MOGAD: A Rare Demyelinating Disease of the CNS

Intended for Healthcare Professionals
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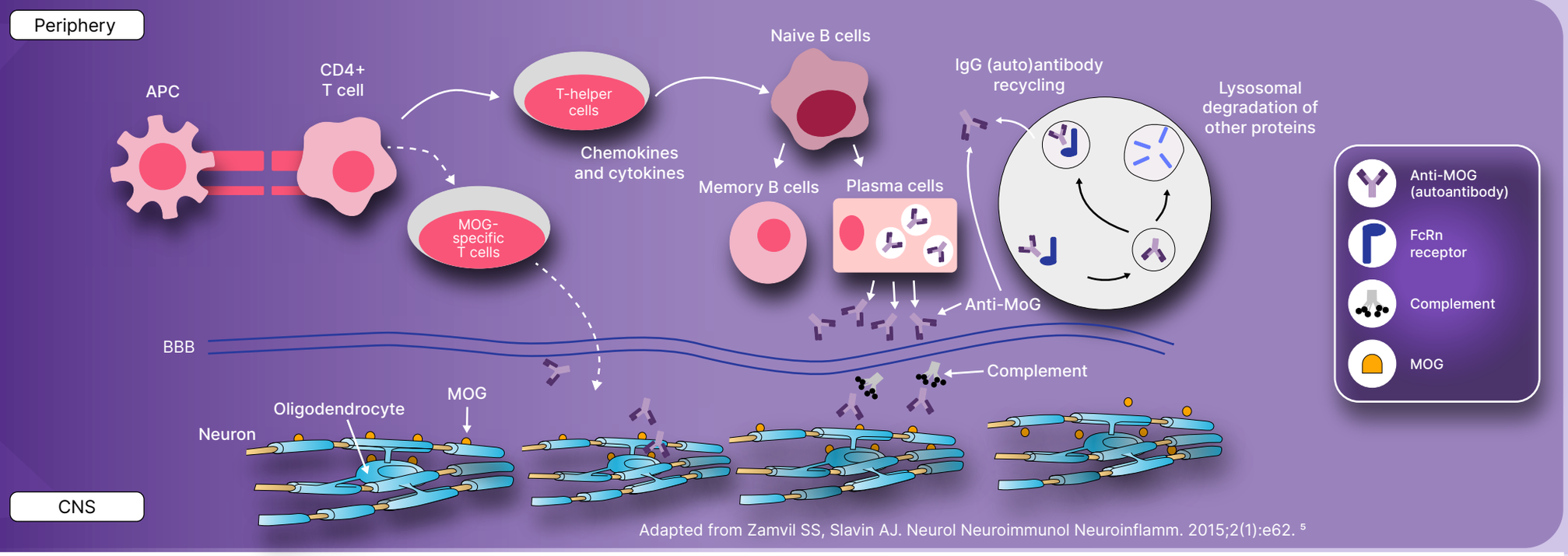
Pathway of Pathophysiology

In the periphery:

- Priming APCs activate T cells to drive B cell maturation.[1]
- The release of IL-6 and other pro-inflammatory cytokines disrupt the BBB allowing MOG-specific T cells to enter the CNS.[2,3]
- Plasma cells release anti-MOG autoantibodies.
- IgG (auto)antibody recycling maintained in the body by FcRn.[4]

In the CNS:

- BBB disruption allows entry of anti-MOG autoantibodies normally excluded from the CNS.
- Anti-MOG autoantibodies target MOG glycoprotein on the myelin sheath and oligodendrocytes.[5]
- Complement activation may trigger lysis and damage to oligodendrocytes.[6,7]



Adapted from Zamvil SS, Slavin AJ. Neurol Neuroimmunol Neuroinflamm. 2015;2(1):e62. [5]

Clinical Manifestations[8-12]

Clinical manifestations of MOGAD are heterogeneous.

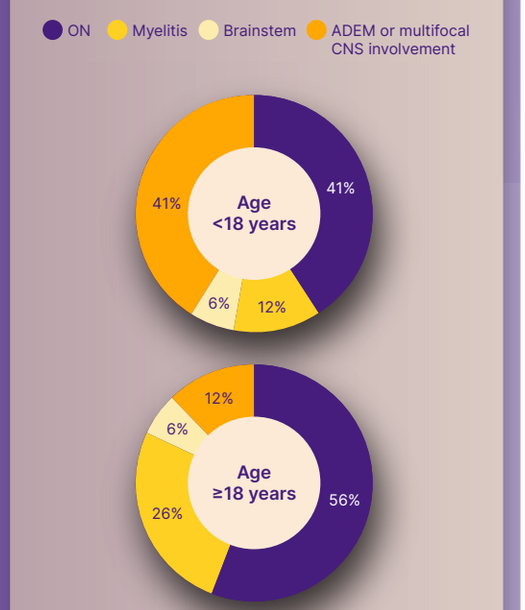
Acute Disseminated Encephalomyelitis
Inflammation attacks in the brain and/or anterior spinal cord causing rapidly developing encephalopathy and altered consciousness, occurs mostly in children.

Optic Neuritis
Inflammation damaging the optic nerve causing eye pain and temporary loss of vision.

Transverse Myelitis
Inflammation of the spinal cord damaging the myelin causes muscle weakness in the legs, and bowel/bladder issues.

Longitudinal Extensive TM
TM affecting the lower thoracic spinal cord with lesions extending ≥3 vertebral segments.

Distribution of disease phenotypes at presentation stratified by age. Frequency of ADEM is significantly higher in younger patients.[13]



Adapted from Sechi E et al. Front Neurol. 2022;13:885218.[13]

Proposed Diagnostic Criteria by International Consensus (requires fulfilment of A, B, and C)

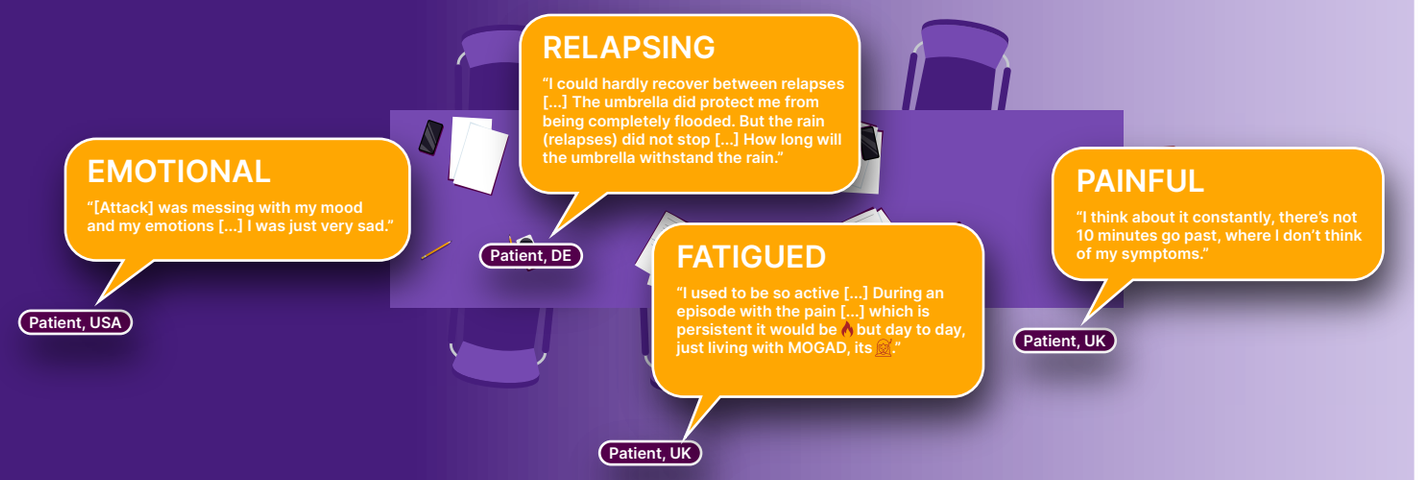
Delays in diagnosis occur due to low disease recognition and misdiagnosis as other demyelinating conditions.

1. Varied access to anti-MOG autoantibodies diagnostic testing; live CBA testing is preferred due to high sensitivity and specificity.
2. Anti-MOG autoantibodies presence alone is not sufficient for current diagnosis; accompanying clinical-MRI assessment is needed.
3. RxGuidelines have previously been lacking.

A	Core clinical demyelinating event	ON* Myelitis† ADEM‡ Cerebral monofocal or polyfocal deficits§ Brainstem or cerebellar deficits¶ Cerebral cortical encephalitis often with seizures‖		
B	Positive MOG-IgG test	Cell-based assay: serum**	Clear positive††	No additional supporting features required
			Low positive‡‡	• AQP4-IgG seronegative AND • ≥supporting clinical or MRI feature
			Positive without reported titre	
			Negative but CSF positive§§	
		ON	• Bilateral simultaneous clinical involvement • Longitudinal optic nerve involvement (>50% length of the optic nerve) • Perineural optic sheath enhancement • Optic disc oedema	
		Myelitis	• Longitudinally extensive myelitis • Central cord lesion of H-sign • Conus lesion	
		Brain, brainstem, or cerebral syndrome	• Multiple ill-defined T2 hyperintense lesions in supratentorial and often infratentorial white matter • Deep grey matter involvement • Ill-defined T2-hyperintensity involving pons, middle cerebellar peduncle, or medulla • Cortical lesion with or without lesional and overlaying meningeal enhancement	
C	Exclusion of better diagnoses, including MS¶¶			

Adapted from Banwell B et al. Lancet Neurol. 2023;22(3):268-82.[14] For more information on qualifying requirements, click here.

Patient Burden



Acronyms

Ab: Antibody; ADEM: acute disseminated encephalomyelitis; APC: antigen-presenting cell; AQP4: aquaporin-4; BBB: blood brain barrier; CBA; cell-based assay; CNS: central nervous system; FcRn: neonatal Fc receptor; MOG: myelin oligodendrocyte glycoprotein; MOGAD: myelin oligodendrocyte glycoprotein antibody-associated disorder; MS: multiple sclerosis; NMOSD: neuromyelitis optica spectrum disorders; ON: optic neuritis; TM: transverse myelitis.

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