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MRI Characteristics of Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease
A Review

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IMPORTANCE Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is a demyelinating disease distinct from multiple sclerosis (MS) and aquaporin-4 antibody-positive neuromyelitis optica spectrum disorder (AQP4+NMOSD). Magnetic resonance imaging (MRI) is central to confirming attacks, defining lesion distribution, and excluding alternative diagnoses and is a key component of the 2023 MOGAD diagnostic criteria. However, its imaging spectrum and lesion evolution remain underrecognized in practice, and variability in imaging parameters can contribute to delayed diagnosis and suboptimal treatment.

OBSERVATIONS This article summarizes the hallmark MRI features of optic nerve, brain, and spinal cord involvement in MOGAD, including key findings from the 2023 diagnostic criteria, supported by illustrative figures and detailed tables. The characteristic evolution of MRI abnormalities in MOGAD is highlighted, including radiologic lag, lesion dynamics during acute attacks, and frequent T2-lesion resolution, contrasting with the persistent lesions typical of MS. A recommended MRI protocol for acute attacks is proposed, and the timing and utility of rebaselining MRI (ie, repeating the MRI to establish a new baseline) after onset are reviewed. The clinical course of MOGAD is of attack-related neuroinflammation evident clinically and radiologically, and asymptomatic radiological activity is rare, suggesting that surveillance MRI has less clinical utility than in MS and less value as a surrogate biomarker in clinical trials. MRI features that differentiate MOGAD from MS and AQP4+NMOSD are summarized and imaging red flags suggestive of alternative diagnoses are highlighted. Finally, emerging advanced imaging, artificial intelligence in MOGAD imaging, and the link between imaging and immunopathogenesis are reviewed.

CONCLUSIONS AND RELEVANCE MRI is central to MOGAD evaluation, and recognition of the characteristic imaging features and lesion dynamics outlined in this review can aid diagnosis. Application of the standardized MRI protocol summarized here can optimize use in clinical practice and promote harmonization across research studies. Future imaging and artificial intelligence applications may improve diagnosis, disease monitoring, and understanding of MOGAD pathogenesis.

Supplemental content

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Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is a distinct central nervous system (CNS) inflammatory demyelinating disease, separate from multiple sclerosis (MS) and aquaporin 4 (AQP4) immunoglobulin G (IgG)–positive neuromyelitis optica spectrum disorder (AQP4+NMOSD). MRI is crucial in suspected MOGAD, as it supports classification in 2023 diagnostic criteria, guides antibody testing, helps confirm attacks, and defines the extent of CNS involvement.[1] Despite some overlap with MS and AQP4+NMOSD, important differences exist in lesion distribution, morphology, and dynamics that remain poorly appreciated. These distinctions are important as false-positive MOG-IgG results occur,[2] especially at low titer, making familiarity with MOGAD MRI features and its differential diagnosis essential to avoiding misdiagnosis. Accurate discrimination is also critical because treatment approaches and prognosis differ from MS and AQP4+NMOSD. This review summarizes the MRI spectrum, proposes practical acute and follow-up MRI protocols, and discusses emerging advanced imaging and artificial intelligence (AI) applications to refine diagnosis and guide future practice.

Methods

A consortium comprising international experts in imaging of MOGAD was constituted by the coleads of the project (E.P.F, J.P). This comprised diverse representation of sex, academic rank, geographic region, and MRI expertise in MOGAD, including pediatric and adult clinicians across neurology, neuro-ophthalmology and neuroradiology. Initial virtual meetings reviewed and amended the proposal drafted by the coleads. Working groups were developed for each section as follows: MRI recommendations during attacks and follow-up (K.M., A.R.), MRI orbits (J.J.C., F.P., S.R.), MRI head supratentorial (E.C.C., M.J., M.L.), MRI head infratentorial (K.F., R.M., S.M.), MRI spine (G.F., H.J.K., E.S.), MRI lesion dynamics (L.C., Y.H.), MRI differential diagnosis (R.G., S.T.), and advanced MRI and AI (B.B., R.C.). Each working group reviewed the relevant literature and drafted their section and tables. Composite MRI images from MOGAD and mimics and a medical illustration were compiled (**Figure 1**, **Figure 2**, **Figure 3**, and **Figure 4** and eFigures 1-3 in the Supplement) and a section linking MRI to pathology was added during the revision stage. All authors reviewed the manuscript and approved the final version.

MRI Recommendations During Attacks and Surveillance of MOGAD

MOGAD-Attack MRIs

At initial clinical presentation and during subsequent MOGAD attacks, MRI scans with and without contrast should be performed as early as possible after symptom onset and should include the symptomatic region (brain, cerebral attacks; spinal cord, myelitis; orbits, optic neuritis [ON]). At the onset attack, when MOGAD is suspected, imaging of brain and spinal cord regions not already covered by symptom-directed imaging should be completed to assess the extent of CNS involvement. The details of the MRI protocol for attacks are outlined in the **Table**.[3] Orbital MRI is generally reserved for symptomatic ON or when visual deficits are unreliable or ophthalmologic assessment is unavailable, such as in young children or patients with encephalopathy. During subsequent relapses, MRI is generally limited to the symptomatic region following the same protocol (Table).[3] During a suspected MOGAD attack, if the initial study is negative or if symptoms rapidly worsen, repeat MRI of the symptomatic region within 1 to 2 weeks is recommended as radiologic lag can occur.[4,5]

Follow-Up MRI Outside of Clinical Attacks

In those with brain or spinal cord parenchymal T2 lesions in the onset attack, a follow-up scan of involved regions is recommended 3 to 12 months after the onset attack. This can help support the diagnosis, as T2-lesion resolution strongly favors MOGAD over MS and AQP4+NMOSD[6-8] and serves as a new baseline for assessing future attacks (Table).[3] However, follow-up orbital MRI after ON is not necessary and optical coherence tomography (OCT) is better for confirming prior ON. Rebaseline MRI (ie, repeating the MRI to establish a new baseline) after subsequent cerebral or myelitis attacks is considered optional but can be useful in adjudication of subsequent relapses to determine if T2 hyperintensity is new or residual from prior attacks. Longer-term surveillance MRI of the brain and spinal cord in MOGAD is considered optional as silent lesions outside of attacks are less frequent in MOGAD (<5%) (Table)[3] than in MS,[9-11] but their presence may shorten time to next relapse and may lead to consideration of initiation or adjustment of maintenance attack-prevention treatment.[4,9]

Harmonization With Imaging Recommendations in MS

These recommendations and technical acquisition parameters mostly align with recommended MRI protocols for MS promoting standardization across CNS demyelinating diseases.[3]

Imaging Definitions

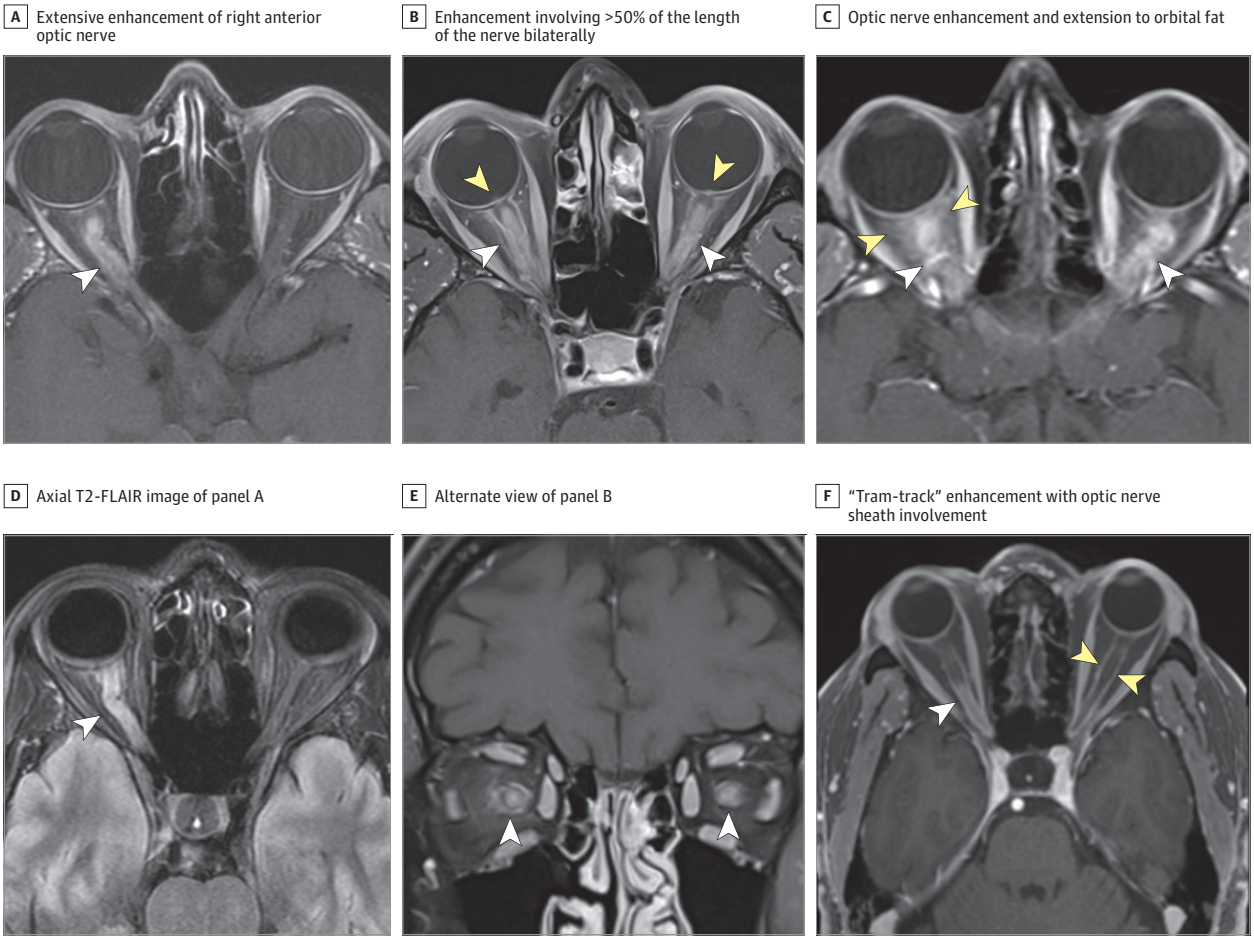
A list of definitions relevant to MRI in MOGAD are included in eTable 1 in the Supplement.

Orbital MRI in MOGAD ON

MRI plays a critical diagnostic role in MOGAD ON, accounting for 50% of onset attacks and up to 70% of relapses, and is more overrepresented in adults than in children.[12-15] OCT can also be useful in the diagnosis of acute ON.[16] MOGAD-ON manifestations include eye pain (worse with eye movement) and subsequent subacute vision loss in 1 or both eyes. The 2023 MOGAD diagnostic criteria supporting MRI features for ON (some of which overlap with clinical features) include bilateral simultaneous clinical involvement, longitudinal optic nerve involvement (>50% optic nerve length), perineural optic sheath enhancement, and optic disc edema.[1] High-quality orbital MRI with contrast-enhanced, fat-suppressed sequences is essential for optimal visualization of optic nerve pathology in MOGAD. Lack of fat suppression or failure to use contrast markedly reduce sensitivity for ON.[17] Optic nerve contrast enhancement helps confirm acute MOGAD ON and is found in 83% to 97.7% of onset orbital MRIs (Figure 1).[17] Optic nerve T2 hyperintensity is common acutely (Figure 1D) but less useful diagnostically to confirm acute ON. Approximately 60% have isolated MOGAD ON; the remaining 40% have concomitant brain or spinal cord involvement on MRI.[17] There are radiologic features that help differentiate MOGAD ON from that

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Figure 1. Orbital Magnetic Resonance Imaging (MRI) Findings During Optic Neuritis Attacks in Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease (MOGAD)



Orbital MRIs from 4 separate patients with MOGAD optic neuritis are shown. A, Axial T1 postcontrast with fat saturation shows longitudinally extensive enhancement of the right anterior optic nerve extending greater than 50% of the length of the nerve with some swelling and tortuosity (arrowhead). D, Axial T2 fluid-attenuated inversion recovery image shows longitudinally extensive T2 hyperintensity in the same region of the right optic nerve (arrowhead). B, Axial T1 postcontrast fat-saturated images show bilateral anterior enhancement involving greater than 50% of the length of the nerve bilaterally (white arrowheads) with subtle flattening of the posterior globe associated with disc swelling and bilateral optic nerve head elevation with enhancement extending into the vitreous (yellow arrowheads). C, Axial T1 postcontrast fat-saturated images show bilateral anterior optic nerve enhancement and swelling on axial images (white arrowheads) with some extension to the orbital fat (yellow arrowheads). F, Axial T1 postcontrast with fat saturated images reveal tram-track enhancement (yellow arrowheads) of both optic nerve sheaths with proximal nerve involvement also on the right (white arrowhead).

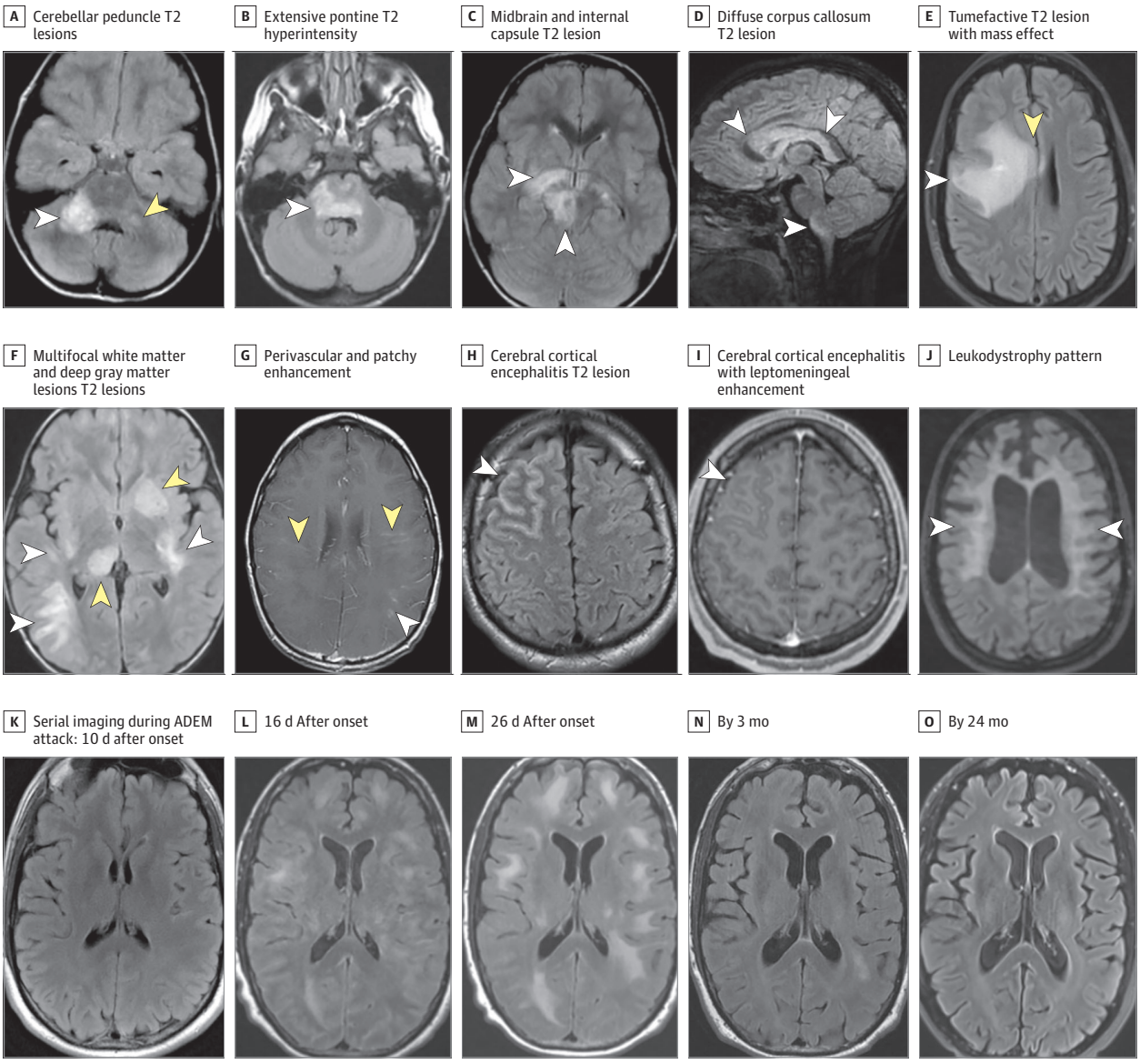
of MS or AQP4+NMOSD. Longitudinally extensive optic nerve enhancement affecting more than 50% of the nerve length is seen in approximately 50% to 80% of patients with MOGAD ON (Figure 1A, B, and F), a feature also seen in AQP4+NMOSD ON and distinct from the shorter, more focal enhancement typical of MS ON (eFigure 1 in the Supplement).[12,18-20] Bilateral optic nerve involvement occurs in up to 50% of MOGAD ON cases (Figure 1B-F) vs 20% to 30% in AQP4+NMOSD ON and 5% in MS ON.[12,21-23] MOGAD ON predominantly affects the anterior optic nerve segments (Figure 1)[12,15,24,25] and less frequently extends to the chiasm (10%-20%), whereas posterior optic nerve, isolated chiasm, or optic tract involvement are much more typical of AQP4+NMOSD ON (eFigure 1 in the Supplement).[12,19,25-27] Perineural optic nerve sheath enhancement (Figure 1F) and orbital fat involvement (Figure 1C) are characteristic of MOGAD ON occurring in approximately 50% often concurrent with optic nerve enhancement.[12,14,15] Isolated optic perineuritis without optic nerve enhancement can also occur in MOGAD ON,[18,19,28] but careful interpretation is needed as mild perineural enhancement can be a normal finding.[29] Optic nerve head swelling and/or enhancement on MRI can occasionally be an MRI accompaniment (Figure 1B) of optic disc edema in MOGAD ON.[18,25] Optic nerve enhancement can also can occur with sarcoidosis, glioma, lymphoma, and infectious etiologies and should be carefully considered particularly with low MOG antibody titers.

Supratentorial Brain MRI in MOGAD Attacks

Cerebral attacks with supratentorial MRI involvement include acute disseminated encephalomyelitis (ADEM), cerebral cortical encephalitis, and cerebral monofocal or polyfocal deficits and account for approximately 25% of initial attacks of all patients with MOGAD and

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Figure 2. Brain Magnetic Resonance Imaging (MRI) Findings During Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease (MOGAD) Attacks and Their Evolution Over Time



Axial T2 fluid-attenuated inversion recovery (FLAIR) image reveals a T2-hyperintense lesion in the right middle cerebellar peduncle (A, white arrowhead) with less well-defined subtle T2 lesion in the left middle cerebellar peduncle (A, yellow arrowhead), extensive pontine T2 hyperintensity (B, arrowhead), and large right midbrain T2-hyperintense lesion (C, lower arrowhead) with extension to the internal capsule (C, upper arrowhead). Sagittal T2 FLAIR reveals diffuse corpus callosum lesion (D, upper arrowheads) and a concomitant medulla T2 lesion (D, lower arrowhead). Axial T2 FLAIR image reveals a large tumefactive T2 lesion in the right hemisphere (E, white arrowhead) with ventricular effacement and midline shift (E, yellow arrowhead), whereas in a separate patient, multifocal white matter (F, white arrowheads) and deep gray matter lesions (F, yellow arrowheads) are shown with some lesions having mild T1 hypointensity (not shown). Axial T1-weighted postcontrast image reveals linear radial perivascular enhancement (G, yellow arrowheads) and more patchy foci of enhancement (G, white arrowhead). Axial T2 FLAIR in a patient with a cerebral cortical encephalitis attack has cortical T2 hyperintensity and swelling (H, arrowhead) with axial T1 postcontrast images show overlying leptomeningeal enhancement (I, arrowhead). A follow-up image after multiple acute disseminated encephalomyelitis (ADEM) attacks reveals a residual leukodystrophy pattern with symmetric white matter T2 hyperintensity (J, arrowheads). Serial imaging during an ADEM attack reveals an initial normal MRI 10 days after onset (K) followed by the development of ill-defined multifocal T2 hyperintensity (L) 16 days after onset that become more well-defined at neurologic nadir 26 days after onset (M). Follow-up MRI reveals resolution of most of the T2 lesions by 3 months (N) and all the T2 lesions by 24 months after onset but with diffuse cerebral atrophy also noted (O).

up to 50% of onset attacks in children.[1,17] Symptoms can include subacute encephalopathy, seizures, and other focal neurologic deficits, and ON or myelitis may coexist.[1] The 2023 MOGAD diagnostic criteria supporting MRI features for supratentorial involvement include multiple and ill-defined supratentorial white matter T2 lesions, deep gray matter involvement, or cortical lesion with or without meningeal enhancement observed in the appropriate clinical presentation.[1] Brain T2 lesions occur in approximately 50% of on-

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Figure 3. Spine Magnetic Resonance Imaging (MRI) Findings During Myelitis Attacks of Myelin Oligodendrocyte Glycoprotei Antibody-Associated Disease (MOGAD)

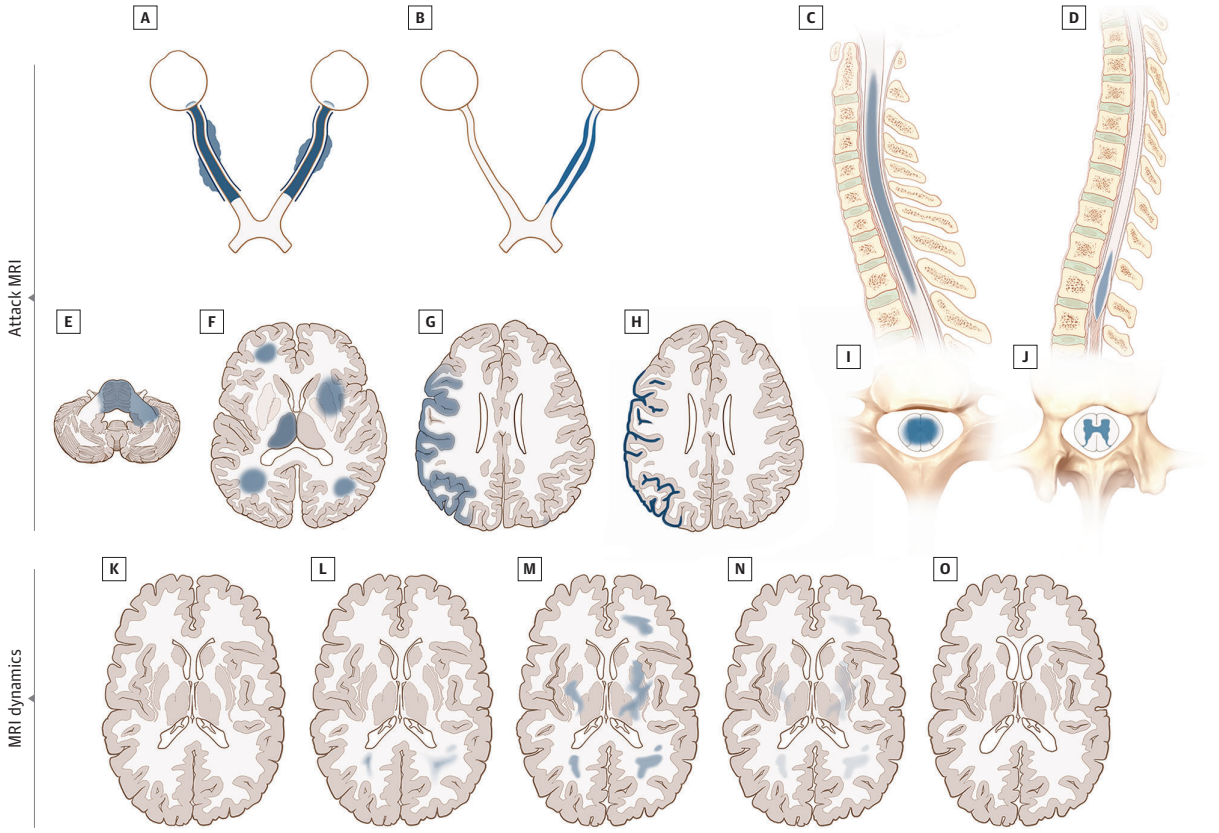


Cervical or thoracic spine MRIs from 2 separate patients with MOGAD are shown. A, Sagittal T2 cervical spine image reveals a longitudinally extensive hyperintensity extending more than 3 vertebral segments from cervical 2 (C2) to C7 with an incomplete sagittal line within the lesion (A, upper image, arrowheads) and axial T2 image revealed hyperintensity restricted to the gray matter forming an H sign (A, lower image, arrowhead). T1 postcontrast sequences revealed faint enhancement on sagittal (B, upper image, arrowhead) and axial (B, lower image, arrowhead) images. C, Sagittal T2 image of the thoracic spine revealed a short T2 hyperintensity extending less than 3 vertebral segments in the conus (C, upper image, arrowhead) with central white and gray matter T2 hyperintensity on axial image (C, lower image, arrowhead). T1 postcontrast images revealed no definitive enhancement on sagittal or axial images (D, upper and lower images).

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Figure 4. Medical Illustration of Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease (MOGAD) Imaging Involvement in Attacks and the Imaging Evolution



Single-attack magnetic resonance images (MRIs, A-J) are illustrated in top section with blue color used to show abnormalities. Depiction of optic nerve enhancement features in MOGAD optic neuritis revealing bilateral longitudinally extensive lesions with sheath and orbital fat involvement and optic disc edema visible on axial postcontrast image (A) and unilateral left sided optic perineuritis with predominantly optic nerve sheath involvement on axial postcontrast image (B). MOGAD myelitis reveals a longitudinally extensive T2 lesion extending more than 3 vertebral segments involving mostly the cervical spine but extending to the thoracic spine on sagittal T2 image (C) with central involvement involving the white and gray matter axial T2 image (I), whereas the thoracic spine image shows a short T2 lesion extending less than 3 vertebral segments and involving the conus on sagittal T2 image (D) with T2 signal restricted to the gray matter forming an H sign on axial T2 image (J). Brain involvement is shown with a brainstem or cerebellar core demyelinating event showing a T2 lesion involving the pons diffusely and middle cerebellar peduncle unilaterally on axial T2 fluid-attenuated inversion recovery (FLAIR) image (E), whereas an acute disseminated encephalomyelitis (ADEM) attack revealed multifocal T2 lesions involving the white and gray matter on axial T2 FLAIR image (F) and a cerebral cortical encephalitis attack revealed unilateral cortical T2 hyperintensity on axial T2 FLAIR (G) with accompanying leptomeningeal enhancement on axial postcontrast image (H). The bottom section (K-O) depicts a MOGAD ADEM attack and its lesion dynamics with abnormalities depicted in blue color. On axial T2 FLAIR images within a couple of days after onset revealing a normal MRI (K), whereas many days, later faint T2 lesions begin to emerge (L) become most prominent 14 days in (M) begin to resolve within a few months (N) and are resolved completely by 6 months, although some slight enlargement of the lateral ventricles is noted from some global atrophy arising after the attack (O).

set attacks, but silent lesions during attacks in other regions can occur and should be discriminated from other etiologies.[9,30] Although supratentorial brain abnormalities are a frequent accompaniment of MOGAD cerebral attacks, particularly in children,[31] 10% of encephalitis attacks have an initial normal MRI due to radiologic lag of up to a few weeks (Figure 2K-O).[4] In contrast to MS, MOGAD white matter T2 lesions are often fluffy or cloudlike with poorly defined borders (Figure 2L) and transient mild T1 hypointensity may occur acutely (approximately 50%).[32,33] Most MOGAD lesions lack restricted diffusion, but this is occasionally encountered in children and very rarely in adults.[34,35] Susceptibility-based imaging further differentiates MOGAD from MS by the absence of paramagnetic rim lesions in MOGAD. The central vein sign, detectable in more than 40% of MS lesions, has been documented at a lower frequency in MOGAD lesions, although the exact relative frequency remains to be further defined.[36,37]

T2 lesions can involve the internal capsule (Figure 2C),[17,32] gray matter cortical (approximately 52%), corticosubcortical interface (approximately 55%), or deep gray nuclei (thalamus [approximately 36%]; basal ganglia [approximately 33%]) (Figure 2F).[17] MOGAD parenchymal T2 lesions can have faint or patchy enhancement (approximately 25%) (Figure 2G), but extensive acute brain T2 lesions without enhancement are also well recognized (Figure 2M).[17] Rarely, linear perivascular enhancement can occur with MOGAD (Figure 2G). Corpus callosum lesions of the genu, body, splenium, or combinations thereof occur in 22% of MOGAD (Figure 2D), with frequent extracallosal extension from prominent associated edema, and differ from the Dawson fingers or typical callososeptal

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Table. Standardized Magnetic Resonance Imaging (MRI) Protocol for Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease (MOGAD) Attacks and Recommendations for Asymptomatic Regions and Repeating the MRI to Establish a New Baseline in MOGAD

Parameter	Brain	Spine	Orbits
Imaging during attacks			
Attack type	ADEM, cerebral polyfocal/monofocal, brainstem/cerebellar deficits, cerebral cortical encephalitis, meningoencephalitis, other cerebral attack	Myelitis	Optic neuritis
Field strength	≥1.5 T[a] (3 T preferred)	≥1.5 T	≥1.5 T (3 T preferred)
Acquisition	3D preferred	2D or 3D	2D or 3D
Slice thickness	3D: ≤1 mm Iso; 2D: ≤3 mm, No gap	Sagittal ≤3 mm, no gap; axial ≤3 mm, no gap	2D: ≤2-3 mm, No gap; 3D: ≤1 mm iso
In-plane resolution	≤1 mm × 1 mm	≤1 mm × 1 mm	≤1 mm × 1 mm
Coverage	Whole brain	Cervical and thoracic spinal cord (thoracic cord to include the conus and cauda equina roots)	Optic nerves and chiasm
Axial orientation	Subcallosal or AC-PC plane	Perpendicular to sagittal axis	Align to optic nerve and chiasm (2D)
Recommended Sequences for regions involved symptomatically in first or subsequent attack	3D T2-FLAIR with sagittal and axial reformats;[b] axial 2D T2w (single or dual echo); pre-GBCA 2D/3D T1w (pediatric); post-GBCA 2D/3D T1w;[c,d] DWI (diagnosis)	At least 2 sagittal sequences (2D T2, 2D PD, 2D STIR, 3D PSIR, 3D MPRAGE; 3D FLAWS) in 2 steps (cervical and thoracic) to achieve enough spatial resolution; axial 2D T2w post-GBCA sagittal 2D T1w[c]	2D Coronal and axial FS T2w or STIR; 2D coronal and axial with or without 3D sagittal[d] post-GBCA FS T1w[c]
During onset attack for regions not symptomatic what is recommended or optional and any adjustment from attack protocol	Recommended (no adjustment)	Recommended (adjustment: axial 2D T2w can just cover lesions seen on sagittal)	Optional[e]
During subsequent attacks for regions not symptomatic	Optional	Optional	Optional[e]
Optional sequences	3D T2[b] GRE/ SWI for CVS and PRL;[f] DWI (monitoring); 3D sagittal DIR; 3D sagittal MPRAGE (for assessing brain atrophy)	Post-GBCA 2D axial T1w through lesions	Axial FS T2w; 3D sagittal DIR
Follow-up imaging outside attacks			
Rebaselining 3-12 mo after onset attack for regions with acute lesions at onset	Recommended	Recommended	Not recommended
Subsequent surveillance imaging outside attacks	Optional (can consider particularly in the first 1-2 y)	Optional (can consider particularly in the first 1-2 y)	Not recommended

Abbreviations: AC-PC, anterior commissure–posterior commissure; ADEM, acute disseminated encephalomyelitis; CUBE, GE 3D Fast Spin-Echo Sequence; CVS, central vein sign; DIR, double inversion recovery; DWI, diffusion-weighted imaging; FLAWS, fluid and white matter suppression; FS, fat suppressed; FLAIR, fluid-attenuated inversion recovery; GBCA, gadolinium-based contrast agent; GRE, gradient-recalled echo; iso, isotropic; MPRAGE, magnetization-prepared rapid acquisition gradient echo; PD, proton density; PRL, paramagnetic rim lesion; PSIR, phase-sensitive inversion recovery; SPACE, Sampling Perfection With Application-Optimized Contrasts Using Different Flip-Angle Evolutions (Siemens); STIR, short tau inversion recovery; T1w, T1 weighted; T2w, T2 weighted; 2D, 2 dimensional; 3D, 3 dimensional; VIBE, volumetric interpolated breath-hold examination; VISTA, Volume Isotropic Turbo Spin-Echo Acquisition (Philips).

[a] Low field portable MRIs are emerging in the developing world and as more data arises about their utility may become an option.

[b] Obtain after GBCA injection, only when contrast is used, for assessment of leptomeningeal involvement. It should be acquired at least 5 to 10 minutes after injection; this waiting time can be used to acquire the T2-weighted sequence. If a good quality 3D sequence is not available, 2D T2-FLAIR sequences are an acceptable alternative.

[c] Dose and type: macrocyclic GBCA, 0.1 mmol/kg. Contrast-enhanced sequences should be acquired at least 5 to 10 minutes postinjection to achieve optimal tissue contrast.

[d] Whole-brain sagittal 3D turbo/fast spin-echo (SPACE, CUBE, or VISTA), radial 3D fat-suppressed T1-weighted gradient-echo (Radial-VIBE) or 3D FLAWS sequences allow simultaneous assessment of both brain and optic nerves similar to what was reported in MS guidelines for MRI.[3]

[e] Consider for younger children or patients with encephalopathy who may not report vision loss accurately.

[f] Recommended when differential diagnosis with multiple sclerosis is considered in cases of brain lesions.

lesions of MS.[6] Patients with MOGAD can develop tumefactive demyelinating T2 lesions (≥2 cm; in approximately 22%), sometimes mimicking neoplasms (Figure 2E).[17,38] Fulminant life-threatening MOGAD attacks rarely occur accompanied by either large lesion(s) with mass effect (Figure 2E) or diffuse cerebral edema and may require ventilatory support, aggressive intracranial pressure–lowering measures, or potentially decompressive hemicraniectomy.[39,40] Cerebral cortical encephalitis[41] manifests with seizures, focal cortical deficits, encephalopathy, fever, or combinations thereof and has also been termed *fluid-attenuated inversion recovery (FLAIR) hyperintense lesions in anti–MOG-associated encephalitis with seizures (FLAMES)*.[41-43] MRI usually shows unilateral or bilateral cortical swelling and T2 FLAIR hyperintensity often in isolation (Figure 2H) but occasionally with other brain involvement.[41-44] Underlying subcortical T2 hypointensity or overlying leptomeningeal enhancement (Figure 2I) are reported, and hyperperfusion can occur.[41-43,45] Notably, a meningoencephalitis phenotype can occur, and leptomeningeal contrast enhancement (Figure 2I) favors MOGAD (46% of cerebral attacks) over AQP4+NMOSD (7%) and MS (4%).[46,47] At follow-up, chronic T1 hypointensities are infrequent and favor MS, and brain atrophy is infrequent but may occur in recurrent or severe disease (Figure 2J and 2O).[17,33,38] A residual leukodystrophylike appearance can rarely oc-

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cur after multiple cerebral attacks and is more common in children (Figure 2J), potentially relating to immature myelin.[17,48]

Infratentorial Brain MRI in MOGAD Attacks

The most common symptoms of brainstem or cerebellar involvement are imbalance, diplopia, vertigo, facial numbness, or weakness, but also nausea, vomiting, and respiratory failure have been described.[40,49,50] The 2023 MOGAD diagnostic criteria recognize brainstem or cerebellar involvement, as a core clinical characteristic, with ill-defined (fluffy) T2/FLAIR hyperintensities involving the pons, middle cerebellar peduncle, or medulla, listed as supportive MRI features.[1] Approximately 30% of patients with MOGAD demonstrate brainstem or cerebellar MRI involvement, and two-thirds of these individuals are symptomatic.[49] Symptomatic brainstem or cerebellar attacks may rarely be isolated or much more often coexist with myelitis or ADEM attacks. Cranial nerve involvement is also recognized.[51] In the acute phase, symptomatic brainstem or cerebellar T2/FLAIR hyperintense lesions are typically large and poorly demarcated, most often involving the pons, bilateral middle and superior cerebellar peduncles, and/or cerebellar parenchyma,[30,32,52] accounting for approximately 70% of symptomatic brainstem or cerebellar involvement (Figure 2A and B). Brainstem or cerebellar MRI abnormalities have also been described in the medulla, midbrain, and around the fourth ventricle. Isolated area postrema involvement with intractable nausea, vomiting, and hiccups is extremely rare in MOGAD in contrast to AQP4+NMOSD.[50] MOGAD can mimic the imaging features of chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids (known as *CLIPPERS*) or hemophagocytic lymphohistiocytosis.[46] Tumefactive lesions have been described in the middle cerebellar peduncle and brainstem.[38] Contrast-enhancement occurs in approximately 50% of MOGAD infratentorial attacks and can be nodular or puntiform.[46]

Spinal Cord MRI in MOGAD Myelitis

Myelitis is the presenting MOGAD attack in 20% to 25% of patients and represents the second most common disease manifestation in adults.[1,17] ON or brain manifestations may coexist, sometimes with ADEM episodes. Symptoms are generally severe, with patients often requiring a gait aid, being bedridden, or needing bladder catheterization at their nadir. Spinal cord MRI may provide important clues to orient the diagnostic workup, and 2023 diagnostic criteria supporting MRI features for myelitis include 1 or more of a longitudinally extensive T2-hyperintense lesion (≥3 contiguous vertebral segments on sagittal images), central cord involvement or axial H sign, and a conus lesion.[1] The spine MRI shows variable T2 hyperintensities or enhancement, although the initial MRI is normal in approximately 10% of patients.[5]

A longitudinally extensive T2 lesion is observed in 70% to 80% of patients during myelitis attacks, either in isolation (Figure 3A, top image) or coexisting with shorter lesions, which occur in 20% to 30%.[17,53] Isolated short myelitis lesions are possible (Figure 3C, top image), and should be differentiated from smaller and peripherally located axial MS lesions (eFigure 2 in the Supplement). In MS, the coalescence of multiple short T2 lesions may rarely appear as a longitudinally extensive T2 lesion on sagittal images.[54] Spinal cord T2 lesions are often central or diffuse on axial images (Figure 3C, bottom image). A similar central or holocord involvement is also common in AQP4+NMOSD myelitis (eFigure 2 in the Supplement) and can be rarely seen in MS due to marked perilesional edema.[55] The central gray matter–predominant T2 hyperintensity (termed *H sign*) is observed in 30% to 40% of patients axially (Figure 3A, bottom image). Although suggestive of MOGAD, this sign can be seen with other myelitis etiologies.[17,53] Lastly, conus medullaris involvement is more common in MOGAD myelitis occurring in up to 40%[53] (Figure 3C and D, top and bottom images) vs AQP4+NMOSD and MS[56] and supports the diagnosis particularly when central.[53] Conus lesions should also lead to consideration of glial fibrillary acidic protein antibody–IgG myelitis, neurosarcoidosis, or spinal dural arteriovenous fistula. Of note, a brighter spotty T2 lesion on axial view favors AQP4+NMOSD. Approximately half of MOGAD myelitis cases show intralesional enhancement, whereas most AQP4+NMOSD myelitis cases have enhancement. When present, lesional enhancement is generally nonspecific, and ringlike enhancement (common in AQP4+NMOSD and MS) is rare. Spinal cord or cauda equina leptomeningeal enhancement is also common in MOGAD myelitis, especially in children.[57]

MRI Lesion Dynamics in MOGAD

MRI abnormalities in MOGAD are unusually dynamic compared with other demyelinating diseases. Radiological lag is common; approximately 10% of patients show a normal early MRI despite clear clinical symptoms (Figure 2K-O).[4,5] Even within a single clinical attack, lesion evolution is frequent. On serial MRI during the same attack (within 30 days), 47% of patients developed additional new T2 lesions (Figure 2K-O), 7% showed disappearance of at least 1 previously seen lesion, and 4% showed both new and resolving lesions simultaneously, in contrast to MS and AQP4+ AQP4+NMOSD, where the acute lesion burden is typically stable after symptom onset.[4] When comparing acute and remission MRI, resolution of at least 1 T2 lesion is observed in approximately 70% of individuals with MOGAD, a phenomenon much less frequent in AQP4+NMOSD and very rare in MS (eFigure 3 in the Supplement).[6,7,38,49,57-59] Contrast enhancement of brain or spinal cord lesions usually disappears within 3 months in MOGAD, which is similar in MS and AQP4+NMOSD.[46] T2-lesion resolution appears to be an intrinsic feature of MOGAD across age groups,[7] although the probability decreases with increasing number of relapses.[59] Corticosteroids and plasma exchange may increase the likelihood of T2-lesion resolution, but it occurs even without treatment.[7,59] Radiological predictors of T2-lesion persistence include acute T1 hypointensity, the central vein sign, and a history of smoking.[7,37,60] In contrast to MS, silent new brain T2 lesions outside of clinical attacks are rare (<5%) in MOGAD irrespective of treatment (eFigure 3 in the Supplement).[9-11] These features support targeted use of repeat MRI. When the initial acute MRI is negative or symptoms evolve, repeat imaging within 1 to 2 weeks should be considered, and lumbar puncture can help as CSF pleocytosis is frequent even without imaging abnormalities.[4,61] Because T2 lesions typically resolve within months,[7,8,58,59] rebaseline MRI 3 to 12 months after can aid diagnosis and help with confirming future re-

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lapses; notably, disappearance of at least 1 T2 lesion is suggestive of MOGAD over MS, and resolution of 2 or more T2 lesions completely separates MOGAD from MS.[8] Similar to brain T2 lesions, spinal cord T2 lesions resolve completely on follow-up MRI in approximately 70% of individuals, with minimal residual atrophy. Silent spinal cord lesions rarely occur between clinical attacks in MOGAD.[9] Optic nerve T2 hyperintensity can resolve in up to 60% of cases but does not correlate with outcomes.[12,62] Mild persistent optic nerve enhancement occurs in 13% of MOGAD cases, often at sites of prior involvement,[63] but prominent asymptomatic enhancement beyond 3 months is rare. Figure 4 provides a schematic overview of the characteristic distribution of CNS involvement in MOGAD and its distinctive lesion evolution.

Differential Diagnosis of MOGAD

A summary highlighting red flags that may suggest MS or AQP4+NMOSD is outlined in eTable 2 in the Supplement, whereas a more detailed comparison is outlined in eTable 3 in the Supplement. However, there is a broad differential diagnosis that can vary based on age. eTable 4 in the Supplement outlines the range of MRI features that may suggest an alternative diagnosis.

Advanced and Quantitative MRI and AI in MOGAD: A Look to the Future

Advanced MRI techniques provide unique insights into mechanisms of tissue injury and recovery in MOGAD beyond those captured by conventional MRI, although this has been assessed in just a few small studies. Diffusion-based techniques, including diffusion tensor imaging and neurite orientation dispersion and density imaging, reveal microstructural abnormalities within lesions and along affected white matter tracts. After ON, reduced fractional anisotropy (FA) and increased radial and mean diffusivity have been demonstrated within the optic radiations, suggesting secondary degeneration along the visual pathway.[64,65] Importantly, although lesional FA is reduced in MOGAD, abnormalities within normal-appearing white matter are considerably less pronounced than in MS.[65] Longitudinal studies[66,67] in pediatric MOGAD further suggest that both a single incident attack (with brain lesions) as well as recurrent attacks may disrupt normal brain maturation, resulting in altered growth trajectories of whole-brain and deep gray matter structures. Greater gray matter volume loss over time has been associated with lesion persistence and relapsing disease in children.[68] Focal tissue loss in the brain and spinal cord localizes to regional lesions and to recurrent attacks in the same location.[64,69] Although these measures are not currently used in routine care, they may ultimately help identify patients at risk of accumulating tissue damage despite apparent clinical recovery and provide more sensitive markers of long-term disease impact. Myelin-sensitive MRI techniques may be particularly informative in MOGAD, for capturing acute tissue edema, tissue damage, and repair processes. Magnetization transfer imaging has shown reduced magnetization transfer ratio within the optic chiasm and affected visual pathways after ON, indicating residual myelin damage despite apparent lesion resolution on conventional MRI.[70] These findings highlight the potential dissociation between radiological lesion disappearance and residual microstructural damage. Emerging quantitative techniques, including myelin water imaging and quantitative susceptibility mapping, remain underexplored in MOGAD but may provide complementary information to explain the rapid apparent resolution of large lesions and will quantify myelin and iron content.[71] In the future, such measures could help quantify tissue recovery after attacks and serve as biomarkers in clinical trials evaluating remyelinating therapies. Slowly expanding lesions, characteristic of the persistent inflammation that is often present in focal lesions in MS, are largely absent in MOGAD.[72] AI-based imaging approaches are increasingly being applied to MOGAD. Deep-learning models leveraging lesion location, morphology, and quantitative MRI metrics have demonstrated promising performance in differentiating MOGAD from MS.[73] However, the greatest value of AI may extend beyond diagnostics. By integrating MRI, OCT, serum and CSF biomarkers, and longitudinal clinical outcomes, AI has the potential to identify biologically meaningful disease trajectories that are not currently predictable.[73] In MS, such approaches have identified active but clinically silent disease, predicted disability trajectories, estimated treatment response, and refined patient stratification.[74] Similar strategies could be particularly valuable in MOGAD. However, the very tight link between relapse-related MRI new disease (and relative paucity of silent new lesions) and near absence of progression irrespective of relapse activity differentiates MOGAD from MS, and thus, AI features predictive of outcomes may vary considerably. Beyond prognostication, AI may also provide insights into MOGAD pathophysiology by identifying imaging signatures associated with myelin edema, axonal injury, remyelination, and tissue recovery. Despite multicenter harmonization challenges, integrating advanced MRI, AI, and biological biomarkers represents a promising avenue toward a more mechanistic and personalized understanding of MOGAD.

Linking MRI to Underlying Pathology and Pathogenesis

Linking MRI features to underlying immunopathology is important. Pathologic analyses of MOGAD reveal frequent cortical demyelination and leptomeningeal inflammation that are often not evident on MRI.[75] T2-lesion disappearance in MOGAD could reflect resolution of edema or remyelination,[7] although further studies are needed to determine the biologic basis of vanishing T2-lesions. Notably, some regions that lack MOG expression exhibit involvement radiologically (eg, optic nerve sheath, orbital fat, cauda equina, meninges), and we hypothesize that spread of inflammation from adjacent regions with MOG expression (eg, optic nerve, conus, cortex) may explain this discordance. Despite greater MOG expression in white matter, MOGAD can have a predilection for gray matter during acute attacks, and chronic atrophy may develop in these regions, including the spinal cord gray matter[53,64]; the underlying mechanisms of this remain uncertain and warrant further investigation. Future studies directly comparing MRI features and pathology from biopsied or autopsied MOGAD cases can better elucidate the immunopathologic basis of MRI changes.

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Conclusions

MRI is central to the evaluation of MOGAD. Application of a standardized MRI protocol can optimize its use in clinical practice and promote harmonization across research studies. Advanced and quantitative MRI and AI represent important future directions that may improve diagnosis, disease surveillance, and understanding of pathogenesis, with the ultimate goal of improving outcomes in MOGAD.

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REFERENCES

1. Banwell B, Bennett JL, Marignier R, et al. Diagnosis of myelin oligodendrocyte glycoprotein antibody-associated disease: international MOGAD Panel proposed criteria. *Lancet Neurol*. 2023;22(3):268-282. doi:10.1016/S1474-4422(22)00431-8

2. Sechi E, Buciuc M, Pittock SJ, et al. Positive predictive value of myelin oligodendrocyte glycoprotein autoantibody testing. *JAMA Neurol*. 2021;78(6):741-746. doi:10.1001/jamaneurol.2021.0912

3. Barkhof F, Reich DS, Oh J, et al; Magnetic Resonance Imaging Network in Multiple Sclerosis; Consortium of Multiple Sclerosis Centers; North American Imaging in Multiple Sclerosis Cooperative MRI guidelines working group. 2024 MAGNIMS-CMSC-NAIMS consensus recommendations on the use of MRI for the diagnosis of multiple sclerosis. *Lancet Neurol*. 2025;24(10):866-879. doi:10.1016/S1474-4422(25)00304-7

4. Cacciaguerra L, Abdel-Mannan O, Champsas D, et al. Radiologic lag and brain MRI lesion dynamics during attacks in MOG antibody-associated disease. *Neurology*. 2024;102(10):e209303. doi:10.1212/WNL.0000000000209303

5. Sechi E, Krecke KN, Pittock SJ, et al. Frequency and characteristics of MRI-negative myelitis associated with MOG autoantibodies. *Mult Scler*. 2021;27(2):303-308. doi:10.1177/1352458520907900

6. Chia NH, Redenbaugh V, Chen JJ, Pittock SJ, Flanagan EP. Corpus callosum involvement in MOG antibody-associated disease in comparison to AQP4-IgG–seropositive neuromyelitis optica spectrum disorder and multiple sclerosis. *Mult Scler*. 2023;29(6):748-752. doi:10.1177/13524585221150743

7. Cacciaguerra L, Redenbaugh V, Chen JJ, et al. Timing and predictors of T2-lesion resolution in patients with myelin oligodendrocyte glycoprotein antibody-associated disease. *Neurology*. 2023;101(13):e1376-e1381. doi:10.1212/WNL.0000000000207478

8. Syc-Mazurek SB, Cacciaguerra L, Tajfirouz DA, et al. MRI characteristics during attack and remission distinguish patients with MOG antibody-associated disease from multiple sclerosis. *J Neurol Neurosurg Psychiatry*. 2026;97(2):120-128. doi:10.1136/jnnp-2025-336684

9. Camera V, Holm-Mercer L, Ali AAH, et al. Frequency of new silent MRI lesions in myelin oligodendrocyte glycoprotein antibody disease and aquaporin-4 antibody neuromyelitis optica spectrum disorder. *JAMA Netw Open*. 2021;4(12):e2137833. doi:10.1001/jamanetworkopen.2021.37833

10. Fadda G, Banwell B, Waters P, et al; Canadian Pediatric Demyelinating Disease Network. Silent new brain MRI lesions in children with MOG-antibody associated disease. *Ann Neurol*. 2021;89(2):408-413. doi:10.1002/ana.25957

11. Syc-Mazurek SB, Chen JJ, Morris P, et al. Frequency of new or enlarging lesions on MRI outside of clinical attacks in patients with MOG antibody-associated disease. *Neurology*. 2022;99(18):795-799. doi:10.1212/WNL.0000000000201263

12. Bennett JL, Costello F, Chen JJ, et al. Optic neuritis and autoimmune optic neuropathies: advances in diagnosis and treatment. *Lancet Neurol*. 2023;22(1):89-100. doi:10.1016/S1474-4422(22)00187-9

13. Sechi E, Cacciaguerra L, Chen JJ, et al. Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD): a review of clinical and MRI features, diagnosis, and management. *Front Neurol*. 2022;13:885218. doi:10.3389/fneur.2022.885218

14. Chen JJ, Bhatti MT. Clinical phenotype, radiological features, and treatment of myelin oligodendrocyte glycoprotein-immunoglobulin G (MOG-IgG) optic neuritis. *Curr Opin Neurol*. 2020;33(1):47-54. doi:10.1097/WCO.0000000000000766

15. Chen JJ, Flanagan EP, Jitprapaikulsan J, et al. Myelin oligodendrocyte glycoprotein antibody-positive optic neuritis: clinical characteristics, radiologic clues, and outcome. *Am J Ophthalmol*. 2018;195:8-15. doi:10.1016/j.ajo.2018.07.020

16. Chen JJ, Sotirchos ES, Henderson AD, et al. OCT retinal nerve fiber layer thickness differentiates acute optic neuritis from MOG antibody-associated disease and multiple sclerosis: RNFL thickening in acute optic neuritis from MOGAD vs MS. *Mult Scler Relat Disord*. 2022;58:103525. doi:10.1016/j.msard.2022.103525

17. Trewin BP, Brilot F, Reddel SW, Dale RC, Ramanathan S. MOGAD: a comprehensive review of clinicoradiological features, therapy, and outcomes in 4699 patients globally. *Autoimmun Rev*. 2025;24(1):103693. doi:10.1016/j.autrev.2024.103693

18. Jeyakumar N, Lerch M, Dale RC, Ramanathan S. MOG antibody-associated optic neuritis. *Eye (Lond)*. 2024;38(12):2289-2301. doi:10.1038/s41433-024-03108-y

19. Akaishi T, Nakashima I, Takeshita T, et al. Different etiologies and prognoses of optic neuritis in demyelinating diseases. *J Neuroimmunol*. 2016;299:152-157. doi:10.1016/j.jneuroim.2016.09.007

20. Biotti D, Bonneville F, Tournaire E, et al. Optic neuritis in patients with anti-MOG antibodies spectrum disorder: MRI and clinical features from a large multicentric cohort in France. *J Neurol*. 2017;264(10):2173-2175. doi:10.1007/s00415-017-8615-8

21. Darakdjian M, Chaves H, Hernandez J, Cejas C. MRI pattern in acute optic neuritis: comparing multiple sclerosis, NMO and MOGAD. *Neuroradiol J*. 2023;36(3):267-272. doi:10.1177/19714009221124308

22. Ramanathan S, Reddel SW, Henderson A, et al. Antibodies to myelin oligodendrocyte glycoprotein in bilateral and recurrent optic neuritis. *Neurol Neuroimmunol Neuroinflamm*. 2014;1(4):e40. doi:10.1212/NXI.0000000000000040

23. Salama S, Khan M, Levy M, Izbudak I. Radiological characteristics of myelin oligodendrocyte glycoprotein antibody disease. *Mult Scler Relat Disord*. 2019;29:15-22. doi:10.1016/j.msard.2019.01.021

24. Ciotti JR, Eby NS, Brier MR, et al. Central vein sign and other radiographic features distinguishing myelin oligodendrocyte glycoprotein antibody disease from multiple sclerosis and aquaporin-4 antibody-positive neuromyelitis optica. *Mult Scler*. 2022;28(1):49-60. doi:10.1177/13524585211007086

25. Ramanathan S, Prelog K, Barnes EH, et al. Radiological differentiation of optic neuritis with myelin oligodendrocyte glycoprotein antibodies, aquaporin-4 antibodies, and multiple sclerosis. *Mult Scler*. 2016;22(4):470-482. doi:10.1177/1352458515593406

26. Carnero Contentti E, López PA, Criniti J, et al. Chiasmatic lesions on conventional magnetic resonance imaging during the first event of optic neuritis in patients with neuromyelitis optica spectrum disorder and myelin oligodendrocyte glycoprotein-associated disease in a Latin American cohort. *Eur J Neurol*. 2022;29(3):802-809. doi:10.1111/ene.15178

27. Tajfirouz D, Padungkiatsagul T, Beres S, et al. Optic chiasm involvement in AQP-4 antibody-positive NMO and MOG

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antibody-associated disorder. *Mult Scler*. 2022;28 (1):149-153. doi:10.1177/13524585211011450

28. Lopez-Chiriboga AS, Van Stavern G, Flanagan EP, et al. Myelin oligodendrocyte glycoprotein antibody (MOG-IgG)–positive optic perineuritis. *Neuroophthalmology*. 2019;44(1):1-4. doi:10.1080/01658107.2019.1607883

29. Becker M, Masterson K, Delavelle J, Viallon M, Vargas MI, Becker CD. Imaging of the optic nerve. *Eur J Radiol*. 2010;74(2):299-313. doi:10.1016/j.ejrad.2009.09.029

30. Cobo-Calvo A, Ruiz A, Maillart E, et al; OFSEP and NOMADMUS Study Group. Clinical spectrum and prognostic value of CNS MOG autoimmunity in adults: the MOGADOR study. *Neurology*. 2018; 90(21):e1858-e1869. doi:10.1212/WNL.0000000000005560

31. Marignier R, Hacohen Y, Cobo-Calvo A, et al. Myelin-oligodendrocyte glycoprotein antibody-associated disease. *Lancet Neurol*. 2021;20 (9):762-772. doi:10.1016/S1474-4422(21)00218-0

32. Juryńczyk M, Geraldes R, Probert F, et al. Distinct brain imaging characteristics of autoantibody-mediated CNS conditions and multiple sclerosis. *Brain*. 2017;140(3):617-627. doi:10.1093/brain/aww350

33. Hooshmand SJ, Vorasoot N, Li X, et al. Application of the ADEM definition to cerebral attacks of MOG antibody-associated disease. *Mult Scler*. 2025;31(14):1629-1640. doi:10.1177/13524585251359450

34. Wang J, Fang J, Wang J, Xiong Y, Zhu W. The magnetic resonance imaging (MRI) features of intracranial lesions in myelin oligodendrocyte glycoprotein-immunoglobulin G-associated disease (MOGAD). *Clin Radiol*. 2025;81:106764. doi:10.1016/j.crad.2024.106764

35. Kim NN, Champsas D, Eyre M, et al. Pediatric MOG-Ab-associated encephalitis: supporting early recognition and treatment. *Neurol Neuroimmunol Neuroinflamm*. 2024;11(6):e200323. doi:10.1212/NXI.0000000000200323

36. Cortese R, Prados Carrasco F, Tur C, et al. Differentiating multiple sclerosis from AQP4-neuromyelitis optica spectrum disorder and MOG-antibody disease with imaging. *Neurology*. 2023;100(3):e308-e323. doi:10.1212/WNL.0000000000201465

37. Nistri R, Cacciaguerra L, Sacco S, et al. Investigating the frequency and outcome of central vein sign and paramagnetic rim lesions in children with MOGAD. *Neurology*. 2026;106(3):e214410. doi:10.1212/WNL.0000000000214410

38. Cacciaguerra L, Morris P, Tobin WO, et al. Tumefactive demyelination in MOG Ab-associated disease, multiple sclerosis, and AQP-4-IgG-positive neuromyelitis optica spectrum disorder. *Neurology*. 2023;100(13):e1418-e1432. doi:10.1212/WNL.0000000000206820

39. McLendon LA, Gambrah-Lyles C, Viaene A, et al. Dramatic response to anti-IL-6 receptor therapy in children with life-threatening myelin oligodendrocyte glycoprotein-associated disease. *Neurol Neuroimmunol Neuroinflamm*. 2023;10(6): e200150. doi:10.1212/NXI.0000000000200150

40. Zhao-Fleming HH, Valencia Sanchez C, Sechi E, et al. CNS demyelinating attacks requiring ventilatory support with myelin oligodendrocyte glycoprotein or aquaporin-4 antibodies. *Neurology*. 2021;97(13):e1351-e1358. doi:10.1212/WNL.0000000000012599

41. Ogawa R, Nakashima I, Takahashi T, et al. MOG antibody-positive, benign, unilateral, cerebral cortical encephalitis with epilepsy. *Neurol Neuroimmunol Neuroinflamm*. 2017;4(2):e322. doi:10.1212/NXI.0000000000000322

42. Budhram A, Mirian A, Le C, Hosseini-Moghaddam SM, Sharma M, Nicolle MW. Unilateral cortical FLAIR-hyperintense lesions in anti–MOG-associated encephalitis with seizures (FLAMES): characterization of a distinct clinicoradiographic syndrome. *J Neurol*. 2019;266 (10):2481-2487. doi:10.1007/s00415-019-09440-8

43. Valencia-Sanchez C, Guo Y, Krecke KN, et al. Cerebral cortical encephalitis in myelin oligodendrocyte glycoprotein antibody-associated disease. *Ann Neurol*. 2023;93(2):297-302. doi:10.1002/ana.26549

44. Pace S, Messina S, Chen B, et al. Cerebral cortical encephalitis in adults with myelin oligodendrocyte glycoprotein antibody-associated disease: a national case series. *Eur J Neurol*. 2025; 32(1):e16550. doi:10.1111/ene.16550

45. Fujimori J, Ogawa R, Murata T, Takai Y, Misu T, Nakashima I. Decreased subcortical T2 FLAIR signal with cortical T2 FLAIR hyperintense lesions in unilateral cerebral cortical encephalitis with myelin oligodendrocyte glycoprotein antibody. *Neuroimmunol Rep*. 2022;2:100096. doi:10.1016/j.nerep.2022.100096

46. Elsbernd P, Cacciaguerra L, Krecke KN, et al. Cerebral enhancement in MOG antibody-associated disease. *J Neurol Neurosurg Psychiatry*. 2023;95(1): 14-18. doi:10.1136/jnnp-2023-331137

47. Aboseif A, Kim NN, Bou G, et al. Meningitis as an attack phenotype of myelin oligodendrocyte glycoprotein antibody-associated disease. *JAMA Neurol*. 2025;82(8):871-873. doi:10.1001/jamaneurol.2025.1774

48. Hacohen Y, Rossor T, Mankad K, et al. 'Leukodystrophy-like' phenotype in children with myelin oligodendrocyte glycoprotein antibody-associated disease. *Dev Med Child Neurol*. 2018;60(4):417-423. doi:10.1111/dmcn.13649

49. Banks SA, Morris PP, Chen JJ, et al. Brainstem and cerebellar involvement in MOG-IgG–associated disorder vs aquaporin-4 IgG and MS. *J Neurol Neurosurg Psychiatry*. Published online December 28, 2020. doi:10.1136/jnnp-2020-325121

50. Kunchok A, Krecke KN, Flanagan EP, et al. Does area postrema syndrome occur in myelin oligodendrocyte glycoprotein-IgG–associated disorders (MOGAD)? *Neurology*. 2020;94(2):85-88. doi:10.1212/WNL.0000000000008786

51. Cobo-Calvo A, Ayrignac X, Kerschen P, et al. Cranial nerve involvement in patients with MOG antibody-associated disease. *Neurol Neuroimmunol Neuroinflamm*. 2019;6(2):e543. doi:10.1212/NXI.0000000000000543

52. Matsumoto Y, Misu T, Mugikura S, et al. Distinctive lesions of brain MRI between MOG-antibody–associated and AQP4-antibody–associated diseases. *J Neurol Neurosurg Psychiatry*. Published online December 30, 2020. doi:10.1136/jnnp-2020-324818

53. Dubey D, Pittock SJ, Krecke KN, et al. Clinical, radiologic, and prognostic features of myelitis associated with myelin oligodendrocyte glycoprotein autoantibody. *JAMA Neurol*. 2019;76 (3):301-309. doi:10.1001/jamaneurol.2018.4053

54. Asnafi S, Morris PP, Sechi E, et al. The frequency of longitudinally extensive transverse myelitis in MS: a population-based study. *Mult Scler Relat Disord*. 2020;37:101487. doi:10.1016/j.msard.2019.101487

55. Zara P, Greco G, Masi F, et al. Applying the supporting features for MOGAD diagnosis to patients with multiple sclerosis. *Neurol Neuroimmunol Neuroinflamm*. 2025;12(6):e200503. doi:10.1212/NXI.0000000000200503

56. Etemadifar M, Salari M, Kargaran PK, et al. Conus medullaris involvement in demyelinating disorders of the CNS: a comparative study. *Mult Scler Relat Disord*. 2021;54:103127. doi:10.1016/j.msard.2021.103127

57. Fadda G, Alves CA, O'Mahony J, et al; Canadian Pediatric Demyelinating Disease Study Group. Comparison of spinal cord magnetic resonance imaging features among children with acquired demyelinating syndromes. *JAMA Netw Open*. 2021; 4(10):e2128871. doi:10.1001/jamanetworkopen.2021.28871

58. Sechi E, Krecke KN, Messina SA, et al. Comparison of MRI lesion evolution in different central nervous system demyelinating disorders. *Neurology*. 2021;97(11):e1097-e1109. doi:10.1212/WNL.0000000000012467

59. Abdel-Mannan O, Champsas D, Tur C, et al; UK-Childhood Neuroinflammatory Disease Network. Evolution of brain MRI lesions in pediatric myelin-oligodendrocyte glycoprotein antibody-associated disease (MOGAD) and its relevance to disease course. *J Neurol Neurosurg Psychiatry*. 2024;95(5):426-433. doi:10.1136/jnnp-2023-332542

60. Berhanu D, Leal Rato M, Messina S, Leite MI, Geraldes R, Palace J. The effect of smoking on MRI lesion resolution in NMOSD-AQP4 and MOGAD. *Mult Scler*. 2023;29(10):1250-1256. doi:10.1177/13524585231188485

61. Cacciaguerra L, Hacohen Y, Flanagan EP. Author response: radiologic lag and brain MRI lesion dynamics during attacks in MOG antibody-associated disease. *Neurology*. 2024;103(12): e209683. doi:10.1212/WNL.0000000000209683

62. Shor N, Aboab J, Maillart E, et al. Clinical, imaging and follow-up study of optic neuritis associated with myelin oligodendrocyte glycoprotein antibody: a multicenter study of 62 adult patients. *Eur J Neurol*. 2020;27(2):384-391. doi:10.1111/ene.14089

63. Tajfirouz D, Madhavan A, Pacheco Marrero JM, et al. Frequency of asymptomatic optic nerve enhancement in 203 patients with MOG antibody-associated disease. *Neurol Neuroimmunol Neuroinflamm*. 2024;11(5):e200277. doi:10.1212/NXI.0000000000200277

64. Mariano R, Messina S, Roca-Fernandez A, Leite MI, Kong Y, Palace JA. Quantitative spinal cord MRI in MOG-antibody disease, neuromyelitis optica, and multiple sclerosis. *Brain*. 2021;144(1):198-212. doi:10.1093/brain/awaa347

65. Messina S, Mariano R, Roca-Fernandez A, et al. Contrasting the brain imaging features of MOG-antibody disease, with AQP4-antibody NMOSD and multiple sclerosis. *Mult Scler*. 2022;28 (2):217-227. doi:10.1177/13524585211018987

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66. Bells S, Longoni G, Berenbaum T, et al. Patterns of white and gray structural abnormality associated with paediatric demyelinating disorders. *Neuroimage Clin*. 2022;34:103001. doi:10.1016/j.nicl.2022.103001

67. Fadda G, Cardenas de la Parra A, O'Mahony J, et al; Canadian Pediatric Demyelinating Disease Network. Deviation from normative whole brain and deep gray matter growth in children with MOGAD, MS, and monophasic seronegative demyelination. *Neurology*. 2023;101(4):e425-e437. doi:10.1212/WNL.0000000000207429

68. De Meo E, Nistri R, Eyre M, et al. Understanding mechanisms of whole brain and regional grey matter atrophy in children with MOGAD. *Ann Clin Transl Neurol*. 2025;12(10):1971-1982. doi:10.1002/acn3.70123

69. Cortese R, Battaglini M, Prados F, et al; MAGNIMS Study Group. Grey matter atrophy and its relationship with white matter lesions in patients with myelin oligodendrocyte glycoprotein antibody-associated disease, aquaporin-4 antibody-positive neuromyelitis optica spectrum disorder, and multiple sclerosis. *Ann Neurol*. 2024;96(2):276-288. doi:10.1002/ana.26951

70. Bianchi A, Cortese R, Prados F, et al. Optic chiasm involvement in multiple sclerosis, aquaporin-4 antibody-positive neuromyelitis optica spectrum disorder, and myelin oligodendrocyte glycoprotein-associated disease. *Mult Scler*. 2024;30(6):674-686. doi:10.1177/13524585241240420

71. Granziera C, Wuerfel J, Barkhof F, et al; MAGNIMS Study Group. Quantitative magnetic resonance imaging towards clinical application in multiple sclerosis. *Brain*. 2021;144(5):1296-1311. doi:10.1093/brain/awab029

72. Fadda G, Banwell B, Elliott C, et al; Canadian Pediatric Demyelinating Disease Network. Slowly expanding lesions differentiate pediatric multiple sclerosis from myelin oligodendrocyte glycoprotein antibody disease. *Ann Neurol*. 2024;96(6):1086-1091. doi:10.1002/ana.27066

73. Cortese R, Sforazzini F, Gentile G, et al; MAGNIMS Study Group. Deep learning modeling to differentiate multiple sclerosis from MOG antibody-associated disease. *Neurology*. 2025;105(6):e214075. doi:10.1212/WNL.0000000000214075

74. Willard C, Puglisi L, Ravi D, et al. Combined magnetic resonance imaging and serum analysis reveals distinct multiple sclerosis types. *Brain*. 2025;148(12):4578-4591. doi:10.1093/brain/awaf331

75. Höftberger R, Guo Y, Flanagan EP, et al. The pathology of central nervous system inflammatory demyelinating disease accompanying myelin oligodendrocyte glycoprotein autoantibody. *Acta Neuropathol*. 2020;139(5):875-892. doi:10.1007/s00401-020-02132-y

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