BMC Medicine

RESEARCH

Open Access

Performance of the 2023 diagnostic criteria for MOGAD: real-world application in a Chinese multicenter cohort of pediatric and adult patients

Meng-Ting Cai[1†], Yi Hua[2†], Qi-Lun Lai[3†], Sheng-Yao Su[1], Chun-Hong Shen[1], Song Qiao[3], Yong-Feng Xu[1], Zhe-Feng Yuan[2*] and Yin-Xi Zhang[1*]

Abstract

Background The clinical phenotypes of myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) have been found to overlap with several other diseases. The new criteria proposed in 2023 were designed to better identify the disease but require validation across various populations to ascertain its clinical utility. We aimed to investigate the diagnostic performance in phenotypically diverse patients.

Methods This multicenter study retrospectively included adult and pediatric patients who were hospitalized for a first suspected demyelinating event and tested positive for MOG immunoglobulin G (IgG) during the acute phase. The 2023 *Lancet Neurology* criteria were assessed against the benchmark of empirical clinical diagnosis, and the 2018 *JAMA Neurology* and *Journal of Neuroinflammation* criteria were also evaluated for comparative analysis.

Results Among the 291 eligible patients (82 adults, 209 children), 282 (96.9%) were clinically diagnosed as definite MOGAD (77 adults, 205 children), while 262 (90.0%) fulfilled the 2023 diagnostic criteria (78 adults, 184 children). A total of 265 patients met the criteria for core clinical demyelinating events, and 76 (26.1%) had serum clear positive MOG-IgG (≥ 1:100). The sensitivity of the 2023 criteria was 0.91 (adults vs. children = 0.97 vs. 0.89), the specificity was 0.56 (adults vs. children = 0.40 vs. 0.75), positive likelihood ratio was 2.06 (adults vs. children = 1.62 vs. 3.57), and negative likelihood ratio (NLR) was 0.15 (adults vs. children = 0.06 vs. 0.14). Additionally, 264 and 256 cases were classified as definite MOGAD by the 2018 *JAMA Neurology* and *Journal of Neuroinflammation* criteria, respectively. Compared to the 2023 diagnostic criteria, the *2018 JAMA Neurology* criteria demonstrated similar diagnostic performance. However, the 2018 *Journal of Neuroinflammation* criteria exhibited comparable sensitivity (0.92, adults vs. children = 0.96 vs. 0.89), higher specificity (1.00, adults vs. children = 1.00 vs. 1.00) and better NLR (0.09, adults vs. children = 0.04 vs. 0.11).

†Meng-Ting Cai, Yi Hua, and Qi-Lun Lai contributed equally to this work.

*Correspondence:
Zhe-Feng Yuan
chyzf@zju.edu.cn
Yin-Xi Zhang
zyx-neurology@zju.edu.cn
Full list of author information is available at the end of the article

Conclusions The 2023 criteria demonstrated good sensitivity in adult and pediatric patients in China yet modest specificity. Close follow-up is needed for patients with atypical phenotypes but high-titer MOG-IgG to avoid underdiagnosis.

Keywords Myelin oligodendrocyte glycoprotein antibody-associated disease, 2023 diagnostic criteria, Core demyelinating event, Antibody titer, Real-world application, Multicenter cohort

Background

In recent years, myelin oligodendrocyte glycoprotein-immunoglobulin G (MOG-IgG) has been detected in patients with demyelinating diseases of the central nervous system (CNS). Despite various descriptions of this phenomenon, the prevailing terminology used is MOG antibody-associated disease (MOGAD) [1]. The clinical manifestations of MOGAD are diverse, overlapping with various conditions such as multiple sclerosis (MS), neuromyelitis optica spectrum disorder, and acute disseminated encephalomyelitis (ADEM), posing a challenge for diagnosis [2]. In 2018, two research groups proposed the concepts and diagnostic criteria of "MOG-IgG-associated disorder" and "MOG-IgG-associated encephalomyelitis" based on clinical phenotypes and MOG-IgG testing results [3, 4], which have since been widely applied in clinical practice in China. However, numerous issues have emerged during the clinical application of these criteria, particularly when low-titer MOG-IgG was identified in patients with suspected MS or other CNS inflammatory demyelinating diseases, thereby complicating the diagnostic process [5].

In 2023, new diagnostic criteria for MOGAD were proposed by an international expert group [6]. They are based on demyelinating phenotypes, antibody titers, supportive criteria, and exclusion criteria for diagnostic evaluation. Their diagnostic performance have been confirmed in several single-center and small-sample studies [7–13], yet they have not been validated in China as of yet. Pediatric patients constitute a significant proportion of the overall patient population, and their clinical presentation differs significantly from adults [2, 14–16]. Currently, only three pediatric studies have been conducted [10, 11, 13]. However, as there are potential differences in disease presentation between different countries and ethnicities, it is important to ascertain the performance of the new criteria in large, diverse cohorts including both pediatric and adult patients. Furthermore, specific phenotypes, such as short-segment myelitis (STM), aseptic meningitis, and clinical presentations of seizures with negative magnetic resonance imaging (MRI) findings [17–23], have not been studied using the new criteria. Clarification of their classification in the diagnostic criteria is needed to facilitate diagnosis and treatment.

This study aimed to evaluate the performance of the 2023 MOGAD diagnostic criteria in children and adults in a multi-center Chinese cohort, analyzing its clinical utility and application challenges.

Methods

Patients

This was a multi-center-based retrospective study of adult (≥ 18 years old) and pediatric (< 18 years old) patients from the Second Affiliated Hospital, School of Medicine, Zhejiang University, Children's Hospital, Zhejiang University School of Medicine, and Zhejiang Hospital, between September 2016 and July 2023. All participants had a suspected inflammatory demyelinating event, and positive MOG-IgG was detected in either serum or cerebrospinal fluid (CSF) using a fixed cell-based assay (CBA). The inclusion criteria were as follows: (1) first episode and hospitalized during the acute phase; (2) complete clinical data and all available brain ± spinal cord ± orbital MRI and/or ophthalmic examination. Patients who were not experiencing their initial attack and those with clinical information lacking or with incomplete data were excluded (Fig. 1).

Demographic, clinical, and paraclinical data, including sex, age of onset, disease duration (period from the onset of symptoms to the time of hospital admission), clinical phenotypes, MOG-IgG titers, radiological features, and ophthalmic examination results from the first attack were collected from medical records during the diagnostic workup. The following MRI sequences were used: T1-weighted imaging, T2-weighted imaging, fluid-attenuated inversion recovery (FLAIR) imaging, and contrast-enhanced T1-weighted imaging. This research was approved by the local ethics committee of each participating center. The requirement to obtain patient consent was waived for this retrospective study.

MOG-IgG assay

The MOG-IgG assay was performed at the acute phase of disease within 1 week of admission using commercial fixed CBA kits (Euroimmun, Lübeck, Germany) with HEK293A cells transfected with full-length human MOG, following the manufacturer's instructions at all centers [24]. Screening of serum samples was performed at 1:10 dilution, and if positive, titrated at 1:10, 1:32,

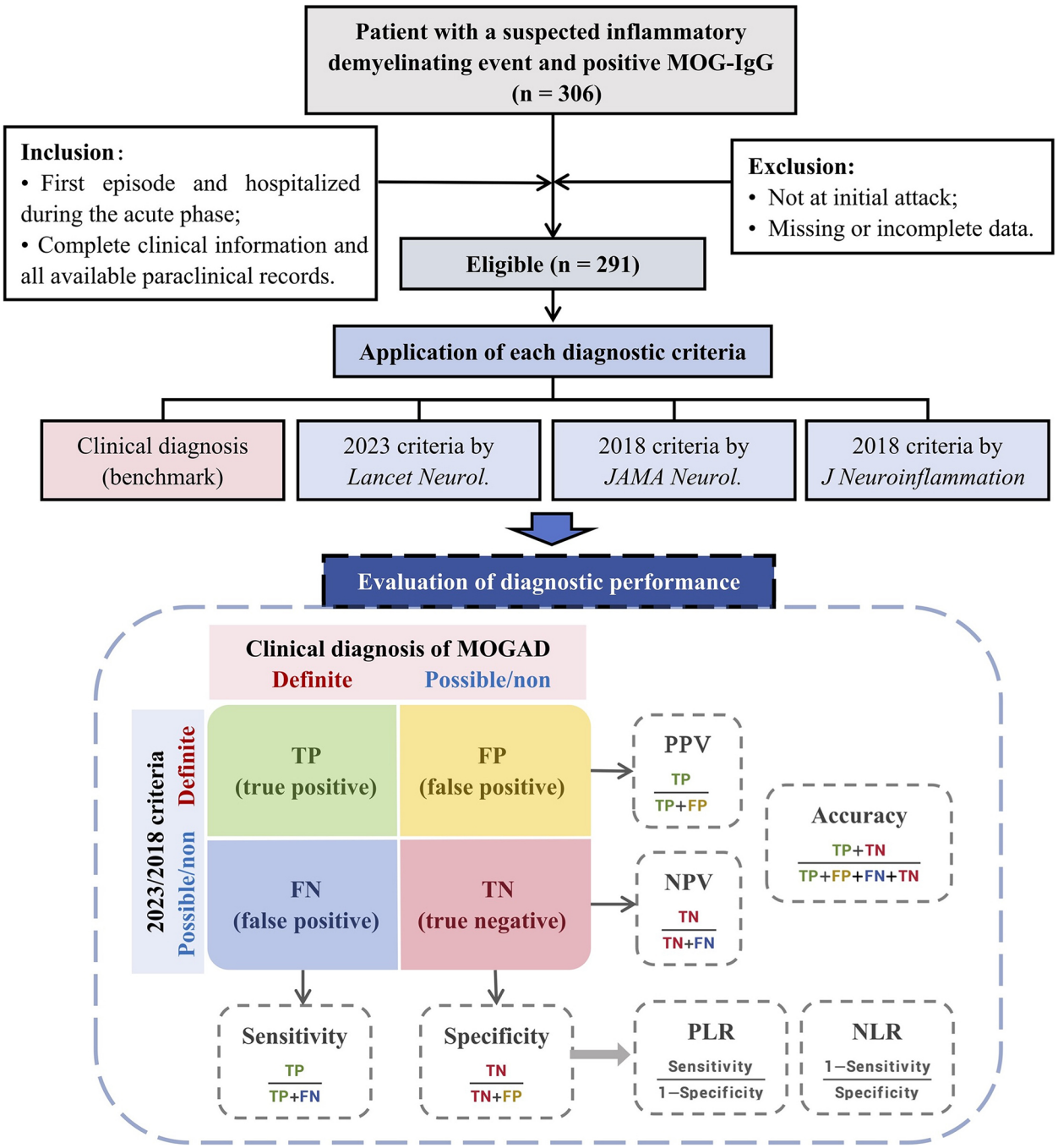

Fig. 1 Flowchart of study cohort and application of MOGAD criteria. Abbreviations: FN, False negative; FP, False positive; MOG-IgG, Myelin oligodendrocyte glycoprotein-immunoglobulin G; MOGAD, Myelin oligodendrocyte glycoprotein antibody-associated disease; NLR, Negative likelihood ratio; NPV, Negative predictive value; PLR, Positive likelihood ratio; PPV, Positive predictive value; TN, True negative; TP, True positive

1:100, 1:320, 1:1000, and 1:3200. CSF samples were initially screened at 1:1 dilution, and then serially diluted at 1:3.2, 1:10, 1:32, etc. MOG-IgG titers were determined according to the fluorescence of the different sample dilutions by two independent examiners using indirect immunofluorescence test. According to the 2023 criteria, a "clear positive" MOG-IgG was established when the serum titer greater than or equal to 1:100 [6].

Diagnostic criteria assessment

Before applying the 2023 and 2018 MOGAD diagnostic criteria, two neurologists independently assigned a

"clinical diagnosis" to each patient, classifying them as either definite MOGAD or non-MOGAD, based on their initial clinical and paraclinical characterizations as well as subsequent follow-up observations. This approach provided a robust benchmark for evaluating the proposed diagnostic criteria. Patients were also assessed at the time of their initial clinical onset using the 2023 *Lancet Neurology* criteria [6], the 2018 *JAMA Neurology* [3] and 2018 *Journal of Neuroinflammation* criteria [4] (Additional file 1: Fig. S1), with subsequent classification into definite and possible/non-MOGAD categories. "Possible MOGAD" referred to patients exhibiting diagnostic "red flags" according to the 2018 *Journal of Neuroinflammation* criteria [4], but whose antibody status could not be confirmed via additional CBA testing since no second, methodologically different CBA was available at our center. The concordance rates for these diagnostic criteria were 95%, 97%, 98%, and 95%, respectively. In instances of diagnostic discordance, resolution was achieved through team discussion.

Statistical analysis

The study results were presented using percentages, medians, and interquartile range (IQR). The Mann–Whitney *U* test was used to compare differences between continuous variables in two groups, while the chi-square test or Fisher's exact test was used to compare differences between categorical variables. Spearman's rank correlation coefficient was used to measure the association between two variables. To assess the performance of the 2023 and 2018 diagnostic criteria against the clinical diagnosis, we calculated the true positives (TP), true negatives (TN), false negatives (FN), and false positives (FP), along with their respective ratios. These ratios included sensitivity, specificity, accuracy, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (PLR), and negative likelihood ratio (NLR), each with a 95% confidence interval (CI) (Fig. 1) [25]. All statistical analyses were performed using R version 4.3.2. A two-tailed *p*-value ($p < 0.05$) was considered statistically significant.

Results

Demographic characteristics and clinical features

Among the 306 patients who tested positive for MOG-IgG, 15 were excluded based on the inclusion and exclusion requirements (Fig. 1). Of the remaining 291 eligible patients, 28.2% ($n = 82$) were adults, and 71.8% ($n = 209$) were children. As shown in Table 1, the male-to-female ratio was approximately 1:1 in the overall cohort, with no significant differences observed between the two age groups. The median age of onset was 35.5 years in adults (IQR = 27.0–54.0, range = 18.0–75.0), and 6.8 years in children (IQR = 5.0–10.1, range = 0.4–17.0). Adults also had a significantly longer duration of disease at admission compared to children ($p = 0.013$).

Referring to the clinical phenotypes, optic neuritis (ON) was predominant in adults ($n = 22$, 26.8%), followed by myelitis ($n = 16$, 19.5%), while ADEM was predominant in children ($n = 84$, 40.2%). Two hundred and eighty-seven cases showed positive serum antibodies, with a median titer of 1:32 (IQR = 1:10–1:100, range = 1:10–1:1000). The remaining four cases with negative serum antibodies tested positive for CSF MOG-IgG (1:10). The median interval from the first attack to MOG-IgG testing was 12.0 days (IQR = 8.0–20.0, range = 2.0–125.0), with no significant correlation with antibody titer ($p = 0.737$). All patients with visual impairment ($n = 68$) underwent fundoscopy, with 44 cases showing optic disc edema, and 10 out of 30 patients who received orbital enhanced MRI found perineural optic sheath enhancement, which was more common in adults than children (9 vs. 1, $p < 0.001$) (Table 1). Additionally, all patients with symptoms suggesting involvement of the brain and/or spinal cord underwent comprehensive MRI examinations of the brain and spinal cord. Among them, intracranial lesions, including involvement of the cortex, white matter, and deep gray matter, were significantly more common in adults than children (Table 1). Notably, seven patients along with clinical presentation of acute encephalitis exhibited special imaging types, including five cases (one adult and four children) with a leukodystrophy-like phenotype consistent with previous reports (confluent and bilateral, essentially symmetric, white matter abnormalities) [18], and two cases (one adult and one child) with tumefactive demyelination. Moreover, 15 patients (three adults and 12 children) with clinical features of encephalitis or myelitis without detectable abnormalities on T2/FLAIR and contrast-enhanced MRI were defined as "MRI-negative encephalitis/myelitis". Additionally, 12 cases (all children) presented as meningitis, characterized by headache, nuchal rigidity, CSF pleocytosis, or leptomeningeal enhancement, without evidence of focal or multifocal neurological deficits or parenchymal imaging abnormalities, as previously suggested [26]. All cases underwent rigorous evaluation to exclude infectious or other potential diagnostic alternatives.

Above all, 282/291 (96.9%) patients were identified with a clinical diagnosis of MOGAD. Among the remaining nine patients with low-titer MOG-IgG, four met the diagnostic criteria for MS [27]. Additionally, four patients presenting with encephalitis were also positive for CSF N-methyl-D-aspartate receptor (NMDAR)-IgG, leading to a diagnosis of "MOG antibody and NMDAR antibody overlapping syndrome (MNOS)" [28]. One case with longitudinally extensive transverse myelitis (LETM) was

Table 1 Clinical characteristics and diagnostic classification of adult and pediatric patients

	Total	Adults	Children	*P*-value
Number of patients	291	82	209	
Male, *n* (%)	147 (50.5)	45 (54.9)	102 (48.8)	0.423
Age at onset, year, median (IQR)	9.5 (5.8–22.5)	35.5 (27.0–54.0)	6.8 (5.0–10.1)	< 0.001
Disease duration, day, median (IQR)	9.0 (5.0–15.0)	10.0 (7.0–20.0)	8.0 (5.0–15.0)	0.013
Patients with definite MOGAD by different criteria, n (%)				
Clinical diagnosis	282 (96.9)	77 (93.9)	205 (98.1)	0.123
2023 *Lancet Neurology*	262 (90.0)	78 (95.1)	184 (88.0)	0.110
2018 *JAMA Neurology*	264 (90.7)	78 (95.1)	186 (89.0)	0.163
2018 *Journal of Neuroinflammation*	256 (88.0)	74 (90.2)	182 (87.1)	0.585
Fulfillment of the 2023 criteria				
(A) Core clinical demyelinating events, *n* (%)				
ON	50 (17.2)	22 (26.8)	28 (13.4)	< 0.001
Myelitis	24 (8.2)	16 (19.5)	8 (3.8)	
ADEM	90 (30.9)	6 (7.3)	84 (40.2)	
Cerebral monofocal or polyfocal deficits	40 (13.7)	10 (12.2)	30 (14.4)	
Brainstem or cerebellar deficits	9 (3.1)	5 (6.1)	4 (1.9)	
Cerebral cortical encephalitis often with seizures	22 (7.6)	10 (12.2)	12 (5.7)	
Combined events	30 (10.3)	10 (12.2)	20 (9.6)	
(B) Clear positive serum MOG-IgG test, *n* (%)	76 (26.1)	27 (32.9)	49 (23.4)	0.132
(C) Supporting clinical or MRI features, *n* (%)				
ON				
Bilateral simultaneous clinical involvement	32 (11.0)	10 (12.2)	22 (10.5)	0.841
Longitudinal optic nerve involvement	25 (8.6)	10 (12.2)	15 (7.2)	0.254
Perineural optic sheath enhancement	10 (3.4)	9 (11.0)	1 (0.5)	< 0.001
Optic disc edema	44 (15.1)	12 (14.6)	32 (15.3)	> 0.999
Myelitis				
Longitudinally extensive myelitis	66 (22.7)	20 (24.4)	46 (22.0)	0.779
Central cord lesion or H-sign	57 (19.6)	19 (23.2)	38 (18.2)	0.423
Conus lesion	17 (5.8)	2 (2.4)	15 (7.2)	0.203
Brain, brainstem, or cerebral syndrome				
Multiple ill-defined T2-hyperintensity lesions in supratentorial and often infratentorial white matter	132 (45.4)	17 (20.7)	115 (55.0)	< 0.001
Deep grey matter involvement	91 (31.3)	8 (9.8)	83 (39.7)	< 0.001
Ill-defined T2-hyperintensity involving pons, middle cerebellar peduncle, or medulla	90 (30.9)	21 (25.6)	69 (33.0)	0.276
Cortical lesion with or without lesional and overlying meningeal enhancement	105 (36.1)	18 (22.0)	87 (41.6)	0.003

Abbreviations: ADEM, Acute disseminated encephalomyelitis; *IQR,* Interquartile range; *MOG-IgG,* Myelin oligodendrocyte glycoprotein-immunoglobulin G; *MOGAD,* Myelin oligodendrocyte glycoprotein antibody-associated disease; *MRI,* Magnetic resonance imaging; *ON,* Optic neuritis

ultimately diagnosed with ependymoma upon pathological examination (patient 1–9 in Additional file 1: Table S1).

Evaluation and application of the 2023 criteria

We assessed the overall cohort according to the steps outlined in the 2023 diagnostic criteria (Fig. 2). In Step 1, 265/291 (91.1%) MOG-IgG-positive patients met the criteria for core clinical demyelinating events, including 50 cases of ON, 24 cases of myelitis, 90 cases of ADEM, 40 cases of cerebral monofocal or polyfocal deficits, 9 cases of brainstem or cerebellar deficits, 22 cases of cerebral cortical encephalitis often with seizures, and 30 cases of combined phenotypes (Table 1, Fig. 3). Meanwhile, 26 cases exhibiting atypical phenotypes were classified as non-MOGAD, including 14 cases (adults: $n=3$; children: $n=11$) of MRI-negative encephalitis (Patient 6–19 in Additional file 1: Table S1), and 12 cases (all children) of meningitis (Patient 20–31 in Additional file 1: Table S1).

In Step 2a, 68/265 (25.7%) patients (adults: $n=25$; children: $n=43$) met the criteria for serum clear positive MOG-IgG. Among the remaining 197 patients, 195

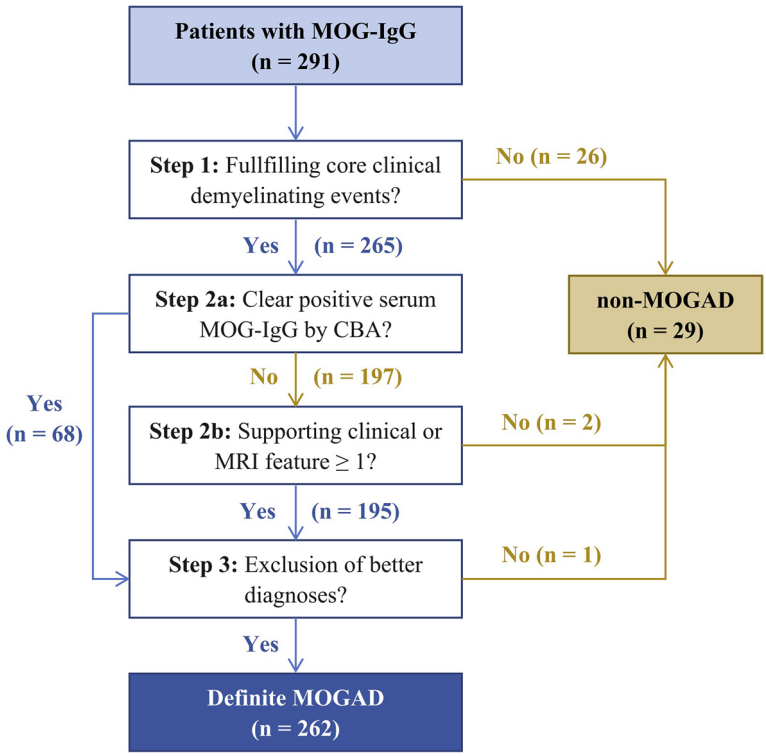

Fig. 2 Diagnosis workflow for patients with suspected MOGAD (based on the 2023 diagnostic criteria [6]). Abbreviations: CBA, Cell-based assay; MOG-IgG, Myelin oligodendrocyte glycoprotein-immunoglobulin G; MOGAD, Myelin oligodendrocyte glycoprotein antibody-associated disease; MRI, Magnetic resonance imaging

(adults: $n=54$; children: $n=141$) fulfilled the supportive criteria in Step 2b and advanced to Step 3 for further evaluation (Fig. 3). The remaining two patients (all children) including one case of STM and one case of MRI-negative myelitis were classified as non-MOGAD (Patient 32–33 in Additional file 1: Table S1). Consequently, in the Step 3, except for one case of ependymoma (Patient 5 in Additional file 1: Table S1), a total of 262 patients were diagnosed with definite MOGAD (adults: $n=78$; children: $n=184$).

Among the 282 patients clinically diagnosed as definite MOGAD, 258 were confirmed as definite MOGAD by the 2023 criteria (TP), while the remaining 24 were diagnosed as non-MOGAD (FN; 10 cases of MRI-negative encephalitis, 12 cases of meningitis, one case of STM, and one case of MRI-negative myelitis) (Patients 10–33 in Additional file 1: Table S1). Additionally, five patients were classified as non-MOGAD according to both the clinical diagnosis and the 2023 criteria (TN; four cases of MNOS and one case of ependymoma) (Patients 5–9 in Additional file 1: Table S1). Notably, four patients initially fulfilled the 2023 criteria for MOGAD during their first episode of demyelination. Nonetheless, as their disease progressed, further neuroimaging studies revealed evidence consistent with MS, culminating in a conclusive diagnosis of MS (FP) (Patients 1–4 in Additional file 1: Table S1). Overall, the sensitivity of the 2023 MOGAD diagnostic criteria compared to clinical diagnosis was 0.91 (95% CI = 0.88–0.94), specificity was 0.56 (95% CI = 0.21–0.86), and accuracy was 0.90 (95% CI = 0.86–0.94). Notably, sensitivity was higher in adult patients (0.97 vs. 0.89), while specificity was greater in children (0.75 vs. 0.40). Additionally, we further calculated PPV, NPV, and PLR and NLR values, adjusted for prevalence, to assess the significance of positive and negative diagnostic results, as shown in Table 2.

Significance of each item of the 2023 diagnostic criteria

To further elucidate the role and significance of each step in the 2023 diagnostic criteria, we conducted a comprehensive analysis (Additional file 1: Fig. S2). In Step 1 of core demyelinating events, 262 patients who met this criterion were diagnosed as definite MOGAD according to the 2023 criteria (TP). However, three patients were subsequently excluded and reclassified as non-MOGAD (FP) during the later steps of the diagnostic process, including one case of ependymoma, one case of STM, and one case of MRI-negative myelitis (Patients 5, 32, 33 in Additional file 1: Table S1). All the 26 patients who did not meet the core demyelinating events were classified

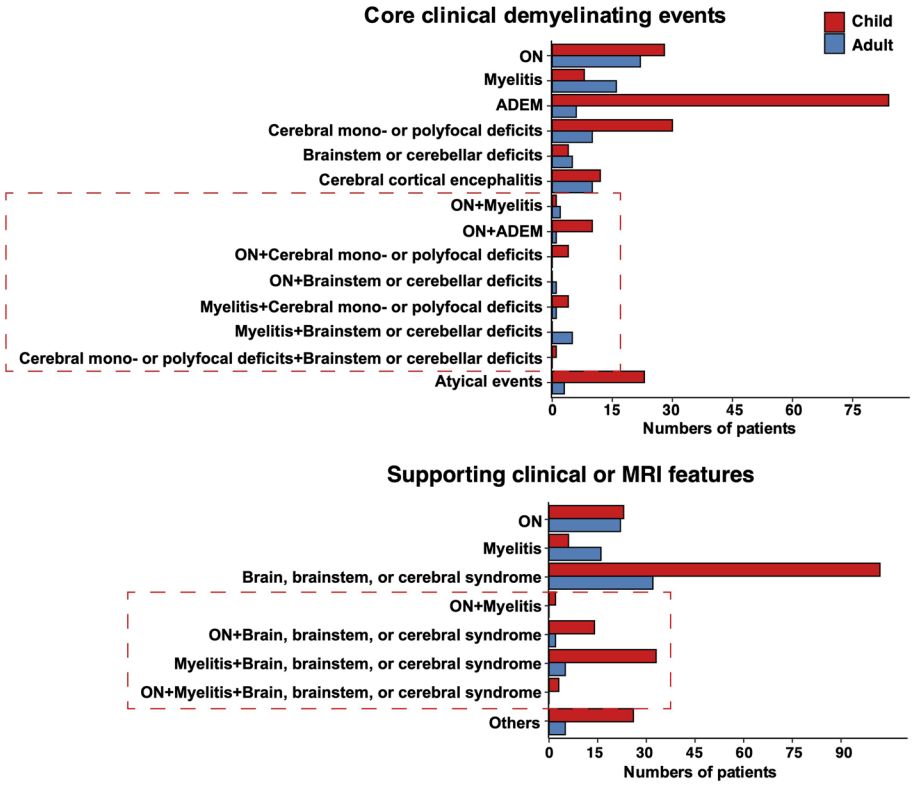

Fig. 3 Core clinical demyelinating events and supporting clinical or MRI features between adult and child patients (the combined characteristics are shown inside the red dashed box). Abbreviations: ADEM, Acute disseminated encephalomyelitis; MRI, Magnetic resonance imaging; ON, Optic neuritis

as non-MOGAD. Among them, 8 patients (adults: $n=2$, children; $n=6$) met the serum clear positive MOG-IgG test requirement, including four cases of MRI-negative encephalitis and four cases of meningitis (Patients 12, 16, 17, 19, 21, 25, 28, 29 in Additional file 1: Table S1). In summary, the diagnostic sensitivity and specificity of core demyelinating events within the 2023 criteria were 1.00 (95% CI = 0.99–1.00) and 0.90 (95% CI = 0.73–0.98), respectively (Additional file 1: Table S2).

In the evaluation of the serum clear positive MOG-IgG criterion, 68 out of the 76 patients who met this requirement were ultimately diagnosed with definite MOGAD according to the 2023 diagnostic criteria (TP). The remaining 8 patients were classified as non-MOGAD (FP) (Patients 12, 16, 17, 19, 21, 25, 28, 29 in Additional file 1: Table S1). The sensitivity and specificity of this diagnostic step within the 2023 criteria were 0.74 (95% CI = 0.68–0.79) and 0.28 (95% CI = 0.13–0.47), respectively (Additional file 1: Table S2).

Among the 260 patients who met the supportive criteria, all except one case of ependymoma (Patients 5 in Additional file 1: Table S1) were classified as definite MOGAD according to the 2023 criteria (TP). Moreover, among the 31 patients who did not meet the supportive criteria, three with serum MOG-IgG at 1:100 were diagnosed as definite MOGAD (TP): two cases of unilateral short-segment ON without enhancement and optic disc edema, and one case of STM. The sensitivity and specificity for these criteria under the 2023 criteria were 0.99 (95% CI = 0.97–1.00) and 0.97 (95% CI = 0.82–1.00), respectively (Additional file 1: Table S2). We further analyzed the diagnostic performance of each supportive criterion for ON, myelitis, and brain lesions (Additional file 1: Table S3). Among 68 patients meeting any ON supportive criterion, optic disc edema was most frequent (44, 64.7%), while perineural optic sheath enhancement was least frequent (10, 14.7%). For myelitis, 74 patients met the criteria, with LETM being the most common (66, 89.2%) and conus involvement the least common (17, 23.0%). Of 194 patients meeting any brain lesion criterion, multiple ill-defined T2-hyperintensity lesions in supratentorial and infratentorial white matter were most common (132, 68.0%). Patients with ON were more frequently associated with serum clear positive MOG-IgG, predominantly with perineural optic sheath enhancement (6/10, 60%), while cortical lesions with or without lesional and overlying meningeal enhancement were less common (17/105, 16.2%). Excluding the LETM (one

Table 2 Performance of the 2023 and 2018 MOGAD criteria based on the benchmark of clinical diagnosis

		TP (n)	FP (n)	FN (n)	TN (n)	Sensitivity (95% CI)	Specificity (95% CI)	Accuracy (95% CI)	PPV (95% CI)	NPV (95% CI)	PLR (95% CI)	NLR (95% CI)
2023 *Lancet Neurology*	Total	258	4	24	5	0.91 (0.88–0.94)	0.56 (0.21–0.86)	0.90 (0.86–0.94)	0.98 (0.96–1.00)	0.17 (0.06–0.36)	2.06 (0.99–4.28)	0.15 (0.08–0.31)
	Adults	75	3	2	2	0.97 (0.91–1.00)	0.40 (0.05–0.85)	0.94 (0.86–0.98)	0.96 (0.89–0.99)	0.50 (0.07–0.93)	1.62 (0.79–3.32)	0.06 (0.01–0.37)
	Children	183	1	22	3	0.89 (0.84–0.93)	0.75 (0.19–0.99)	0.89 (0.84–0.93)	0.99 (0.97–1.00)	0.12 (0.03–0.31)	3.57 (0.65–19.51)	0.14 (0.07–0.29)
2018 *JAMA Neurology*	Total	264	4	22	5	0.92 (0.88–0.95)	0.56 (0.21–0.86)	0.91 (0.87–0.94)	0.98 (0.96–1.00)	0.19 (0.06–0.38)	2.07 (1.00–4.31)	0.14 (0.07–0.29)
	Adults	75	3	2	2	0.97 (0.91–1.00)	0.40 (0.05–0.85)	0.94 (0.86–0.98)	0.96 (0.89–0.99)	0.50 (0.07–0.93)	1.62 (0.79–3.32)	0.06 (0.01–0.37)
	Children	185	1	20	3	0.90 (0.85–0.94)	0.75 (0.19–0.99)	0.90 (0.85–0.94)	1.00 (0.97–1.00)	0.13 (0.03–0.34)	3.61 (0.66–19.72)	0.13 (0.06–0.26)
2018 *Journal of Neuroinflammation*	Total	256	0	26	9	0.91 (0.87–0.94)	1.00 (0.66–1.00)	0.91 (0.87–0.94)	1.00 (0.99–1.00)	0.26 (0.12–0.43)	∞ (NA–∞)	0.09 (0.06–0.13)
	Adults	74	0	3	5	0.96 (0.89–0.99)	1.00 (0.48–1.00)	0.96 (0.90–0.99)	1.00 (0.95–1.00)	0.62 (0.24–0.91)	∞ (NA-∞)	0.04 (0.01–0.12)
	Children	182	0	23	4	0.89 (0.84–0.93)	1.00 (0.40–1.00)	0.89 (0.84–0.93)	1.00 (0.98–1.00)	0.15 (0.04–0.34)	∞ (NA-∞)	0.11 (0.08–0.16)

Abbreviations: CI, Confidence interval; *FN,* False negative; *FP,* False positive; *MOGAD,* Myelin oligodendrocyte glycoprotein antibody-associated disease; *NA,* Not applicable; *NLR,* Negative likelihood ratio; *NPV*, Negative predictive value; *PLR*, Positive likelihood ratio; *PPV,* Positive predictive value; *TN,* True negative; *TP,* True positive

case of ependymoma), all other criteria met the definition of definite MOGAD by the 2023 criteria. Additionally, a comparative analysis between patients with LETM ($n=66$) and STM ($n=7$) revealed no significant differences in meeting the serum clear MOG-IgG criteria (16 vs. 1, $p>0.999$) or in the diagnosis of definite MOGAD (65 vs. 6, $p>0.999$). Notably, perineural optic sheath enhancement, optic disc edema, conus lesion, and deep grey matter involvement exhibited 100% specificity for clinically diagnosed MOGAD.

Comparison of diagnostic performance among each criteria

To evaluate the performance differences between the 2023 and the 2018 diagnostic criteria, we reassessed 291 MOG-IgG positive patients and identified 264 and 256 cases as definite MOGAD by 2018 *JAMA Neurology* criteria and 2018 *Journal of Neuroinflammation* criteria, respectively. As illustrated in Fig. 4, in comparison to the clinical diagnosis, 22 cases of MRI-negative encephalitis and meningitis classified as non-MOGAD under the two 2018 diagnostic criteria were FN (Patients 10–31 in Additional file 1: Table S1). And four cases of MNOS and one case of ependymoma were TN (Patients 5–9 in Additional file 1: Table S1). Additionally, there were four FN cases under the 2018 *Journal of Neuroinflammation* criteria, including one case of MRI-negative myelitis (Patients 33 in Additional file 1: Table S1) classified as non-MOGAD and three cases (one with ON + encephalitis, one with ADEM, one with ON + ADEM) classified as possible MOGAD due to the presence of red flag (CSF-restricted MOG-IgG positivity). Meanwhile, the 2018 *JAMA Neurology* criteria also yielded four FP cases of MS (Patients 1–4 in Additional file 1: Table S1).

All patients classified as definite MOGAD under the 2023 criteria met the requirements of the 2018 *JAMA Neurology* criteria. However, seven cases with red flags (three with CSF-restricted MOG-IgG positivity, four with typical MRI features of MS) classified as possible MOGAD under the 2018 *Journal of Neuroinflammation* criteria were identified as definite MOGAD in the 2023 criteria. By contrast, one case of STM (Patients 32 in Additional file 1: Table S1) classified as non-MOGAD by the 2023 criteria met the two 2018 criteria, and one

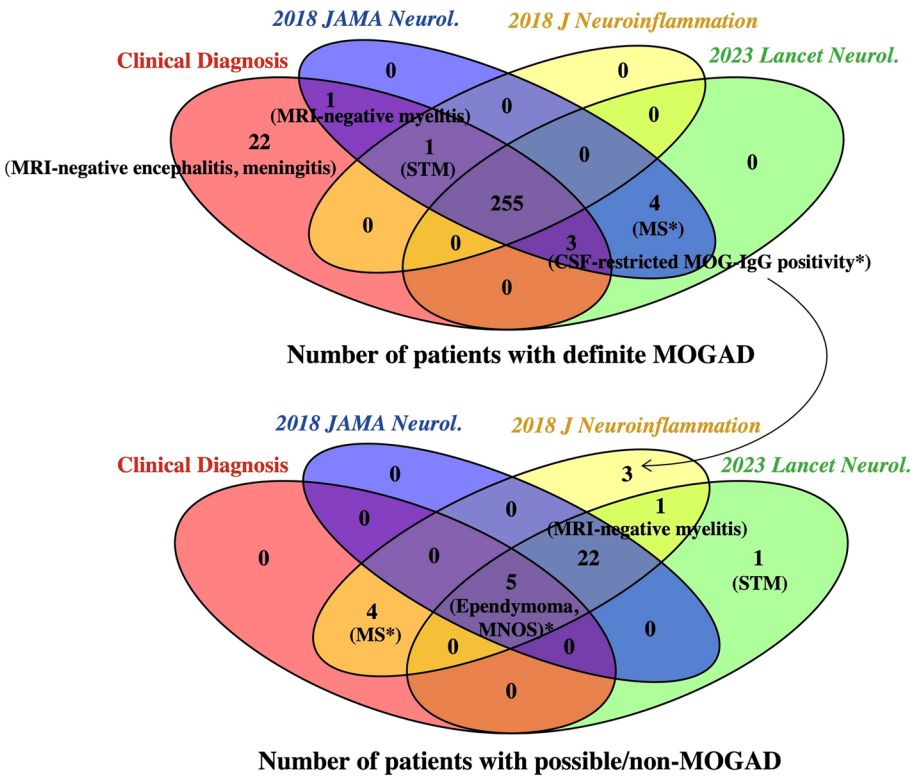

Fig. 4 Venn diagram of patients with definite or possible/non-MOGAD by each diagnostic criteria. *Possible MOGAD with red flags, but unable to verify antibody status through additional CBA testing due to technical limitations (three cases with CSF-restricted MOG-IgG positivity, four MS cases with typical MRI features, four cases with MNOS, one case with ependymoma). Abbreviations: CBA, Cell-based assay; CSF, Cerebrospinal fluid; MOG-IgG, Myelin oligodendrocyte glycoprotein-immunoglobulin G; MOGAD, Myelin oligodendrocyte glycoprotein antibody-associated disease; MRI, Magnetic resonance imaging; MS, Multiple sclerosis; MNOS, Myelin oligodendrocyte glycoprotein antibody and N-methyl-d-aspartate receptor antibody overlapping syndrome; STM, Short-segment myelitis

MRI-negative myelitis case (Patients 33 in Additional file 1: Table S1) met the 2018 *JAMA Neurology* criteria.

Following the clinical diagnosis, we evaluated the diagnostic performance of the two criteria. As shown in Table 2, the performance of the 2018 *JAMA Neurology* criteria was similar to the 2023 criteria. When compared to the 2018 *Journal of Neuroinflammation* criteria, the 2023 criteria exhibited comparable sensitivity (0.92, 95% CI = 0.88–0.95 vs. 0.91, 95% CI = 0.87–0.94) and accuracy (0.91, 95% CI = 0.87–0.94 vs. 0.91, 95% CI = 0.87–0.94) but lower specificity (0.56, 95% CI = 0.21–0.86 vs. 1.00, 95% CI = 0.66–1.00) and worse NLR (0.14, 95% CI = 0.07–0.29 vs. 0.09, 95% CI = 0.06–0.13) and PLR (2.06, 95% CI = 0.99–4.28 vs. ∞, 95% CI = NA–∞). All three sets of criteria showed better sensitivity, accuracy, and NLR among adult patients than among children. In contrast, the 2023 criteria and the 2018 *JAMA Neurology* criteria both showed lower specificity and PLR in adults than in children, while the 2018 *Journal of Neuroinflammation* criteria showed 100% specificity and a nominally infinite PLR in both adults and children.

Discussion

This study was a real-world application of the 2023 MOGAD diagnostic criteria using the largest cohort of adult and pediatric patients as yet studied for this set of criteria. We found that the 2023 MOGAD criteria demonstrated high diagnostic sensitivity and accuracy across different age groups, but lower specificity and a worse NLR compared to previously published criteria with similar sensitivity. Nevertheless, cautious differentiation is essential in cases with overlapping clinical and imaging features of MS. While the inclusion of core clinical demyelinating events has facilitated the diagnosis of MOGAD, regular follow-up and close monitoring are still warranted for patients presenting with atypical phenotypes accompanied by high-titer MOG-IgG.

Upon evaluation using the 2023 diagnostic criteria, 262 out of 291 MOG-IgG-positive patients were classified as definite MOGAD. A comparison with clinical diagnosis revealed four FP and 24 FN cases, indicating the potential for misdiagnosis and underdiagnosis. Although these FP cases did not receive an MS diagnosis at the time of their initial attack, subsequent evaluations revealed that they indeed had MS. This underscores the diagnostic challenge, as the differentiation between MOGAD and MS remains inherently complex [21, 22, 29–31]. Similarly, the research conducted by Lipps et al. corroborated the concern that the 2023 diagnostic criteria may not adequately distinguish between MOGAD and MS [29]. Given the incomplete specificity and pathogenic potential of MOG-IgG, particularly at low titers, the clinical relevance of these antibodies in disease pathogenesis warrants further investigation [5]. Considering the risk of low-titer false-positive MOG-IgG results in adult patients with a first demyelinating event typical of MS, Jarius et al. and Geraldes et al. highlighted the importance of pre-test probability [4, 30]. Overall, accurate diagnosis of MOGAD might necessitate a comprehensive approach, repeat serological assessment, use of confirmatory assays, reevaluation of imaging, and vigilant monitoring of clinical progression and therapeutic response [31]. Keep in mind that diagnosing MOGAD necessitates the exclusion of other more likely conditions, particularly MS, and this distinction is of utmost importance for patients with low MOG-IgG titers. Even if patients initially meet the diagnostic criteria for MOGAD, ongoing regular follow-ups and dynamic re-examinations are indispensable. If features emerge that are consistent with MS, it is imperative to reconsider the original diagnosis. Future refinements to diagnostic criteria are essential to improve specificity and better differentiate between MOGAD and MS.

Among the 24 FN cases, 22 presented with meningitis (12 cases) and MRI-negative encephalitis (10 cases), which were excluded due to not meeting the criteria for core demyelinating events. All cases of meningitis in our study were in children, and, as reported in previous studies, meningitis is not uncommon in pediatric MOGAD [32, 33]. These patients typically presented with increased CSF cell counts, and symptoms such as fever and headache. Most patients have favorable responses to immunotherapy, while MOG-IgG titers tend to decrease following treatment [17, 33]. Although patients with MOG-IgG-positive meningitis may not be diagnosed as definite MOGAD according to the 2023 criteria, this clinical phenotype might fundamentally belong on the MOGAD spectrum, especially when presenting with clear positive MOG-IgG. Further study into the pediatric meningitis phenotype is needed, to evaluate its use as a core clinical demyelinating event. Referring to the MRI-negative encephalitis, the negative findings may be due to delayed imaging manifestations compared to clinical symptoms, small lesions that are not visible, or detection biases resulting from instrument parameter settings [34]. Actually, pediatric patients constitute 80% of these FN MRI-negative encephalitis cases, and their relatively shorter disease course compared to adults might increase the incidence of MRI-negative findings. Nonetheless, the presence of neurological deficits strongly suggests inflammatory CNS damage, and the possibility of MOGAD cannot be ruled out, especially in the presence of high-titer MOG-IgG. Repeated MRI examinations during the disease course may facilitate the identification of underlying demyelinating events. Moreover, cases with MRI-negative findings but concurrent clinical features such as seizures, psychiatric symptoms, or altered

consciousness may fulfill the diagnostic criteria for autoimmune encephalitis [35]. Considering the broad spectrum of MOGAD and the overlaps in pathophysiology [36, 37], these cases may still fall within the MOGAD spectrum. Overall, in light of the diversity and complexity of MOGAD phenotypes, we recommend combining these atypical phenotypes and diagnosing patients with clear positive MOG-IgG as "possible MOGAD" to avoid underdiagnosis and to facilitate treatment decision-making.

Moreover, the remaining two FN patients with core demyelinating events of STM and MRI-negative myelitis were categorized as non-MOGAD due to the low-titer MOG-IgG and the absence of supportive criteria. These findings corroborated the discoveries of Forcadela et al., who suggested that delayed testing or insufficient investigation may result in low positive MOG-IgG titers and a lack of supportive features, thereby contributing to missed diagnosis [8]. Consequently, the integration of antibody testing with clinical and paraclinical findings was imperative for accurate MOGAD diagnosis. An evaluation of each step of 2023 diagnostic criteria revealed that antibody titer exhibited a high NLR (0.94, 95% CI = 0.50–1.76), underscoring its significance in excluding non-MOGAD though with potential risk for underdiagnosis [38]. Another study by Kurd et al. also reported that the 2023 criteria did not improve the diagnostic accuracy of the antibody test alone [10]. Indeed, merely 26% of our patients met the criteria for clear positive serum MOG-IgG ($\geq$ 1:100), a proportion lower than that reported in other studies. This discrepancy may be attributed to the fact that a substantial number of patients were in the acute phase of the disease, with a relatively short duration of disease, and most sought medical attention and antibody testing promptly after onset. During the early stages of the disease, antibody titers may be low, gradually increasing as the disease progresses, and then decreasing in the later stages [30, 39]. Some patients in our cohort may have lower serum MOG-IgG which could be attributed to the early stage of the disease, while their antibody titers could reach the requirement for clear positivity later in the disease. Another study by Kim et al. also reported a sensitivity of 93% for the 2023 criteria after a median observation period of 24 months and only 84% at disease onset [9]. Therefore, these patients might be "potential" MOGAD. Meanwhile, current antibody detection methods have not yet achieved standardization, as there are weaknesses in their consistency and repeatability, which may result in false positive or false negative results [39]. To facilitate timely diagnosis and treatment, patients with suspected diagnoses and low serum MOG-IgG titers or positive MOG-IgG antibodies only in the CSF should undergo antibody retesting [4]. Furthermore, MOG-IgG levels might be influenced by factors such as ethnicity and geographic region, as low titers have also been observed in other studies conducted in China [40–42]. Further research is needed to confirm these findings.

The integration of supportive criteria as ancillary evidence in case of low-titer MOG-IgG was crucial for enhancing the sensitivity of MOGAD diagnosis and thereby reducing the risk of underdiagnosis. However, among patients with optic nerve enhancement, the proportion of cases with serum clear positive MOG-IgG was the highest, whereas cortical lesions were the least common. Previous studies have suggested that MOG-IgG titers were associated with brain lesions. Optic nerve enhancement might indicate more pronounced inflammatory damage, whereas cortical lesions may be related to relatively lower titers due to the lesions being localized or early disease stage [43]. Intracranial involvement, including white matter, deep gray matter, and cortical regions, was common in CNS demyelinating diseases but lacked specificity, potentially leading to FP diagnoses like MS [44]. In such cases, the requirement for serum clear positive MOG-IgG could reduce the risk of misdiagnosis. Further research into the intracranial imaging characteristics of MOGAD is warranted to improve diagnostic specificity and avoid misdiagnosis. Additionally, after comparing MOG-IgG-positive patients with STM and LETM, we found no differences in terms of meeting the criteria for "serum clear positive MOG-IgG" or "definite MOGAD". Vigilance regarding a potential diagnosis of MOGAD remains essential in cases of STM [20]. However, due to the limited number of STM patients in this study, further investigations with larger cohorts are warranted to assess its specificity in MOGAD.

Overall, we found that the 2023 diagnostic criteria exhibit high sensitivity (91%) but relatively lower specificity (56%). This finding aligns with the validation study by Alaboudi et al., which reported high sensitivity (100%) but low specificity (56%) for the 2023 criteria [7]. The low specificity was primarily associated with FP in MS cases. In other validation studies, a single-center study from the USA conducted by Filippatou et al. supported the diagnostic utility of the MOGAD criteria, suggesting its accuracy in distinguishing MOGAD from serologically low-titer MOG-IgG positive mimics [11]. Additionally, the 2023 criteria have demonstrated favorable diagnostic performance in cohorts from South Korea [9], the UK [13], and Israel [10, 12]. Compared to the two 2018 criteria [3, 4], the 2023 criteria exhibited comparable sensitivity, underscoring its efficacy in identifying true MOGAD cases. However, its relatively lower specificity when comparing with the 2018 *Journal of Neuroinflammation* criteria indicated persistent challenges in

excluding FP diagnoses, particularly in distinguishing MOGAD from MS. By contrast, another study by Forcadela et al. found no difference in specificity between these two criteria, which may be attributed to differences in the study populations and methodologies between the two studies [8]. It is noteworthy that the 2018 *Journal of Neuroinflammation* criteria were primarily intended for use in adults and adolescents [4]. Nonetheless, when applied to pediatric patients, we found these criteria to demonstrate robust diagnostic performance. By convention, tests, including diagnostic criteria, are deemed clinically useful if they have a PLR > 10 and a NLR < 0.1 [45]. In our study, only the 2018 *Journal of Neuroinflammation* criteria met both of these conditions. Importantly, the 2023 criteria demonstrated a higher NLR, meaning that their efficacy in ruling out MOGAD (in case the criteria are not met) was lower. When considering the exclusion of atypical phenotypes and FP cases, the 2023 criteria offered a more detailed diagnostic framework, providing clearer guidance for clinical practice in some situations and addressing the diagnostic uncertainties caused by data deficiencies [6]. In details, compared to the 2018 *JAMA Neurology* criteria, the 2023 criteria explicitly classified STM and MRI-negative myelitis with low-titer MOG-IgG as non-MOGAD, thereby potentially increasing diagnostic specificity and reducing the burden of overdiagnosis and overtreatment. Compared to the 2018 *Journal of Neuroinflammation* criteria, the 2023 criteria increased clinical practicability by supplementing supportive criteria for CSF-restricted MOG-IgG-positive cases, i.e., by addressing diagnostic uncertainties arising from the reliance on CSF antibody testing alone due to sample acquisition issues or data loss.

Interestingly, the 2023 criteria exhibit higher diagnostic specificity in children compared to adult patients, albeit with lower sensitivity. Previous research by Kurd et al. also supported the good diagnostic performance of the new criteria in pediatric patients [10]. However, Varley et al. reported that the 2023 criteria exhibited higher sensitivity in children compared to adults, with similar specificity, primarily due to a higher incidence of FN ON in adults [13]. In contrast, our cohort showed more FN cases of MRI-negative encephalitis and meningitis in children, leading to reduced sensitivity.

Our study has several limitations. First, as a retrospective study, it was inherently prone to bias. Second, the use of fixed CBA for MOG-IgG detection may result in slightly lower sensitivity compared to live CBA, potentially leading to lower antibody titers [46, 47]. Notably, MOG-IgG testing was susceptible to measurement errors. According to the 2018 *Journal of Neuroinflammation* criteria, patients with borderline, unequivocal, or low-titer antibodies were required to undergo a secondary test to confirm a positive MOG-IgG result [4]. In contrast, the 2023 diagnostic criteria permitted diagnosis based on supporting criteria, yet clinical or paraclinical features cannot transform a truly FP laboratory results into a TP. Additionally, the 2023 criteria used the same clinical or paraclinical features both to confirm questionable antibody results and as triggers for MOG-IgG testing, potentially creating a circular reasoning that could result in the erroneous reclassification of genuine FP cases as TP. Hence, future multicenter studies with larger cohorts and diverse antibody testing methods are needed to validate the diagnostic criteria and refine testing requirements to improve specificity.

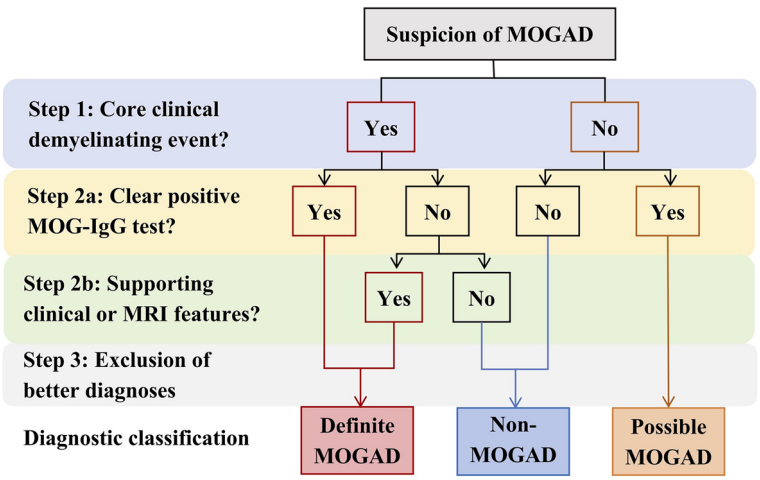

Fig. 5 Recommended diagnostic workflow for MOGAD. Abbreviations: MOG-IgG, Myelin oligodendrocyte glycoprotein-immunoglobulin G; MOGAD, Myelin oligodendrocyte glycoprotein antibody-associated disease; MRI, Magnetic resonance imaging

Conclusions

The 2023 diagnostic criteria demonstrated good sensitivity but relatively modest specificity in Chinese pediatric and adult cohorts. We suggest a supplementary diagnostic subtype of "possible MOGAD" for patients presenting with non-core clinical demyelinating events, i.e., meningitis, or MRI-negative encephalitis/myelitis, but who also met the requirement of serum clear positive MOG-IgG (Fig. 5). Close follow-up is needed for these patients to avoid missed diagnoses. Furthermore, a more comprehensive analysis is warranted for MOG-IgG positive patients who do not fulfill the diagnostic criteria to thoroughly exclude alternative genetic, metabolic, or infectious etiologies.

Abbreviations

ADEM	Acute disseminated encephalomyelitis
CBA	Cell-based assay
CI	Confidence interval
CNS	Central nervous system
CSF	Cerebrospinal fluid
FLAIR	Fluid-attenuated inversion recovery
FN	False negative
FP	False positive
IgG	Immunoglobulin G
IQR	Interquartile range
LETM	Longitudinally extensive transverse myelitis
MNOS	Myelin oligodendrocyte glycoprotein antibody and N-methyl-d-aspartate receptor antibody overlapping syndrome
MOG	Myelin oligodendrocyte glycoprotein
MOGAD	MOG antibody-associated disease
MRI	Magnetic resonance imaging
MS	Multiple sclerosis
NLR	Negative likelihood ratio
NMDAR	N-methyl-d-aspartate receptor
NPV	Negative predictive value
ON	Optic neuritis
PLR	Positive likelihood ratio
PPV	Positive predictive value
STM	Short-segment myelitis
TN	True negative
TP	True positive

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12916-025-03875-9.

Additional file 1: Fig. S1 Diagnostic criteria of MOGAD in 2018 [3, 4] and 2023 [6]. Fig. S2 Detailed steps of the 2023 diagnostic criteria. Table S1 The 2023 diagnostic criteria identified false positive, false negative, and true negative cases when compared to clinical diagnosis. Table S2 Diagnostic performance of each item in the 2023 diagnostic criteria. Table S3 Specificity of supporting clinical or MRI features in the diagnosis of MOGAD.

Acknowledgements

We would like to extend our sincere appreciation to all the patients who have been involved in this clinical study, and we are grateful to all the members of the participating institutions for their invaluable expertise and support.

Authors' contributions

MC: Conceptualization, data curation, formal analysis, investigation, writing-original draft, writing-review & editing. YH: Conceptualization, data curation, formal analysis, investigation, writing-original draft, writing-review & editing. QL: Conceptualization, data curation, formal analysis, investigation, writing-original draft, writing-review & editing. SS: Data curation, formal analysis, investigation, writing-review & editing. CS: Data curation, formal analysis, investigation, writing-review & editing. SQ: Data curation, formal analysis, investigation, writing-review & editing. YX: Data curation, formal analysis, investigation, writing-review & editing. ZY: Conceptualization, data curation, formal analysis, investigation, supervision, validation, writing-review & editing. YZ: Conceptualization, data curation, formal analysis, investigation, supervision, validation, writing-review & editing. All authors read and approved the final manuscript.

Funding

None.

Data availability

Anonymized data not published within this article will be made available upon reasonable request from any qualified investigator within 5 years after publication.

Declarations

Ethics approval and consent to participate

This research was approved by the local ethics committee of each participating center (Second Affiliated Hospital, School of Medicine, Zhejiang University [approval number: 2024-LSY-0682], Children's Hospital, Zhejiang University School of Medicine [approval number: 2024-IRB-0238-P-01], and Zhejiang Hospital [approval number: 2024-095K]). Patient consent was waived for this retrospective study.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

[1]Department of Neurology, Second Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou 310009, China. [2]Department of Neurology, Children's Hospital, Zhejiang University School of Medicine, National Clinical Research Center for Child Health, Hangzhou 310052, China. [3]Department of Neurology, Zhejiang Hospital, Hangzhou 310013, China.

Received: 17 June 2024 Accepted: 14 January 2025
Published online: 23 January 2025

References

1. Graus F, Dalmau J. MOGAD comes of age with new criteria. Lancet Neurol. 2023;22(3):193–4.
2. de Mol CL, Wong Y, van Pelt ED, Wokke B, Siepman T, Neuteboom RF, Hamann D, Hintzen RQ. The clinical spectrum and incidence of anti-MOG-associated acquired demyelinating syndromes in children and adults. Mult Scler. 2020;26(7):806–14.
3. Lopez-Chiriboga AS, Majed M, Fryer J, Dubey D, McKeon A, Flanagan EP, Jitprapaikulsan J, Kothapalli N, Tillema JM, Chen J, et al. Association of MOG-IgG serostatus with relapse after acute disseminated encephalomyelitis and proposed diagnostic criteria for MOG-IgG-associated disorders. JAMA Neurol. 2018;75(11):1355–63.
4. Jarius S, Paul F, Aktas O, Asgari N, Dale RC, de Seze J, Franciotta D, Fujihara K, Jacob A, Kim HJ, et al. MOG encephalomyelitis: international recommendations on diagnosis and antibody testing. J Neuroinflammation. 2018;15(1):134.
5. Levy M, Yeh EA, Hawkes CH, Lechner-Scott J, Giovannoni G. Implications of low-titer MOG antibodies. Mult Scler Relat Disord. 2022;59:103746.
6. Banwell B, Bennett JL, Marignier R, Kim HJ, Brilot F, Flanagan EP, Ramanathan S, Waters P, Tenembaum S, Graves JS, et al. Diagnosis of myelin oligodendrocyte glycoprotein antibody-associated disease: International MOGAD Panel proposed criteria. Lancet Neurol. 2023;22(3):268–82.
7. Alaboudi M, Morgan M, Serra A, Abboud H. Utility of the 2023 international MOGAD panel proposed criteria in clinical practice: An institutional cohort. Mult Scler Relat Disord. 2024;81:105150.

8. Forcadela M, Rocchi C, San Martin D, Gibbons EL, Wells D, Woodhall MR, Waters PJ, Huda S, Hamid S. Timing of MOG-IgG testing is key to 2023 MOGAD diagnostic criteria. Neurol Neuroimmunol Neuroinflamm. 2024;11(1):e200183.
9. Kim KH, Kim SH, Park NY, Hyun JW, Kim HJ. Validation of the International MOGAD Panel proposed criteria. Mult Scler. 2023;29(13):1680–3.
10. Kurd M, Pratt LT, Gilboa T, Fattal-Valevski A, Vaknin-Dembinsky A, Gadoth A, Hacohen Y, Meirson H. Validation of the 2023 international diagnostic criteria for MOGAD in a pediatric cohort. Eur J Paediatr Neurol. 2024;49:13–6.
11. Filippatou AG, Said Y, Chen H, Vasileiou ES, Ahmadi G, Sotirchos ES. Validation of the international MOGAD panel proposed criteria: a single-centre US study. J Neurol Neurosurg Psychiatry. 2024;95(9):870–3.
12. Rechtman A, Freidman-Korn T, Zveik O, Shweiki L, Hoichman G, Vaknin-Dembinsky A. Assessing the applicability of the 2023 international MOGAD panel criteria in real-world clinical settings. J Neurol. 2024;271(8):5102–8.
13. Varley JA, Champsas D, Prossor T, Pontillo G, Abdel-Mannan O, Khaleeli Z, Petzold A, Toosy AT, Trip SA, Wilson H, et al. Validation of the 2023 International diagnostic criteria for MOGAD in a selected cohort of adults and children. Neurology. 2024;103(1):e209321.
14. Chen L, Chen C, Zhong X, Sun X, Zhu H, Li X, Yang H, Shu Y, Chang Y, Hu X, et al. Different features between pediatric-onset and adult-onset patients who are seropositive for MOG-IgG: A multicenter study in South China. J Neuroimmunol. 2018;321:83–91.
15. Padungkiatsagul T, Chen JJ, Jindahra P, Akaishi T, Takahashi T, Nakashima I, Takeshita T, Moss HE. Differences in Clinical Features of Myelin Oligodendrocyte Glycoprotein Antibody-Associated Optic Neuritis in White and Asian Race. Am J Ophthalmol. 2020;219:332–40.
16. Xu J, Liu L, Xiong J, Zhang L, Huang P, Tang L, Xiao Y, Li X, Li J, Luo Y, et al. The clinical, radiologic, and prognostic differences between pediatric and adult patients with myelin oligodendrocyte glycoprotein antibody-associated encephalomyelitis. Front Neurol. 2021;12:679430.
17. Gu M, Mo X, Fang Z, Zhang H, Lu W, Shen X, Yang L, Wang W. Characteristics of aseptic meningitis-like attack-an underestimated phenotype of myelin oligodendrocyte glycoprotein antibody-associated disease. Mult Scler Relat Disord. 2023;78:104939.
18. Jiang Y, Tan C, Li X, Jiang L, Hong S, Yuan P, Zheng H, Fan X, Han W. Clinical features of the first attack with leukodystrophy-like phenotype in children with myelin oligodendrocyte glycoprotein antibody-associated disorders. Int J Dev Neurosci. 2023;83(3):267–73.
19. ZhangBao J, Huang W, Zhou L, Wang L, Chang X, Lu C, Zhao C, Lu J, Quan C. Myelitis in inflammatory disorders associated with myelin oligodendrocyte glycoprotein antibody and aquaporin-4 antibody: A comparative study in Chinese Han patients. Eur J Neurol. 2021;28(4):1308–15.
20. Li EC, Lai QL, Cai MT, Fang W, Ding MP, Zhang YX. Criteria for myelin oligodendrocyte glycoprotein antibody-associated disease: Balancing underdiagnosis with overdiagnosis. Clin Transl Discovery. 2023;3(4):e225.
21. Al-Ani A, Chen JJ, Costello F. Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD): current understanding and challenges. J Neurol. 2023;270(8):4132–50.
22. Ciccarelli O, Toosy AT, Thompson A, Hacohen Y. Navigating through the recent diagnostic criteria for MOGAD: challenges and practicalities. Neurology. 2023;100(15):689–90.
23. Hwangbo J, Oh SI. A case of MRI-negative encephalomyelitis in a patient with long-term stable myelin oligodendrocyte glycoprotein antibody-associated disease. J Clin Neurol. 2023;19(4):422–4.
24. Waters PJ, Komorowski L, Woodhall M, Lederer S, Majed M, Fryer J, Mills J, Flanagan EP, Irani SR, Kunchok AC, et al. A multicenter comparison of MOG-IgG cell-based assays. Neurology. 2019;92(11):e1250–5.
25. Barrett BJ, Fardy JM. Evaluation of diagnostic tests. Methods Mol Biol. 2021;2249:319–33.
26. Putz K, Hayani K, Zar FA. Meningitis. Prim Care. 2013;40(3):707–26.
27. Thompson AJ, Banwell BL, Barkhof F, Carroll WM, Coetzee T, Comi G, Correale J, Fazekas F, Filippi M, Freedman MS, et al. Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. Lancet Neurol. 2018;17(2):162–73.
28. Du BQ, Lai QL, Li EC, Cai MT, Fang GL, Shen CH, Zhang YX, Ding MP. Myelin oligodendrocyte glycoprotein antibody and N-methyl-d-aspartate receptor antibody overlapping syndrome: insights from the recent case reports. Clin Exp Immunol. 2024;215(1):27–36.
29. Lipps P, Gomes ABAGR, Kulsvehagen L, Mutke MA, Kuhle J, Papadopoulou A, Probstel AK. Ongoing challenges in the diagnosis of myelin oligodendrocyte glycoprotein antibody-associated disease. JAMA Neurol. 2023;80(12):1377–9.
30. Geraldes R, Arrambide G, Banwell B, Rovira A, Cortese R, Lassmann H, Messina S, Rocca MA, Waters P, Chard D, et al. The influence of MOGAD on diagnosis of multiple sclerosis using MRI. Nat Rev Neurol. 2024;20(10):620–35.
31. Manzano GS, Levy M, Salky R, Mateen FJ, Klawiter EC, Chitnis T, Vasileiou ES, Sotirchos ES, Gibbons E, Huda S, et al. Assessment of international MOGAD diagnostic criteria in patients with overlapping MOG-associated disease and multiple sclerosis phenotypes. J Neurol. 2024;217(9):6160–71.
32. Bruijstens AL, Lechner C, Flet-Berliac L, Deiva K, Neuteboom RF, Hemingway C, Wassmer E, consortium EUpM, Baumann M, Bartels F, et al. EU paediatric MOG consortium consensus: Part 1 - Classification of clinical phenotypes of paediatric myelin oligodendrocyte glycoprotein antibody-associated disorders. Eur J Paediatr Neurol. 2020;29:2–13.
33. Lin S, Long W, Wen J, Su Q, Liao J, Hu Z. Myelin oligodendrocyte glycoprotein antibody-associated aseptic meningitis without neurological parenchymal lesions: A novel phenotype. Mult Scler Relat Disord. 2022;68:104126.
34. Abunada M, Nierobisch N, Ludovichetti R, Simmen C, Terziev R, Togni C, Michels L, Kulcsar Z, Hainc N. Autoimmune encephalitis: Early and late findings on serial MR imaging and correlation to treatment timepoints. Eur J Radiol Open. 2024;12:100552.
35. Graus F, Titulaer MJ, Balu R, Benseler S, Bien CG, Cellucci T, Cortese I, Dale RC, Gelfand JM, Geschwind M, et al. A clinical approach to diagnosis of autoimmune encephalitis. Lancet Neurol. 2016;15(4):391–404.
36. Takai Y, Misu T, Kaneko K, Chihara N, Narikawa K, Tsuchida S, Nishida H, Komori T, Seki M, Komatsu T, et al. Myelin oligodendrocyte glycoprotein antibody-associated disease: an immunopathological study. Brain. 2020;143(5):1431–46.
37. McCombe JA, Flanagan EP, Chen JJ, Zekeridou A, Lucchinetti CF, Pittock SJ. Investigating the immunopathogenic mechanisms underlying MOGAD. Ann Neurol. 2022;91(2):299–300.
38. Grimes DA, Schulz KF. Refining clinical diagnosis with likelihood ratios. Lancet. 2005;365(9469):1500–5.
39. Reindl M, Rostasy K. Serum MOG IgG titres should be performed routinely in the diagnosis and follow-up of MOGAD: Yes. Mult Scler. 2023;29(8):926–7.
40. Fan X, Li Q, Li T, He X, Feng C, Qin B, Xu Y, He L. Radiological features for outcomes of MOGAD in children: a cohort in Southwest China. Neuropsychiatr Dis Treat. 2022;18:1875–84.
41. Li X, Wu W, Hou C, Zeng Y, Wu W, Chen L, Liao Y, Zhu H, Tian Y, Peng B, et al. Pediatric myelin oligodendrocyte glycoprotein antibody-associated disease in southern China: analysis of 93 cases. Front Immunol. 2023;14:1162647.
42. ZhangBao J, Huang W, Zhou L, Tan H, Wang L, Wang M, Yu J, Lu C, Lu J, Quan C. Clinical feature and disease outcome in patients with myelin oligodendrocyte glycoprotein antibody-associated disorder: a Chinese study. J Neurol Neurosurg Psychiatry. 2023;94(10):825–34.
43. Elsbernd P, Cacciaguerra L, Krecke KN, Chen JJ, Gritsch D, Lopez-Chiriboga AS, Sechi E, Redenbaugh V, Morris PP, Carter JL, et al. Cerebral enhancement in MOG antibody-associated disease. J Neurol Neurosurg Psychiatry. 2023;95(1):14–8.
44. Wildner P, Stasiolek M, Matysiak M. Differential diagnosis of multiple sclerosis and other inflammatory CNS diseases. Mult Scler Relat Disord. 2020;37:101452.
45. Jaeschke R, Guyatt GH, Sackett DL. Users' guides to the medical literature. III. How to use an article about a diagnostic test. B. What are the results and will they help me in caring for my patients? The Evidence-Based Medicine Working Group. JAMA. 1994;271(9):703–7.
46. Budhram A, Rotstein DL, Yang L, Yeh EA. Myelin oligodendrocyte glycoprotein antibody titers by fixed cell-based assay: positive predictive value and impact of sample collection timing. Front Neurol. 2024;15:1380541.
47. Reindl M, Schanda K, Woodhall M, Tea F, Ramanathan S, Sagen J, Fryer JP, Mills J, Teegen B, Mindorf S, et al. International multicenter examination of MOG antibody assays. Neurol Neuroimmunol Neuroinflamm. 2020;7(2):e674.

Publisher's Note