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Clinical Features of Children With MOG-IgG Who Fulfill Criteria of Multiple Sclerosis and Overlapping Disorders

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Abstract

Objectives

The aim of this study was to report the clinical features, disease-modifying treatment (DMT) response, and outcomes of children with MOG-IgG who fulfill the 2017 McDonald criteria for multiple sclerosis (MS).

Methods

This prospective observational study included children (<18 years) with a suspected acquired demyelinating syndrome (ADS) whose serum or CSF was positive for MOG-IgG, who met the indicated MS criteria, and who had ≥1 year of clinical follow-up. MOG-IgG was tested using live cell-based assays.

Results

Of 554 children with confirmed ADS (196 with MOG-IgG), 8 (median age 11 years, interquartile range 9–14) harbored MOG-IgG and fulfilled MS criteria: 2 had typical MS and 6 had overlapping MOGAD-MS features at onset, but 5 of the latter group developed an MS-like course during follow-up. Five of 7 patients with assessable samples were Epstein-Barr virus seropositive at disease onset, and all 8 had persistent silent radiologic activity with lesional location and morphology suggestive of MS, leading to initiation of DMT. All initial treatments were well tolerated, but eventually, 7 of 8 children (88%) required high-efficacy DMT.

Discussion

In this pediatric cohort, 4% of patients with MOG-IgG met criteria for MS. The clinical-radiologic spectrum ranged from typical MS to overlapping MOGAD-MS, and patients usually required high-efficacy DMT.

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Supplementary Material

Introduction

Diagnosis of myelin oligodendrocyte glycoprotein antibody–associated disease (MOGAD) requires a core demyelinating syndrome, serum and/or CSF MOG-IgG positivity, and additional clinico-radiologic supporting features in cases with low serum titers or CSF positivity only.[1] In addition, exclusion of alternative diagnoses such as multiple sclerosis (MS) is required, which can be challenging in clinical practice. Although recent studies highlighted the high

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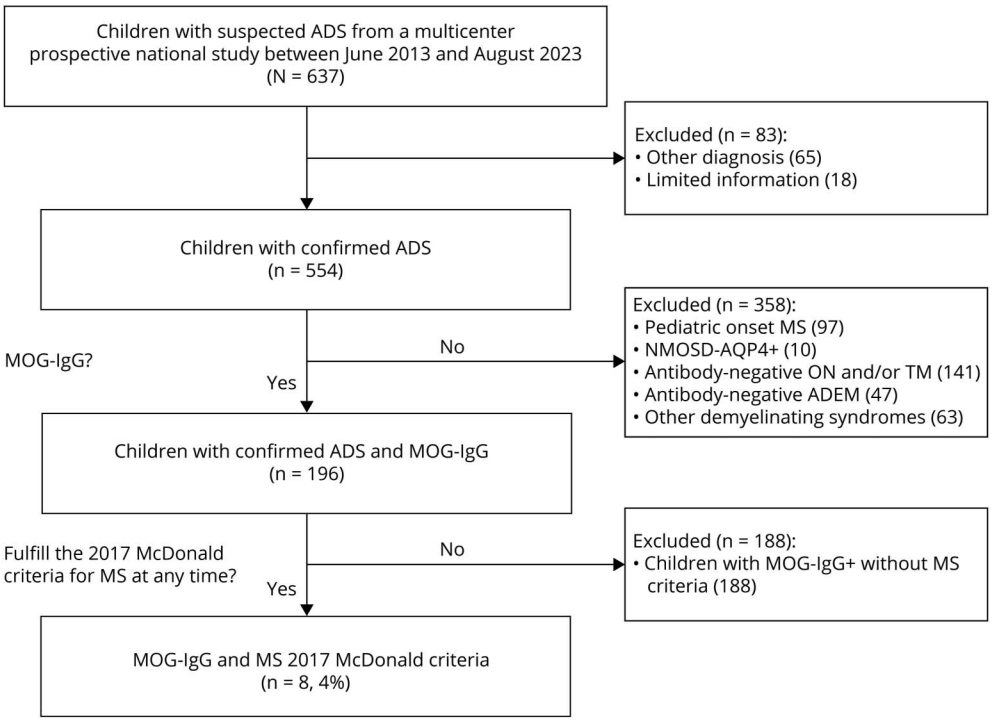
Figure 1 Flowchart of Children Included in the Study



*The recruitment of patients is part of a prospective ongoing study that involves more than 40 secondary and tertiary centers in Spain, in which all children with suspected demyelinating disorders are investigated for autoantibodies in serum and/or CSF (eMethods). Abbreviations: ADEM = acute disseminated encephalomyelitis; ADS = acquired demyelinating syndrome; AQP4+ = aquaporin-4 antibody positive; FU = follow-up; IgG = immunoglobulin G; MOG = myelin oligodendrocyte glycoprotein; MS = multiple sclerosis; NMOSD = neuromyelitis optica spectrum disorder; ON = optic neuritis; TM = transverse myelitis.

accuracy of MOGAD criteria in pediatric and adult populations,[2,3] there are still concerns for patients who might meet both sets of criteria, i.e., MOGAD and MS.[4] Moreover, the experience in the pediatric population with overlapping MOGAD-MS features is very limited.[5] In this study, we examined a large prospective pediatric cohort of patients with acquired demyelinating syndromes (ADSs) for these overlapping features and report the clinical manifestations, response to disease-modifying treatments (DMTs), and outcomes.

Methods

We reviewed the clinical and immunologic features of a cohort of 637 children (<18 years) with suspected ADS whose samples (427 paired serum and CSF, and 210 only serum) were sent between June 1, 2013, and August 31, 2023, to our laboratory (IDIBAPS-Hospital Clinic, Barcelona, Spain) as part of a prospective multicenter study. MOG-IgG was determined with a live cell-based assay as previously reported.[3] Patients with MOG-IgG who met the 2017 McDonald diagnostic criteria for MS[6] at any time during the disease were included in this study. Patients without sufficient clinical information or follow-up <12 months were excluded (eMethods).

Standard Protocol Approvals, Registrations, and Patient Consents

This study was approved by the Ethical Committee of Hospital Clínic de Barcelona. Written informed consents were obtained from patients or proxies.

Data Availability

Anonymized data not published within this article will be made available by reasonable request from any qualified investigator.

Results

Of 554 children with confirmed ADS, 196 were MOG-IgG positive and 8 of them (median age at onset 11 years [interquartile range (IQR): 9–14], 5 [63%] female) fulfilled MS criteria[6] (Figure 1). Of these 8 patients, 7 had CSF-restricted MOG-IgG and one had MOG-IgG in both serum and CSF. Two clinical and radiologic presentations were identified: 2 patients showed typical MS features at onset and follow-up, and the other 6 patients had overlapping MOGAD-MS features at disease onset, 5 of them following a MS-like course (Table).

The 2 patients with typical MS features had a clinically isolated syndrome with initial brain and spinal cord MRI lesions characteristic of MS (#1–2, Table, Figure 2, A.a–A.d). Despite MOG-IgG positivity and supportive radiologic features of MOGAD in one of them (#1), MS was believed to be the most plausible diagnosis based on the presenting syndrome, a high lesion load on brain MRI, and the presence of CSF oligoclonal bands (CSF-OCBs). DMT (anti-CD20; interferon-beta1a) was initiated at 1 month and 6 months after disease onset. During follow-up, both patients had persistent T2-FLAIR hyperintense and T1 hypointense lesions (Figure 2, A.e–A.f),

Table Children With MOG-IgG Positivity Who Fulfilled the 2017 McDonald Criteria for Multiple Sclerosis at Any Time

Case #, age range (y)[a] Presenting syndrome (supportive clinico-radiologic features of MOGAD)	MRI at onset		Follow-up			Biomarkers at onset and follow-up		
	Brain MRI	Spinal cord MRI	Clinical relapses/ asymptomatic radiologic activity	DMT (time from disease onset to initiation)	EDSS (mo: FU) persistent brain T2-hyper/T1-hypo lesions	CSF-OCBs	MOG-IgG	EBV-IgG
Children with typical MS features at onset and follow-up								
#1 13–15 y; Polyfocal syndrome (Yes, at onset: LETM but not typical of MOGAD)[b]	Typical of MS >30 lesions: PV, juxtacortical, and CC with Gd+. T1-hypo lesions since onset (Figure 2A.a-A.c)	Typical of MS Ill-defined lesion in cervical region[b] with additional short lesions in C4, C6, and D5 (Figure 2A.d)	1 relapse in the first week after DMT (brainstem syndrome) /no	RTX (1 mo)	EDSS : 4 (60 mo) MRI: >30 T2 lesions (Figure 2A.e)/yes (Figure 2A.f)	Positive (onset)	Onset: S – (CSF +1:2) FU: S – (1, 2, 3 y)	Positive
#2 13–15 y; short myelitis (no)	Typical of MS >15 lesions: PV, CC, subcortical WM, and brainstem Gd- and T1-hypo lesions since onset	Typical of MS A tumefactive central lesion in D10-11 with Gd+, short lesions in C3 and D5 Gd-	3 relapses under first DMT (2 with brainstem syndrome, 1 with short myelitis)/yes, after first DMT	First IFN-β1a (6 mo) Second NTZ (18 mo)	EDSS : 1.5 (156 mo) MRI: >30 T2 lesions/yes	Positive (onset)	Onset: S – (CSF + 1:2) FU: n.a.	n.a.
Children with overlapping MOGAD-MS features								
#3 10–12 y; Bilateral ON (yes, at onset)	Nonspecific Punctate lesions in subcortical and juxtacortical WM Gd+	Typical of MS Short peripheral lesions in cervical and dorsal region Gd- (C2, C3, C5-C6, and D4)	1 relapse (unilateral ON) before first DMT/ yes, after first DMT	First FTY (5 mo), second OFA (24 mo)	EDSS : 0 (33 mo) MRI: <15 T2 lesions/yes	Negative (onset and 2 y[c])	Onset: S – (CSF + 1:2) FU: S and CSF – (2 y)[c]	Positive
#4 7–9 y;[d] Bilateral ON (yes, at onset)	Typical of MOGAD/NMOSD Bilateral optic nerve involvement Gd+. Ill-defined lesions in brainstem and subcortical WM Gd+	Typical of MS Short and peripheral lesions in cervical and lower dorsal spine with ill-defined Gd+ (C2, C6, D8-9, and D11-12)	No/yes, before DMT	RTX (15 mo)[e]	EDSS : 1.0 (56 mo) MRI: 15-20 T2 lesions/no	Positive (onset)	Onset: S – (CSF + 1:5) FU: S – (2 y)	Positive
#5 10–12 y; cortical encephalitis (yes, at onset)	Typical of MOGAD Right frontal cortical gyri and sulci hyperintensity in T2/ FLAIR (Figure 2B.a)	Not performed at onset	4 relapses (unilateral ON, brainstem syndrome, short myelitis, hemispheric syndrome) before and on first DMT/yes, after second DMT (Figure 2B.b–B.c)	First GA (3 mo), second TERI (62 mo); third OCRE (89 mo)	EDSS : 3.0 (132 mo) MRI: >20 T2 lesions (Figure 2B.e)/yes (Figure 2B.f)	Positive (onset)	Onset: S – (CSF +1: 10) FU: S – (1, 10 y)	Positive
#6 7–9 y; bilateral ON (yes, at onset)	Typical of MOGAD Bilateral optic nerve involvement with Gd+. Patchy lesions in cortico-subcortical, PV, and juxtacortical regions Gd- (Figure 2C.a)	Typical of MS Short peripheral lesions in cervical and dorsal spine with Gd+ (C2, C5, D1, and D5) (Figure 2C.b)	No/yes, before and 4 mo after DMT, but then stability (Figure 2C.c–C.d)	IFN-β1a (initiated at 13 mo, discontinued at 84 mo)	EDSS : 1.0 (90 mo) MRI: <5 T2 lesions/yes (Figure 2C.e–C.f)	Positive (onset) Negative (7 y)	Onset: S – (CSF +1:2) FU: S – (1, 7 y), CSF – (7 y)	Positive

Continued

Table Children With MOG-IgG Positivity Who Fulfilled the 2017 McDonald Criteria for Multiple Sclerosis at Any Time *(continued)*

Case #, age range (y)[a] Presenting syndrome (supportive clinico-radiologic features of MOGAD)	MRI at onset		Follow-up			Biomarkers at onset and follow-up		
	Brain MRI	Spinal cord MRI	Clinical relapses/ asymptomatic radiologic activity	DMT (time from disease onset to initiation)	EDSS (mo: FU) persistent brain T2-hyper/T1-hypo lesions	CSF-OCBs	MOG-IgG	EBV-IgG
#7 **10–12 y;** **Brainstem-cerebellar (yes, at onset)**	Overlap MOGAD-MS Combined well-defined and ill-defined lesions in middle cerebellar peduncle and brainstem Gd+, and one PV well-defined lesion (Figure 2D.a--D.c)	Typical of MS Patchy, ill-defined cervical and lower dorsal spine lesions Gd+ (C2-C3, C5, D5-6, D10-11) (Figure 2D.d)	No/yes, before DMT (Figure 2D.e)	FTY (7 mo)	EDSS : 1.0 (68 mo) MRI: <5 T2 lesions/yes (Figure 2D.f)	Positive (onset) Negative (7 y)	Onset: S + (1: 160),CSF + (1:5) FU: S – (6 mo) S + (1 y, 1:80) S - (2, 5, 7 y)	Negative
#8 **7–9 y;** **Short myelitis (yes, at FU)**	Typical of MS Well-defined brainstem-cerebellar lesions, and subcortical and PV lesions (Figure 2E.a–E.c)	Typical of MS Tumefactive, central dorsal cord lesion (D5-6) (Figure 2E.d)	Yes, bilateral almost subclinical ON[f]/yes, before (Figure 2D.e) and after first DMT[g], as well 4 and 8 mo after second DMT[h]	First FTY (7 mo), second RTX (12 mo)	EDSS : 1.5 (20 mo) MRI: <15 T2 lesions/yes (Figure 2E.f)	Negative (onset and 6 mo[c])	Onset: S – (CSF +1: 10) FU: S + (6 mo, 1:160) S – (8 mo, 1 y, 2 y) CSF + (6 mo, 1:5)[c]	Negative

Abbreviations: CC = corpus callosum; DMT = disease-modifying treatment; EDSS = Expanded Disability Status Scale; Figure = figure; FU = follow-up; FTY = fingolimod; GA = glatiramer acetate; Gd+ = gadolinium enhancement; Gd- = without gadolinium enhancement; IFN-β1a = interferon beta-1a; LETM = longitudinally extensive transverse myelitis; MS = multiple sclerosis; MOGAD = myelin oligodendrocyte glycoprotein antibody–associated disease; n.a. = not available; NTZ = natalizumab; OCB = oligoclonal band; OCT = optic coherence tomography; OCRE = ocrelizumab; OFA = ofatumumab; ON = optic nerve; PV = periventricular; RTX = rituximab; S = serum; TERI = teriflunomide; T1-hypo = T1 hypointense lesions; T1-hyper = T1 hyperintense lesions; WM = white matter.

[a] In patients with typical MS features (patients #1 and 2), gender distribution was equal. Among those with overlapping MOGAD-MS features (patients #3 to 8), 4 (67%) were female and 2 (33%) were male. The ancestry distribution was as follows: European in 4 patients, Latin-American in 3, and North African in 1. The median (IQR) age at onset in patients with typical MS features was 14 y (IQR: 14-14) while in patients with overlapping features, it was 10 y (IQR: 9–12).

[b] Image not typical of MOGAD due to additional short spinal cord lesions; longitudinal involvement (≥3 segments) was more suggestive of extensive involvement due to high lesion load (Figure 2A.d).

[c] Repeated CSF studies were performed after the detection of new silent radiologic activity typical for MS.

[d] This patient was previously reported (reference 3 of Supplementary Material).

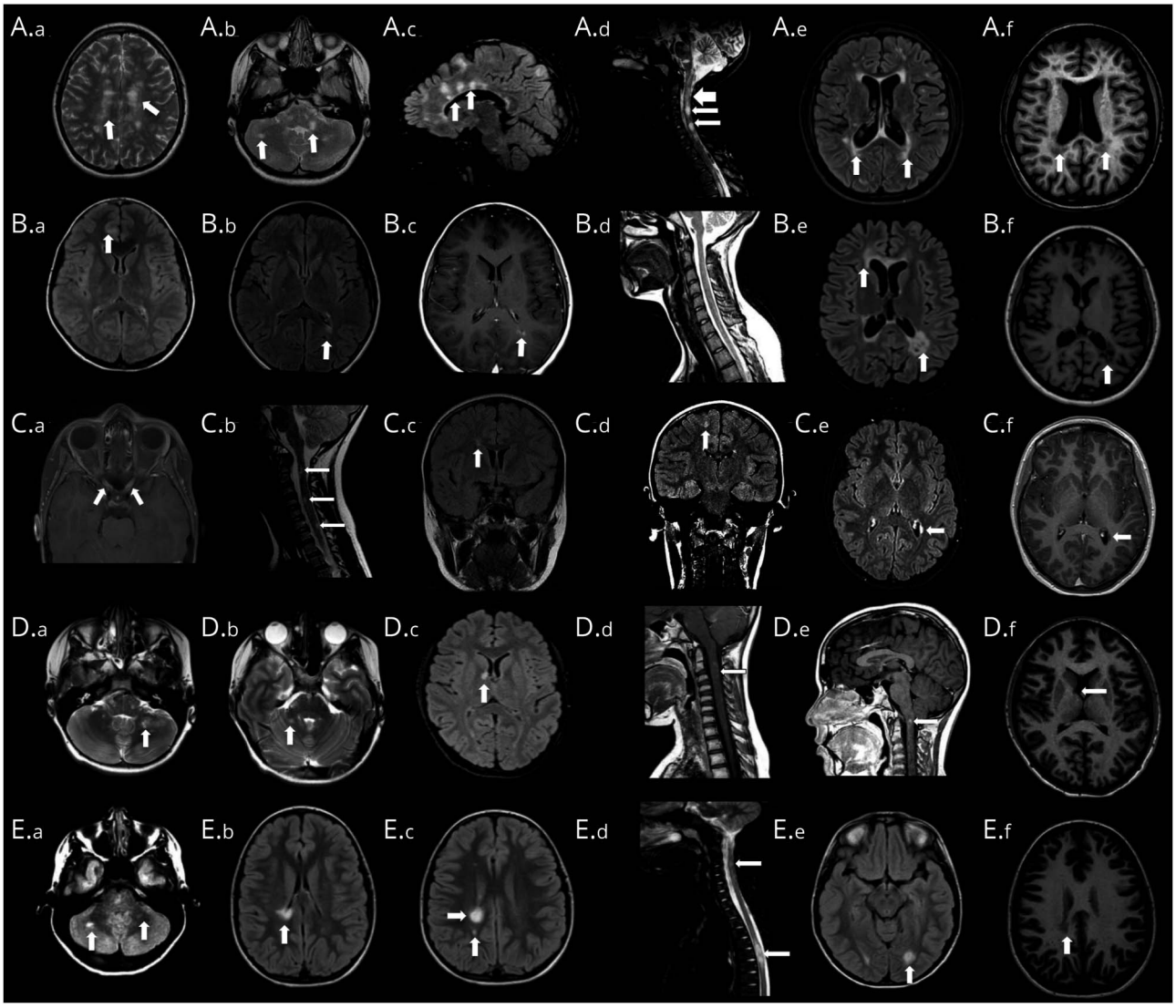
[e] Rituximab was given during the acute episode because of poor response to first-line therapy, but rituximab as maintenance treatment was not started until 15 mo later when new silent typical MS lesions appeared.

[f] OCT showed severe bilateral reduction in thickness of both the ganglion cell layer (GCL) and the retinal nerve fiber layer (RNFL).

[g] At the time of silent radiologic activity 4 mo after starting fingolimod (0.25 mg/daily because of body weight <40 kg), blood white cell count did not show lymphopenia.

[h] Although reduced, silent radiologic activity with new T2/FLAIR lesions with typical MS location and morphology was still observed in follow-up brain MRI scans performed at 4 and 8 mo after switching to RTX, so close monitoring of radiologic activity is still ongoing.

Figure 2 Representative MRI Scans of Each Patient Group



Panel A: Representative patient (#1) with MOG-IgG and typical MS features: T2-weighted/axial FLAIR brain and cervical spinal cord MRI at onset (A.a–A.d) showed well-defined supra and infratentorial typical MS lesions (vertical white arrows). Note that despite spinal cord MRI showing involvement of ≥3 consecutive segments (A.d wide horizontal arrow), the image is not typical for MOGAD because it showed additional short spinal cord lesions (A.d, narrow horizontal arrows); T2-weighted/axial FLAIR brain MRI at last follow-up (5 years) (A.e) showed persistent T2 typical MS lesions, global atrophy, and hypointense lesions in T1 sequences (A.f). (B, C, D, and E) Representative patients with overlapping MOGAD-MS features. Panel B (patient #5): T2-weighted/axial FLAIR brain MRI at onset with right frontal cortical gyri and sulci hyperintensity (B.a); T2-weighted/axial FLAIR and T1-weighted postcontrast MRI after 3 months of follow-up showed new silent periventricular lesions (B.b), one with Gd+ enhancement (B.c); T2-weighted sagittal spinal cord MRI at 5-year follow-up showed no abnormalities (B.d); T2-weighted/axial FLAIR brain MRI at last follow-up (9 years) (B.e) showed persistent T2/FLAIR periventricular and CC typical MS lesions along with global atrophy and hypointense lesions in T1 sequences (B.f). Panel C (patient #6): Axial T1-weighted postcontrast brain MRI (C.a) and sagittal T1-weighted postcontrast cervical-thoracic spine MRI (C.b) at disease onset demonstrate bilateral optic nerve involvement with gadolinium enhancement (C.a) and 3 short spinal cord lesions (C.b). T2-weighted/axial FLAIR brain MRI (C.c-C.d) showed new silent periventricular lesions before the initiation of disease-modifying treatment (DMT) (C.c), as well as a new juxtacortical lesion 4 months after initiation of interferon beta-1a (C.d). At the last follow-up, T2-weighted/axial FLAIR brain MRI (C.e) and axial T1-weighted postcontrast MRI (C.f) revealed persistence of the left periventricular lesion. Panel D (patient #7): T2-weighted axial (D.a-D.b), axial FLAIR brain (D.c), and sagittal T1-weighted postcontrast cervical (D.d) MRI sequences at onset showing mixed well and ill-defined brainstem lesions (D.a-D.b), one well-defined right periventricular lesion (D.c), and one short spinal cord lesion with Gd+ enhancement (D.d). Sagittal T1-weighted postcontrast spinal cord MRI at 3 months of follow-up (D.e) showed a new silent short spinal cord lesion with Gd+ enhancement; axial T1 brain MRI (D.f) at last follow-up (6 years) showed persistence of the right periventricular T1 hypointense lesion (D.f). Panel E (patient #8): T2-weighted/axial FLAIR brain and spinal cord MRI at onset (E.a–E.d) with well-defined silent brainstem (E.a) and periventricular (E.b and E.c) lesions typical of MS and short symptomatic spinal cord lesion (E.d). T2-weighted/axial FLAIR brain MRI at 4 months after disease onset showed a new silent periventricular lesion (E.e); T2-weighted/axial FLAIR brain MRI performed 3 months after the initiation of fingolimod therapy, as well as a subsequent brain MRI scans at 3 and 8 months following the initiation of anti-CD20 therapy revealed new silent lesions typical of MS (not shown). (E.f) T1 hypointense lesions typical of MS.

developed relapses or silent MRI lesions typical of MS, and required high-efficacy DMTs (anti-CD20 and natalizumab).

Among the 6 patients with overlapping features, 5 (patients #3–7, Table) presented with characteristic clinical features of MOGAD (3 with bilateral optic neuritis, 1 with cortical encephalitis, and 1 with brainstem-cerebellar syndrome) (Figure 2, B.a, C.a, D.a), 4 of them had CSF-OCBs, 4 were Epstein-Barr virus (EBV) seropositive, and 4 with available spinal cord MRI obtained at presentation had silent short

spinal cord lesions. The remaining patient (#8, Table), however, presented with a short myelitis and well-delimited brain MRI lesions typical of MS (Figure 2, E.a–E.d), CSF-OCBs and EBV serology were negative, and he relapsed with subclinical bilateral optic neuritis accompanied by severe changes in optical coherence tomography. Because MOGAD diagnosis could not be definitively excluded, chronic treatment was not initially considered in any of the 6 patients. However, 2 patients had typical MS clinical relapses, and all 6 patients developed silent brain MRI lesions with the morphology and location similar to those seen in MS (Figure 2, B.b–B.c, C.c–C.d, D.e, E.e), which led to start DMTs (3 fingolimod, 1 anti-CD20, 1 interferon-beta1a, 1 acetate glatiramer) at a median of 7 months (IQR: 6–12) after disease onset.

At the last follow-up (64 months, IQR: 50–101), 2 of the 6 patients with overlapping MOGAD-MS criteria (#4 and 7) showed sustained clinical and radiologic stability after their initial DMT (1 fingolimod, 1 anti-CD20). In contrast, #3 and #8 (initially on fingolimod) and #5 (initially on glatiramer acetate) had to be switched to anti-CD20 therapy because of ongoing clinical and/or radiologic activity. In patient #6, after 7 years of interferon-beta1a treatment, it was discontinued because of the absence of clinical-radiologic activity and the disappearance of CSF-MOG-IgG and CSF-OCBs. All 6 patients with overlapping MOGAD-MS had persistent T2-FLAIR lesions, and 5 of them (83%) had additional T1-hypointense lesions on follow-up MRI (Figure 2, B.f, C.f, D.f, E.f).

Discussion

This study demonstrates that 4% of children with MOG-IgG meet criteria for MS at some point during their disease course. It also identifies 2 distinct clinical profiles: (1) patients who exhibit typical MS features and follow a disease trajectory indistinguishable from prototypical MS and (2) patients who initially present with overlapping features of MOGAD and MS but predominantly follow an MS-like course.

The response to DMT in the 2 patients with typical MS features was consistent with outcomes observed in pediatric patients with MS without MOG-IgG.[7] However, treatment decisions were more challenging for patients with overlapping features because of the diagnostic complexity of differentiating MS and MOGAD because the criteria for these diseases are mutually exclusive. In such cases, several factors—including the frequent presence of CSF-OCBs, short silent spinal cord lesions at disease onset, and the appearance of new silent radiologic activity—provided critical guidance in diagnosing MS and initiating therapy. Although new silent lesions have been reported in approximately 10% of patients with MOGAD[8] (some explained by a radiologic lag[3,9]), the morphology and location of new lesions in our patients, along with the persistence of the T2/FLAIR hyperintensity and T1 hypointensity, supported an MS diagnosis. By contrast, MOGAD lesions typically resolve almost completely.[10]

The overlapping clinical and paraclinical features of MOGAD and MS in some patients (e.g., EBV seronegative in 2 cases, as commonly reported in MOGAD)[11] may indicate a continuum between these conditions in rare subsets of patients. While MS-specific treatments seemed safe in these patients and therapies such as anti-CD20 may be effective for both conditions, the long-term use of immunotherapy in MOGAD remains less well defined. It may not always be necessary in all patients with overlapping MOGAD-MS features (e.g., patient #6).

Of interest, while low titers of MOG-IgG in serum have been described in a small subgroup of adult and pediatric patients with MS,[12-14] our series revealed 7 patients with CSF-restricted MOG-IgG and one patient with low titers in both CSF and serum. Whether this immunologic profile also occurs in adult patients remains uncertain, and CSF testing for MOG-IgG is less commonly performed in adult cohorts, particularly in MS-like presentations.[14] In typical MS cases, MOG-IgG may represent one of several autoantibodies present in the CSF,[15] but further research is needed to elucidate its role in cases with overlapping features.

This study has some limitations, including the small sample size of patients with overlapping features and the partial availability of follow-up CSF samples. However, its prospective design, systematic assessment of MOG-IgG in both CSF and serum at disease onset, and the long-term clinical and radiologic follow-up are notable strengths.

Our findings carry important implications: (1) a small subset of children with MOG-IgG and overlapping MOGAD-MS features may progress to a highly active, MS-like disease course and (2) key diagnostic and therapeutic indicators include presence of silent short spinal cord lesions and CSF-OCBs at disease onset, the emergence of new silent brain MRI lesions during follow-up, and the persistence of T2/FLAIR hyperintense and T1 hypointense lesions.

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Author Contributions

E.G. Fonseca: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; analysis or interpretation of data. G. Olivé-Cirera: drafting/revision of the manuscript for content, including medical writing for content; analysis or interpretation of data. L.-W. Chen: drafting/revision of the manuscript for content, including medical writing for content. F. Paredes-

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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. Varley JA, Champsas D, Prossor T, et al. Validation of the 2023 international diagnostic criteria for MOGAD in a selected cohort of adults and children. *Neurology*. 2024;103(1):e209321. doi:10.1212/WNL.0000000000209321
3. Fonseca E, Olivé-Cirera G, Martinez-Hernandez E, et al. Investigating the 2023 MOGAD criteria in children and adults with MOG-antibody positivity within and outside attacks. *Neurology*. 2024;103(6):1-12. doi:10.1212/WNL.0000000000209682
4. Lipps P, Ayroza Galvão Ribeiro Gomes AB, Kulsvehagen L, et al. Ongoing challenges in the diagnosis of myelin oligodendrocyte glycoprotein antibody-associated disease. *JAMA Neurol*. 2023;80(12):1377-1379. doi:10.1001/jamaneurol.2023.3956
5. Manzano GS, Levy M, Salky R, et al. Assessment of international MOGAD diagnostic criteria in patients with overlapping MOG-associated disease and multiple sclerosis phenotypes. *J Neurol*. 2024;271(9):6160-6171. doi:10.1007/S00415-024-12585-W
6. Thompson AJ, Banwell BL, Barkhof F, et al. Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. *Lancet Neurol*. 2018;27(2):162-173. doi:10.1016/S1474-4422(17)30470-2
7. Huppke P, Huppke B, Ellenberger D, et al. Therapy of highly active pediatric multiple sclerosis. *Mult Scler*. 2019;25(1):72-80. doi:10.1177/1352458517732843
8. 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
9. 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
10. 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
11. Fadda G, Yea C, O'Mahony J, et al. Epstein–Barr virus strongly associates with pediatric multiple sclerosis, but not myelin oligodendrocyte glycoprotein-antibody-associated disease. *Ann Neurol*. 2024;95(4):700-705. doi:10.1002/ANA.26890
12. Armangue T, Olivé-Cirera G, Martínez-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
13. Hennes EM, Baumann M, Schanda K, et al. Prognostic relevance of MOG antibodies in children with an acquired demyelinating syndrome. *Neurology*. 2017;89(9):900-908. doi:10.1212/WNL.0000000000004312
14. Cobo-Calvo Á, d'Indy H, Ruiz A, et al. Frequency of myelin oligodendrocyte glycoprotein antibody in multiple sclerosis: a multicenter cross-sectional study. *Neurol Neuroimmunol Neuroinflamm*. 2019;7(2):e649. doi:10.1212/NXI.0000000000000649
15. Höftberger R, Lassmann H, Berger T, Reindl M. Pathogenic autoantibodies in multiple sclerosis—from a simple idea to a complex concept. *Nat Rev Neurol*. 2022;18(11):681-688. doi:10.1038/s41582-022-00700-2