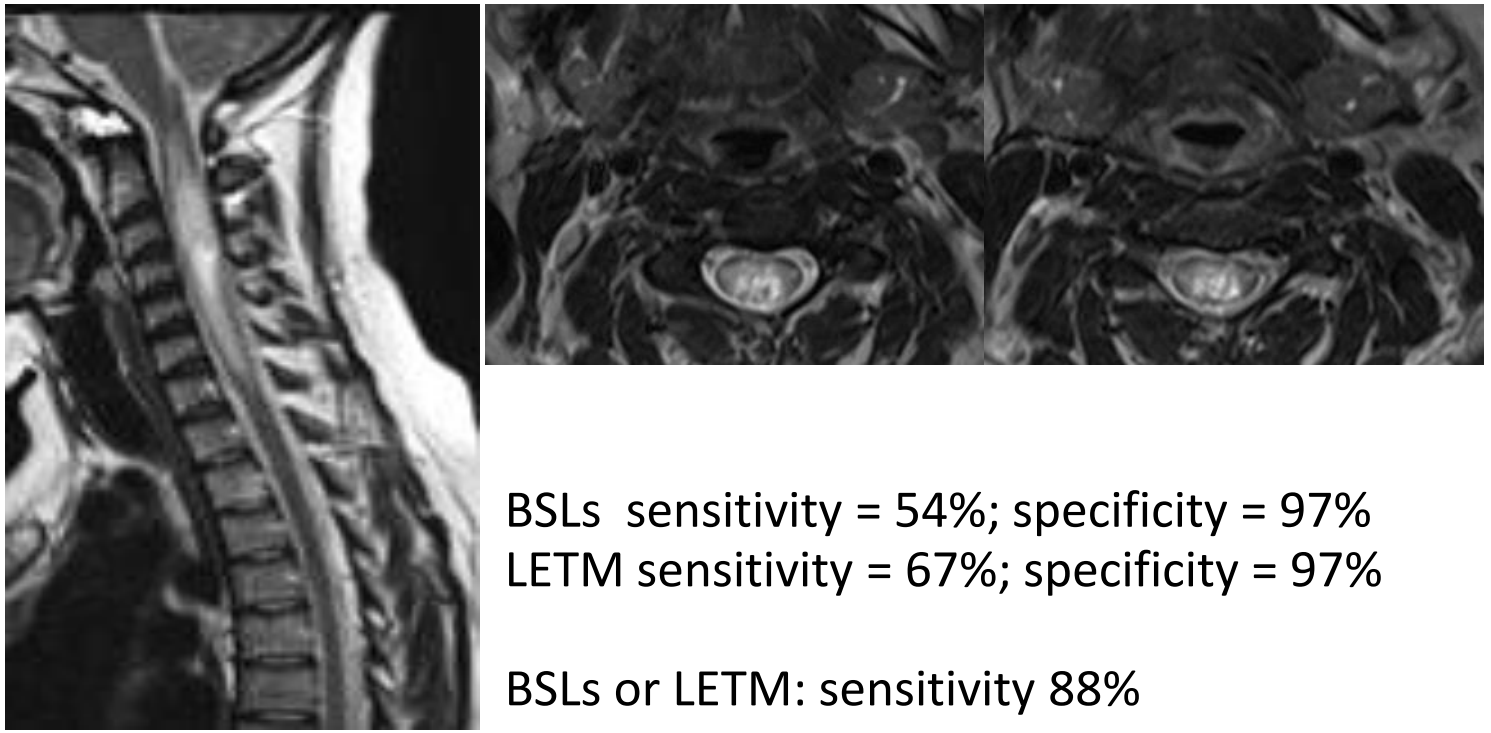
Modified from Dubey et al. JAMA Neurol 2018

NMOSD, Neuromielitis optica spectrum disorder; MOG, Myelin oligodendrocyte glycoprotein; MS, multiple sclerosis; AQP4, aquaporin 4

Bright spotty lesion pattern: specific pattern for NMOSD

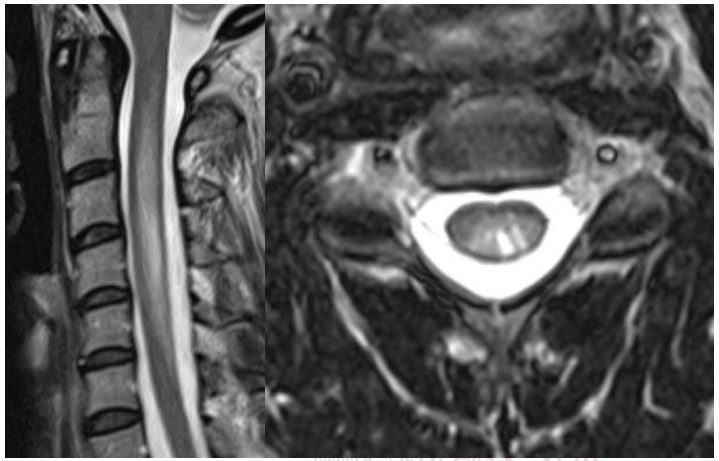
- Very hyperintense spotty lesions on axial T2WI
- More hyperintense than that of surrounding cerebrospinal fluid

Yonezu T et al. Mult Scler 2013

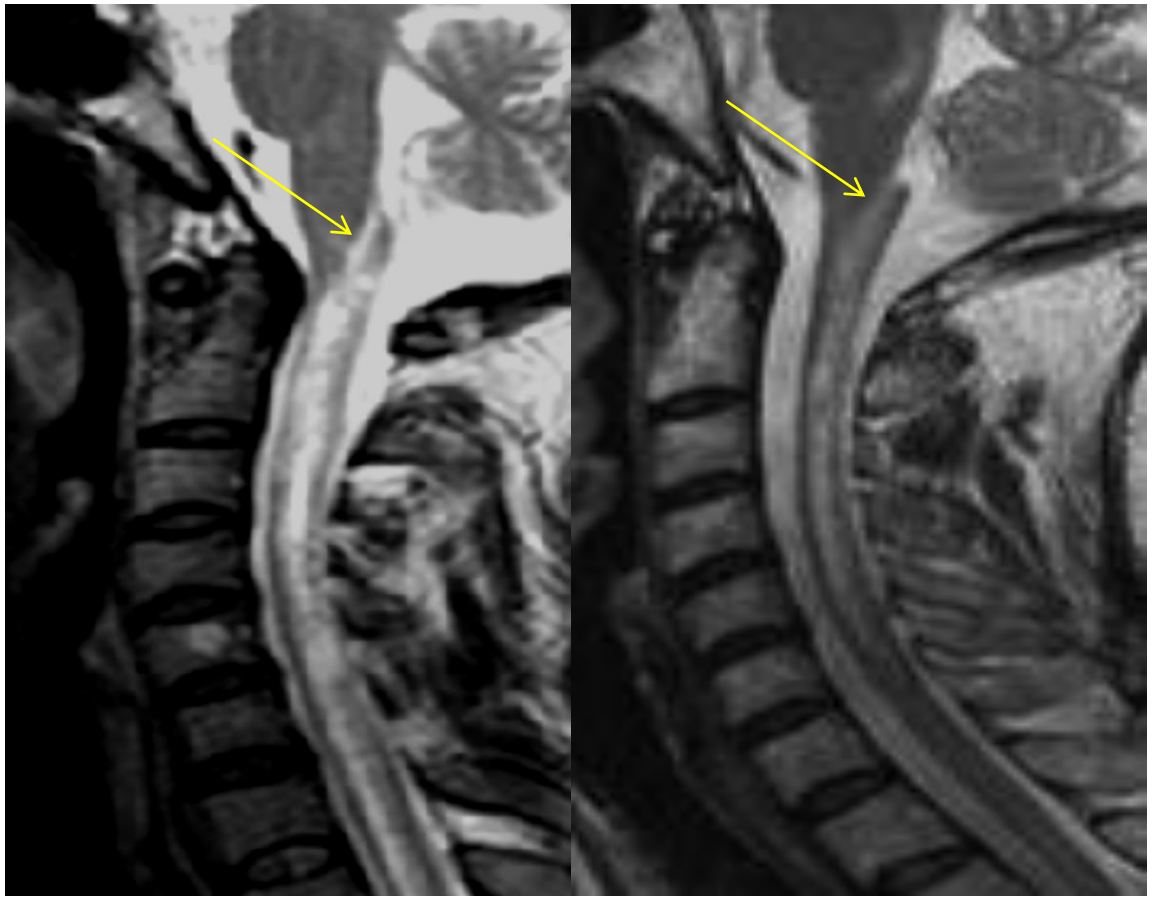


BSLs sensitivity = 54%; specificity = 97%
LETM sensitivity = 67%; specificity = 97%

BSLs or LETM: sensitivity 88%

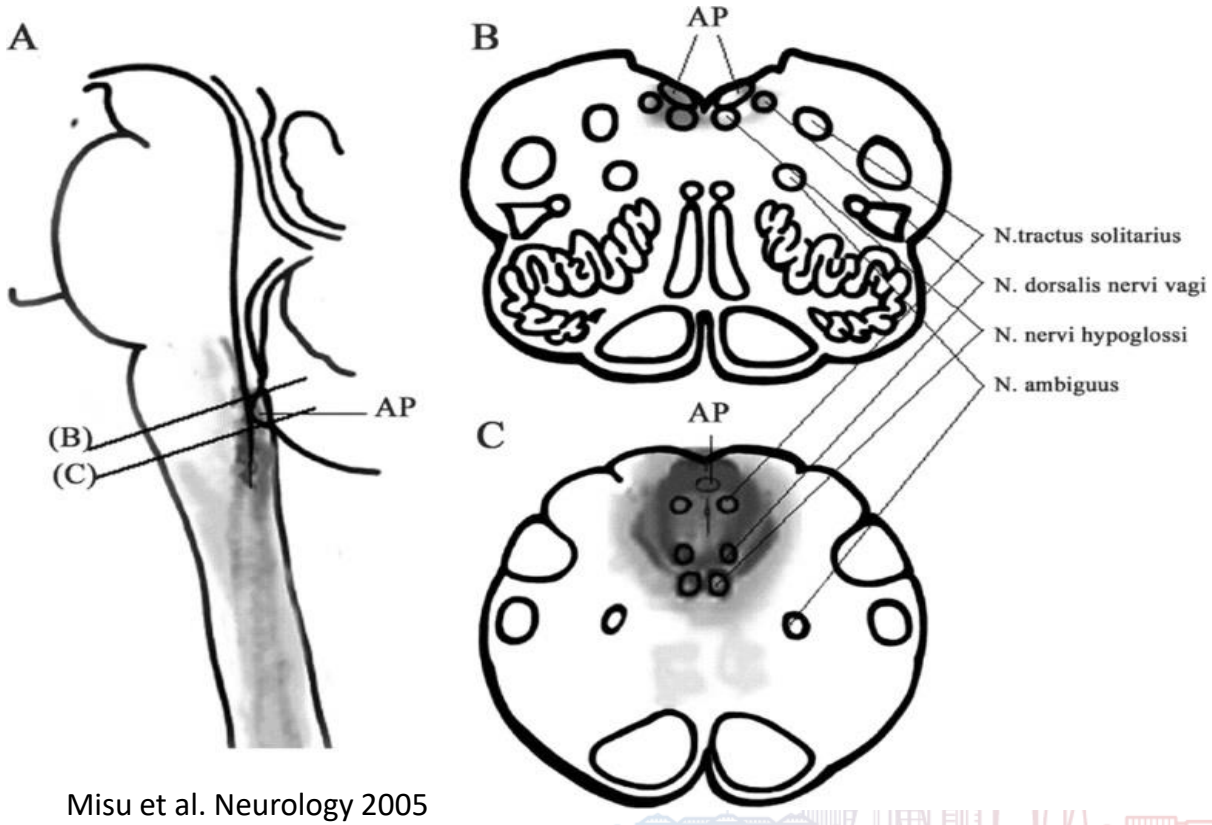


Area postrema extension: specific pattern for AQP4+ NMOSD



Intractable hiccup and nausea

Linear lesion at the region of area postrema typically seen in NMOSD and causes intractable vomiting



Misu et al. Neurology 2005

Spinal cord MRI features (transverse): MS, AQP4, Anti-MOG

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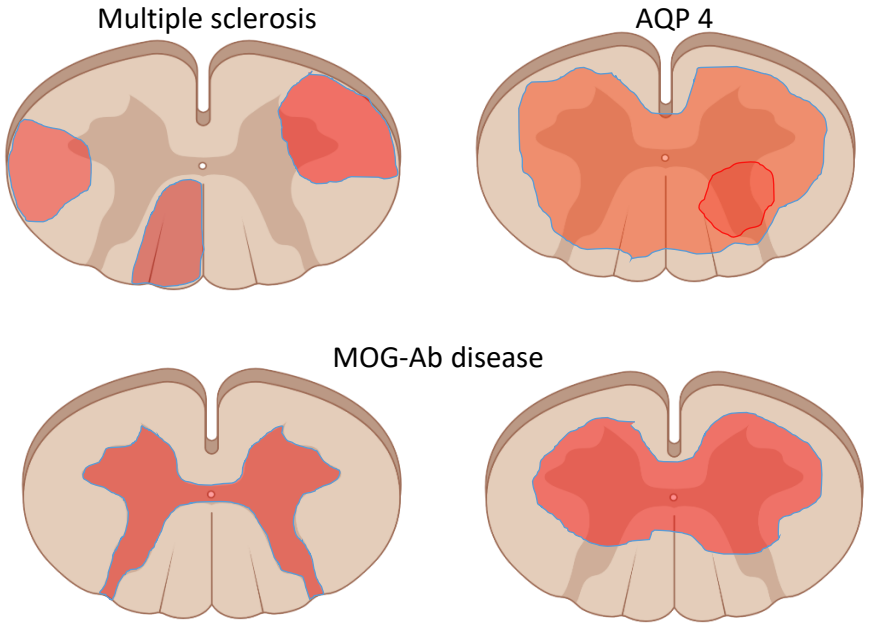

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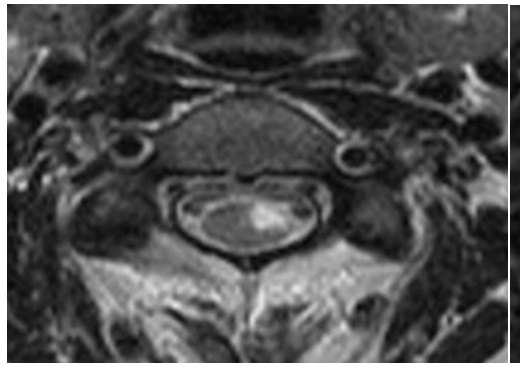
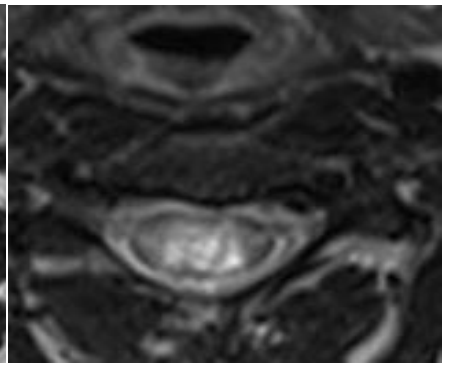
Enhancement	Infrequent	Frequent (lens shape)	Frequent (nodular/ring)

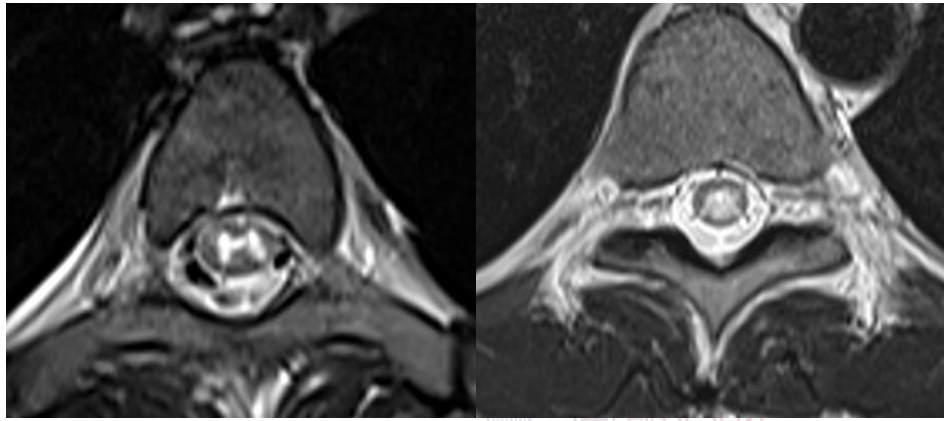
Multiple sclerosis



AQP 4

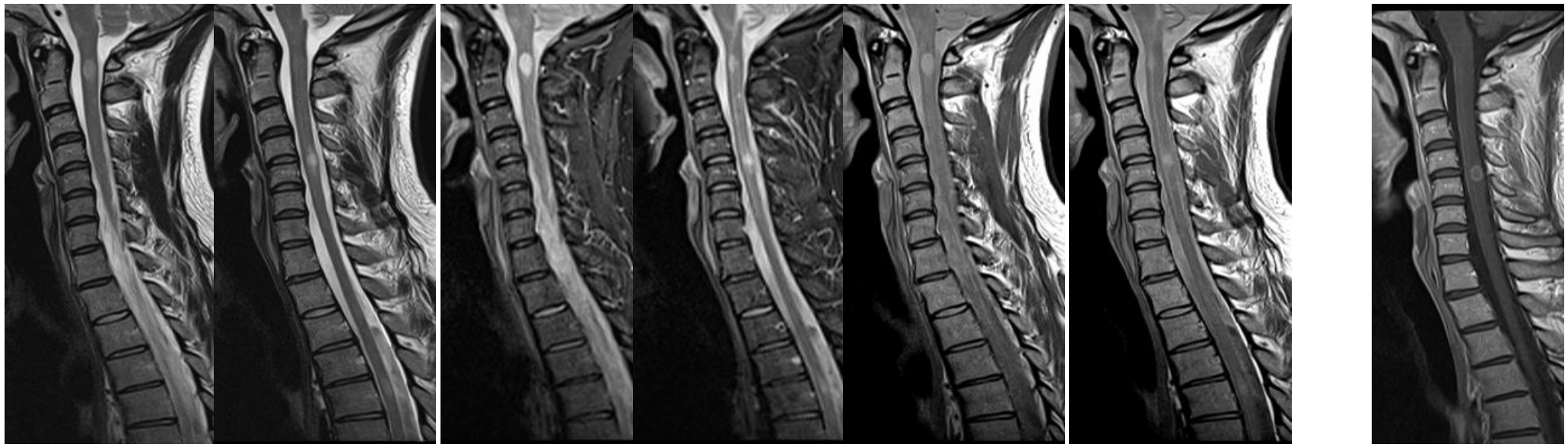


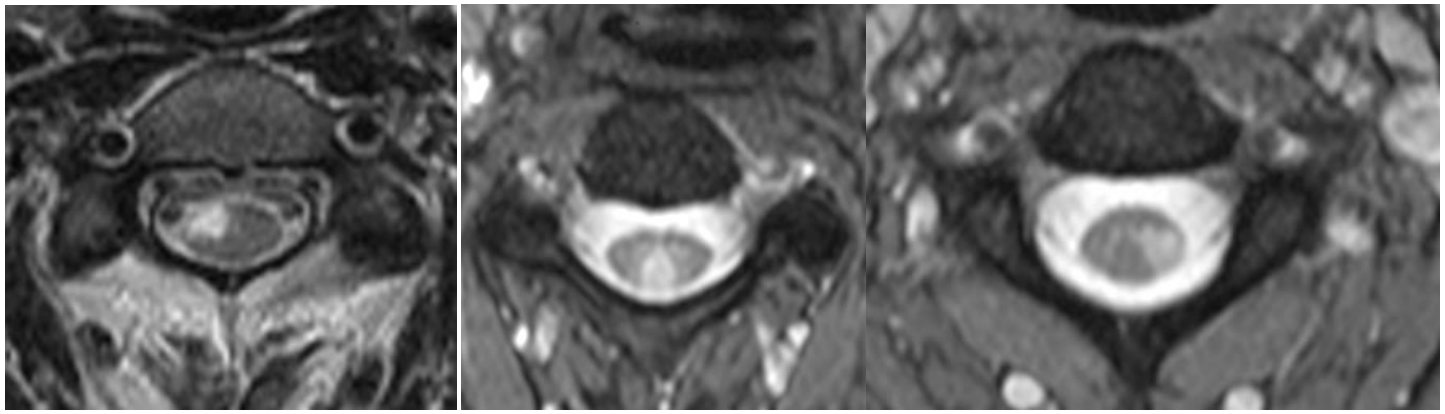
MOG-Ab disease

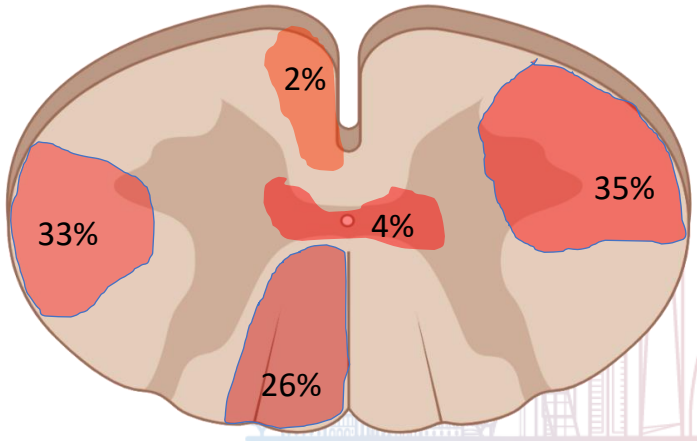


NMOSD, Neuromielitis optica spectrum disorder; MOG, Myelin oligodendrocyte glycoprotein; MS, multiple sclerosis; AQP4, aquaporin 4

Short-segment mielitis plus eccentric tract-specific pattern



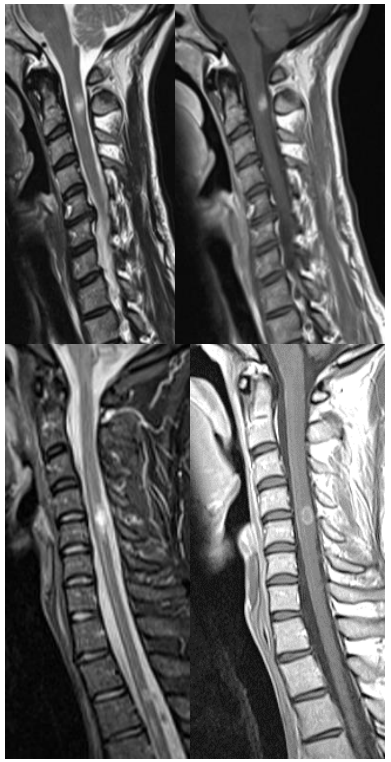




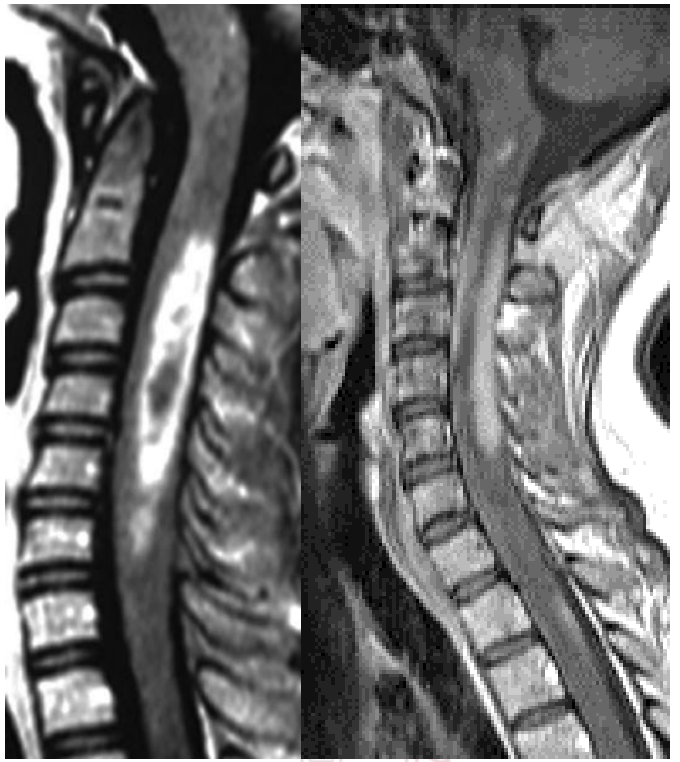
Modified from Weier et al. Mult Scler 2012;18:1560-9

Spinal cord MRI features (transverse): MS, AQP4, Anti-MOG

Characteristics MRI spine	MOG-IgG	AQP4 IgG	MS
Longitudinal extensive T2 lesion(s)	Frequent	Very frequent	Very rare (pediatric)
Short T2 lesion (s)	Frequent	Infrequent	Very frequent
Grey matter restricted (axial H shape, sagittal line)	Frequent (30-50%)	Infrequent (8%)	Not seen
Marginal (dorsal, lateral)	Rare	Rare	Very frequent (wedge-shaped)
Conus involvement	25%	Rare	Rare
Multiple lesions	Frequent	Rare	Frequent
Enhancement	**Infrequent**	**Frequent (lens shape, peripheral)**	**Frequent (nodular/ring)**



MS: nodular/ring



NMOSD: lens/peripheral

NMOSD, Neuromielitis optica spectrum disorder; MOG, Myelin oligodendrocyte glycoprotein; MS, multiple sclerosis; AQP4, aquaporin 4

MS diagnosis: McDonald 2017 criteria

Dissemination in space (DIS)

- **≥1 T2 lesion* in 2 out of 4 regions of the CNS**
  - Periventricular
  - Cortico-Juxtacortical
  - Infratentorial
  - Spinal cord

CNS= central nervous system; Gd=gadolinium, CSF=cerebrospinal fluid
*Gd not needed for demonstration of DIS

Dissemination in time (DIT)

- Simultaneous presence of Gd+ and non-enhancing lesions at any time

- New T2 and/or Gd+ lesion on follow-up MRI
  - Compared to reference (baseline) MRI

Alternative to DIT

- Presence of CSF specific oligoclonal bands

Thompson AJ et al. Lancet Neurol 2017

Primary progressive multiple sclerosis

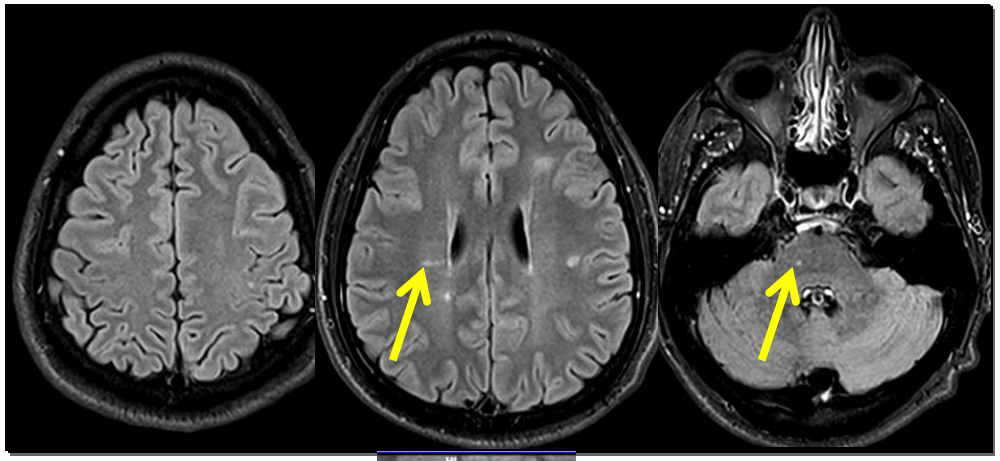
One year of disability progression (retrospectively or prospectively determined) independent of clinical relapse and demonstration of **two of the following**:

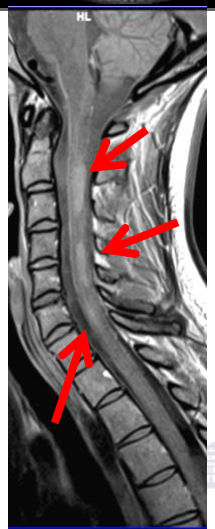
≥1 T2-hyperintense lesions[a] characteristic of MS in ≥1 of 3 areas of the central nervous system:

- Periventricular
- Cortical/juxtacortical
- Infratentorial

≥2 T2-hyperintense spinal cord lesions

CSF-specific OBs





[a] **No distinction between symptomatic and asymptomatic** MRI lesions is required

MS, multiple sclerosis; OB, oligoclonal bands; CSF, cerebrospinal fluid

Thompson AJ et al. Lancet Neurol 2017

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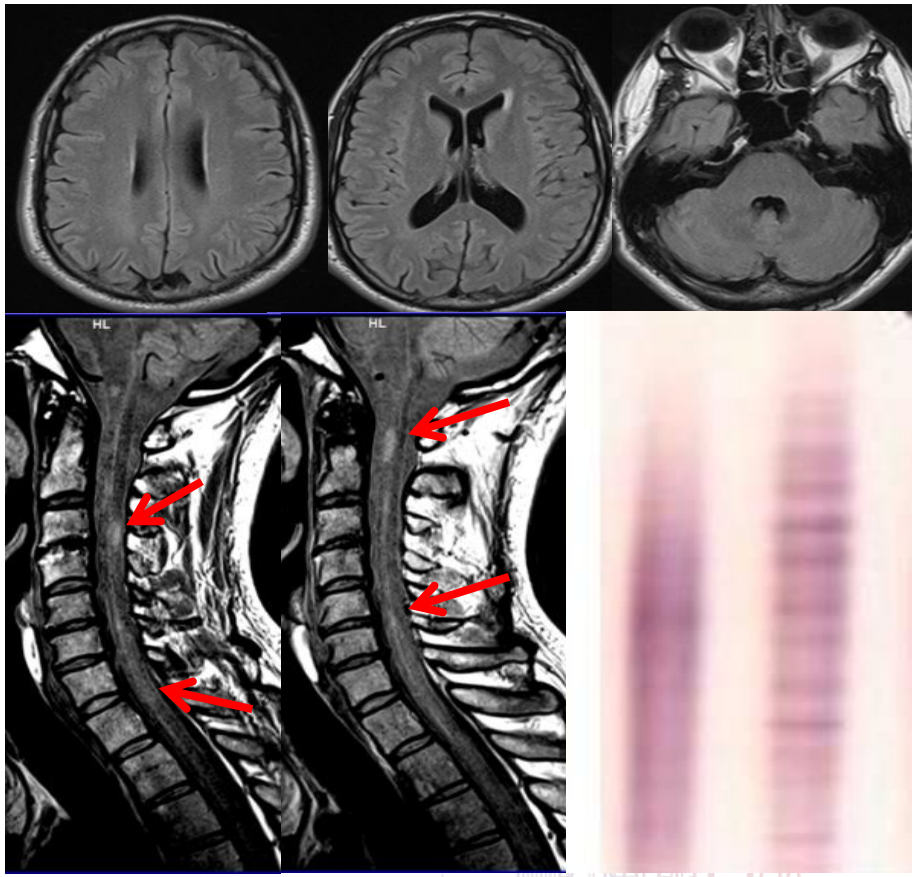


[a] **No distinction between symptomatic and asymptomatic** MRI lesions is required

Thompson AJ et al. Lancet Neurol 2017

NMOSD: 2015 diagnostic criteria

Emphasis on clinical diagnosis rather than solely AQP4-IgG positivity: integration of clinical, serologic, and MR imaging data

+ AQP4-IgG

At least one of the following core clinical characteristics:

- Optic neuritis
- Acute mielitis
- Area postrema syndrome
- Acute brainstem syndrome
- Acute diencephalic syndrome **(typical MRI)**
- Cerebral syndrome **(typical MRI)**

- AQP4-IgG
NMOSD with unknown/nve AQP4-IgG status

At least two of the following core clinical chara

- Optic neuritis **(typical MR**
- Acute mielitis **(typi**
- Area postrem **(typical MRI)**
- Acute h ndrome **(typical MRI)**
- A phalic syndrome **(typical MRI)**
- al syndrome **(typical MRI)**

Additional MR imaging requirements

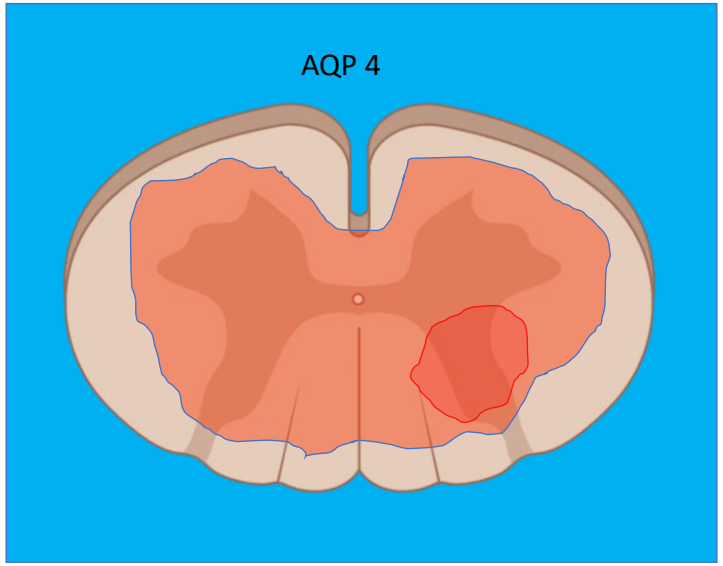
Wingerchuk DM, et al. Neurology. 2015

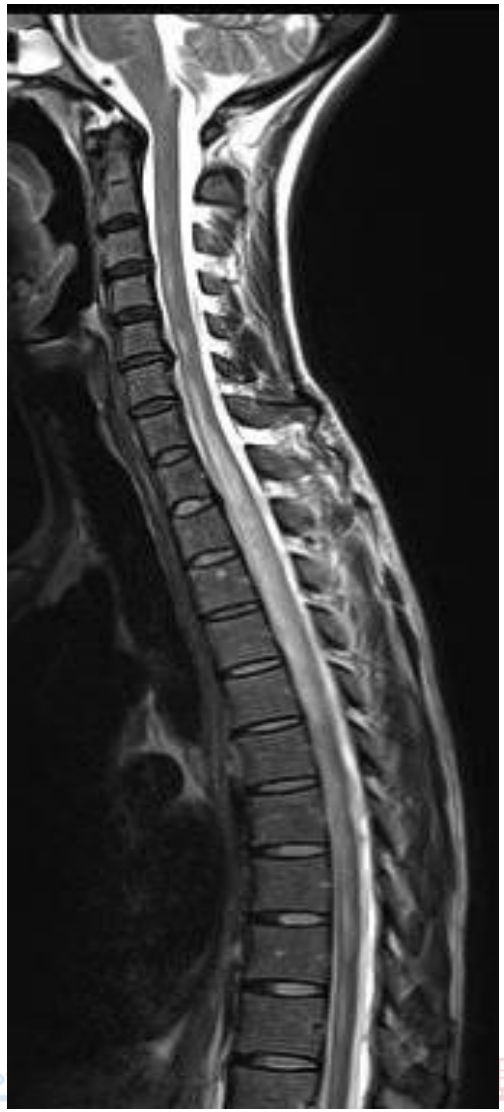
NMOSD: 2015 diagnostic criteria

Additional MRI requirements (AQP4-IgG negative/unknown)

Acute myelitis:

Intramedullary lesions ≥ 3 contiguos segments (LETM)
≥ 3 contiguos segments spinal cord atrophy (history of myelitis)

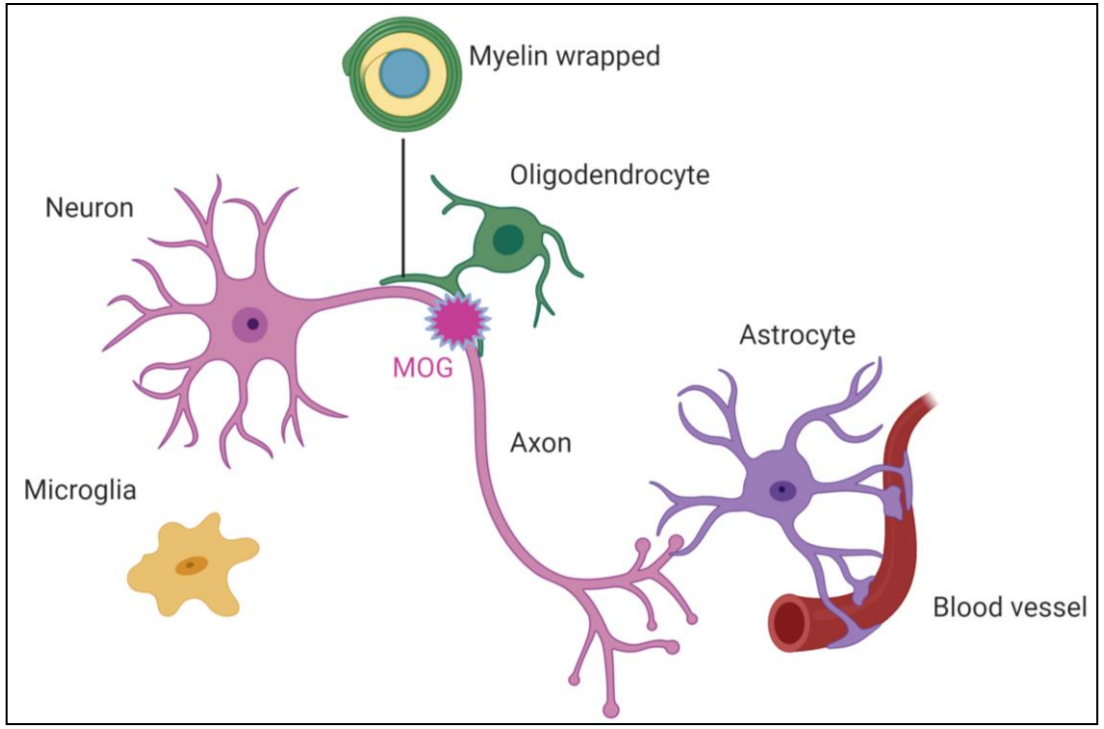




Wingerchuk DM, et al. Neurology. 2015

Myelin Oligodendrocyte Glycoprotein (MOG)-antibody disease (MOGAD)

- Female : Male equal
- No non-Caucasian predominance
- ~ 50% monophasic
- Better outcome than AQP4-antibody disease
- Not associated with other auto-immunity
- Onset with both **Optic Neuritis** + **Transverse Myelitis** common
- Overlap with ADEM (monophasic & relapsing)



Parrotta and Kister. Front Neurol 2020

MOGAD diagnosis requires: MOG-IgG positivity + compatible clinical-MRI phenotype
Risk of false positive MOG-IgG (up to 28%) with low titers

MOGAD diagnostic criteria

Banwell et al. Lancet Neurol 2023

A/ Core clinical demyelinating event

- Optic neuritis
- Myelitis
- ADEM
- Cerebral monofocal or polyfocal deficits
- Brainstem or cerebelar déficits
- Cerebral cortical encephalitis often with seizures

B/ Positive MOG-IgG test (Cell-based assay: serum)

- **Clear positive**: no additional supporting features required
- **Low positive/positive without reported titre, negative but CSF positive:** additional supporting features required:
  - AQP4-IgG seronegative AND
  - ≥ 1 supporting clinical or MRI features

C/ Exclusion of better diagnoses including multiple sclerosis

Supporting clinical or MRI features:

- **Optic neuritis**
  - Bilateral simultaneous clinical involvement
  - Longitudinal optic nerve involvement (>50% lenght)
  - Perineural optic sheath enhancement
- **Myelitis**
  - LETM
  - Central cord lesión or H-sign
  - Conus lesion
- **Brain, brainstem or cerebelar syndrome**
  - Multiple ill-defined T2 lesions in supratentorial and often infratentorial WM
  - Deep grey matter involvement
  - Ill-defined T2 lesions involving pons, middle cerebelar peduncles or medulla
  - Cortical lesions with or without lesional and overlying meningeal enhancement

MOGAD diagnostic criteria

Banwell et al. Lancet Neurol 2023

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Banwell et al. Lancet Neurol 2023

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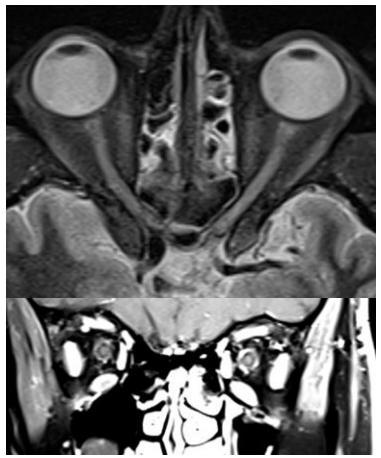

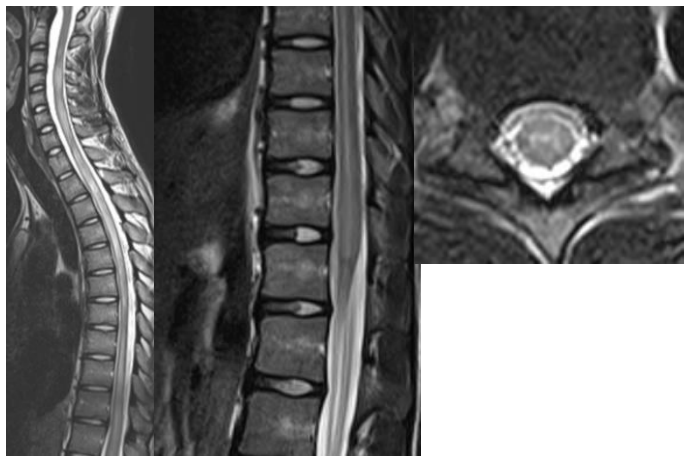

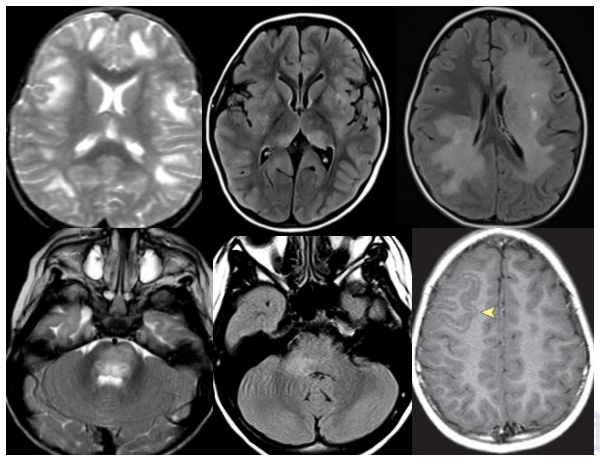

Diagnostic criteria: MS, AQP4+, MOGAD

Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria

Alan J Thompson, Brenda L Banwell, Frederik Barkhof, William M Carroll, Timothy Coetzee, Giancarlo Comi, Jorge Correale, Franz Fazekas, Massimo Filippi, Mark S Freedman, Kazuo Fujihara, Steven L Galetta, Hans Peter Hartung, Ludwig Kappos, Fred D Lublin, Ruth Ann Marrie, Aaron E Miller, David H Miller, Xavier Montalban, Ellen M Mowry, Per Soelberg Sorensen, Mar Tintoré, Anthony L Traboulsee, Maria Trojano, Bernard M J Uitdehaag, Sandra Vukusic, Emmanuelle Waubant, Brian G Weinshenker, Stephen C Reingold, Jeffrey A Cohen

Lancet Neurol 2017

VIEWS & REVIEWS

International consensus diagnostic criteria for neuromyelitis optica spectrum disorders

OPEN

Dean M. Wingerchuk,

ABSTRACT

Neurology 2015

Diagnosis of myelin oligodendrocyte glycoprotein antibody-associated disease: International MOGAD Panel proposed criteria

Brenda Banwell, Jeffrey L Bennett*, Romain Marignier*, Ho Jin Kim*, Fabienne Brilot, Eoin P Flanagan, Sudarshini Ramanathan, Patrick Waters, Silvia Tenembaum, Jennifer S Graves, Tanuja Chitnis, Alexander U Brandt, Cheryl Hemingway, Rinze Neuteboom, Lekha Pandit, Markus Reindl, Albert Saiz, Douglas Kazutoshi Sato, Kevin Rostasy*, Friedemann Paul*, Sean J Pittock*, Kazuo Fujihara*, Jacqueline Palace**

Lancet Neurol 2023

Conclusions

- MR imaging is the only imaging technique able to directly visualize the spinal cord, and therefore is considered the first imaging modality to be used in the diagnostic work up of patients with suspected inflammatory-infectious conditions involving the spinal cord.

- MR imaging findings are not disease-specific and an accurate diagnosis requires not only a detailed analysis of the extension and topography of the spinal cord lesions, but also of the additional imaging findings that may affect the spinal column and the brain, together with relevant demographic, clinical and laboratory data.

- Of crucial clinical relevance is the distinction between inflammatory and vascular spinal cord lesions, being relatively frequent to overdiagnoses demyelinating lesions in ischemic related lesions.

Vall d'Hebron Hospital

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