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ORIGINAL ARTICLE

Clinical spectrum, treatment and outcome of myelin oligodendrocyte glycoprotein (MOG) antibody-associated disease in children: a tertiary care experience

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Abstract
Anti-myelin oligodendrocyte glycoprotein antibodies have been associated with a wide range of clinical presentations including monophasic and relapsing disease courses. Lack of a definitive marker for predicting further relapses and the final diagnoses complicates the clinical follow-up and treatment decisions for patients with the first episode. This study retrospectively analyzed the clinical spectrum, treatment protocols and outcome of nine children with MOG antibody-associated demyelinating disease. Diagnoses at first presentation were acute disseminated encephalomyelitis (ADEM) in six cases (67%), optic neuritis in two cases (22%), and clinically isolated syndrome in one case (11%). The disease remained monophasic in five (56%) cases. All cases with a monophasic disease course were negative for anti-MOG antibody titers in the third month. The initial diagnosis of all relapsing cases was ADEM. Three of the four cases with a relapsing disease course were available for anti-MOG antibody testing at the third month and all were positive, however, antibody titers at the sixth month were inconsistent. Cases with a relapsing disease course had no further attacks after monthly intravenous immunoglobulin treatment. Relapsing disease course is not rare in childhood MOG-antibody associated demyelinating disease. Monthly IVIG treatment may be a good alternative for the long-term treatment of relapsing cases with a low side effect profile. Anti-MOG antibody serostatus at remission periods should be interpreted cautiously. Further studies are needed to better understand and predict the clinical course of pediatric patients with MOG-antibody associated diseases.

Keywords Myelin oligodendrocyte glycoprotein antibody · Childhood · Inflammatory demyelinating diseases · Treatment · Outcome

Introduction

Myelin oligodendrocyte glycoprotein (MOG) is a central nervous system (CNS) specific protein expressed on the surface of myelin sheath and oligodendrocytes [1]. The possible relation of MOG antibodies with multiple sclerosis (MS) and other demyelinating conditions first appeared in the literature in the late 1980s [2]. However, MOG antibodies associated with pediatric demyelinating diseases were first described in 2007 [3, 4]. Later studies have shown the presence of MOG antibodies in one-third of all pediatric cases with a first episode of an acute demyelinating syndrome [5–9].

MOG-antibody associated disease has been associated with a range of phenotypic presentations which include monophasic diseases such as acute disseminated encephalomyelitis (ADEM), optic neuritis (ON), and transverse myelitis (TM). The forms of relapsing MOG-antibody associated diseases include; multiphasic disseminated encephalomyelitis (MDEM), recurrent optic neuritis (RON), acute disseminated encephalomyelitis followed by optic neuritis (ADEM-ON) [7–9]. Additionally, some MOG-antibody positive patients may present with a clinical phenotype similar to NMOSD. However, due to the distinct underlying mechanisms of these two entities, it would be appropriate to evaluate these patients as uncategorized MOG-antibody

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associated disease until a better classification is recommended [10].

Although most MOG-antibody positive cases show a monophasic course, relapses are not rare and the lack of a definitive marker for predicting the further relapses and the final diagnoses complicates the clinical follow-up and treatment decisions for patients with a first episode. While current knowledge regarding MOG-antibody associated demyelinating diseases in children is constantly expanding through case reports and series, there is still a lot to learn.

Methods

The study was conducted in Ege University Faculty of Medicine, Department of Child Neurology between January 2015 and February 2020. Children presenting with a clinical episode consistent with an acute demyelinating syndrome with positive MOG-antibody titers and were followed-up for at least 24 months were retrospectively analyzed. All patients underwent comprehensive clinical assessments, had brain magnetic resonance imaging (MRI) scans. The initial and final diagnoses of the cases including ADEM, MDEM, ADEM-ON and CIS were based on the most recent diagnostic criteria for these diseases [11, 12].

MOG-antibodies were studied in a single center using serum cell-based assay (Euroimmun, Lübeck, Germany) and titers higher than 1:10 were considered as a positive result. Serum samples of seven patients with myelitis and/or recurrent episodes of ON were also analyzed for anti-aquaporin-4/AQP4 antibody using serum cell-based assay in the same laboratory (Euroimmun, Lübeck, Germany).

All cases were evaluated in terms of their clinical, radiological findings and MOG-antibody titers at disease onset. Treatment modalities, MOG-antibody titers during follow-up, clinical and radiological disease courses and final diagnoses of each case were discussed in detail.

This study was reviewed and approved by Ege University Faculty of Medicine Ethics Committee for Noninvasive Clinical Research (Date: 22.05.2018, Number: 18-5.1/19).

Results

Clinical characteristics

The mean age was 7.66 ± 3.12 years. Six (66.6%) cases were female and 3 (33.3%) were male. The most common findings on admission were encephalopathy (55.5%), ataxia (44.4%), headache (22.2%), vision loss (33.3%), dysphagia (11.1%) and speech impairment (11.1%). The mean follow-up period was 49.33 ± 58.92 months. Five (55.5%) cases (Cases 1–5) remained monophasic during the follow-up period while the remaining four (44.4%) (Cases 6–9) had relapsing disease course. Initial diagnoses on the first presentation were ADEM in six (67%) cases, ON in two (22%) cases, and CIS in one (11%) case (11%). The initial diagnosis of all relapsing cases was ADEM and it was changed to MDEM in one (11.1%) case, ADEM-ON in one (11.1%) case and uncategorized relapsing MOG-associated disease in two (22.2%) cases. The number of episodes ranged from 1 to 23 and the mean time interval between the episodes were 8.75 ± 4.71 months (Table 1).

MRI features

The cranial and spinal magnetic resonance imaging (MRI) of all cases, and the orbital MRIs of cases with ON, were obtained. Six cases were found to have spinal cord involvement, with four of them showing signs of longitudinally extensive transverse myelitis (LETM). Cranial MRIs of two cases with isolated ON were normal and orbital MRIs demonstrated bilateral optic nerve thickening and contrast enhancement. All cases had follow-up MRIs at 3–6 months. Cases with monophasic disease course had normal cranial MRIs at follow-up. Among four cases with relapsing disease course, MRI at 3–6 months was normal in two, while the remaining two cases demonstrated incomplete regression of the lesions despite normal neurological examination. Case 9, who had undergone 17 years of follow-up, with a final diagnosis of uncategorized MOG-antibody associated disease with NMOSD phenotype, had both cortical and spinal cord atrophy at the last follow-up MRI. Descriptive cranial and spinal MR images of the study group are given in Fig. 1.

Laboratory findings

Cerebrospinal fluid (CSF) sampling was performed at an initial presentation on all cases except one (Case 2) who was admitted to the intensive care unit and mechanically ventilated. Biochemical analysis of CSF in all cases was normal. None of the patients had pleocytosis in CSF except two cases (Cases 2, 8) with 20 white blood cells/mm^3. Viral and bacterial serological studies, and CSF cultures were all negative. All cases with CSF samples were also negative for oligoclonal bands (OCBs) and IgG indexes were found within normal limits (< 0.8). Serum bacterial and viral serology of all cases were negative, as was the test for antinuclear antibodies.

Regarding the MOG-antibody serostatus of the cases with monophasic and relapsing disease courses, all five cases with a monophasic disease course were negative for MOG-antibody titers at the third month of follow-up. Three of the remaining four cases (Cases 6–7–8) with a relapsing disease course were available for MOG-antibody testing in the third month of disease onset, and all three remained

Table 1 Clinical features, serological findings, treatment protocols, initial and final diagnosis of the study group

Case no.	Age at onset (years)/sex	Presenting symptom	Serum anti-MOG Ab titer				Anti-AQP4 Ab titer	Acute attack/long term therapy	Number of attacks	Initial diagnosis	Final diagnosis	Follow-up duration (months)
			1st episode	3rd month	6th month	Relapse						
1	10/F	Encephalopathy	1:100	Negative	ND	NA	ND	IV PMP + oral steroid/–	1	ADEM	ADEM	24
2	8/M	Encephalopathy	1:100	Negative	ND	NA	ND	IV PMP + oral steroid/–	1	ADEM	ADEM	25
3	6/F	Blurred vision	1:100	Negative	ND	NA	Negative	IV PMP + oral steroid/–	1	ON	ON	30
4	13/M	Blurred vision	1:100	Negative	ND	NA	Negative	IV PMP + oral steroid/–	1	ON	ON	34
5	11/F	Ataxia	1:100	Negative	ND	NA	Negative	IV PMP + oral steroid/–	1	CIS	CIS	25
6	6/F	Headache, ataxia	1:100	1:10	Negative	1:10	Negative	IV PMP + oral steroid/monthly IVIG	2	ADEM	ADEM-ON	28
7	6/M	Ataxia, encephalopathy	1:10	1:10	1:10	1:10	Negative	IV PMP + oral steroid/monthly IVIG	2	ADEM	MDEM	28
8	6/F	Headache, encephalopathy ataxia, blurred vision	1:32	1:10	Negative	1:100	1:32-Negative	IV PMP + oral steroid/ AZT + monthly IVIG	3	ADEM	Uncategorized relapsing MOG-antibody associated disease	54
9	3/F	Ataxia, encephalopathy, dysphagia, vomiting	ND	ND	Negative[a]	1:32	Negative	IV PMP + oral steroid/AZT, monthly IVIG, monthly IV PMP	23	ADEM	Uncategorized relapsing MOG-antibody associated disease	196

Ab antibody, *F* female, *M* male, *ND* not done, *NA* not applicable, *IV PMP* pulse methylprednisolone, *ADEM* acute disseminated encephalomyelitis, *ON* optic neuritis, *CIS* clinically isolated syndrome, *IVIG* intravenous immunglobulin, *AZT* azathioprine

[a]Performed at thirteen months of attack-free period

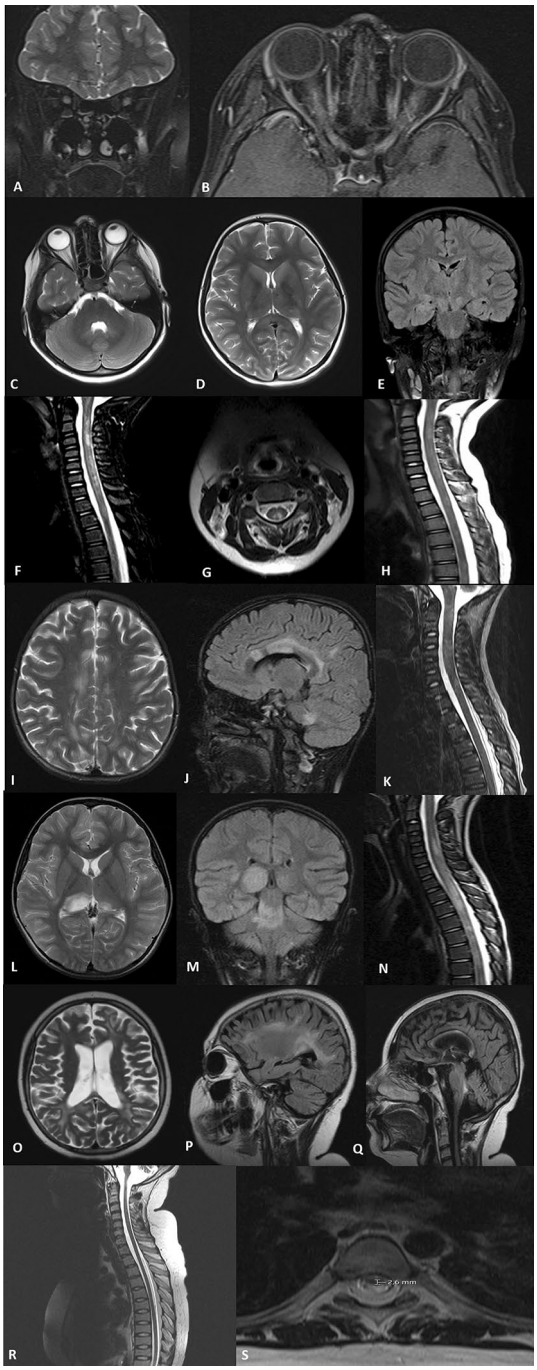

Fig. 1 Bilateral optic nerve thickening and high signal intensity on coronal fluid-attenuated inversion recovery (FLAIR) (**a**) image and pathological contrast enhancement of optic nerves on post-contrast (**b**) T1 image (Case 3). Axial T2 (**c**, **d**) and coronal FLAIR (**e**) MR images with hyperintense lesions at the level of bilateral dentate nuclei and left thalamus. Multiple hyperintense lesions at different levels of the cervical spinal cord on sagittal TIRM (**f**), axial T2 (**g**) and sagittal T2 (**h**) images (Case 6). Multiple callosal, sub-cortical white matter and pontine hyperintense lesions on axial T2 (**i**) and sagittal FLAIR (**j**) images, hyperintense cervical spinal cord lesions on sagittal T2 (**k**) image (Case7). Multiple bithalamic and posterior fossa hyperintensities on axial T2 (**l**) and coronal FLAIR (**m**) image and diffuse hyperintense lesions in cervical and upper thoracic spinal cord on sagittal (**n**) T2 image (Case 8). Axial T2 (**o**) and sagittal FLAIR (**p**, **q**) MR images demonstrating chronic white matter changes, global atrophy of cerebral hemispheres and corpus callosum. Sagittal T2 (**r**) image of the spinal cord and axial T2 (**s**) image at the level of T6 vertebrae demonstrating the spinal cord atrophy (Case 9 at the 14th year of follow-up)

positive. Although two of these cases (Cases 6 and 8) were negative for MOG-antibody at the sixth month, they both relapsed and their final diagnosis were changed to ADEM-ON and uncategorized relapsing MOG-antibody associated disease with NMOSD phenotype, respectively. Case 9 could not be analyzed for MOG-antibody titers during her initial episodes because the test was commercially unavailable at the time. The first analysis for serum MOG-antibody titers could only be performed at the 14th year of her follow-up. This was done following 13 months of attack-free period and was found negative. Interestingly, just three months after this analysis, she presented with a relapse and her MOG-antibody titer was found 1/32 positive. She was finally diagnosed as relapsing MOG-antibody associated disease with NMOSD phenotype.

The detailed characteristics of cases including demographic and clinical features, MOG-antibody titers at disease onset and follow-up, treatment modalities, initial and final diagnoses are given in Table 1.

Treatment protocols and outcome

All cases received a standard high-dose intravenous methylprednisolone treatment (30 mg/kg/day, 5 days, max. 1 g/day) following the first episode of demyelinating disease, with a tapering oral steroid regimen for 4–6 weeks. All cases with a single attack (Cases 1–5) recovered without neurologic sequela and follow-up MRIs performed 3–6 months after the disease onset demonstrated complete resolution of the lesions. The MOG-antibody titers of the cases who did not have relapses within 24 months of follow-up were all negative in the third month of disease onset. The clinical, radiological courses and the laboratory findings of the cases with a relapsing course are discussed below:

Case 6, whose initial diagnosis was ADEM, was re-admitted with the complaint of blurred vision in the right eye at the ninth month of follow-up. Ophthalmologic evaluation revealed a decrease in visual acuity, color vision and contrast sensitivity in the right eye. Cranial MRI was normal while orbital MRI findings were consistent with unilateral ON. The MOG-antibody titer was 1:10 in the third month and negative at the sixth month following the first episode. At the second attack, antibody titer was again 1:10 positive. After high-dose methylprednisolone treatment, monthly intravenous immunoglobulin (IVIG) treatment was initiated as a long-term treatment, in conjunction with oral

steroid tapering. The diagnosis of the case was changed to ADEM-ON and no further relapses occurred over the next 16 months.

Case 7, whose final diagnosis was MDEM, demonstrated MOG-antibody persistence both at the third and sixth month of follow-up. High-dose intravenous methylprednisolone with a six-week tapering oral steroid regimen was applied. Following a relapse at the fifteenth month of follow-up, MOG-antibody titer was found 1:10 positive and a monthly IVIG treatment protocol was started. The case is attack-free for 21 months after the monthly IVIG treatment and the diagnosis remained as MDEM.

Case 8 experienced three episodes in the three-year follow-up. The initial diagnosis was ADEM on the first admission, with positive MOG-antibody and negative anti-AQP4 antibody. The case presented with ataxia and oculomotor nerve palsy nine months after the first episode and tested double positive for both anti-AQP4 antibody (1/32) and MOG-antibody (1:100). The initial treatment was intravenous and oral steroids, however, due to the relapsing disease course, azathioprine (AZT) was initiated (1 mg/kg/day, titrated up to 2 mg/kg/day) and low dose oral steroid treatment was continued. At the end of a further one-year uneventful follow-up, MOG-antibody titer was still 1:10 positive. However, the side effects of steroid/AZT combination (weight gain, hirsutism and frequent upper respiratory system infections) were evident. The steroid treatment was discontinued and the dosage of AZT was reduced to 0.5 mg/kg/day. The case then presented with visual acuity loss in the right eye two months after the discontinuation of steroid treatment and one month after AZT dose modification. Anti-MOG antibody was 1:100 positive and anti-AQP4 was found to be negative. This episode was treated with high-dose methylprednisolone, followed by additional oral steroid therapy. A monthly IVIG treatment was also added due to the side effects of steroids and AZT. MOG-antibody was negative at the sixth-month of the last episode. The case has been followed for 22 months without any relapses or clinical sequela (Table 2).

Case 9, who had a history of 23 demyelinating attacks beginning at the age of three dating back to 2003, had been followed-up at different centers with varying diagnoses ranging from MDEM and MS to tumor necrosis factor receptor-associated periodic syndrome (TRAPS). She was found to be negative for MOG-antibody back when MOG-antibody testing first became available and she was in remission for thirteen months. Three months later, she presented with another episode and MOG-antibody was found to be positive (1/32). She has been followed up for 17 years and history includes interferon beta-1a therapy following a diagnosis of MS. This caused a remarkable clinical deterioration as well as an increase in disease relapse frequency. Over the course of her illness, the case has also received long-term oral steroid therapy, various immunosuppressive therapies (AZT, cyclosporine, rituximab, oral and intravenous cyclophosphamide, mycophenolate mofetil, etanercept, infliximab, colchicine, methotrexate) and monthly IVIG treatment. The relapses were mostly controlled with intravenous cyclophosphamide treatment. The treatment was then continued with monthly IVIG and low dose oral steroids. The patient has been followed-up for 18 months without any relapses. She has bilateral optic atrophy, spasticity cognitive impairment and bladder dysfunction as sequela with an extended disability status score (EDSS) of 5. All the remaining cases with monophasic and relapsing disease course recovered without clinical sequela (EDSS = 0).

Table 2 Radiological findings of the study group at diagnosis and follow-up

Case no.	Lesion location in MRI at disease onset	Follow-up MRI at 3–6 months	Last MRI on follow-up
1	Subcortical WM, cervico-thoracic LETM	Normal	ND
2	PV, subcortical WM, BS	Normal	ND
3	Bilateral ON	Normal	ND
4	Bilateral ON	Normal	ND
5	BS, CC, C1	Normal	ND
6	BS, BG, DN, C2–C3, T	Normal	Bilateral optic neuritis
7	Subcortical WM, PV, CC, cerebellar peduncles, BS, cervical LETM	Normal	Normal
8	Subcortical WM, BS, thalamus, cervico-thoracic LETM	Incomplete regression of subcortical WM lesions	Normal
9	Subcortical WM, CC, BS, cervico-thoracic LETM	Incomplete regression of CC, BS and spinal cord lesions	Chronic white matter changes, cerebral atrophy, cervical and thoracal spinal cord atrophy

BS brain stem, *BG* basal ganglia, *DN* dentate nucleus, *CC* corpus callosum, *WM* white matter, *PV* periventricular, *LETM* longitudinally extensive transvers myelitis, *ND* not done

Discussion

The relationship of MOG-antibody with childhood demyelinating diseases was first demonstrated by O'Connor et al. [3] in a group of children with ADEM. Following this initial description, studies from different ethnic groups provided a better understanding of the demographic, clinical and prognostic features of the disease [5–8, 13]. However, MOG-antibody associated disease has many aspects that are not yet fully understood.

Clinical characteristics

Male-to-female ratio in MOG-antibody associated disease described in the literature is mostly around 1:1–1.5 [7, 13]. In this study, the number of female cases was found higher with a male-to-female (M/F) ratio of 1:2. Similar to the present study, Ramanathan et al. [14] also reported the M/F ratio as 1:2 in their cohort. Encephalopathy has been reported as the most common initial symptom in demyelinating diseases associated with MOG-antibody in children [9, 15, 16]. Fernandez et al. [17] evaluated MOG-antibody positive patients and encephalopathy was the presenting symptom in 71.4% of the patients under 10 years of age. Older children, however, were found to initially present with optic neuritis in most studies [8, 17]. In our study, encephalopathy was the most common (55.5%) initial finding and all cases with encephalopathy were 10 years or younger. There were only two cases who initially presented with ON in the present study (Cases 3–4) and the age of these cases were 6 and 13, respectively. Brainstem findings, classically associated with anti-AQP4 antibody-related diseases, have also been reported in MOG-antibody associated disease [16]. Case 9, with the final diagnosis of relapsing MOG antibody-associated disease with NMOSD phenotype, had symptoms of brainstem involvement such as persistent vomiting, difficulty in swallowing and diplopia in most of her relapses.

MRI features

Baumann et al. [18] evaluated the cerebral and spinal MRIs of 69 children who presented with the first event of a MOG-antibody associated demyelinating disease, in terms of the distribution and characteristics of the lesions. Children with ADEM or NMOSD phenotype had a pattern of imaging characterized by predominantly poorly demarcated lesions with a supra- and infratentorial distribution. Younger children also tended to have more poorly identifiable extensive lesions; including corpus callosum and basal ganglia. Fernandez et al. [17] reported no lesions in the corpus callosum of their MOG-antibody positive patients. A multicenter study conducted in Turkey reported callosal involvement is present in patients with ADEM, MDEM and RON [8]. In the present study, three cases (Cases 5, 7, 9) with diagnoses of CIS, MDEM and uncategorized relapsing MOG-antibody associated disease, respectively, were found to have callosal lesions. Although LETM lesions are reported to be more common in the cervical region, cervicothoracic involvement was found to be the most common in our cases. Two of our cases with a single ON episode were also found to have bilateral optic nerve thickening and contrast enhancement without any cerebral lesions.

Serological findings

Double seropositivity for both AQP4-IgG and MOG-IgG is a rare finding when cell-based assays are used, possibly indicating distinct disease processes for each antibody [19]. Marignier et al. [20] reported that the indirect immunofluorescence method for detecting anti-AQP4 antibodies was very specific, but not very sensitive, and the best method was cell-based assay with a sensitivity of 74.4% and a specificity of 100%. There are only a small number of cases with double seropositivity reported to date in the literature and currently there is not enough information to place these patients in a separate phenotypic subgroup [19, 21]. Cases with double seropositivity are generally reported to have higher relapse rates, residual disability and MRI lesion burden; and more compatible with the disease course of AQP4-IgG-seropositive NMOSD [19, 21]. In the present study, Case 8 demonstrated double seropositivity in the second attack. Both anti-AQP4 and anti-MOG antibody titers were studied in serum via cell-based assay. Anti-AQP4 antibody was found negative at the last episode while MOG-antibody was 1:100 positive. This case had an average of one attack annually all of which improved without sequela. Due to young age and short follow-up duration of our case, it is still too early to make a clear prediction of her clinical course.

Although the majority of MOG-antibody positive cases in the literature are monophasic; recent studies have shown that MOG-antibody associated demyelinating diseases may have a relapsing course [6–9]. Relapse rates in different studies are reported between 32.2 and 65% in cases with a first MOG-antibody related demyelinating event [1, 7, 8, 13, 17, 22, 23]. Similar to the current literature, the relapse rate was 44.4% in this study.

Data on the relationship between MOG-antibody titers and the clinical course of the disease have yielded contradictory results and are still extensively investigated. While prior studies have indicated that MOG-antibody titer can be a guide for further relapses, more recent studies with long term follow-up periods have shown that MOG-antibody serostatus should be interpreted cautiously [24–28]. Oliveira et al. [25] evaluated 31 MOG-antibody positive patients (23

relapsing diseases, 8 monophasic) and found that all patients with monophasic disease and most of the patients with the relapsing disease were seronegative during the remission period. They also observed that patients exhibiting disease activity within the last 2 years were more likely to remain positive than patients in clinical remission. In a recent study by Lopez-Chiriboga et al. [29], reported relapses occurred in 88% of ADEM patients presenting with persistent anti-MOG seropositivity while this ratio was only 12% in ADEM patients with transient seropositivity. They defined persistent MOG-antibody seropositivity as positive results in both the initial and follow-up samples at 3 months or later. Contrary to this, Jarius et al. [26] evaluated the MOG-antibody titers with a median interval between first and last sampling of 16.5 months (range 0–123) and they reported that MOG-antibody positivity persisted in most of their patients with clinical remission. In a recent study by Waters et al. [30], the relapse rates of the persistent seropositive group and seronegative group during follow-up were 38% and 13%, respectively. The authors concluded that, despite the persistence of MOG-antibody, most children will demonstrate a monophasic disease course. In the present study, all five cases with a monophasic disease course were negative for MOG-antibody titers in the third month of follow-up. Three of the remaining four cases (Cases 6, 7, 8) with a relapsing disease course were available for MOG-antibody testing at the third month of disease onset and all were positive. However, MOG-antibody serostatus of the relapsing cases at the sixth month was inconsistent with two negative (Cases 6 and 8) and one positive (Case 7) result. Case 9, first analyzed at the 13th year of her disease onset following 13 months of attack-free period, was negative for MOG-antibody. Only three months later, she relapsed and was found positive for MOG-antibody. This case may suggest that even if the MOG-antibody associated disease is long-lasting, MOG-antibody titers may revert to negative during attack-free periods. However, this negativity does not exclude the possibility of further attacks. Therefore, antibody titer follow-up should not be superior to clinical follow-up of the patients and should not play a primary role in determining the long-term treatment decision. Prospective studies and case series are needed to clarify the follow-up and treatment of MOG-antibody associated demyelinating syndromes and to establish treatment protocols.

Treatment and outcome

Intravenous pulse methylprednisolone and a taper of oral prednisone is the mainstay treatment for acute demyelinating diseases in childhood. Oral steroids, IVIG, AZT, mycophenolate mofetil, methotrexate and rituximab are other therapeutic agents recommended as second-line therapy [7–9, 13, 14]. In a recent study, 59 adult and pediatric patients with recurrent MOG-antibody associated demyelinating disease were evaluated. Although most patients were steroid-responsive initially, relapses occurred at a rate of 70% during steroid taper or within two months of cessation. The lowest treatment failure rate was observed when a maintenance dose oral steroid treatment was continued [14]. Hacohen et al. [9] reported that, although widely used in patients with MS, disease-modifying drugs did not contribute to the clinical improvement in children with MOG-antibody associated disease. AZT, mycophenolate mofetil, rituximab and IVIG were reported to cause a decrease in relapse frequency. Moreover, IVIG treatment was found to be associated with a reduction in the extended disability status scale (EDSS) score. In the presented study, intravenous pulse methylprednisolone in the acute period, and a maintenance oral steroid treatment was used in all cases. Cases with relapsing MOG-antibody associated disease were treated with immunosuppressive drugs (AZT, cyclosporine, rituximab) or monthly IVIG. The case with MDEM (Case 7) continues to be given monthly IVIG treatment and has been followed-up without further relapses or sequela. Although the follow-up period of this cohort is short, as described by Hacohen et al. [9], we are of the opinion that; monthly IVIG treatment may be an effective treatment option for relapsing MOG-antibody associated demyelinating disorders in childhood with the advantage of fewer side effects when compared to other immunosuppressive agents. At the end of monthly IVIG for two years, it was planned to decide the treatment based on the clinical and radiological status of the patients by evaluating the MOG-antibody titers cautiously. Determining the most appropriate treatment period will be possible with future prospective and retrospective studies.

Retrospective design, small sample size and short follow-up periods are the limitations of this study. Despite these limitations, our study reflects the wide clinical spectrum of the disease and provides detailed treatment modalities and clinical experience in pediatric cases with MOG-antibody associated disease.

Conclusions

Childhood MOG-antibody associated disease has a wide clinical spectrum ranging from a monophasic course to a chronic relapsing disease. Currently, no definite markers to predict the clinical course, prognosis or the final diagnosis are available. Although a possible relationship between positive MOG-antibody titers at the third month and relapsing disease course was found in this study, sixth-month antibody titers did not support this finding. Thus, it was concluded that therapeutic decision making for patients with MOG-antibody associated diseases should not be based on MOG-antibody titers. Limiting treatment side effects while preventing relapses remains a serious challenge in childhood

demyelinating diseases. Monthly IVIG treatment with a low side effect profile may present as a good option for the long-term treatment.

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Compliance with ethical standards

Conflict of interest None.

Ethical standards The study was approved by the Local Ethics Committee of Ege University and carried out in accordance with the principles of the Helsinki Declaration.

Informed consent The consent form was received from the parents of the patient.

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