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Radiologic Lag and Brain MRI Lesion Dynamics During Attacks in MOG Antibody–Associated Disease

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Abstract

Background and Objectives

Knowledge of the evolution of CNS demyelinating lesions within attacks could assist diagnosis. We evaluated intra-attack lesion dynamics in patients with myelin oligodendrocyte glycoprotein antibody–associated disease (MOGAD) vs multiple sclerosis (MS) and aquaporin-4 antibody seropositive neuromyelitis optica spectrum disorder (AQP4+NMOSD).

Methods

This retrospective observational multicenter study included consecutive patients from Mayo Clinic (USA) and Great Ormond Street Hospital for Children (UK). Inclusion criteria were as follows: (1) MOGAD, MS, or AQP4+NMOSD diagnosis; (2) availability of ≥2 brain MRIs (within 30 days of attack onset); and (3) brain involvement (i.e., ≥1 T2 lesion) on ≥1 brain MRI. The initial and subsequent brain MRIs within a single attack were evaluated for the following: new T2 lesions(s); resolved T2 lesion(s); both; or no change. This was compared between MOGAD, MS, and AQP4+NMOSD attacks. We used the Mann-Whitney *U* test and χ^2/Fisher exact test for statistical analysis.

Results

Our cohort included 55 patients with MOGAD (median age, 14 years; interquartile range [IQR] 5–34; female sex, 29 [53%]) for a total of 58 attacks. The comparison groups included 38 patients with MS, and 19 with AQP4+NMOSD. In MOGAD, the initial brain MRI (median of 5 days from onset [IQR 3–9]) was normal in 6/58 (10%) attacks despite cerebral symptoms (i.e., radiologic lag). The commonest reason for repeat MRI was clinical worsening or no improvement (33/56 [59%] attacks with details available). When compared with the first MRI, the second intra-attack MRI (median of 8 days from initial scan [IQR 5–13]) showed the following: new T2 lesion(s) 27/58 (47%); stability 24/58 (41%); resolution of T2 lesion(s) 4/58 (7%); or both new and resolved T2 lesions 3/58 (5%). Findings were similar between children and adults. Steroid treatment was associated with resolution of ≥1 T2 lesion (6/28 [21%] vs 1/30 [3%], $p = 0.048$) and reduced the likelihood of new T2 lesions (9/28 vs 18/30, $p = 0.03$). Intra-attack MRI changes favored MOGAD (34/58 [59%]) over MS (10/38 [26%], $p = 0.002$) and AQP4+NMOSD (4/19 [21%], $p = 0.007$). Resolution of ≥1 T2 lesions was exclusive to MOGAD (7/58 [12%]).

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Glossary

ADEM = acute disseminated encephalomyelitis; **AQP4+NMOSD** = aquaporin-4 antibody seropositive neuromyelitis optica spectrum disorder; **FLAIR** = fluid-attenuated inversion recovery; **GOSH** = Great Ormond Street Hospital; **Ig** = immunoglobulin; **IQR** = interquartile range; **MOGAD** = myelin oligodendrocyte glycoprotein antibody–associated disease; **MS** = multiple sclerosis.

Discussion

Radiologic lag is common within MOGAD attacks. Dynamic imaging with frequent appearance and occasional disappearance of lesions within a single attack suggest MOGAD diagnosis over MS and AQP4+NMOSD. These findings have implications for clinical practice, clinical trial attack adjudication, and understanding of MOGAD pathogenesis.

Introduction

Myelin oligodendrocyte glycoprotein antibody–associated disease (MOGAD) is a newly recognized demyelinating disorder distinct from multiple sclerosis (MS) and aquaporin-4 antibody seropositive neuromyelitis optica spectrum disorder (AQP4+NMOSD).[1-3]

Despite clinical overlap with MS and AQP4+NMOSD, including the presence of optic neuritis, myelitis, and brain involvement,[1] studies have highlighted certain clinical and radiologic features that can discriminate between these diseases.[4-6] Investigations of postattack brain T2 lesions demonstrate that T2 lesions almost invariably persist in MS, rarely disappear in AQP4+NMOSD, and resolve in approximately 60%–83% in MOGAD.[7-12]

When physicians encounter a patient with an acute attack of CNS inflammation, knowledge of the brain MRI lesion dynamics, evolving and changing, within an attack may provide important clinical data that informs differential diagnosis, directs additional diagnostic testing, and guides early treatment. To date, studies evaluating lesion dynamics within MOGAD attacks are lacking. This study provides an analysis of MRI lesion dynamics within a single MOGAD attack and compares the findings with MS and AQP4+NMOSD, 2 disorders commonly considered in the MOGAD differential diagnosis.

Methods

Standard Protocol Approvals, Registrations, and Patient Consents

This study was approved by the Mayo Clinic institutional review board (IRB 08-006647) and by Great Ormond Street Hospital (GOSH) Research and Development Department (reference: 16NC10). All participants at Mayo Clinic gave written consent to the passive use of their medical records for research purposes, while consent was waived in London as per institutional review board decision.

Patient Identification, Inclusion Criteria, and Study Design

This is a retrospective observational study using routine clinical care data. Both pediatric and adult patients were enrolled at 2 tertiary referral centers for autoimmune demyelinating disorders, Mayo Clinic (Rochester [MN], Jacksonville [FL], Scottsdale [AZ]; USA) and GOSH for Children NHS Trust (London, United Kingdom). The CNS demyelinating disease databases from the 2 centers were searched to identify consecutive patients with MOGAD (n = 55: Mayo Clinic, 39; GOSH, 16), relapsing-remitting MS (n = 38: Mayo Clinic, 29; GOSH, 9), and AQP4+NMOSD (n = 19: Mayo Clinic, 17; GOSH, 2).

Inclusion criteria for the disease of focus (MOGAD) and our comparison groups (MS and AQP4+NMOSD) were as follows: (1) MOGAD,[1] MS,[13] or AQP4+NMOSD[14] diagnosis; (2) 2 or more brain MRI scans all acquired within 30 days of attack onset; and (3) brain involvement demonstrated by the presence of at least 1 typical inflammatory T2 hyperintense lesion on 1 or more of the acute MRIs defined as per the respective diagnostic criteria for each disease.[1,13,14] A 30-day cutoff for imaging within an attack was chosen based on prior literature of the definition of the duration of attacks in MOGAD, MS, and AQP4+NMOSD.[1,15,16]

Antibody Testing

All 55 patients with MOGAD were tested for MOG-IgG in the serum as part of the routine clinical care for the 2 participating centers using a cell-based assay (live, 44 [80%], fixed, 11 [20%]).[1,17] Anti–MOG-IgG testing was also performed for research purposes in the CSF (18 patients).[18] Clear positive MOG-IgG tests in the serum were defined based on MOG-IgG titer or microscopy visual score as per 2023 diagnostic criteria.[1] All 19 patients with AQP4+NMOSD tested positive for AQP4-IgG in the serum using a cell-based assay (live, 15 [79%], fixed, 4 [21%]).[14,19]

Collection of Demographics, Clinical, and CSF Data

At least 2 neurologists per center (L.C. and E.P.F., Mayo Clinic; D.C., O.A.-M., and Y.H., GOSH) abstracted demographic and clinical data of patients, including age, sex at birth, disease duration, attack onset, neurologic manifestations during the

Table 1 Between-Group Comparison of Clinical and Demographic Features Between Patients With MOGAD, MS, and AQP4+NMOSD During the Attack

Demographic/clinical features	MOGAD (n = 55)	MS (n = 38)	MOGAD vs MS	AQP4+NMOSD (n = 19)	MOGAD vs AQP4+NMOSD
Age, y	14 (5–34)	26 (15–38)	0.02	41 (15–55)	0.01
Female	29 (53)	28 (74)	0.04	19 (100)	<0.001
White	45 (82)	27 (71)	0.22	9 (47)	0.004
Non-White[a]	10 (18)	11 (29)	0.22	10 (53)	0.004
Relapsing disease	36 (66)	38 (100)	<0.001	14 (74)	0.51
CSF unique oligoclonal bands	6 of 45 (13)	28 of 36 (78)	<0.001	2 of 17 (12)	>0.99[c]
Clinical features at attack	**MOGAD (n = 58)**	**MS (n = 38)**	**MOGAD vs MS**	**AQP4+NMOSD (n = 19)**	**MOGAD vs AQP4+NMOSD**
Pediatric at attack	34 (59)	15 (40)	0.07	5 (26)	0.02
Disease duration during the attack[b]	0 (0–34)	0 (0–46)	0.53	0 (0–158)	0.31
Time to nadir[b]	11 (5–16)	5 (2–12)	0.02	11 (4–16)	0.85
EDSS at nadir	4.25 (3–7)	3.5 (3–4)	0.046	4.5 (3–8)	0.92
Concomitant optic nerve involvement	19 (33)	4 (11)	0.02[c]	1 (5)	0.02[c]
Concomitant spinal cord involvement	24 (41)	10 (26)	0.13	3 (16)	0.054[c]
Acute treatment before second MRI					
Steroids	28 (48)	21 (55)	0.50	13 (68)	0.13
Plasma exchange	4 (7)	2 (5)	>0.99[c]	3 (16)	0.35[c]
IVIgs	4 (7)	0 (0)	0.15[c]	1 (5)	>0.99[c]
Reasons for repeated MRI scan	**MOGAD (n = 56)**	**MS (n = 37)**	**MOGAD vs MS**	**AQP4+NMOSD (n = 15)**	**MOGAD vs AQP4+NMOSD**
Clinical worsening or lack of improvement	33 (59)	10 (27)	0.003	8 (53)	0.70
New baseline after transfer to a new medical center	10 (18)	18 (49)	0.002	2 (13)	>0.99[c]
Assess treatment response	8 (14)	3 (8)	0.52[c]	4 (27)	0.26[c]
Additional sequences needed or biopsy planning	5 (9)	4 (11)	0.74[c]	1 (7)	>0.99[c]
Research MRI scan	0 (0)	2 (5)	0.16[c]	0 (0)	>0.99[c]

Abbreviations: AQP4+NMOSD = aquaporin-4 antibody seropositive neuromyelitis optica spectrum disorder; EDSS = Expanded Disability Status Scale; MOGAD = myelin oligodendrocyte glycoprotein antibody–associated disease; MS = multiple sclerosis.
Unless otherwise specified, categorical variables are presented as frequencies (percentages) and *p* values refer to the Pearson χ^2 test, while continuous variables are median (interquartile range) and *p* values refer to the Mann-Whitney *U* test.
[a] Non-White patients: MOGAD (Asian, 7; Hispanic, 2; and other race/ethnicity; 1), MS (Asian, 5; African, 4; Hispanic, 1; and other race/ethnicity, 1), AQP4+NMOSD (African, 6; Asian, 1; and other race/ethnicity, 3).
[b] Days.
[c] Fisher exact test.

acute attack, presence of CSF white blood cells and CSF unique oligoclonal bands, steroid treatment during the attack, and reason for repeat MRI within a single attack.

MRI Analysis

MRIs were undertaken during routine clinical care except for 2 that were research MRIs. All available MRI reports by the neuroradiologist were reviewed. MRI scans were then independently re-evaluated by 2 neurologists per center (L.C. and E.P.F., Mayo Clinic; O.A.-M. and Y.H., GOSH). For each MRI, the number of T2 hyperintense lesions on T2 fluid-attenuated inversion recovery (FLAIR) or T2-weighted sequences (if T2-FLAIR was unavailable) was collected according to the following categories: absence of lesions, presence of 1 to 5 lesions, 6 to 10 lesions, and more than 10 lesions. To improve readability, unless otherwise specified, the term "lesion(s)" will refer to T2 hyperintense lesions throughout the article.

Table 2 Acute MRI Dynamics and Comparison of Pediatric and Adult Patients With MOGAD

	MRI-2			*p* Values
	All (n = 58)	Pediatric (n = 34)	Adults (n = 24)	Pediatric vs adults
Days from MRI-1	8 (5–13)	7 (4–12)	10 (7–13)	0.08
MRI dynamics (MRI-2 vs MRI-1)				
Lesions				
Stable lesion number[b]	24 (41)	13 (38)	11 (46)	0.56
New lesion(s)[c]	27 (47)	18 (53)	9 (38)	0.25
Resolved lesion(s)[d]	4 (7)	2 (6)	2 (8)	>0.99[a]
Both new and resolved lesion(s)[e]	3 (5)	1 (3)	2 (8)	0.56[a]
Leptomeningeal enhancement				
Persistent	7 of 44 (16)	6 of 26 (23)	1 of 18 (6)	0.21[a]
New	5 of 44 (11)	3 of 26 (12)	2 of 18 (11)	>0.99[a]
Resolved	8 of 44 (18)	4 of 26 (15)	4 of 18 (22)	0.70[a]
Parenchymal enhancement of lesion(s)				
Persistent	11 of 44 (25)	3 of 26 (12)	8 of 18 (44)	0.03[a]
New	8 of 44 (18)	6 of 26 (23)	2 of 18 (11)	0.44[a]
Resolved	5 of 44 (11)	2 of 26 (8)	3 of 18 (17)	0.39[a]

Abbreviation: MOGAD = myelin oligodendrocyte glycoprotein antibody–associated disease.
Unless otherwise specified, quantitative variables are presented as frequencies (percentages) and *p* values refer to the Pearson χ^2 test, while continuous variables are median (interquartile range) and *p* values refer to the Mann-Whitney *U* test.
[a] Fisher exact test.
[b] Stable lesion number: no new lesions and no resolved lesions.
[c] New lesion(s): ≥1 new lesion and no resolved lesions.
[d] Resolved lesion(s): no new lesions and ≥1 resolved lesion.
[e] Both new and resolved lesion (s): ≥1 new lesion and ≥1 resolved lesion.

Postcontrast T1-weighted sequences were also analyzed in terms of presence of leptomeningeal enhancement[20] and of at least 1 gadolinium-enhancing parenchymal lesion. Given the different number of MRI scans per patient and the limited number of individuals with at least 3 MRI scans, we focused the analysis mostly on the dynamics of radiologic findings between the first and the second MRI scans. Changes were classified according to the following definitions:

1. Stable: no new lesions or resolved lesions;
2. New lesion(s): 1 or more new lesions with no resolved lesions;
3. Resolved lesion(s): 1 or more lesions resolved and no new lesions;
4. Both new and resolved lesion(s): 1 or more new lesions and 1 or more lesions resolved.

When there was disagreement, the radiology reports were consulted (if available), images were rereviewed, and a final consensus was reached. The evolution of MRI scans in those patients with at least 3 examinations were descriptively reported.

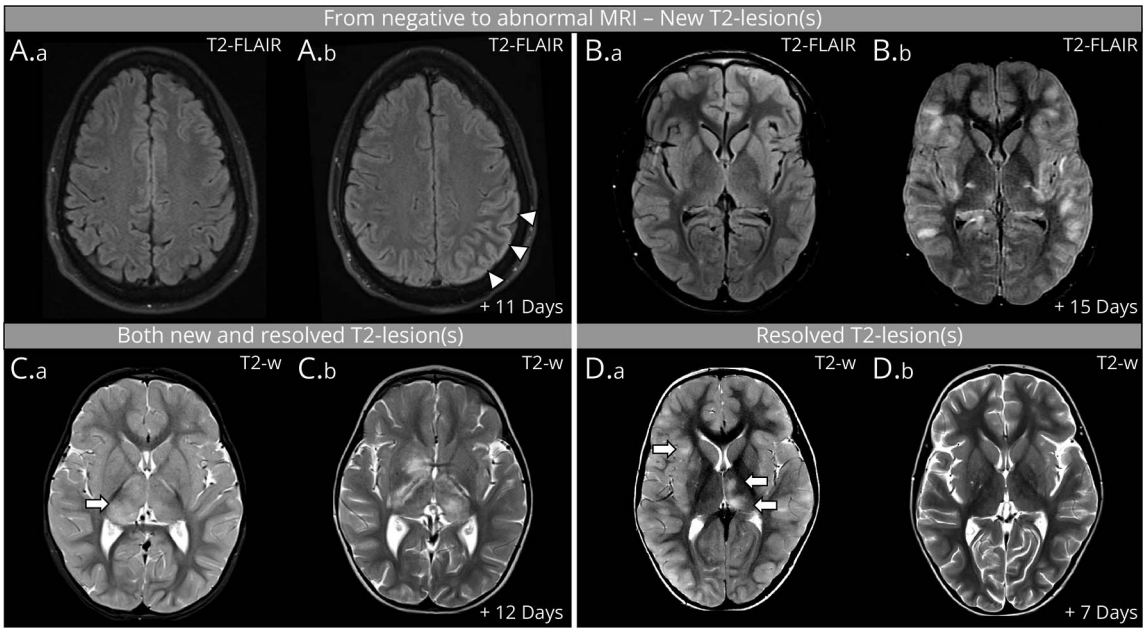
In addition, we merged categories to identify the frequency of the following: (1) at least 1 lesion resolved (i.e., pooled analysis of resolved lesion(s) and both new and resolved lesion(s)); (2) at least 1 new lesion (i.e., pooled analysis of new lesion(s) and both new and resolved lesion(s)), and (3) dynamic findings in either direction (i.e., pooled analysis of new lesion(s), both new and resolved lesion(s), and resolved lesion(s)).

We also reported the frequency of persistent, new, or resolved leptomeningeal and parenchymal enhancement among patients with postcontrast T1-weighted imaging available both at baseline and follow-up MRI.

Statistical Analysis

Continuous variables were compared using the Mann-Whitney *U* test according to the normality assumption. Comparisons of categorical variables were performed with the χ^2 test or Fisher exact test based on the number of observations. A *p* value of <0.05 was considered significant. Analyses were run with BlueSky Statistics version 7.40 (LLC, Chicago, IL), and plots were obtained with R (version 4.3.1; R Core Team 2020).

Figure 1 Examples of Intra-Attack T2 Lesion Dynamics in Patients With MOGAD



All images are in axial view. Resolving T2 lesions are indicated by arrows on first examination. To improve readability, arrows are not displayed when obvious changes are visible. Patients with initial negative MRIs (i.e., radiologic lag A.a and B.a) developed a cortical lesion in the setting of cerebral cortical encephalitis (A.b, arrowheads) and multiple ill-defined supratentorial lesions (B.b). Patient with bilateral thalamic lesions (C.a), 1 resolving (C.a, right thalamic, arrow) and 1 enlarging (C.b, left thalamic) at follow-up (C.b). Additional lesions are also visible in the right globus pallidus and both internal capsules (C.b). Patient with left thalamic lesions and right subcortical lesion (D.a, arrows) had resolved at follow-up (D.b). T2-FLAIR = fluid-attenuated inversion recovery; T2-w = T2-weighted image.

Data Availability

Anonymized data used for this study are available on reasonable request from the corresponding authors.

Results

Demographic and Clinical Features of MOGAD During the Attack

The final cohort included 55 patients with MOGAD (clear positive MOG-IgG in the serum 41 [75%]; double-positive MOG-IgG in the serum and CSF, 15/18 tested [83%]) with 58 attacks analyzed (34 [59%] in pediatrics) (Table 1). Their demographics and clinical details are listed in Table 1.

The 58 attacks in patients with MOGAD included the following: cerebral attacks, 56 (acute disseminated encephalomyelitis [ADEM], 21; cerebral cortical encephalitis, 12; mono/polyfocal cerebral deficits, 5; brainstem/cerebellar deficits, 18) and optic neuritis with asymptomatic acute brain lesions, 2. The reasons for repeat imaging were available in 56 patients with MOGAD and are outlined in Table 1 with clinical worsening or lack of improvement the most common indication.

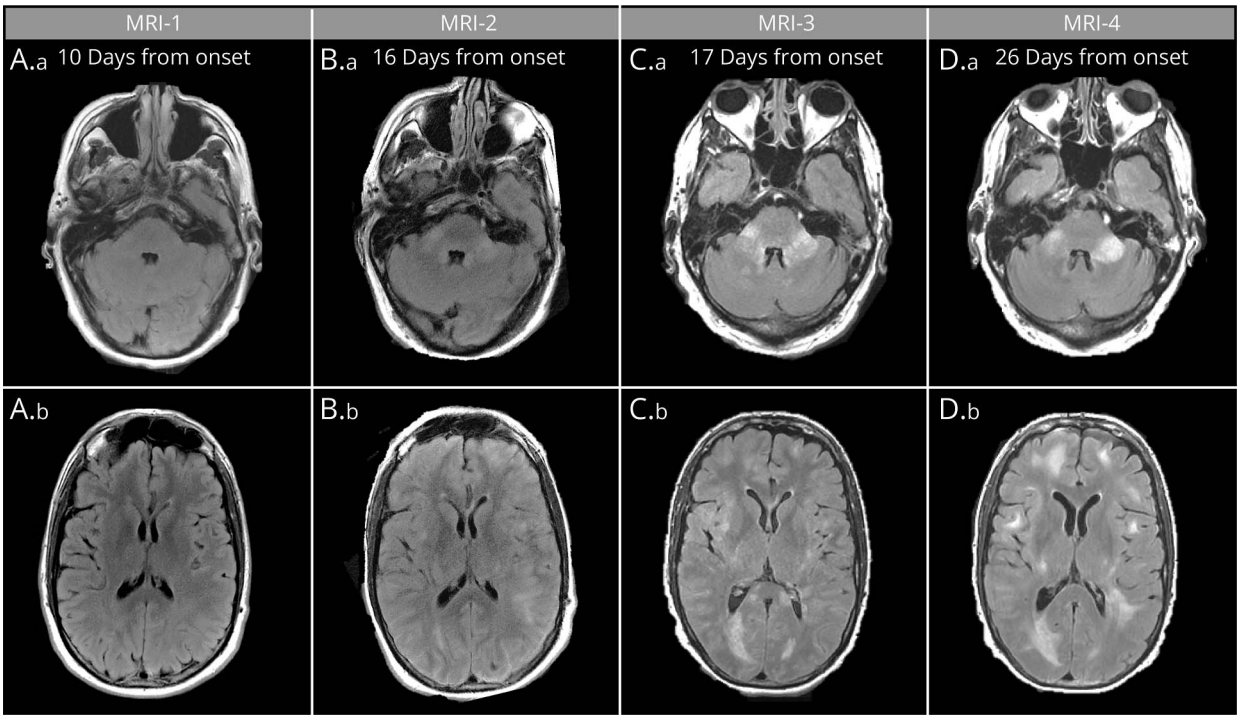
Initial MRI Results and Radiologic Lag in Patients With MOGAD

The first MRI scan was acquired after a median of 5 days from symptom onset (interquartile range [IQR] 3–9) and was normal (i.e., no evidence of brain lesions) in 6/58 patients (10%) (Table 2 and Figure 1). All patients had initial cerebral symptoms (ADEM, 2; cerebral cortical encephalitis, 3; and brainstem/cerebellar deficits, 1). All these patients had abnormalities detected on the second MRI, which was acquired after a median of 10 days from the first MRI (IQR 7.5–15.5); the patient with brainstem/cerebellar deficits received high-dose steroids before the second MRI scan. None of the other patients with initial normal MRI received attack treatments between scans (i.e., steroids, plasma exchange, and IVIgs). CSF was obtained in close proximity to the normal MRI scan in 4 patients, and all demonstrated pleocytosis (i.e., >5 cells/μL; median, 58 cells/μL [IQR 30–84]). Examples of the initial negative MRI and subsequent abnormal MRI within a single attack are shown in Figures 1 and 2. Among the remaining 52 patients with brain T2 lesions on the first MRI, 32 (62%) had from 1 to 5 lesions, 13 (25%) had more than 10 lesions, and 7 (22%) had 6 to 10 lesions. Among the 47 attacks with post-contrast images available from the initial scan, leptomeningeal enhancement was noted in 17 (36%) and parenchymal enhancement in 16 (34%).

Lesion Evolution Within an Attack in Patients With MOGAD

The second MRI was acquired at a median (IQR) of 8 (5–13) days from the first MRI (Table 2, eTable 1, Figures 1 and 2). When compared with the initial MRI, the second MRI within the same attack demonstrated dynamic lesions in 34/58 (59%) including: new lesion(s), 27 (47%); resolved lesion(s), 4 (7%); and both new and resolved

Figure 2 Examples of Intra-Attack T2 Lesion Dynamics in a Patient With MOGAD With 4 MRI Scans Within a Single Attack



All images are in axial view on T2–fluid-attenuated inversion recovery. The patient had progressive increase in number and size of T2 lesions over a span of 16 days. First MRI (A) was normal. The patient developed new and enlarging ill-defined lesions on subsequent examinations (B, C, and D) mainly located in infratentorial and juxtacortical supratentorial white matter. MOGAD = myelin oligodendrocyte glycoprotein antibody–associated disease.

lesion(s), 3 (5%). In the remaining 24 patients (41%), the second MRI was stable. Details of intra-attack lesion evolution in patients with MOGAD are listed in Table 1 and demonstrated in Figures 1, 2 and 4 (A and B). Parenchymal and leptomeningeal enhancement show changes between MRIs, although less frequently than seen with T2 lesions (Table 3).

Twelve patients had more than 2 MRI scans within a single attack. When compared with the second MRI, the third MRI showed new lesions in 5 (42%), stability in 3 (25%), resolution of lesions in 4 (33%), and both new and resolved lesions in 0 (0%). Both patients who had 4 MRIs within a single attack showed new lesion(s) on the fourth MRI compared with the third. Details are reported in eTable 1, and an example of 4 MRIs within a single attack is shown in Figure 2. In patients with multiple attacks analyzed, new lesion(s) at second MRI were observed in 2 of the 3 additional attacks (66%).

Lesion Evolution Within an Attack in Pediatric and Adult Patients With MOGAD

When compared with adults, pediatric patients with MOGAD were broadly similar in terms of MRI dynamics, except for a lower rate of persistent parenchymal enhancement of lesions at follow-up MRI (3/26 [12%] vs 8/18 [44%], p = 0.03) (Table 2). Details are provided in Table 2.

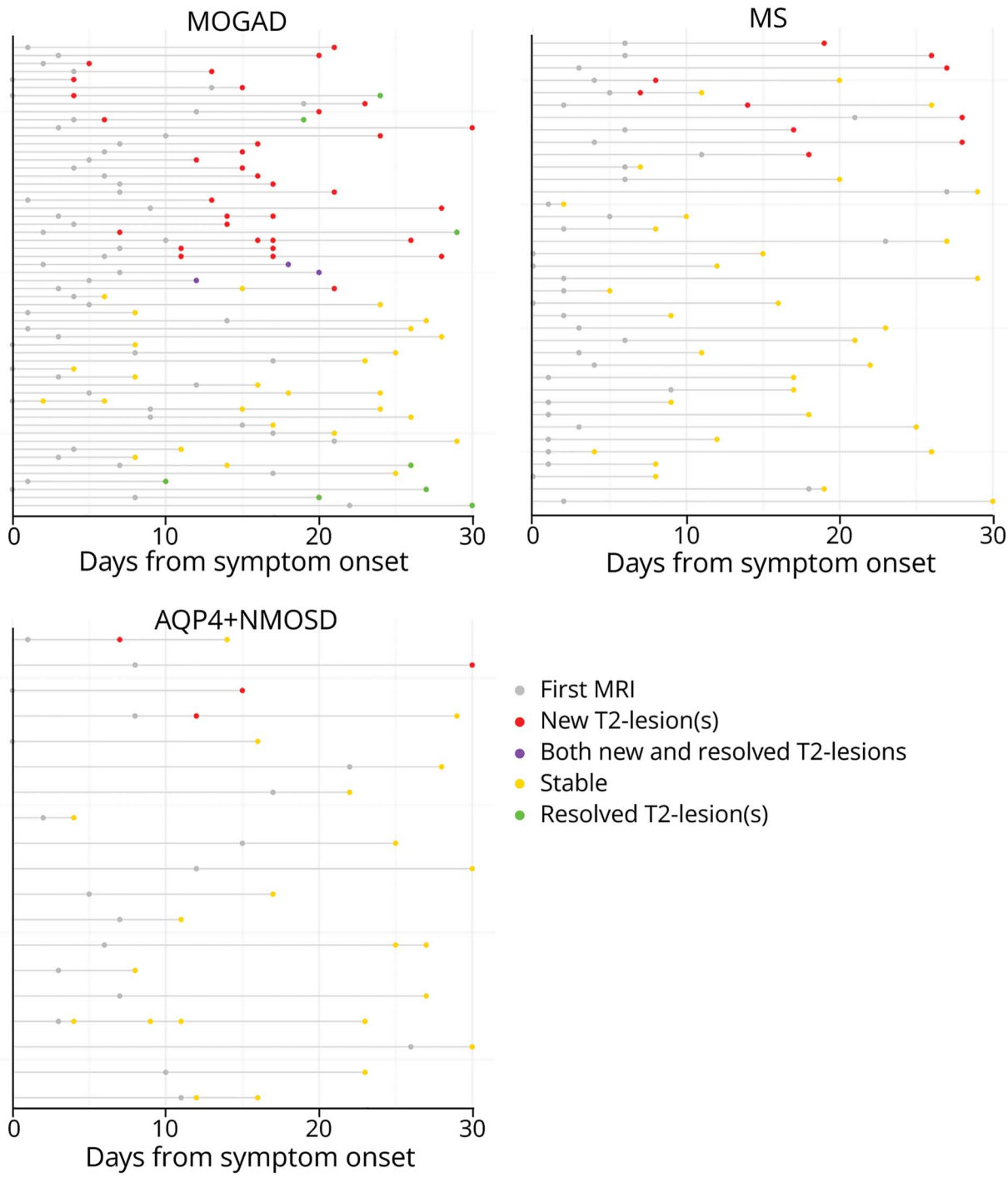
Lesion Evolution Within an Attack in Patients With MOGAD According to Steroid Treatment

Intravenous steroids (methylprednisolone, total dose 1–7 g) were administered before the second MRI in 28 patients, after a median of 7 [IQR 3–13] days from symptom onset (eTable 2). Subsequent oral tapering was started in 10 patients. In patients treated with steroids, new lesion(s) were less common (9/28 [32%] vs 18/30 [60%], p = 0.03), the likelihood of lesion(s) resolving was greater (4/28 [14%] vs 0/30 [0%], p = 0.048), and leptomeningeal enhancement was less frequent (1/24 [4%] vs 6/20 [30%], p = 0.04). In the pooled analysis, the presence of at least 1 lesion resolved was also more common with steroid administration at 6/28 [21%] vs 1/30 [3%], p = 0.048. Full data are listed in eTable 2.

Lesion Evolution Within an Attack in Patients With MOGAD According to Attack Phenotype

Given the small number of patients with mono/polyfocal cerebral deficits and optic attacks with incidental lesions, they were merged into the category "other phenotypes" (eTable 3). The MRI dynamic, including the frequency of radiologic lag, was similar across the attack phenotypes (ADEM, cerebral cortical encephalitis, brainstem/cerebellar deficits, and other phenotypes), except for a higher rate of resolved lesion(s) with the brainstem/cerebellar deficit category (4/18 [22%], vs 0% in the other groups, p = 0.02)

Figure 3 Graphic Representation of MRI Scan Dynamics Over Time in the Study Population



X axis shows the days from symptom onset. Each horizontal line represents 1 attack, with dots corresponding to each MRI scan labeled by its evolution. AQP4+NMOSD = aquaporin-4 antibody seropositive neuromyelitis optica spectrum disorder; MOGAD = myelin oligodendrocyte glycoprotein antibody–associated disease; MS = multiple sclerosis.

and of persistent leptomeningeal enhancement in patients with cerebral cortical encephalitis (4/6 [67%] vs 3/17 [18%] in ADEM, 0/16 [0%] in brainstem/cerebellar attacks, and 0/6 [0%] in other phenotypes, $p = 0.002$). Details are listed in eTable 3.

Comparison of Lesion Evolution With an Attack in Patients With MOGAD, MS, and AQP4+NMOSD

The demographics, clinical features, and reasons for repeat MRI of the 55 patients with MOGAD (58 attacks) are compared with

Table 3 Comparison of Lesion Dynamics at Second MRI Scan Between MOGAD, MS, and AQP4+NMOSD

	MOGAD (n = 58)	MS (n = 38)	MOGAD vs MS	AQP4+NMOSD (n = 19)	MOGAD vs AQP4+NMOSD
Days from MRI 1	8 (5–1)	10 (5–16)	0.52	6 (4–16)	0.74
MRI dynamics (MRI 2 vs MRI 1)					
Lesions					
Stable lesion number[b]	24 (41)	28 (74)	0.002	15 (79)	0.004
New lesion(s)[c]	27 (47)	10 (26)	0.046	4 (21)	0.06[a]
Resolved lesion(s)[d]	4 (7)	0 (0)	0.15[a]	0 (0)	0.57[a]
Both new and resolved lesion(s)[e]	3 (5)	0 (0)	0.15[a]	0 (0)	0.57[a]
Leptomeningeal enhancement					
Persistent	7 of 44 (16)	N/A[f]	—	0 of 14 (0)	0.18[a]
New	5 of 44 (11)	1 of 22 (5)	0.66[a]	0 of 14 (0)	0.32[a]
Resolved	8 of 44 (18)	N/A[f]	—	1 of 14 (7)	0.43[a]
Parenchymal enhancement of lesion(s)					
Persistent	11 of 44 (25)	13 of 22 (59)	0.01	3 of 14 (21)	>0.99[a]
New	8 of 44 (18)	6 of 22 (27)	0.39	1 of 14 (7)	0.43[a]
Resolved	5 of 44 (11)	1 of 22 (5)	0.66[a]	6 of 14 (43)	0.009

Abbreviations: AQP4+NMOSD = aquaporin-4 antibody seropositive neuromyelitis optica spectrum disorder; MOGAD = myelin oligodendrocyte glycoprotein antibody–associated disease; MS = multiple sclerosis; N/A = not applicable.
Unless otherwise specified, categorical variables are presented as frequencies (percentages) and p values refer to the Pearson χ^2 test, while continuous variables are median (interquartile range) and p values refer to the Mann-Whitney U test.
[a] Fisher exact test.
[b] Stable lesion number: no new lesions and no resolved lesions.
[c] New lesion(s): ≥1 new lesion and no resolved lesions.
[d] Resolved lesion(s): no new lesions and ≥1 resolved lesion.
[e] Both new and resolved lesion (s): ≥1 new lesion and ≥1 resolved lesion.
[f] N/A: not applicable because no patients with MS had leptomeningeal enhancement at baseline.

the 38 patients with MS and 19 patients with AQP4+NMOSD in Table 1 (Table 3, Figures 3 and 4). The demographics and clinical features found reflected the expected epidemiologic and clinical differences in the 3 disorders (Table 1). The reasons for repeat imaging were broadly similar between patients with MOGAD and AQP4+NMOSD, with clinical worsening or lack of improvement representing the most common reason, while with MS, repeat imaging for a new baseline after transfer to a new medical center predominated (Table 1).

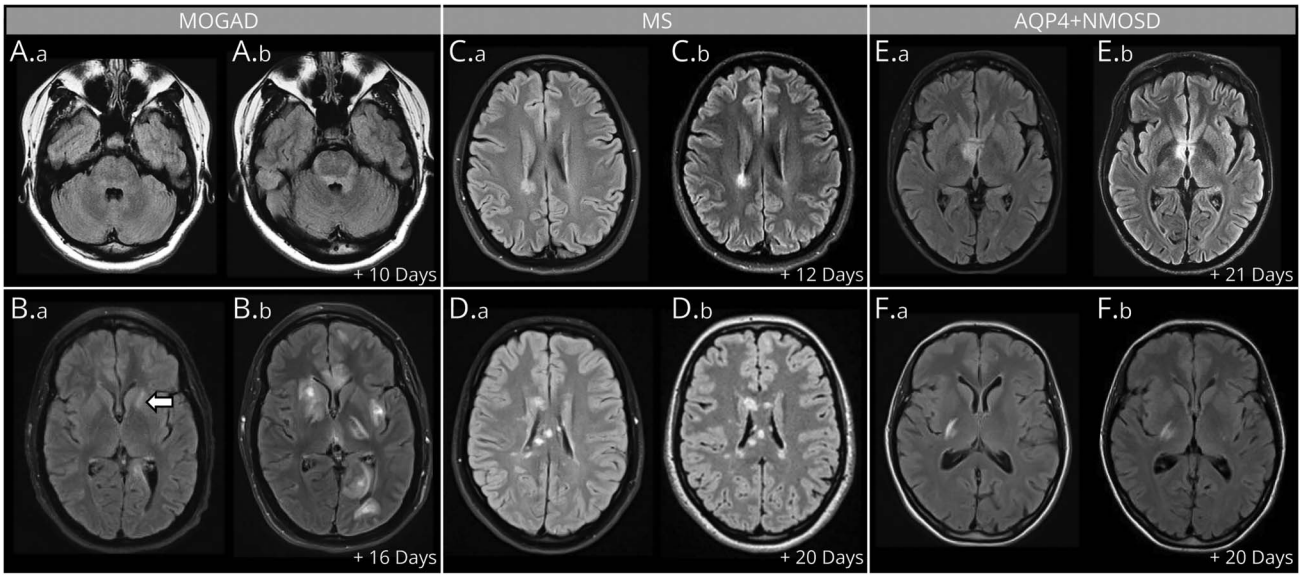
Both MS and AQP4+NMOSD showed a higher rate of stable MRIs than MOGAD, while new lesion(s) were more common in MOGAD than MS. Details are summarized in Table 3 with MRI examples in Figure 4. When we pooled the analysis, the presence of at least 1 new lesion was more common in MOGAD at 30/58 (52%) than in MS at 10/38 (26%, p = 0.01) and in AQP4+NMOSD at 4/19 (21%, p = 0.03). Pooled analysis also showed that at least 1 lesion resolved at the second MRI was observed only in MOGAD at 7/58 (12%), but not in MS at 0/38 (0%, p = 0.04) nor AQP4+NMOSD at 0/19 (0%, p = 0.18).

Dynamic MRI changes were more common in MOGAD (34/58, 59%) than in MS (10/38 [26%], p = 0.002) and AQP4+NMOSD (4/19 [21%], p = 0.007). To assess whether this finding was due to the higher rate of patients with MRI scan repeated for clinical worsening or lack of improvement in the MOGAD group, we ran a post hoc analysis including only patients with MRI scan repeated for other reasons. Dynamic changes were observed in 14/23 patients with MOGAD (61%), 5/27 patients with MS (19%, p = 0.002), and 0/7 patients with AQP4+NMOSD (0%, p = 0.005). This suggests that the higher number of patients with clinical deterioration as an indication for repeat MRI in the MOGAD group vs the MS group did not explain the higher frequency of dynamic changes in the MOGAD group. The complete details of the MRI comparison are outlined in Table 3 and visually summarized in Figure 3.

Discussion

This multicenter study explored the acute dynamics of brain MRI features of MOGAD within a single attack and demonstrated 3 major findings. First, the initial brain MRI can be normal in 10% of attacks despite patients being symptomatic. Second, within a single MOGAD attack, new brain lesions

Figure 4 Comparison of Intra-Attack T2 Lesion Dynamics in Patients With MOGAD, MS, and AQP4+NMOSD



All images are in axial view on T2–fluid-attenuated inversion recovery. Resolving T2 lesions are indicated by arrows on the first examination. To improve readability, arrows are not displayed when obvious changes are visible. MOGAD: 2 patients who developed multiple new ill-defined lesions at the second intra-attack MRI (A.b, B.b) compared with initial MRI (A.a, B.a). The second patient also had resolution of a single lesion in the left putamen (B.a, arrow). MS: a patient with an unchanged periventricular lesion (C.a, C.b) and a patient who developed multiple new focal periventricular lesions (D.a, D.b). AQP4+NMOSD: 2 patients with stable MRIs (E.b, F.b) compared with initial MRIs (E.a, F.a). AQP4+NMOSD = aquaporin-4 antibody seropositive neuromyelitis optica spectrum disorder; MOGAD = myelin oligodendrocyte glycoprotein antibody–associated disease; MS = multiple sclerosis.

often develop and occasionally resolve. Third, MOGAD brain lesions more frequently show changes within a single attack than MS and AQP4+NMOSD, which are more stable.

Our finding of the initial MRI being normal in 10% of MOGAD cerebral attacks is similar to the 10% reported with acute MOGAD myelitis,[21] showing consistent radiologic lag in the brain and spinal cord. This has been previously mentioned in ADEM[22] and in a case of MOGAD,[23] but our study was able to systematically evaluate this among a large multicenter MOGAD group. Recognition of radiologic lag has clear importance for clinical practice, and a normal initial MRI should not exclude MOGAD or consideration of MOG-IgG testing. In this situation, our data suggest that CSF analysis may increase the sensitivity for detecting initial CNS inflammation beyond MRI alone because all patients with an initial normal MRI demonstrated a CSF pleocytosis. In patients with encephalitis and positive MOG-IgG (either low positive or titers not available), a normal MRI may preclude the diagnosis because the diagnostic criteria require typical imaging features of cerebral presentations.[1,24] In these patients, repeat imaging may be diagnostic. Finally, our findings are relevant to clinical trials in MOGAD because an initial normal MRI during a MOGAD attack may preclude such patients from fulfilling the requirements for a MOGAD attack. In this scenario, repeat MRI could also be helpful. However, it also warrants emphasis if the brain MRI is persistently negative and CSF is non-inflammatory, then alternative diagnoses should be explored because MOG-IgG false-positive results (particularly at low titers) are well recognized.[25]

We found that acute lesions in MOGAD are dynamic, with new lesions appearing within an attack in 52% and lesions disappearing in 12%, and this phenomenon occurred with the initial attack and during relapses. Overall, serial imaging in MOGAD in our study often demonstrated radiologic worsening including in those with lesions on the initial MRI, fitting with radiologic lag. The most common reason for repeat imaging was clinical worsening or lack of clinical improvement, so radiologic accumulation of new lesions within an attack is not always radiologic lag but may also occur in the setting of clinical deterioration. We did not find differences in acute MOGAD lesion dynamics between children and adults, and prior analyses of longer-term lesion evolution have shown similar rates of lesion resolution in pediatric and adult MOGAD, suggesting this is related to MOGAD disease biology rather than being age dependent.[10-12] A prior study showed new asymptomatic lesions in MOGAD were most commonly detected at the first follow-up MRI scan after an attack but rarely developed later in the disease course, differing from MS.[26,27] Our data suggest that these asymptomatic lesions may not develop between clinical attacks, but rather more likely arise within the prior attack but are not captured on the initial attack MRI due to radiologic lag.

In contrast to MOGAD, where follow-up MRIs often change, the second MRI was stable in approximately 75% of patients with MS and AQP4+NMOSD. In the MS literature, the main focus has been on intralesional changes of acute microstructural abnormalities[28] and gadolinium enhancement,[29] while longitudinal changes of lesion burden have been assessed over time frames of years and mostly related to the risk of clinical

conversion and disability accrual.[30,31] Increased number of acute lesions over a single attack have been reported, but the comparison with our cohort is challenging because they are presented as examples of patients not responding to acute treatment escalation.[32] In AQP4+NMOSD, serial imaging of the spinal cord within a single attack has shown progressive enlargement of a single lesion.[33] Enlarging lesions are well-recognized in MS also, but this was not the focus of our study that analyzed new lesion occurrence, which was a useful diagnostic clue for MOGAD. Not all new MOGAD lesions had enhancement, and nonenhancing acute lesions are more typical of MOGAD than MS. MS also more frequently had persistent lesional enhancement vs MOGAD while AQP4+NMOSD more often had resolution of enhancement within the attack. Similar to prior analyses,[20] leptomeningeal enhancement was almost exclusive to MOGAD limiting comparisons. Susceptibility-weighted imaging to assess for central vein signs and paramagnetic rim lesions also offers promise as a specific marker of MS and is exceedingly rare in MOGAD.[34]

Prior investigations analyzing lesion resolution in MOGAD,[7-11] mostly compared acute attack MRIs with follow-up MRIs outside an attack and hypothesized that edema resolution, remyelination, or both could contribute to lesion disappearance in MOGAD.[9] The very early disappearance of lesions within days and promoted by steroid treatment could suggest resolution of intramyelin edema as its mechanism,[9] supporting its use as an acute treatment. Experimental models have found that remyelination can begin as soon as 2 weeks from injury,[35] but complete remyelination of lesions, sufficient to allow them to disappear on MRI, might be expected to take many months. We have a few hypotheses on why the initial MRI may be normal. First, it may reflect MOG-IgG exerting a functional interference with neuronal transmission leading to clinical symptoms before becoming overt with conventional imaging. Second, it may relate to CNS inflammation preceding demyelination and lesion development as supported by CSF inflammation in all whose first MRI was normal. Finally, insensitivity of conventional MRI to detect inflammation in MOGAD may have contributed. Post-gadolinium FLAIR sequences could increase the sensitivity for detection of leptomeningeal inflammation in MOGAD and should be considered in MOGAD attacks particularly if the initial MRI head is negative.[20,36]

Our study has some limitations. First, we decided to focus on new lesions appearing and disappearing rather than enlarged lesions or lesions reduced in size. However, without quantitative MRI (as in clinical practice), it can be hard to robustly identify lesion size changes. Moreover, prior studies found that lesions usually reduce their size over time in all 3 disorders (MOGAD, MS, and AQP4+NMOSD), while resolution is almost exclusive to MOGAD.[11] Therefore, lesion appearance and disappearance is a better discriminator. While other parameters (e.g., lesions with ill-defined borders) can discriminate between these diseases and have been previously compared,[8,37] we did not analyze this here because our focus was on lesion dynamics with straightforward endpoints of new lesions, resolved lesions, and stability.

Other potential sources of biases include the retrospective design, which led to repeat MRIs being undertaken on different scanners with variable field strength and different sequence parameters. This variability reflects clinical practice. Obtaining serial research MRIs on the same scanner in patients during an acute attack is generally not feasible given the accompanying clinical status and potential need for MRI under anesthesia (particularly for children). Moreover, the changes between MRIs that we report were not subtle and could likely be identified on repeat imaging with any conventional MRI machine (Figures 1, 2, and 4). The development of new T2 hyperintense lesions, even on different MRI scans and with different MRI protocols, is routinely performed by neuroradiologists and neurologists during MRI surveillance of patients with MS. Despite the lack of standardized protocols and heterogeneity of images, this practice is the basis for the assessment of patients' management and treatment response in clinical practice. Overall, we believe the findings from our study are applicable to clinical practice and that variability in scanner or its parameters did not majorly influence our results.

Another potential limitation is the selection bias in our cohort toward severe or atypical attacks that required additional imaging, and we do not know whether the dynamics would be similar for all MOGAD attacks with brain involvement. A slightly higher proportion of MOGAD than MS had repeat MRI due to clinical worsening, which could have affected that comparison, but post hoc analyses showed the findings remained the same regardless of indication for repeat MRI. Finally, it can be challenging to discriminate new or worsening symptoms within the same attack from a new attack, and we used a cutoff of 30 days for images to be considered within the same attack per 2023 MOGAD diagnostic criteria[1] and definitions in MS[15] and AQP4+NMOSD.[16]

In summary, this study demonstrates that MOGAD lesions are very dynamic during attacks, unlike MS and AQP4+NMOSD. These lesion dynamics are a diagnostic clue to MOGAD and have relevance for attack adjudication in MOGAD clinical trials. Evidence of early lesion resolution may reflect rapidly reversible intramyelin edema rather than demyelination and remyelination. Future studies could consider more advanced imaging techniques and the assessment of blood and CSF biomarkers within attacks to better understand the mechanisms of damage and repair in MOGAD.

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Continued

Appendix *(continued)*

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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. 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
3. Hacohen Y, Absoud M, Deiva K, et al. Myelin oligodendrocyte glycoprotein antibodies are associated with a non-MS course in children. *Neurol Neuroimmunol Neuroinflamm*. 2015;2(2):e81. doi:10.1212/NXI.0000000000000081
4. Hacohen Y, Mankad K, Chong WK, et al. Diagnostic algorithm for relapsing acquired demyelinating syndromes in children. *Neurology*. 2017;89(3):269-278. doi:10.1212/WNL.0000000000004117
5. Cortese R, Battaglini M, Prados F, et al. Clinical and MRI measures to identify non-acute MOG-antibody disease in adults. *Brain*. 2023;146(6):2489-2501. doi:10.1093/brain/awac480
6. Jurynczyk M, Tackley G, Kong Y, et al. Brain lesion distribution criteria distinguish MS from AQP4-antibody NMOSD and MOG-antibody disease. *J Neurol Neurosurg Psychiatry*. 2017;88(2):132-136. doi:10.1136/jnnp-2016-314005
7. Banks SA, Morris PP, Chen JJ, et al. Brainstem and cerebellar involvement in MOG-IgG-associated disorder versus aquaporin-4-IgG and MS. *J Neurol Neurosurg Psychiatry*. 2020;92(4):384-390. doi:10.1136/jnnp-2020-325121
8. 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
9. 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
10. Redenbaugh V, Chia NH, Cacciaguerra L, et al. Comparison of MRI T2-lesion evolution in pediatric MOGAD, NMOSD, and MS. *Mult Scler*. 2023;29(7):799-808. doi:10.1177/13524585231166834
11. 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
12. Abdel-Mannan O, Champsas D, Tur C, et al. Evolution of brain MRI lesions in paediatric myelin-oligodendrocyte glycoprotein antibody-associated disease (MOGAD) and its relevance to disease course. *J Neurol Neurosurg Psychiatry*. 2023. doi:10.1136/jnnp-2023-332542
13. Thompson AJ, Banwell BL, Barkhof F, et al. Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. *Lancet Neurol*. 2018;17(2):162-173. doi:10.1016/S1474-4422(17)30470-2
14. Wingerchuk DM, Banwell B, Bennett JL, et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. *Neurology*. 2015;85(2):177-189. doi:10.1212/WNL.0000000000001729
15. Schumacher GA, Beebe G, Kibler RF, et al. Problems of experimental trials of therapy in multiple sclerosis: report by the panel on the evaluation of experimental trials of therapy in multiple sclerosis. *Ann NY Acad Sci*. 1965;122:552-568. doi:10.1111/j.1749-6632.1965.tb20235.x
16. Kleiter I, Gahlen A, Borisow N, et al. Apheresis therapies for NMOSD attacks: a retrospective study of 207 therapeutic interventions. *Neurol Neuroimmunol Neuroinflamm*. 2018;5(6):e504. doi:10.1212/NXI.0000000000000504
17. Reindl M, Schanda K, Woodhall M, et al. International multicenter examination of MOG antibody assays. *Neurol Neuroimmunol Neuroinflamm*. 2020;7(2):e674. doi:10.1212/NXI.0000000000000674
18. Carta S, Cobo Calvo A, Armangue T, et al. Significance of myelin oligodendrocyte glycoprotein antibodies in CSF: a retrospective multicenter study. *Neurology*. 2023;100(11):e1095-e1108. doi:10.1212/WNL.0000000000201662
19. Waters PJ, McKeon A, Leite MI, et al. Serologic diagnosis of NMO: a multicenter comparison of aquaporin-4-IgG assays. *Neurology*. 2012;78(9):665-671. discussion 669. doi:10.1212/WNL.0b013e318248dec1
20. 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
21. 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
22. Honkaniemi J, Dastidar P, Kahara V, Haapasalo H. Delayed MR imaging changes in acute disseminated encephalomyelitis. *AJNR Am J Neuroradiol*. 2001;22(6):1117-1124.
23. Armangue T, Olive-Cirera G, Martinez-Hernandez E, et al. Associations of paediatric demyelinating and encephalitic syndromes with myelin oligodendrocyte glycoprotein antibodies: a multicentre observational study. *Lancet Neurol*. 2020;19(3):234-246. doi:10.1016/S1474-4422(19)30488-0
24. Ciccarelli O, Toosy AT, Thompson A, Hacohen Y. Navigating through the recent diagnostic criteria for MOGAD: challenges and practicalities. *Neurology*. 2023;100(15):689-690. doi:10.1212/WNL.0000000000207238
25. 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
26. 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
27. Fadda G, Banwell B, Waters P, et al. Silent new brain MRI lesions in children with MOG-antibody associated disease. *Ann Neurol*. 2021;89(2):408-413. doi:10.1002/ana.25957
28. Rovira A, Auger C, Alonso J. Magnetic resonance monitoring of lesion evolution in multiple sclerosis. *Ther Adv Neurol Disord*. 2013;6(5):298-310. doi:10.1177/1756285613484079
29. Gaitan MI, Shea CD, Evangelou IE, et al. Evolution of the blood-brain barrier in newly forming multiple sclerosis lesions. *Ann Neurol*. 2011;70(1):22-29. doi:10.1002/ana.22472
30. Weiner HL, Guttmann CR, Khoury SJ, et al. Serial magnetic resonance imaging in multiple sclerosis: correlation with attacks, disability, and disease stage. *J Neuroimmunol*. 2000;104(2):164-173. doi:10.1016/s0165-5728(99)00273-8
31. Morrissey SP, Miller DH, Kendall BE, et al. The significance of brain magnetic resonance imaging abnormalities at presentation with clinically isolated syndromes suggestive of multiple sclerosis. A 5-year follow-up study. *Brain*. 1993;116(pt 1):135-146. doi:10.1093/brain/116.1.135
32. Pericot I, Rio J, Rovira A, Castella MD, Tintore M, Montalban X. Serial gadolinium-enhanced MRI in acute attack of multiple sclerosis treated with plasma exchange. *J Neurol*. 2003;250(2):243-244. doi:10.1007/s00415-003-0962-y
33. Asgari N, Skejoe HP, Lennon VA. Evolution of longitudinally extensive transverse myelitis in an aquaporin-4 IgG-positive patient. *Neurology*. 2013;81(1):95-96. doi:10.1212/WNL.0b013e318297ef07
34. Sacco S, Virupakshaiah A, Papinutto N, et al. Susceptibility-based imaging aids accurate distinction of pediatric-onset MS from myelin oligodendrocyte glycoprotein antibody-associated disease. *Mult Scler*. 2023;29(14):1736-1747. doi:10.1177/13524585231204414
35. Karttunen MJ, Czopka T, Goedhart M, Early JJ, Lyons DA. Regeneration of myelin sheaths of normal length and thickness in the zebrafish CNS correlates with growth of axons in caliber. *PLoS One*. 2017;12(5):e0178058. doi:10.1371/journal.pone.0178058
36. Tzanetakos D, Tzartos JS, Vakrakou AG, et al. Cortical involvement and leptomeningeal inflammation in myelin oligodendrocyte glycoprotein antibody disease: a three-dimensional fluid-attenuated inversion recovery MRI study. *Mult Scler*. 2022;28(5):718-729. doi:10.1177/13524585211034362
37. Carnero Contentti E, Rojas JI, Criniti J, et al. Towards imaging criteria that best differentiate MS from NMOSD and MOGAD: large multi-ethnic population and different clinical scenarios. *Mult Scler Relat Disord*. 2022;61:103778. doi:10.1016/j.msard.2022.103778