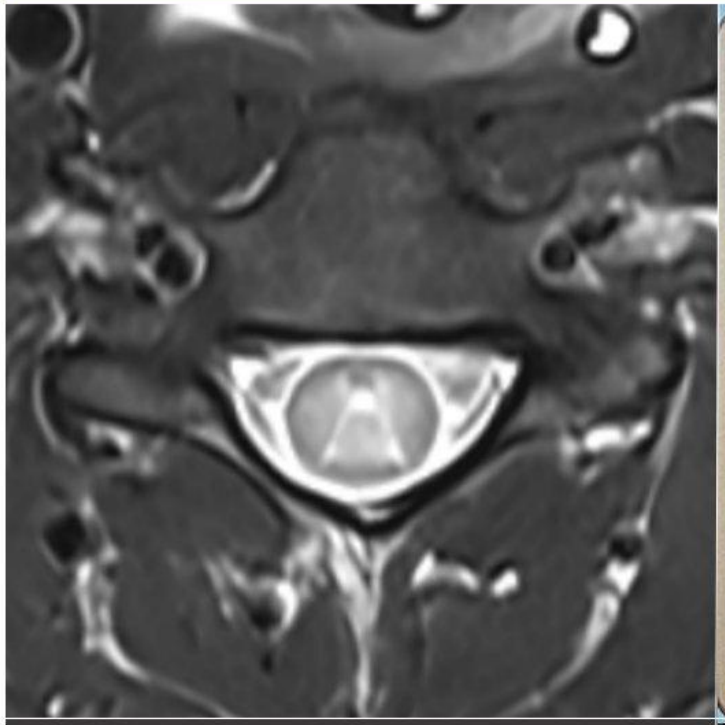
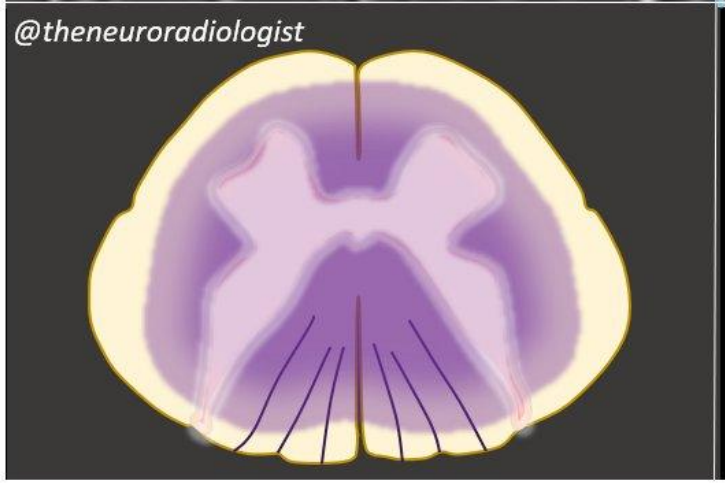
The H-Sign



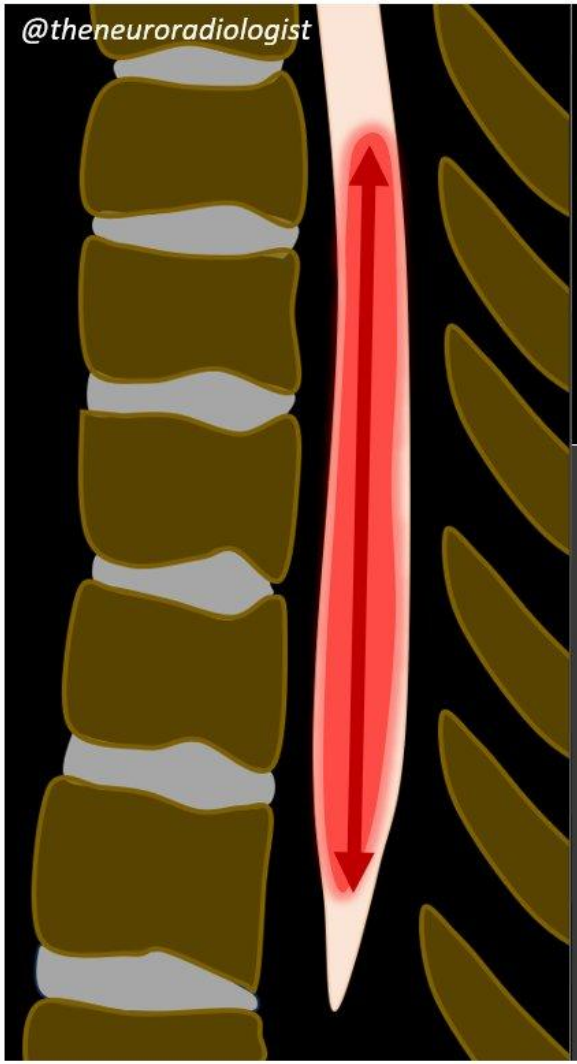


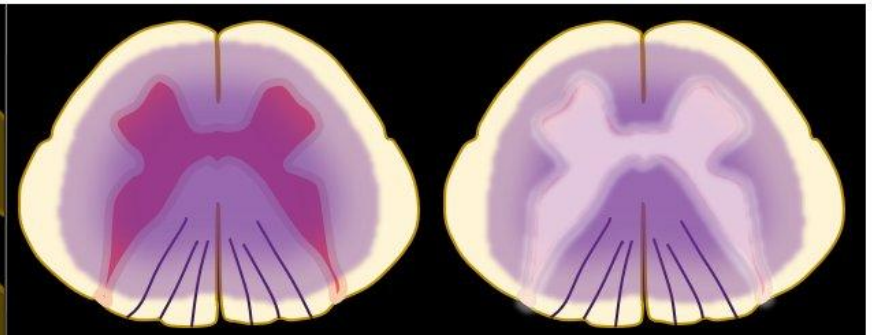
T2-hyperintense appearance of the central gray matter of the spinal cord outlining the anterior & posterior horns

Pattern most suggestive for MOGAD-related myelitis

Can also be seen in idiopathic transverse myelitis & NMOSD

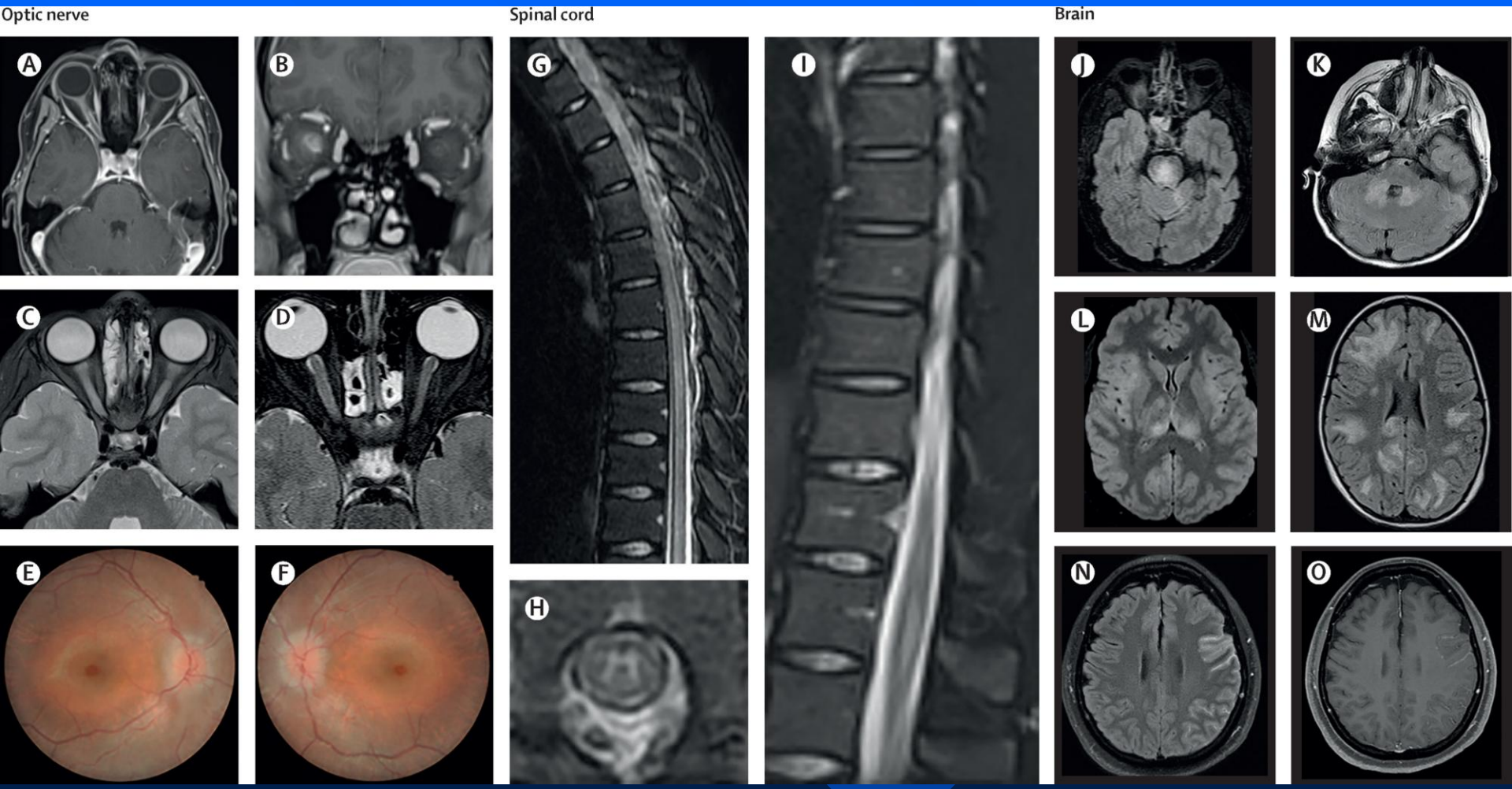
Spinal Cord lesions in MOG-antibody associated disease (MOGAD)





Transverse myelitis H-sign in ~30%

- **Long segment**
  ≥ 3 vertebrae
- **Transverse**
  central myelum
- **Thoracic > cervical**
  (conus involvement)


Optic nerve
Spinal cord
Brain
A
B
C
D
E
F
G
H
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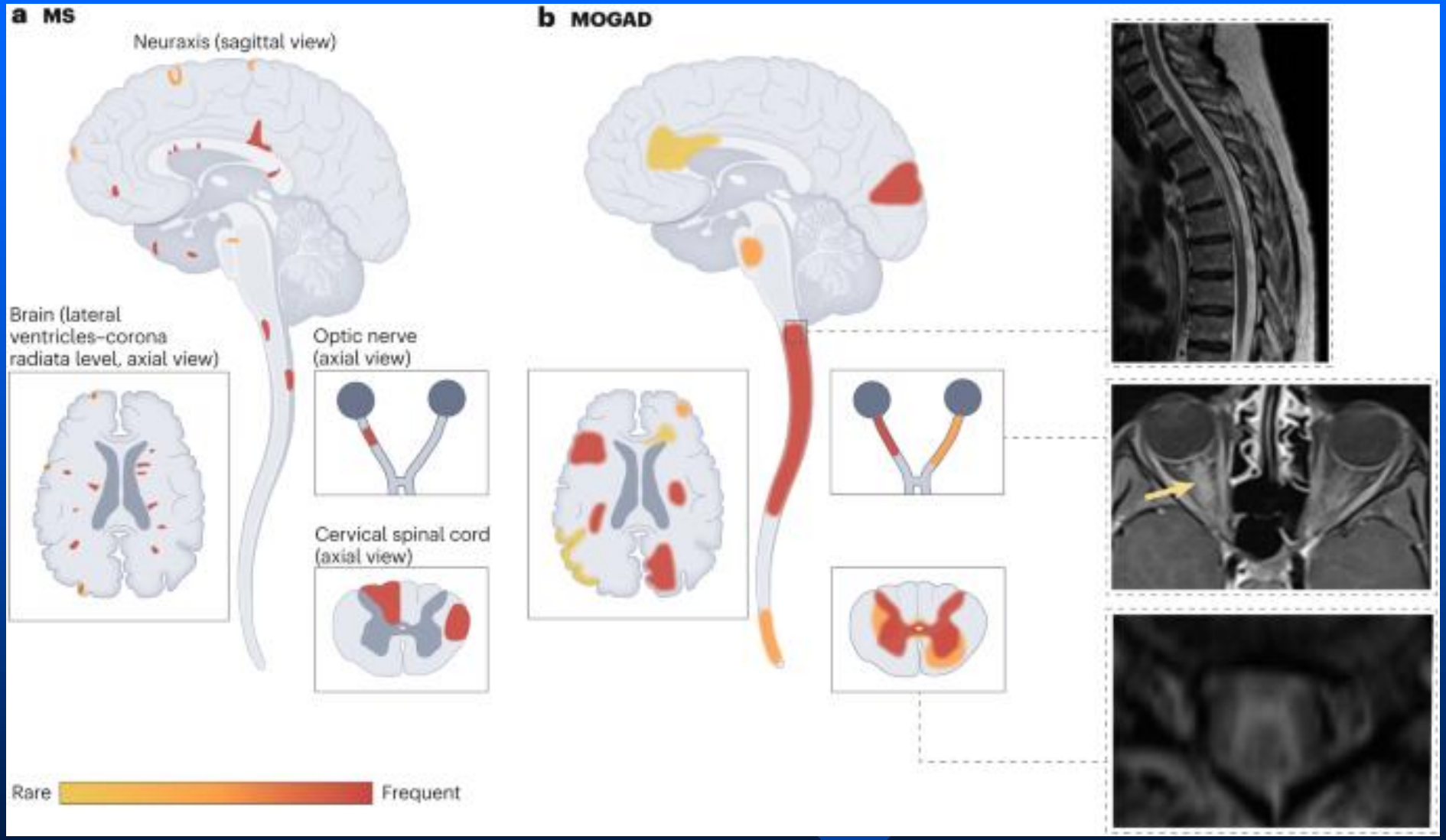
M
N
O

Clinical

- 5-40 years - Younger
- Optic neuritis, transverse myelitis, ADEM (children)
  - Optic neuritis is most common presentation in adults
  - ADEM is most common presentation in children
  - 20% of children may present with acute flaccid myelitis (AFM) mimicking enterovirus D68 (+) AFM
- Acute treatment with IV methylprednisolone
- Plasma exchange, IVIG, immunosuppression

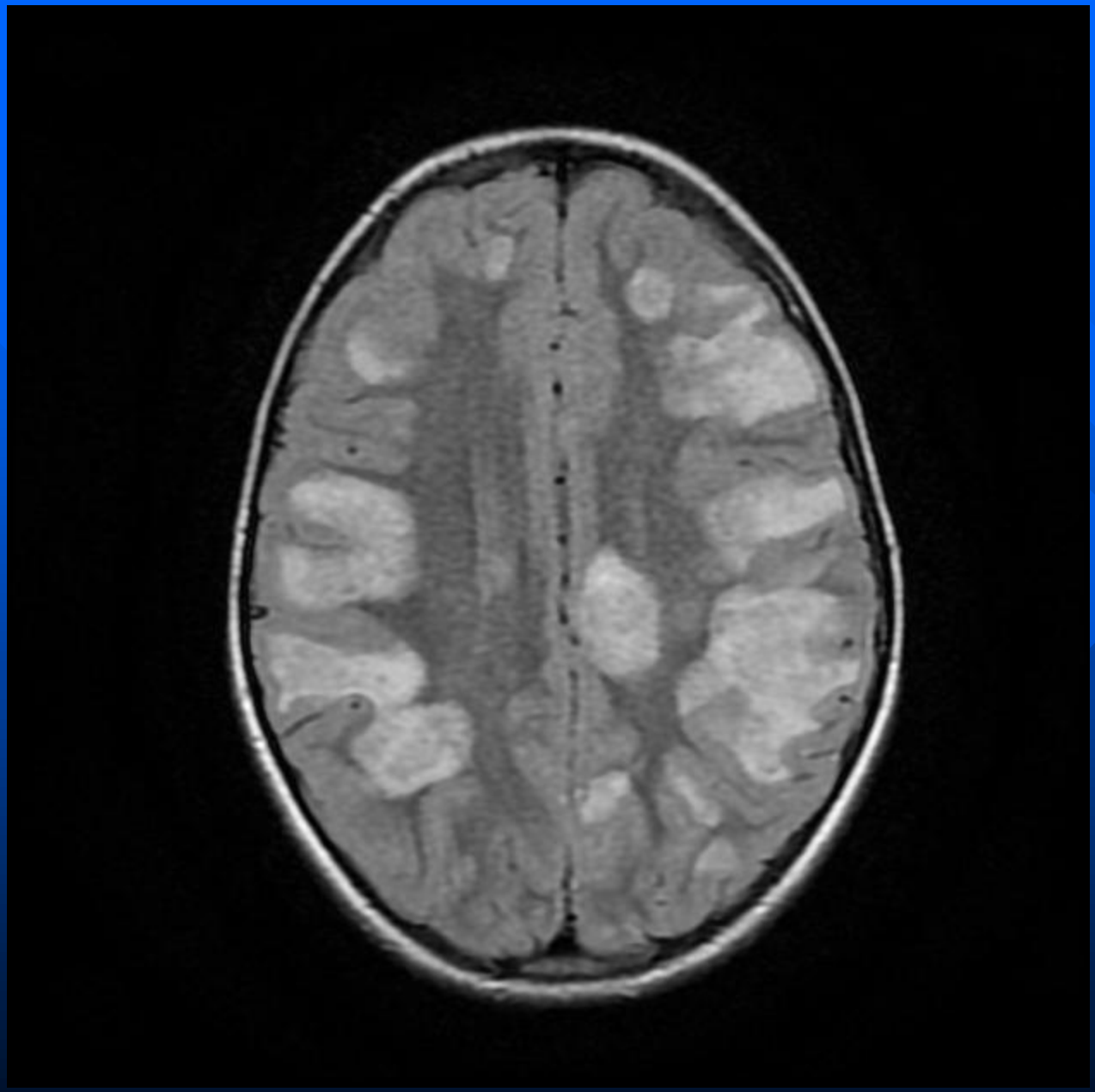

a MS
Neuraxis (sagittal view)
Brain (lateral ventricles–corona radiata level, axial view)
Optic nerve (axial view)
Cervical spinal cord (axial view)
Rare
Frequent
b MOGAD

Optic Nerves

- Optic neuritis typically shows long lesions in the anterior part of the optic nerve, often with periorbital enhancement and frequent bilateral involvement.
- MRI may reveal edematous and tortuous optic nerves, with enhancement of the perioptic nerve sheath and surrounding orbital fat.
- Optic nerve head swelling is common, while chiasmal involvement is rare (about 10% of cases

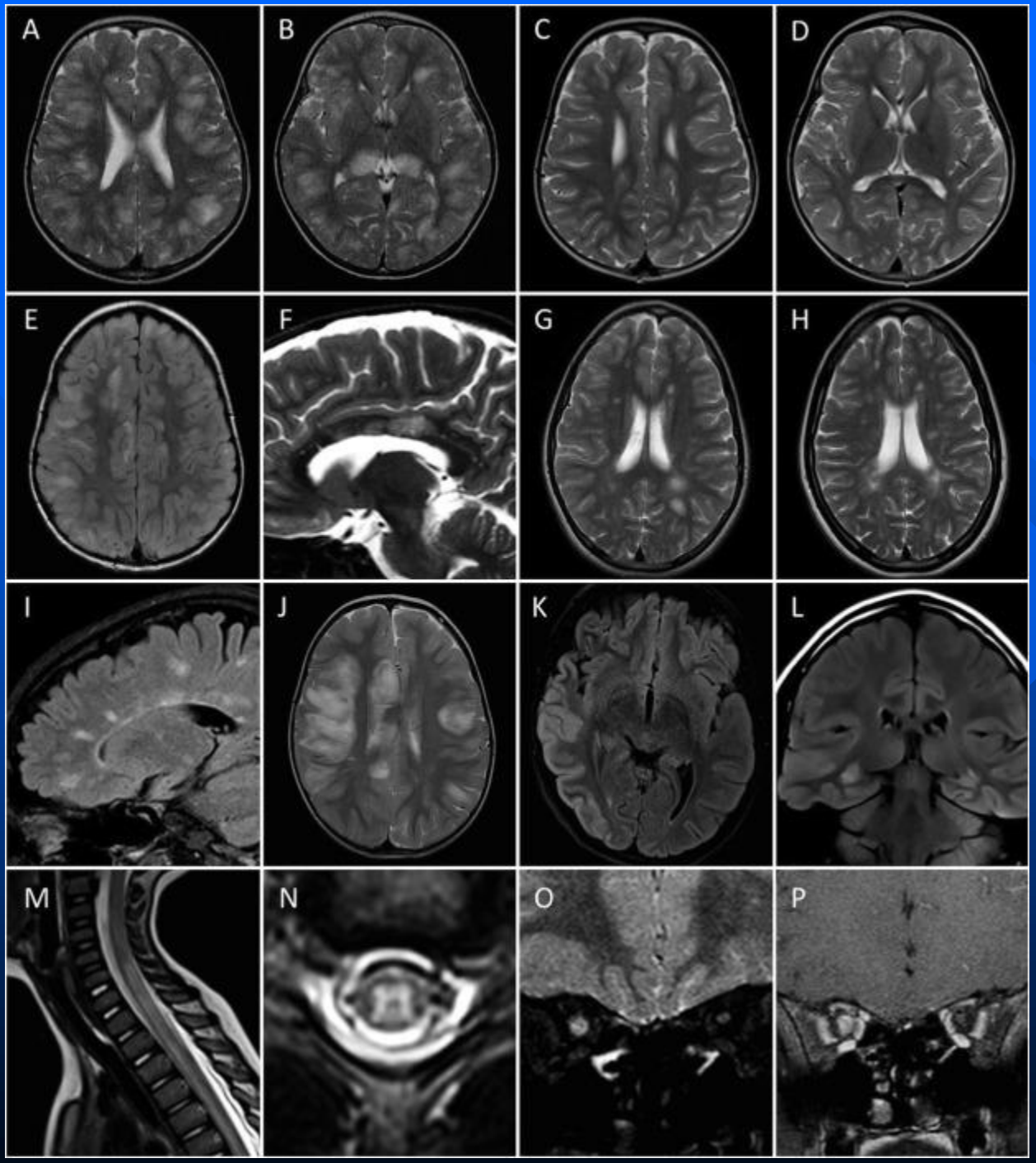
Brain

- Brain MRI may show fluffy, T2 hyperintense lesions, usually few in number and often bilateral.
- Lesions are commonly found in the thalamus and pons; in children, cerebellar peduncle lesions are also observed.
- Leptomeningeal enhancement is relatively common in MOGAD but rare in MS, and can be a helpful distinguishing feature.
- In children, MOGAD may present with a pattern resembling acute disseminated encephalomyelitis (ADEM), showing diffuse signal abnormalities in the cortical gray matter



Spinal Cord

- Longitudinally extensive transverse myelitis (LETM) is a hallmark, often affecting the central gray matter of the spinal cord.
- On axial MRI, this can appear as an "H-sign", reflecting predominant gray matter involvement.
- Lesions typically span more than three vertebral segments and may involve the conus medullaris in up to 40% of cases.
- Compared to AQP4-IgG+ NMOSD, cord edema and enhancement are less pronounced in MOGAD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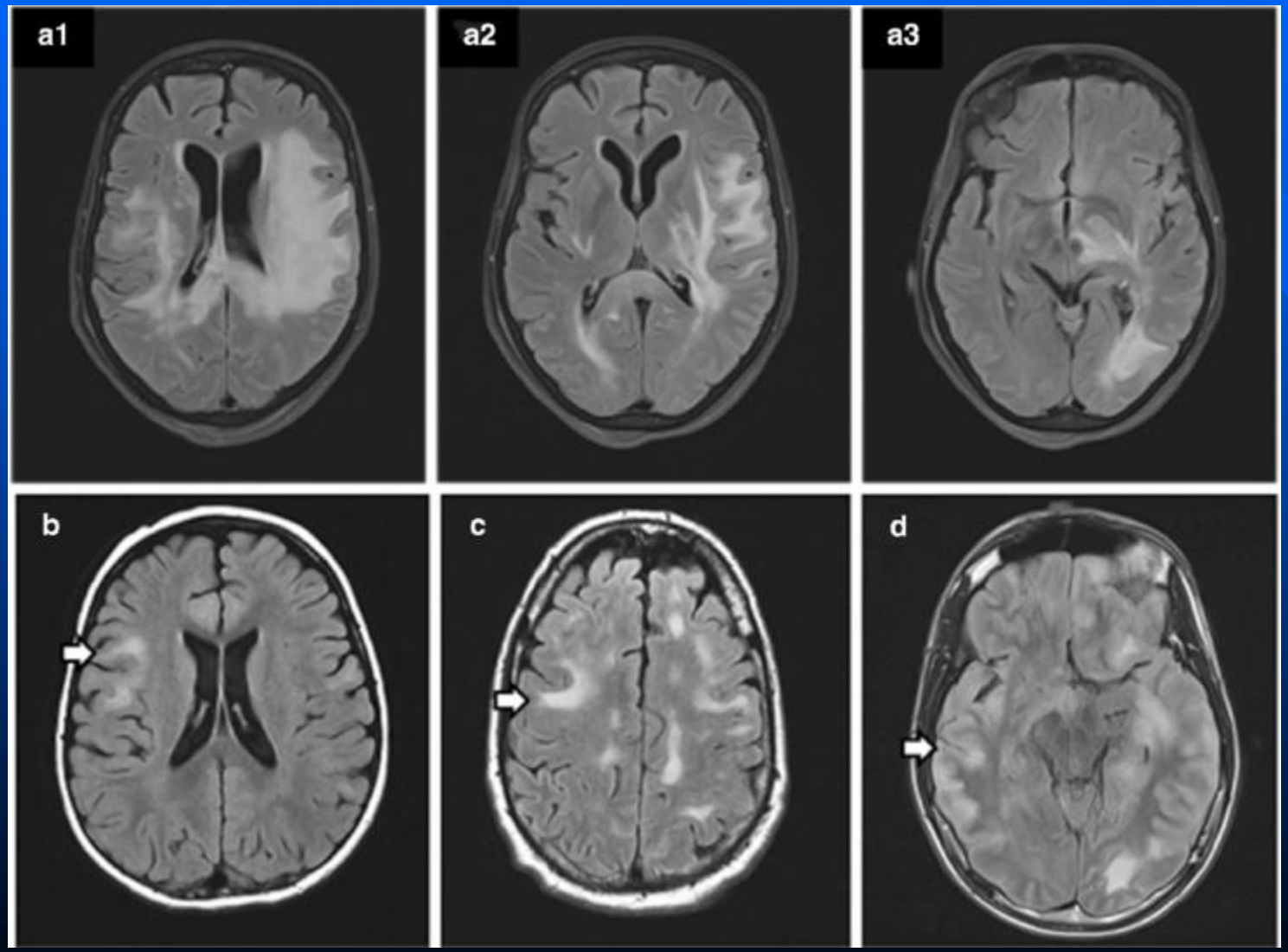
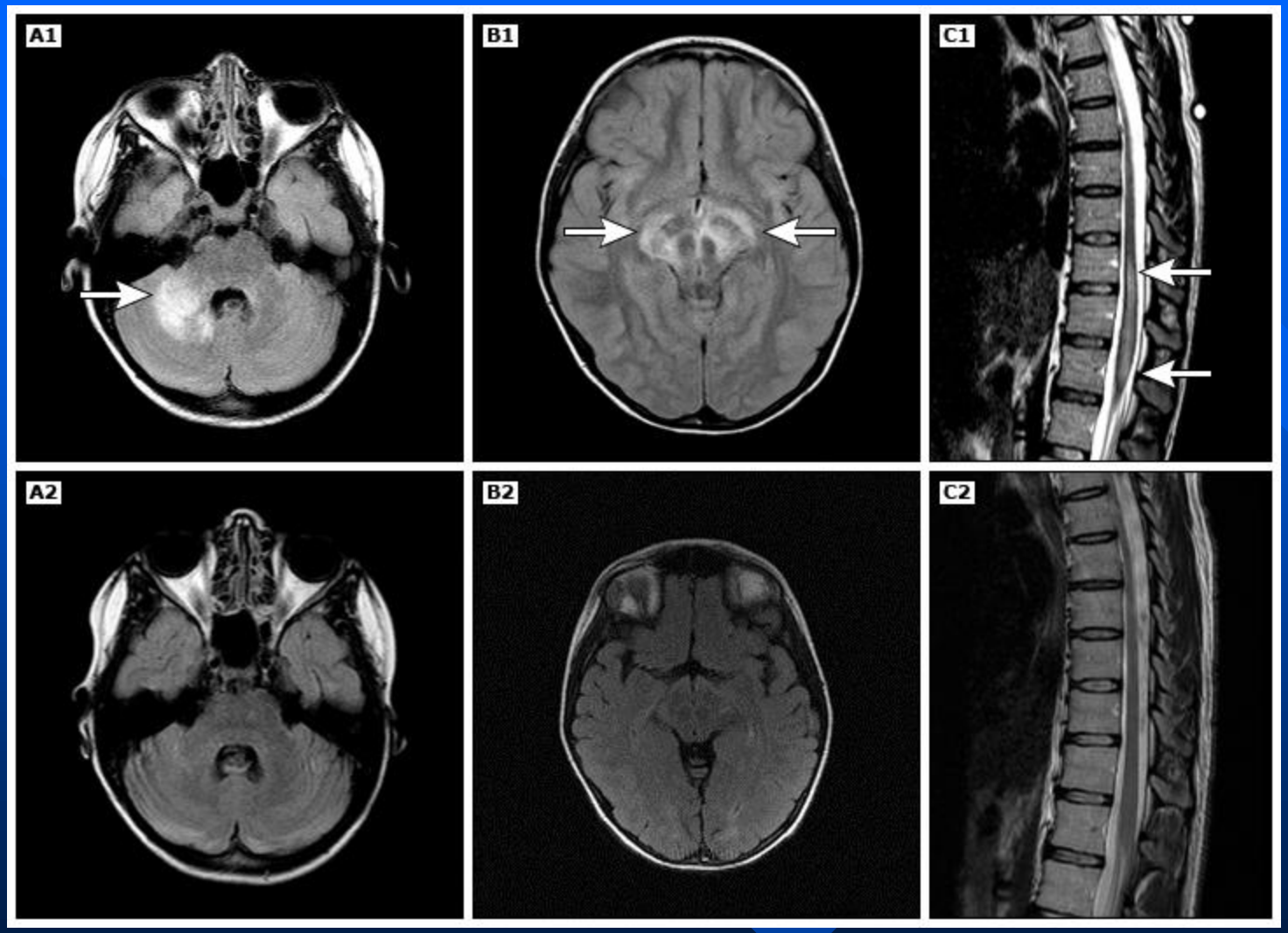
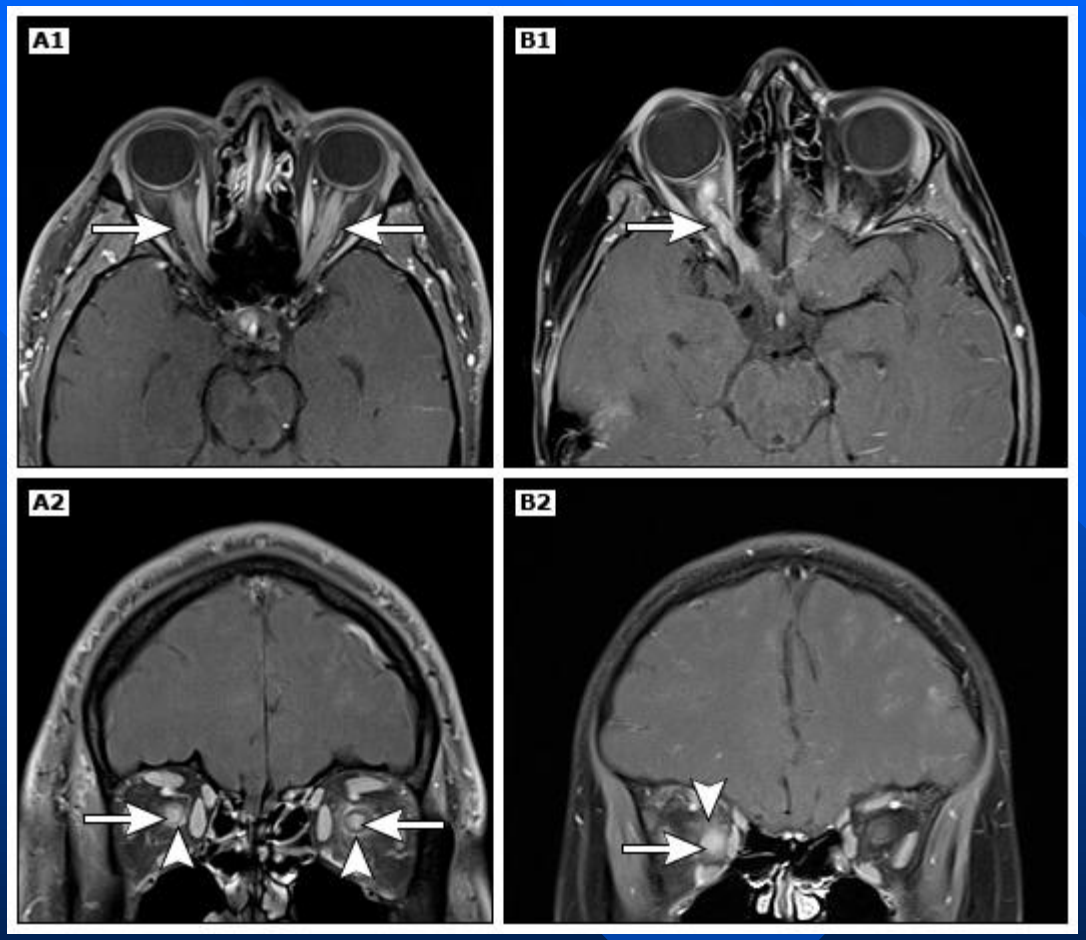
MOG-associated encephalomyelitis




A1
B1
C1
A2
B2
C2


A1
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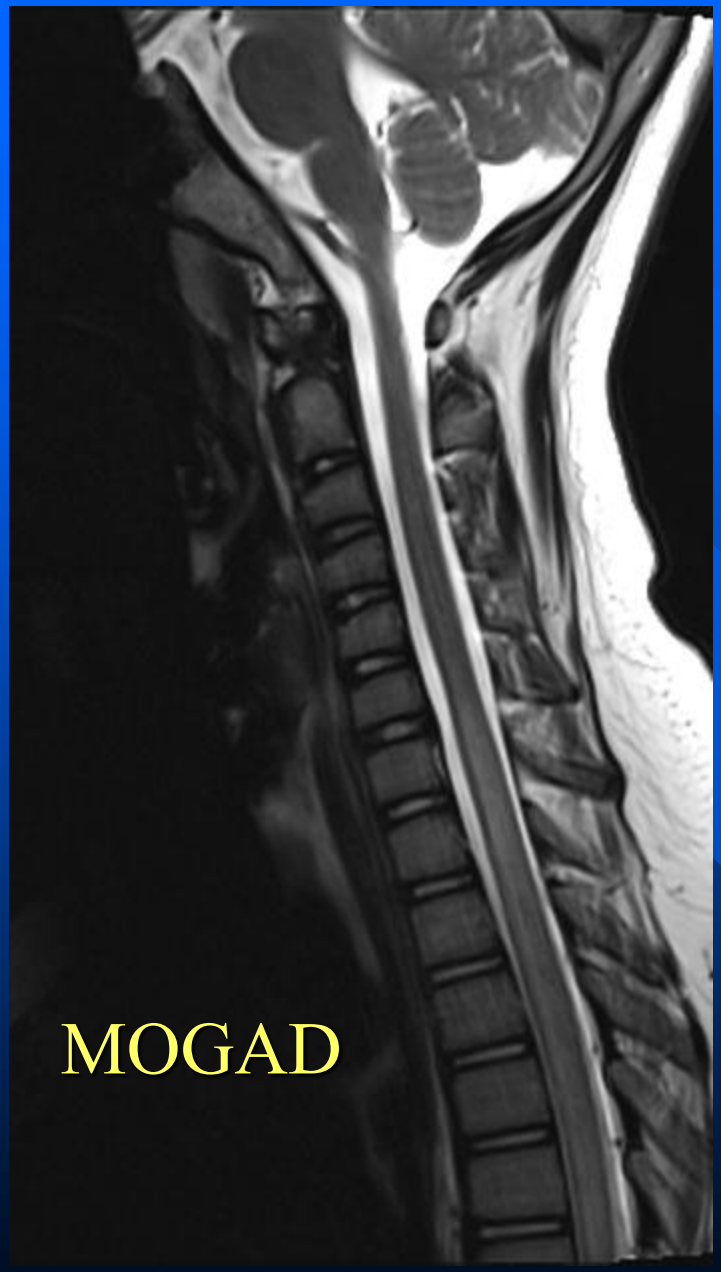
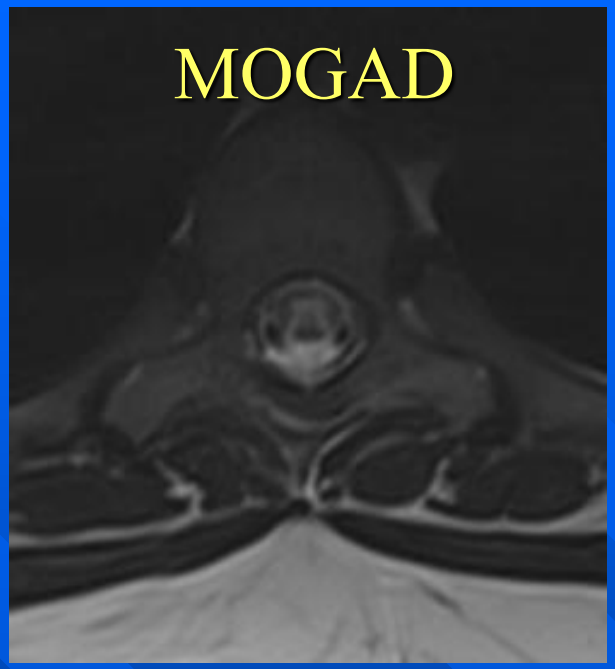




- **Acute flaccid myelitis**
- Uncommon cause of acute flaccid paralysis similar to poliomyelitis, primarily affecting children
- Usually seen following a respiratory viral illness.
- Can Have H sign.
- Related to respiratory enteroviral illness (especially enteroviruses D68 and A71)

Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD)

- Autoimmune disorder that shares some symptoms with multiple sclerosis and may be misdiagnosed as MS.
- It is associated with the presence of antibodies directed against MOG.
- MOG is found in the myelin that insulates the nerves of the central nervous system (CNS), which consists of the brain, spinal cord and optic nerves.
- Damage to myelin causes disruption in the transmission of nerve signals in the body and a variety of symptoms

MOGAD

- Myelin oligodendrocyte glycoprotein (MOG), a protein on the surface of oligodendrocytes.
- There were overlapping features and important differences clinically, radiologically, and on cerebrospinal fluid analysis distinguishing MOGAD from MS and aquaporin-4-IgG seropositive neuromyelitis optica spectrum disorder (AQP4-IgG NMOSD).
- Thus, MOGAD has now been confirmed as a distinct CNS demyelinating disease.

MOGAD

- MOGAD and NMOSD frequently affect both eyes at the same time and cause more severe visual loss compared to MS. There is often better recovery of vision in MOGAD than in NMOSD.
- MOGAD is equally common in men and women, whereas women are more likely to develop both MS and NMOSD.
- In children, MOGAD may cause attacks of the brain rather than the eye or spinal cord. These attacks are called “acute disseminated encephalomyelitis” or “ADEM.”
- People with MOGAD often have an excellent response to steroids and recover much of their function from before an attack.
- After the first attack, about half of people with MOGAD may have no further attacks, unlike people with NMOSD and MS, who are very likely to have further relapses

Clinical Features

- Characteristic attacks
- While none of the clinical features of MOGAD are disease-specific, some are highly characteristic. These include acute attacks of :
  - Unilateral or bilateral optic neuritis resulting in severe visual loss
  - Acute disseminated encephalomyelitis (ADEM), resulting in altered mental status, focal neurologic features, and features of transverse myelitis
  - Transverse myelitis, often causing limb weakness, sensory loss, and bowel, bladder, or sexual dysfunction
- MOGAD may have a monophasic or relapsing course
- Optic neuritis is the most common clinical manifestation of MOGAD at onset and is even more predominant during relapses
- Clinical syndrome termed cerebral cortical encephalitis is now recognized as a characteristic feature of MOGAD

MRI Orbits

- Enhancement of the optic nerve is typical and usually extends >50 percent the length of the nerve , which differs from MS in which <50 percent of the nerve is more common, despite some overlap.
- In MOGAD, enhancement of the optic nerve most often involves the anterior optic nerve pathway extending up to the fundus , which may explain the frequent optic disc edema accompanying it;
- Isolated involvement of the chiasm is more suggestive of aquaporin-4-IgG seropositive neuromyelitis optica spectrum disorder (AQP4-IgG NMOSD).
- Bilateral optic nerve enhancement is noted in approximately 50 percent of cases of MOGAD optic neuritis.
- In some cases, the enhancement involves the optic nerve sheath in isolation (termed optic perineuritis)or can extend into the orbital fatty tissues .

Brain MR

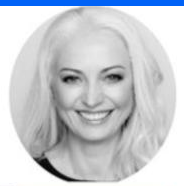
- Multiple large poorly demarcated (fluffy) T2 hyperintensities of the white matter are typical with ADEM or ADEM-like like presentations of MOGAD (image 3) [36].
- Involvement of the deep gray matter with unilateral or bilateral thalamic or basal ganglia T2 hyperintensities is well recognized (image 3) and helps distinguish MOGAD from MS, although these imaging features do have overlap with AQP4-IgG NMOSD
- Tumefactive brain lesions, defined as ≥2 cm diameter T2 hyperintense MRI lesions (image 4), are common in MOGAD. In a retrospective study of 43 patients with MOGAD, at least one tumefactive brain lesion was seen in 22 percent [69].
- Gadolinium enhancement accompanying parenchymal lesions is less well demarcated compared with MS lesions and tends to be patchy, although the pattern has not yet been fully elucidated .
- Leptomeningeal enhancement occurs in less than 10 percent of adults but may occur in up to 33 percent of children.
- Large T2 hyperintense lesions in the middle cerebellar peduncles are a common infratentorial brain lesion , and the large size and indistinct borders can help distinguish MOGAD from MS T2 lesions, which can also involve this region but tend to be smaller and well demarcated
- Diffuse brainstem lesions involving the medulla, pons, or midbrain (account for approximately 20 percent of infratentorial lesions and differ from the focal small, well-demarcated infratentorial T2 lesions of MS
- The cerebral cortical encephalitis clinical phenotype may be accompanied by subtle or more dramatic cortical swelling that is often unilateral and may or may not be associated with enhancement
- A leukodystrophy-like MRI pattern of more diffuse white matter signal abnormality has been noted after one or more attacks of MOGAD

Spine

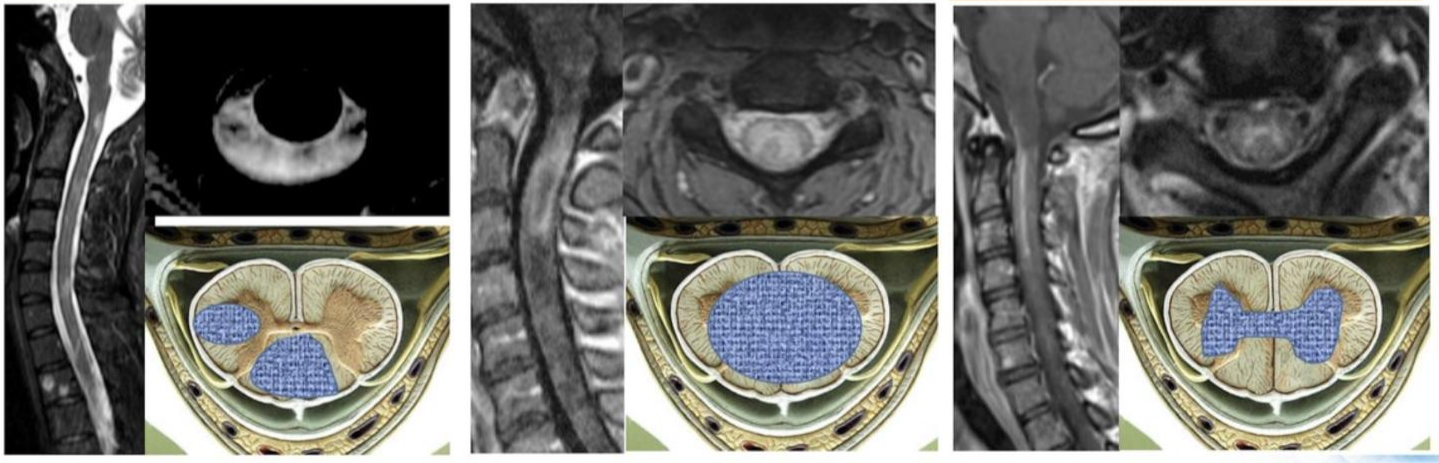
- Longitudinally extensive spinal cord lesions on T2-weighted sagittal spine MRI extending ≥3 vertebral segments are common with MOGAD and found in the majority (60 to 100 percent) of cases
- Can occur in isolation or with additional longitudinally-extensive or short lesions [17,29,30];
  - Isolated short lesions may occur but are less common, and consideration for the possibility of MS should be made, particularly if peripherally located or accompanied by a ring of enhancement.
- On axial images, the lesions are usually central in up to 75 percent [29], and in approximately one-third may be restricted to the gray matter and form a sagittal line and axial H-sign
- Myelitis with MOGAD has a predilection for the conus, which may explain the high frequency of bowel, bladder, and sexual dysfunction .
- The lesions are accompanied by mild to moderate swelling, and accompanying gadolinium enhancement occurs in approximately 50 percent but tends to be faint, patchy, and less avid than with AQP4-IgG NMOSD or MS, which can both have ring enhancement.
- Leptomeningeal enhancement may occur and extend to cauda equina nerve roots and be accompanied by lower motor neuron signs clinically [53]. Differentiation from acute flaccid myelitis is particularly important in these cases. (See "Acute flaccid myelitis".)

Biomarkers and Imaging Findings in Myelitis

Majda M Thurnher, MD, EDiNR



Multiple Sclerosis (MS)	Neuromyelitis Optica Spectrum Disorder (NMOSD)	Myelin Oligodendrocyte Glycoprotein-associated disease (MOGAD)



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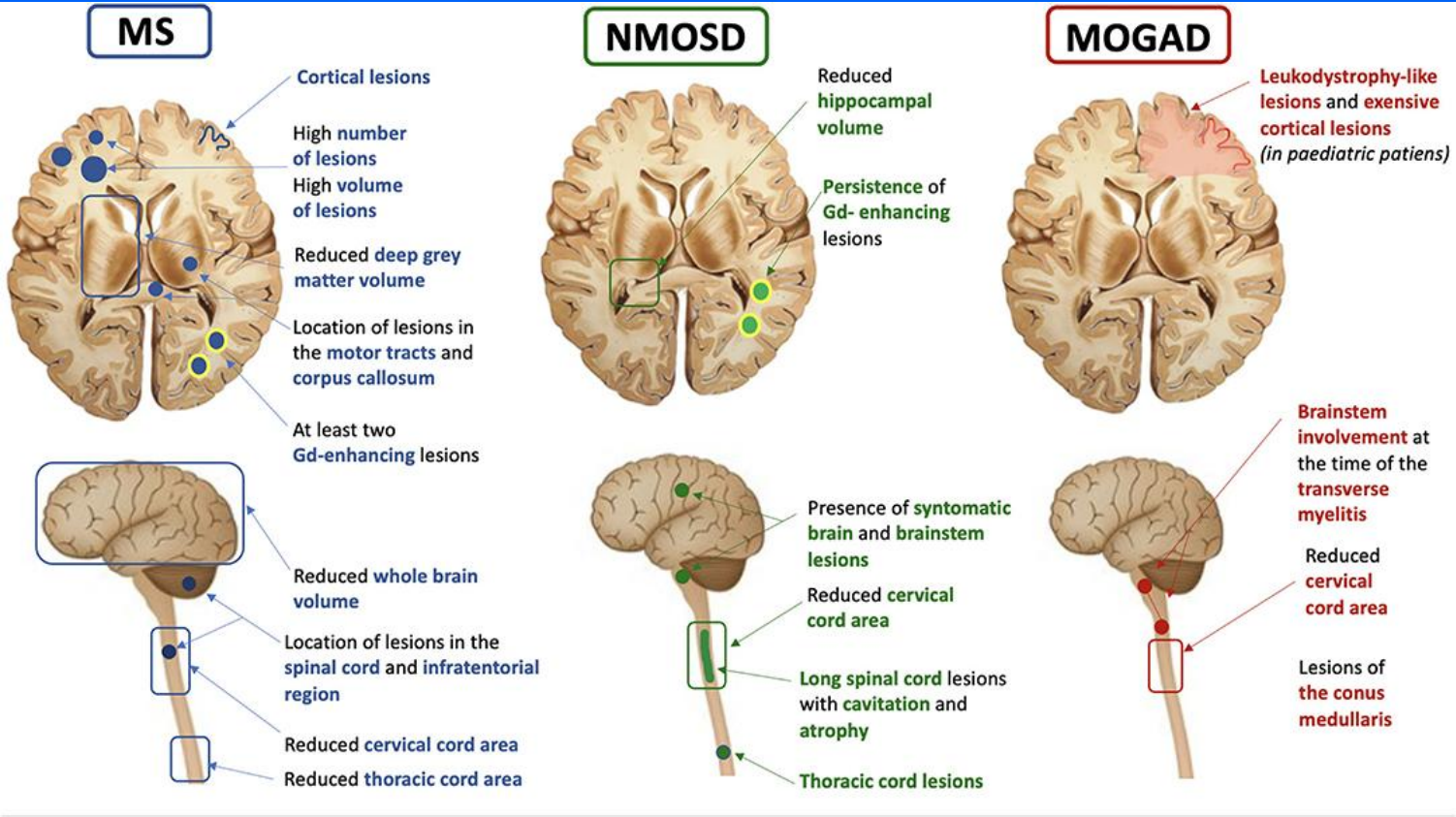
MS
Cortical lesions
High number of lesions
High volume of lesions
Reduced deep grey matter volume
Location of lesions in the motor tracts and corpus callosum
At least two Gd-enhancing lesions
Reduced whole brain volume
Location of lesions in the spinal cord and infratentorial region
Reduced cervical cord area
Reduced thoracic cord area
NMOSD
Reduced hippocampal volume
Persistence of Gd- enhancing lesions
Presence of syntomatic brain and brainstem lesions
Reduced cervical cord area
Long spinal cord lesions with cavitation and atrophy
Thoracic cord lesions
MOGAD
Leukodystrophy-like lesions and exensive cortical lesions (in paediatric patiens)
Brainstem involvement at the time of the transverse myelitis
Reduced cervical cord area
Lesions of the conus medullaris