Clinical characteristics and associated factors of pediatric acute disseminated encephalomyelitis patients with MOG antibodies: a retrospective study in Hangzhou, China

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Research Article

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Abstract

Background: To investigate the clinical characteristics and associated factors of pediatric acute disseminated encephalomyelitis (ADEM) patients positive for anti-myelin oligodendrocyte glycoprotein (MOG) antibodies.

Methods: This retrospective study included pediatric ADEM patients who underwent serum MOG antibody detection from May 2017 to August 2020. The patients were divided into two groups: those with (MOG+, n=35) and without (MOG−, n=50) anti-MOG antibodies in the serum. Our study analyzed the clinical characteristics of MOG-IgG-positive ADEM pediatric patients and conducted a comparative analysis between the two groups.

Results: Thirty-five MOG-IgG-positive ADEM patients (21 males and 14 females) with encephalopathy, multifocal neurological symptoms, and typical magnetic resonance imaging (MRI) abnormalities were enrolled. They usually had a favorable outcome, while some suffered from relapse. Compared to the ADEM patients without MOG antibodies, MOG-IgG-positive ADEM patients suffered from a longer disease duration (median: 10 vs. 6 days), more meningeal involvement (31.4% vs. 8%) and frontal lobe involvement (82.8% vs. 68%), higher relapse rates (14.3% vs. 2%), lower serum tumor necrosis factor (1-12.4 pg/ml, median 1.7 vs. 1-34 pg/ml, median 2.2) and interferon-gamma (1-9.4 pg/ml, median 1.3 vs. 1-64 pg/ml, median 3) (all $P < 0.05$). Multivariate logistic regression analysis indicated that a longer disease duration, meningeal involvement, and frontal lobe involvement were associated factors for ADEM patients with MOG antibodies ($P < 0.05$).

Conclusions: Our findings provide clinical evidence that a longer disease duration, meningeal involvement, and frontal lobe involvement are associated with pediatric MOG-IgG-positive ADEM.

Background

Myelin oligodendrocyte glycoprotein (MOG) antibodies, expressed in the outermost layer of the myelin sheaths in the mammalian central nervous system (CNS), mediate a variety of demyelinating diseases in the CNS [1]. MOG-immunoglobulin G (IgG)-associated disorders (MOGADs), with diverse clinical phenotypes, have been research hotspots in neurology in recent years. The first onset of MOGADs in children involves acute disseminated encephalomyelitis (ADEM) and optic neuritis (ON) [2], and ADEM is especially common in young children [3]. ADEM is an immune-mediated demyelinating CNS disease that presents with encephalopathy, polyfocal neurologic symptoms, and multifocal demyelinating lesions in the brain and spinal cord [4]. Most children with ADEM have a good prognosis, and a small number of them may have recurrence and residual sequelae. To date, the pathological mechanism and risk factors for anti-MOG antibody-positive ADEM are still not well established. This study retrospectively compared the clinical characteristics and prognosis of pediatric ADEM patients with or without MOG antibody positivity to improve the diagnosis and treatment of MOG-IgG-positive ADEM and identify the factors associated with this disease.

Materials And Methods

Clinical data of all ADEM patients who underwent detection of MOG antibodies in the serum were retrospectively collected in the Department of Neurology, Children's Hospital of Zhejiang University School of Medicine, China, from May 2017 to August 2020. The MOG antibodies in the serum were determined using cell-based assays when admission, and the levels of ≥ 1:10 were classified as serum positive. According to the serum MOG antibody status, the 85 patients were divided into two groups. A total of 35 MOG-IgG-positive patients were included in the MOG + group, and the remaining 50 MOG-IgG-negative patients were included in the MOG − group. The diagnostic criteria of ADEM were in accordance with the 2013 International Pediatric Multiple Sclerosis Study Group criteria for pediatric ADEM, including all of the following: (1) the first multifocal CNS event (probably caused by inflammatory demyelination); (2) symptoms of encephalopathy (disorder of consciousness or behavioral changes) that could not be explained by fever; (3) no new clinical or lesions revealed by MRI 3 months after onset; (4) abnormal head MRI in the acute stage (within 3 months); and (5) typical findings in head MRI. The exclusion criteria of this study were (1) less than 3 months of follow-up and (2) other intracranial infectious diseases or systemic autoimmune diseases [5].

All demographic, clinical, laboratory, and MRI data were collected from the two groups. The initial cerebrospinal fluid (CSF) studies and MRI scans were performed within five days of admission. Pathogen evaluations (including viral polymerase chain reaction studies and bacterial culture), autoimmune encephalitis antibodies, anti-aquaporin 4 (AQP4) antibodies, anti-myelin basic protein antibodies, and cytokines were tested in the serum and CSF samples in all patients. In addition, electroencephalogram (EEG), complete blood counts, C-reactive protein, serum chemistry, complements, and erythrocyte sedimentation rates were also collected at admission. All patients were followed up at the outpatient clinic for at least one year. Follow-up brain and spinal cord MRI was performed every 3–6 months.

The SPSS 22.0 statistical software package was used to process the data in this study. Continuous variables with a normal distribution were compared using a t-test, while those that exhibited a nonnormal distribution were compared with the Mann-Whitney U test. Categorical variables were compared with the chi-square test. Factors associated with MOG-IgG-positive ADEM were identified through a binary logistic regression model. The factors with statistical significance in univariate analysis and other potential predictor variables were included in multivariate models for analysis. The test standard was $P = 0.05$, and $P < 0.05$ was considered statistically significant. This study was approved by the Ethics Committee of the Children's Hospital of Zhejiang University School of Medicine, China (2019-IRB-115). All parents of pediatric patients provided informed consent for this study.

Results

Clinical characteristics of ADEM children seropositive for anti-MOG antibodies

We identified 35 patients, 21 males and 14 females (male-to-female ratio of 1.5:1), with a median onset age of 69 months (range: 20-138 months), in the MOG+ group. The disease duration ranged from 1 to 30 days (median: 10 days), with a hospital stay length of 6-35 days (median: 17 days). Seasonal increases in incidence during spring or winter were seen in our cohort (13 cases in winter, 10 cases in spring, 5 cases in summer, and 7 cases in fall). Among the patients, 28.6% (10/35) had an acute upper respiratory history, while the other 71.4% of patients had no preceding or concomitant diagnosis of respiratory infection. None of our patients had a preceding vaccination history. Encephalopathy was seen in all patients, including altered consciousness in 21 patients (60%) and behavioral changes in the other 14 children (40%). Other symptoms included fever (23/35, 65.7%), headache (15/35, 42.9%), vomiting (13/35, 37.1%), limb weakness (13/35, 37.1%), meningeal irritation (11/35, 37.1%), seizures (8/35, 22.3%), optic neuritis (6/35, 17.1%), and ataxia (3/35, 8.6%) (Table 1).

The initial cranial MRI revealed typical multifocal high lesions on fluid attenuated inversion recovery and T2-weighted images in all 35 MOG-IgG-positive ADEM patients. The most commonly involved brain site was the frontal lobe (29/35, 82.9%), followed by the parietal lobe (19/35, 54.3%), temporal lobe (18/35, 51.4%), and occipital lobe (13/35, 37.1%). In addition to the white matter, the basal ganglia (17/35, 48.6%), thalamus (16/35, 45.7%), brainstem (13/35, 37.1%), cerebellum (9/35, 25.7%), and corpus callosum (5/35, 14.3%) were also involved. Lesions in the thalamus, basal ganglia, brainstem, and cerebellum were bilaterally involved in general, and corpus callosum lesions were mainly involved in the compression part (4/5, 80%). Initial spinal cord MRI showed lesions of high signal intensity on T2-weighted images in 42.9% (15/35) of the cases, in which the cervical, thoracic, lumbar, and sacral cord were invaded in 42.9% (15/35), 37.1% (13/35), 17.1% (6/35), and 5.7% (2/35) of patients, respectively (Table 2).

CSF analysis showed pleocytosis (>5/ml, range 12-352/ml, monocyte predominance) in 29 (82.9%) cases and protein elevation in 13 (37.1%) cases (>400 mg/L, range 388-972 mg/L) (Table 2). CSF glucose and chloride were normal in all patients. Oligoclonal bands in CSF were positive in five patients who showed intrathecal synthesis. There were 8 patients (22.9%) with MOG-IgG positivity in the CSF. The results of the autoimmune encephalitis antibodies, AQP 4 antibodies, and anti-myelin basic protein antibodies in the CSF and serum were negative in all children. Interictal EEGs demonstrated that 23 patients (65.7%) had abnormal background activity, and none showed epileptiform discharges. Six patients showed abnormal visual evoked potentials. All children had normal brainstem auditory evoked potentials. The median serum MOG-IgG titre was 1:20 (range 1:10-1:320).

All children received high-dose, intermittent intravenous methylprednisolone therapy (20-30 mg/kg/day, 5 days for 1 course, 1-2 courses in total) followed by tapered oral corticosteroids over 6-8 weeks, whereas 21 patients received intravenous immunoglobulin (2 mg/kg divided over 2 days) therapy, and 6 cases (17.1%) were treated with immunosuppressants. All clinical symptoms and signs were significantly improved within 1-3 weeks of the treatment. With a median follow-up of 1.6 (range, 1.2-2.3) years, 30 cases (85.7%) were diagnosed with monophasic ADEM, while the remaining 5 cases (14.3%) recurred during follow-up. Among the five recurrent cases, the final diagnoses were multiphasic disseminated

encephalomyelitis (MDEM, n=3), neuromyelitis optica spectrum disorders (NMOSDs, n=1), and ADEM-ON (n=1). All recurrent episodes occurred between 4 months and 10 months after the initial event. Five patients (14.3%) suffered from neurological sequelae, including motor deficits (n=3) and secondary epilepsy (n=2). Five recurrent patients showed new MRI lesions during the follow-up period between 4 months and 10 months, and the lesions were significantly improved after subsequent retreatment. Nevertheless, MRI studies at one-year follow-up showed that the lesions in the brain and spinal cord were improved to varying degrees. Brain MRI scans showed complete T2 lesion resolution in 12 patients (34.3%) and partial reduction in the size of the T2 lesion in 23 patients (65.7%), while spinal cord MRI scans showed complete T2 lesion resolution in 31 patients (88.6%). Of the 23 patients with abnormal EEG, the recheck EEG showed that only five cases were mildly abnormal, and the remaining 18 cases recovered to a normal level at the one-year follow-up. At the last follow-up, 18 patients (51.4%) still had positive MOG-IgG in the serum.

Comparison of clinical, MRI, and laboratory features between the MOG+ and MOG− groups

To evaluate what characterizes ADEM children with positive MOG antibodies, a statistical comparison of clinical data, including the general conditions, clinical manifestations, imaging manifestations, laboratory findings, and prognosis after treatment, was performed between the MOG+ and MOG− groups (Tables 1-2). The results showed that the MOG+ group had a significantly longer disease duration (median: 10 vs. 6 days, $P < 0.05$), more meningeal involvement (31.4% vs. 8%, $P < 0.05$), and a higher recurrence rate (14.3% vs. 2%, $P < 0.05$) than the MOG− group (Table 2). Comparison of the initial and follow-up MRI studies between the two groups revealed that MOG-IgG-positive ADEM patients had a higher chance of frontal lobe involvement (82.8% vs. 68%, $P < 0.05$), in contrast to children with absent MOG antibodies. Another finding was that children with or without MOG antibodies did not differ in bilateral lesions, spinal cord involvement, infratentorial lesion involvement, or residual MRI findings. Furthermore, the serum levels of tumor necrosis factor (TNF) and interferon γ (IFN-γ) in the MOG+ group were significantly lower than those in the MOG− group (TNF: 1-12.4 pg/ml, median 1.7 vs. 1-34 pg/ml, median 2.2, $P < 0.05$; IFN-γ: 1-9.4 pg/ml, median 1.3 vs. 1-64 pg/ml, median 3, $P < 0.05$), while no significant differences in serum interleukin (IL)-2, 4, 6, 10, CSF cytokines, or serum complements were noted between the two groups (Table 2). In addition, no significant differences in age, gender, other clinical characteristics, or other laboratory findings were found between the two groups.

Analysis of factors associated with MOG-IgG-positive ADEM in children

To further study the associated factors for seropositive MOG-IgG ADEM patients, all factors with $P < 0.05$ in univariate analyses and other potentially related factors were included in the binary logistic regression analysis. Significant differences in the disease duration, meningeal involvement, and frontal lobe involvement were found between the two groups ($P < 0.05$), indicating that MOG-IgG-positive ADEM patients were predicted by longer disease duration, higher meningeal involvement, and higher frontal lobe involvement (Table 3).

Discussion

ADEM is a common phenotype of MOGADs in pediatric patients. The presence of MOG antibodies in ADEM was higher than that in other demyelinating disorders [6]. Previous data showed that serum MOG-IgG was even identified in more than 50% of children with ADEM [7]. We confirmed that 41.2% (35/85) of pediatric ADEM patients were seropositive for MOG-IgG in our cohort. As already suggested in the literature [6–8], in the present study, MOG-IgG-positive ADEM children had a median age of 69 months, with a high incidence in winter or spring. Although the clinical manifestations of ADEM children with positive serum MOG-IgG were similar to those without, there were still some clues that helped us to differentiate ADEM patients with positive serum MOG-IgG. There was a higher likelihood of MOG antibody positivity in younger patients or patients suffering seizures from previous data [9–10]. Nevertheless, we did not find similar conclusions. On the other hand, we found that the ADEM patients with positive serum MOG-IgG had a longer disease duration than those without, suggesting that the disease course of MOG-IgG-positive ADEM patients was more protracted. Interestingly, meningeal involvement was more common in ADEM children with MOG antibodies (31.4%, 11/35), which was higher than the 12% reported in a previous study [11]. Furthermore, a longer disease duration and meningeal involvement were independent variables associated with MOG-IgG-positive ADEM. Therefore, we demonstrated that ADEM children with positive serum MOG-IgG were more likely to have meningeal involvement and a longer disease duration, and much more attention should be given to the detection of MOG-IgG in pediatric patients with ADEM and prolonged disease duration or meningeal involvement.

MRI is an important measure for the diagnosis of ADEM. In the current study, the manifestations of cranial MRI of MOG-IgG-positive ADEM patients were consistent with previous reports [5, 12], involving multifocal irregular and asymmetric clusters and flaky lesions mainly in the subcortical white matter, accompanied by bilateral involvement of the brainstem, thalamus, and basal ganglia. It was reported that large and bilateral lesions and longitudinally extensive transverse myelitis (LETM) lesions were more common and more likely to resolve in MOG antibody-associated ADEM [13–14]. In contrast, there was no significant difference in bilateral lesions, spinal cord involvement, or infratentorial lesions between the MOG-IgG-positive ADEM and MOG-IgG-negative ADEM children in our cohort. MRI follow-up also revealed that ADEM children with or without MOG antibodies did not differ in the resolution of the initial lesions. In our cohort, frontal lobe involvement was more likely to occur and was an independent associated factor for MOG-IgG-positive ADEM, as described previously, which may be related to the abundant blood supply of the frontal lobe [5, 12]. Thus, we concluded that it was valuable to consider frontal lobe involvement as a diagnostic clue for children who presented with ADEM due to MOG-IgG seropositivity.

The exact pathogeneses of ADEM and MOG-IgG-mediated ADEM have not been fully elucidated. Cytokines and chemokines play important roles in the progression of ADEM. A previous study showed that the acute phase of ADEM is mainly related to T helper cell (Th) 1-related cytokine abnormalities, such as significant increases in TNF, IFN-γ, IL1, IL6, and IL8 levels, and the remission period of ADEM is mainly related to Th2-related increases in IL4, IL10, and transforming growth factor-beta [15]. In this study, the serum TNF and IFN-γ levels in the MOG-IgG-positive ADEM group in the acute phase were significantly

lower than those in the MOG-IgG-negative ADEM group, while no significant difference in the CSF cytokines was found between the two groups, suggesting that the changes in serum Th1-related cytokines were more pronounced in ADEM children without antibodies. Although some in vitro experiments have confirmed that MOG-IgG mediates cell death through the complement pathway [1, 16], no significant differences in complements were found between the two groups in the present study. Further in vitro and in vivo research on the involvement of cytokines and complements in ADEM, especially the pathogenesis of anti-MOG antibody-positive ADEM in pediatric patients, is needed.

In accordance with previous reports [8, 17], the prognosis of ADEM children with MOG antibodies was good in this study, and only 14.3% of ADEM children with positive serum MOG-IgG suffered from neurological sequelae. However, a previous study demonstrated that the recurrence rate of ADEM was as high as 1/3 [8], and patients with persistent anti-MOG serum seropositivity were more likely to have a multiphasic course of ADEM [7, 18–19]. Long-term follow-ups showed that children with primary onset of ADEM might relapse during follow-up with MDEM, ON, or NMOSD [14, 18]. In this study, a total of five ADEM patients with anti-MOG serum seropositivity had a recurrence, with a recurrence rate of 14.3%, which was significantly higher than that in patients without serum MOG antibodies, suggesting that MOG-IgG positivity may be a risk factor for recurrence in ADEM children. Among the recurrence cases, relapse was more common in females (80%, 4/5), with a recurrence interval of less than one year, which was consistent with previous reports [18, 20]. However, another report showed that a second demyelination event might take up to 4 years to develop [18]. Further observation and research are needed to confirm whether the recurrence rate of ADEM will continue to increase over time.

There are limitations to our study. First, this was a single-center study; thus, the findings of this study may not apply to all pediatric ADEM patients seropositive for MOG-IgG in China. Second, MRI data were acquired clinically, and the enhanced MRI sequence data were not available for some patients. Third, this study was a retrospective study and the data of children were retrospectively collected, which may lead to a potential for selection bias. Further long-term prospective studies are needed to verify our findings. Despite these limitations, we believe that our findings in the present study provide some useful information for better understanding the clinical characteristics and associated factors of ADEM children with MOG antibodies.

Conclusion

To summarize, MOG-IgG-positive ADEM frequently occurred in winter and spring, with the main clinical manifestations being encephalopathy and multifocal neurologic signs, and usually had a favorable outcome, while some suffered from mild neurological sequelae. Compared to ADEM patients without MOG antibodies, MOG-IgG-positive ADEM children had a more prolonged disease duration, more meningeal involvement, more frontal lobe involvement, and less serum TNF and INF-γ and were more prone to recurrence. A long disease duration, meningeal involvement, and frontal lobe involvement were associated with MOG-IgG-positive ADEM.

Abbreviations

ADEM: acute disseminated encephalomyelitis; MOG: myelin oligodendrocyte glycoprotein; MRI: magnetic resonance imaging; CNS: central nervous system; IgG: immunoglobulin G; MOGADs: myelin oligodendrocyte glycoprotein-immunoglobulin G-associated disorders; ON: optic neuritis; CSF: cerebrospinal fluid; AQP4: anti-aquaporin 4; EEG: electroencephalogram; MDEM: multiphasic disseminated encephalomyelitis; NMOSD: neuromyelitis optica spectrum disorder; TNF: tumor necrosis factor; IFN-γ interferon γ; IL: interleukin; LETM: longitudinally extensive transverse myelitis; Th: T helper cell.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the Children's Hospital of Zhejiang University School of Medicine, China (2019-IRB-115). All parents of pediatric patients provided informed consent for this study. This study was carried out in accordance with relevant guidelines and regulations.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used or analyzed during the current study are not publicly available due to patient confidentiality but are available from the corresponding author on reasonable request.

Conflicts of interest

The authors declare no conflicts of interest.

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Authors' contributions

FG, KJ, and JS conceptualized and designed the study. JS and TJ acquired and analyzed the data, drafted the text, and prepared the tables. All authors approved the final version of the manuscript to be published.

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Tables

Table 1

Clinical features of MOG-IgG-positive ADEM patients compared to MOG-IgG-negative ADEM patients

Clinical features	MOG+ group n=35	MOG− group n=50	Univariate analyses p value
Gender, male, n (%)	21 (60)	28 (56)	0.71
Onset age, months, median (range)	69 (20-138)	76 (13-178)	0.32
Disease duration, days, median (range)	10 (1-30) *	6 (0.5-30)	0.04
Hospital stay, days, median (range)	17 (6-35)	16 (7-40)	0.57
Relapse, n (%)	5 (14.3) *	1 (2)	0.03
With respiratory symptoms, n (%)	10 (28.6)	17 (34)	0.83
Onset at winter or spring, n (%)	23 (65.7)	24 (48)	0.34
Neurological sequel, n (%)	5 (14.3)	11 (22)	0.72
Encephalopathy, n(%)			
Altered consciousness, n(%)	21 (60)	38 (76)	0.15
Behavioral changes, n (%)	14 (40)	12 (24)	0.15
Fever, n (%)	23 (65.7)	37 (74)	0.47
Headache, n (%)	15 (42.9)	26 (52)	0.51
Vomitting, n (%)	13 (37.1)	22 (44)	0.66
Seizures, n (%)	8 (22.3)	13 (26)	0.80
Optic neuritis, n (%)	6 (17.1)	4 (8)	0.31
Meningeal involvement, n (%)	11 (31.4) *	4 (8)	<0.01
Ataxia, n (%)	3 (8.6)	6 (12)	0.73
Limb weekness, n (%)	13 (37.1)	17 (34)	0.82

ADEM: acute disseminated encephalomyelitis; MOG: myelin oligodendrocyte glycoprotein; MOG+: ADEM patients with positive anti-MOG antibodies in serum; MOG−: ADEM patients without positive anti-MOG antibodies in serum; univariate analyses were confirmed by the t-test, chi-square or Mann-Whitney u test. * indicates MOG+ group *vs.* MOG−group, $p<0.05$.

Table 2

The MRI and laboratory features of MOG-IgG-positive ADEM patients compared to MOG-IgG-negative ADEM patients

MRI lesions, n (%)	MOG+ n=35	MOG− n=50	p value	Laboratory features	MOG+ n=35	MOG− n=50	p value
Brain lesions				EEG abnormality, n(%)	23 (65.7)	31 (62)	0.82
Frontal lobe	29 (82.8) *	34 (68)	0.02	CSF analysis, n(%)			
Parietal lobe	19 (54.3)	27 (54)	0.14	Pleocytosis	29 (82.9)	32 (64)	0.86
Temporal lobe	18 (51.4)	23 (46)	1.00	Protein elevation	13 (37.1)	15 (30)	0.55
Occipital lobe	13 (37.1)	14 (28)	0.67	Positive OB	5 (14.3)	3 (6)	0.27
Basal ganglia	17 (48.6)	22 (44)	0.83	Serum cytokines, (pg/ml)			
Thalamus	16 (45.7)	14 (28)	0.38	IL-2, median (range)	2.1 (1-4.5)	2.0 (1-8.6)	0.97
Brainstem	13 (37.1)	14 (28)	0.48	IL-4, median (range)	2 (1-3.9)	1.9 (1-36.6)	0.41
Cerebellum	9 (25.7)	12 (24)	0.53	IL-6, median (range)	12.4 (1-1436)	12.4 (1.6-5000)	0.75
Corpus callosum	4 (14.3)	5 (10)	0.73	IL-10, median (range)	3.4 (1-11.1)	4.3 (1-116.7)	0.06
Optic nerve	6 (17.1)	4 (8)	0.31	TNF, median (range)	1.7 (1-12.4) *	2.2 (1-34)	0.04
Spinal cord lesions	15 (42.9)	29 (58)	0.66	IFN-γ, median (range)	1.3 (1-9.4) *	3 (1-64)	<0.01
LETM	6 (17.1)	9 (18)	0.58	Serum complements (U/L)			
Infratentorial lesions	16 (45.7)	19 (38)	0.38	C3, median (range)	1.38 (1-18.9)	1.3 (0.8-1.9)	0.07
Bilateral lesions	35 (100)	50 (100)	1.00	C4, mean ± SD	0.38±0.02	0.39±0.02	0.86
Residual cranial lesions	23 (65.7)	29 (58)	0.51				
Residual spinal cord lesions	4 (11.4)	5 (10)	1.00				

ADEM: acute disseminated encephalomyelitis; MOG: myelin oligodendrocyte glycoprotein; MOG+: ADEM patients with positive anti-MOG antibodies in serum; MOG−: ADEM patients without positive anti-MOG antibodies in serum; MRI: magnetic resonance imaging; LETM: longitudinal extensive transverse myelitis; EEG: electroencephalogram; CSF: cerebrospinal fluid; IL: interleukin; TNF: tumor necrosis factor; IFN-γ: interferon γ; univariate analyses were confirmed by the t-test, chi-square or Mann-Whitney u test. * indicates MOG+ group *vs.* MOG−group, p<0.05.

Table 3

Associations of clinical indicators with MOG-IgG-positive ADEM patients

Factors	MOG+ group n=35	MOG− group n=50	B	p value	OR	95% CI
Gender, male, n (%)	21 (60)	28 (56)	0.032	0.97	1.03	(0.193, 5.509)
Onset age, months, median (range)	69 (20-138)	76 (13-178)	-0.007	0.58	0.993	(0.970, 1.017)
Disease duration, days, median (range)	10 (1-30) *	6 (0.5-30)	0.168	<0.01	1.183	(1.045, 1.339)
Meningeal involvement, n (%)	11 (31.4) *	4 (8)	4.445	<0.01	85.158	(6.199, 1169.853)
Frontal lobe involvement, n (%)	29 (82.9) *	29 (58)	2.703	0.03	51.824	(2.867, 936.883)
Relapse, n (%)	5 (14.3)	1 (2)	2.978	0.10	19.639	(0.533, 723.340)
Serum TNF, (pg/ml), median (range)	1.7 (1-12.4)	2.2 (1-34)	-0.147	0.16	0.863	(0.703, 1.060)
Serum IFN-γ, (pg/ml), median (range)	1.3 (1-9.4)	3 (1-64)	-0.114	0.58	0.893	(0.596, 1.336)

ADEM: acute disseminated encephalomyelitis; MOG: myelin oligodendrocyte glycoprotein; MOG+: ADEM patients with positive anti-MOG antibodies in serum; MOG−: ADEM patients without positive anti-MOG antibodies in serum; TNF: tumor necrosis factor; IFN-γ: interferon γ; OR: odds ratio; 95% CI: 95% confidence interval. Binary logistic regression was used for multivariate analyses. * indicates MOG+ group *vs.* MOG−group, p<0.05.