Published in final edited form as:

Mult Scler Relat Disord. 2019 May ; 30: 231–235. doi:10.1016/j.msard.2019.02.023.

Clinical Characteristics of Myelin Oligodendrocyte Glycoprotein Antibody Neuromyelitis Optica Spectrum Disorder.

Sara Salama^{1,2}, Santiago Pardo², and Michael Levy²

¹Department of Neurology, University of Alexandria, Alexandria, Egypt

²Department of Neurology, Johns Hopkins University, Baltimore, MD, USA

Abstract

Background.—Serological antibodies against myelin oligodendrocyte glycoprotein (MOG) are associated with a relapsing autoimmune demyelinating disease of the central nervous system. Initially identified in the context of acute disseminated encephalomyelitis, persistent seropositivity of MOG antibodies is now recognized as a variant of neuromyelitis optica spectrum disorder (NMOSD).

Objectives: The aim of the study is to describe the epidemiological and clinical features of MOG antibody positive cases and compare our findings with those previously published.

Methods.—This is a retrospective descriptive study of 23 patients with MOG antibody disease who were cared for at Johns Hopkins Hospital over the period from 2015 to 2018. MOG testing was done at Johns Hopkins using the cell based assay (CBA). We describe their epidemiological and clinical features.

Results.—Twenty-three patients were included in the study with a female to male ratio of 2.3:1. The mean age of the cohort was 42.6 years, while the mean age at onset was 37 years. The most frequent initial presentation was optic neuritis, followed by ADEM-like encephalopathic clinical picture and transverse myelitis. Five patients showed a monophasic disease course while the rest experienced a relapsing phenotype. Nine patients (39%) experienced immediate relapses on withdrawal of steroids.

conclusions.—Our cohort showed clinical characteristics comparable with previously published reports of MOG antibody disease worldwide. Unique features of MOG antibody disease are: high frequency of optic neuritis attacks, good long term neurological recovery and sensitivity to steroid use and withdrawal.

Keywords

MOG antibody; NMOSD; clinical

Corresponding author: Sara Salama, MD, 600 N. Wolfe St., Pathology 509, Baltimore, MD 21287, ssalamafouad@gmail.com.

Publisher's Disclaimer: sThis is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Disclosure: Santiago Pardo has nothing to report.

Introduction

Serological antibodies against myelin oligodendrocyte glycoprotein (MOG) are associated with a relapsing autoimmune demyelinating disease of the central nervous system (CNS). Initially identified in the context of acute disseminated encephalomyelitis, persistent seropositivity of MOG antibodies is now recognized as a variant of neuromyelitis optica spectrum disorder (NMOSD) called MOG antibody disease.(1) MOG antibody disease occupies the space that overlaps with both aquaporin-4 (AQP4) seronegative NMOSD and multiple sclerosis (MS) (2–6). Similar to NMOSD, MOG antibody disease preferentially targets the optic nerve and spinal cord with severe attacks leading to blindness and paralysis. However the pathology of MOG is more similar to MS with non-necrotic demyelination and generally good long term outcome after relapse.(1) The epidemiology of MOG disease has been recently described in several populations(7–12). Most of these studies showed that MOG patients appear to be relatively younger Caucasian males as compared to AQP4 NMOSD(4, 8, 13–16).

As for the clinical presentation, in comparison to AQP4 NMOSD, MOG antibody disease more commonly presents with bilateral simultaneous optic neuritis,(8, 17, 18) transverse myelitis presentation shows a tendency to involve the conus medullaris,(19) with more frequent focal lesions and better clinical outcome, although poor outcomes with significant disability have been reported.(8) Recently, seizures with or without encephalopathy with cortical changes on brain MRI has become a feature more frequently observed among MOG seropositive patients(20, 21).

It has been observed that MOG antibody attacks respond briskly to steroids with a tendency to relapse upon withdrawal. Prolonged steroid taper has been suggested, and alternative acute therapy with plasma exchange and/or intravenous immunoglobulins (IVIG) have been explored.(8, 22)To prevent attacks, mycophenolate mofetil (23)and rituximab(8, 24) are the most commonly employed drugs, however emerging data suggests that MOG antibody disease responds differently to those medications compared to AQP4 NMOSD. Conventional MS treatments have not been studied in MOG antibody disease.

In this study we report on the clinical features of a cohort of MOG antibody disease in the United States and compare our findings with those previously reported.

Patients and methods.

This is a retrospective descriptive study of patients with MOG antibody disease. For the purpose of this study, MOG antibody disease was defined as an autoimmune syndrome of monophasic or relapsing attacks of demyelinating CNS disease including _but not limited to_ optic neuritis and/or transverse myelitis in the context of a seropositive MOG antibody. A relapse was defined as an acute symptomatic presentation associated with a change in neurological exam and a new T2 or contrast enhancing MRI lesion. All patients were cared for at Johns Hopkins Hospital over the period from 2015 to 2018, and consented to participate in this study, which was approved by the Johns Hopkins University institutional review board.

MOG testing was done at Johns Hopkins using the cell based assay (CBA) as described previously.(25) Briefly, human embryonic kidney cells were transfected with the full length MOG construct (Genecopoeia, cat# EXZ8086-M68) using lipofectamine 2000 per manufacturer instructions. On the following day, the cells were exposed to patients' sera for 40 minutes at 37°C, followed by washing and incubation with anti-human IgG1 secondary antibody (Thermo Fisher, cat# A10631) for 30 minutes at room temperature. Next, repeat washing and fixation with 10% formalin for 10 minutes at 4°C. Positive and negative controls were run with all serum samples. A positive result was considered in the context of staining around the cell membranes (Figure 1) whereas a negative result was not visible. Titers were measured by serial dilutions of the sera and called at the last positive dilution. In all patients MOG antibody was tested within 30 days of a clinical relapse.

Results.

Twenty-three patients met the study definition of MOG antibody disease. The majority were females: 16 as opposed to only 7 males, with a ratio of 2.3:1. The mean age of the cohort was 42.6 years, while the mean age at onset was 37 years (range: 3.5–66). Thirteen patients (56.5%) were Caucasians.

The most frequent initial presentation was optic neuritis, reported in 11 patients (47.8 % of all cases), of whom seven had bilateral involvement (63.6% of optic neuritis presentations). ADEM-like encephalopathic presentation with or without seizures and transverse myelitis were next, experienced by 5 patients (21.7%), and 4 patients (17%) respectively. Simultaneous optic neuritis and transverse myelitis were present initially in one patient (4.3%). Two patients presented with brainstem syndrome (8.7%) (Table 1).

The average number of relapses was 4 over an average disease duration of 5.6 years, with an annualized relapse rate of 0.7. Optic neuritis was the most frequent relapse, followed by ADEM-like encephalopathy and transverse myelitis. Brainstem relapses were the least common. Nine patients (39%) experienced immediate relapses on withdrawal of steroids. Five patients (21.7%) experienced only one attack over a disease duration of 24 months (range: 5–36 months).

The median EDSS was 1.5, ranging from 0–4. All acute relapses were treated with intravenous corticosteroids for 3–10 days, followed by an average of 6 weeks oral taper. Patients who did not briskly respond to corticosteroids underwent plasma exchange or received intravenous immunoglobulins.

Regarding personal and family history, 6 patients (26%) had a background history of other autoimmune disorders including four with thyroid disease, one with ulcerative colitis and one with psoriasis. Seven patients (30.4%) had a positive family history of other autoimmune disorders, while four patients (17%) had a family history of cancer.

Autoantibodies were tested in 14 patients, with antinuclear antibody and anti-Ro60 antibody being positive in only one patient. AQP4 antibody was tested in all patients, all of whom were seronegative except for one who initially tested low positive by ELISA, then negative by CBA.

CSF was available for 15 patients. The number of white blood cell ranged from 2–386 cells with lymphocytic predominant pleocytosis (more than 5 cells) detected in six patients (26%). The protein level ranged from 24–89 mg/dl with elevated protein level detected in six patients (26%). Oligoclonal bands were detected in two patients.

Maintenance immunosuppression was used in 19 patients (82.6%), while 4 of the 5 monophasic cases were not started on treatment. Sixteen patients received rituximab (84.2%), 12 (63%) received mycophenolate mofetil, two received cyclophosphamide, and one each received azathioprine, mitoxantrone and methotrexate. Because patients were on overlapping therapies, we could not calculate failure rates for each treatment. Multiple sclerosis disease modifying therapy (interferon- β and natalizumab) was used in one patient, who suffered two relapses meanwhile until the diagnosis of MOG antibody disease was done.

Among the five patients with no further attacks, three presented with bilateral optic neuritis, one with simultaneous bilateral optic neuritis and transverse myelitis, one had an ADEM-like presentation, with disease durations of 1, 2, 2, 3 years, and 5 months respectively. Three of them were males and two were females.

Discussion.

We characterized the clinical features of 23 MOG antibody disease patients cared for at the Johns Hopkins Hospital. Those included in this study all met the study definition of MOG antibody disease which required a monophasic or relapsing autoimmune disease mainly_ but not only_ involving the spinal cord and/or optic nerve in the context of a seropositive MOG antibody using a cell-based assay.

There were several features of our cohort that were different from other populations of MOG antibody disease recently published. Our cohort median age at onset was 39 years, which is older than that described by the French and German studies; 31 and 36.5 years of age, respectively.(8, 9) An even younger median age of onset (27 years) was reported by the Spanish study. On the other hand, the mean (rather than median) age of our cohort was 42.6 years, older than that reported by the Netherlands study, 36.2 years, but similar to that reported by Kim et al in the Korean study, 42.7 years.(10, 11) In the largest MOG study published to date, Jurynczyk et al reported the mean age of onset to be 30.1 years.(7) Unlike the previously reported male predominance in the French, Spanish and Dutch MOG studies, (9, 10, 12) our cohort was mainly females with a ratio of 2.3:1. Interestingly the German, UK and the Korean studies reported the same, with female to male ratios of 2.8, 2.3 and 1.4:1, respectively.(8, 11) Similar to previous observations, (10, 26, 27) MOG antibody positive patients are more likely to be Caucasians (56% of our cohort).

As with other previously published studies, our MOG patients showed a tendency for attacks of the optic nerves and spinal cord. In our cohort, the most frequent phenotype at disease onset was optic neuritis, reported in 47.8% of cases – and in 63.6% of those, it was bilateral. Transverse myelitis was experienced in 17% of patients. These findings were comparable to the French, German, Korean and Dutch studies, where 60.9%, 74%, 82.4% and 40%

respectively presented at onset with optic neuritis and 22.3%, 34%, 11.8% and 20% with transverse myelitis.(8–11) In the Dutch study, 75% of optic neuritis relapses were bilateral, which is slightly more than our findings.(10)

When accounting for the presentation during clinical relapses (rather than onset attack), optic neuritis was the most common, followed by transverse myelitis. The same findings were observed in the German and Dutch studies.(8, 10) Interestingly, the Korean cohort relapsed only with optic neuritis.(11)

ADEM-like presentation is a well-recognized phenotype of MOG antibody disease in children but can also occur in adults.(28–30) Five subjects in our cohort had an initial presentation of ADEM-like attack with or without seizures, of which 3 were adults, which was the second most frequent type of attack, either at onset or relapse. Whether to call the presentation ADEM or MOG encephalitis needs to be addressed in future studies. We believe there is a clinical overlap between the two, and only prospective pathological study can resolve the debate.

The fact that one of our patients has been misdiagnosed as MS for many years with a very poor response to MS disease modifying drugs might reflect what was reported by Sapadaro et al. (5)where MOG antibodies were detected in 5% of MS patients with typical clinical and radiological disease features

In our cohort, the annualized relapse rate was 0.7, higher than the French (0.37), but similar to the Korean (0.7) study. Only 21.7% of MOG patients were considered to have a monophasic disease course, despite the short follow up duration (median= 24 months). In contrast, 78.3% of our patients showed a relapsing course with a median follow up duration of 54 months. The same discrepancy between the follow up time was observed in the Dutch study, but unlike our finding, they reported a monophasic course in 70% of their patients with a median follow up of 8 months.(10) Similarly, the UK study also differed from our findings, as it reported 56% of its cohort to show a monophasic disease course.(7) In line with our observation, both German and Spanish cohorts had a relapsing disease course in 80% and 59% of patients respectively.(8, 12)

The median time between first and second attack was only 2.5 months, much shorter than other reports by the German (5 months),(8) French (15.8 months) and Spanish (7.5 month) cohorts. That could be explained by the fact that 45% of relapses in our cohort occurred on withdrawal of steroids, which averages approximately 6 weeks for a typical oral taper. Steroid sensitivity was also a prominent feature noted in the UK cohort.(7) Despite the frequent attacks, the median EDSS at final follow up was 1.5 as compared to 1.5 and 1 in the Spanish and the Dutch studies.(10, 12) Although attacks of optic neuritis and transverse myelitis initially presented with severe disability, they generally improved over the course of 6–12 months with only minor residual disabilities from any one attack.

Regarding the personal and family history, 30.4% of our patients had a positive family history of autoimmune diseases as compared to 28% in the Dutch study.(10) Almost one-third of our cohort reported a background history of other autoimmune disorders, with hypothyroidism being the most frequent (21.7%). The same observation was reported in

11% and 5% respectively of the French and the Dutch cohort.(9, 10) As compared to the Dutch population this could represent a true difference, but the French study included far more patients, which could explain the discrepancy. Anti-nuclear antibodies were detected in only one patient (5%), as opposed to 42.2% and 20.1% in the German and French cohorts. (8, 9) This also can be explained by the different number of patients included in different studies. In the CSF, the white blood cell count was elevated (more than 5) in 26% of our cohort, with lymphocytes being the predominant cell type. The Spanish study reported a similar value of 25%, but they used a higher cut off point of 50 cells/ μ l. More patients were reported to have CSF pleocytosis from the German study (69%). Of those, 28% had a pleocytosis of 100 at least once.(12) Oligoclonal bands were detected in two patients from our cohort (8.7%), and was similarly positive in 19%, 13.3%, 6% and 5.7% of the Dutch, German, Spanish and French cohorts respectively.(8–10, 12)

Conclusion.

Our findings are comparable with those previously published in the literature. The relatively older age at onset, and female predominance are important features. The majority of our patients experienced a relapsing disease course with a relatively good recovery on follow up. Tendency to involve the optic nerve and spinal cord is now a well-recognized feature of the disease as well as sensitivity to steroids and relapse upon rapid withdrawal.

Finally, encephalopathy with or without seizures are becoming an interesting symptomatology that requires further research.

The main limitations of the study are the fact that it is a retrospective one, conducted at a single center and the relatively few number of patients.

Funding:

This work was supported by a scholarship from the Egyptian ministry of higher education, JS-3725 (SS), as well as a grant from the National Institute of Neurological Disease and Stroke, NS-078555 (ML).

References.

1. Reindl M, Jarius S, Rostasy K, Berger T. Myelin oligodendrocyte glycoprotein antibodies: How clinically useful are they? *Curr Opin Neurol*. 2017;30(3):295–301. [PubMed: 28248700]
2. Kitley J, Waters P, Vincent A, Palace J. Features of neuromyelitis optica spectrum disorders and aquaporin-4 with myelin-oligodendrocyte glycoprotein antibodies-reply. *JAMA neurology*. 2014;71(7):924.
3. Hacohen Y, Mankad K, Chong WK, Barkhof F, Vincent A, Lim M, et al. Diagnostic algorithm for relapsing acquired demyelinating syndromes in children. *Neurology*. 2017;89(3):269–78. [PubMed: 28615429]
4. Jurynczyk M, Gerales R, Probert F, Woodhall MR, Waters P, Tackley G, et al. Distinct brain imaging characteristics of autoantibody-mediated CNS conditions and multiple sclerosis. *Brain*. 2017;140(3):617–27. [PubMed: 28364548]
5. Spadaro M, Gerdes LA, Krumbholz M, Ertl-Wagner B, Thaler FS, Schuh E, et al. Autoantibodies to MOG in a distinct subgroup of adult multiple sclerosis. *Neurol Neuroimmunol Neuroinflamm*. 2016;3(5):e257. [PubMed: 27458601]
6. Narayan R, Simpson A, Fritsche K, Salama S, Pardo S, Mealy M, et al. MOG antibody disease: A review of MOG antibody seropositive neuromyelitis optica spectrum disorder. *Mult Scler Relat Disord*. 2018;25:66–72. [PubMed: 30048919]

7. Jurynczyk M, Messina S, Woodhall MR, Raza N, Everett R, Roca-Fernandez A, et al. Clinical presentation and prognosis in MOG-antibody disease: a UK study. *Brain*. 2017;140(12):3128–38. [PubMed: 29136091]
8. Jarius S, Ruprecht K, Kleiter I, Borisow N, Asgari N, Pitarokoili K, et al. MOG-IgG in NMO and related disorders: a multicenter study of 50 patients. Part 2: Epidemiology, clinical presentation, radiological and laboratory features, treatment responses, and long-term outcome. *J Neuroinflammation*. 2016;13(1):280. [PubMed: 27793206]
9. Cobo-Calvo A, Ruiz A, Maillart E, Audoin B, Zephir H, Bourre B, et al. Clinical spectrum and prognostic value of CNS MOG autoimmunity in adults: The MOGADOR study. *Neurology*. 2018;90(21):e1858–e69. [PubMed: 29695592]
10. van Pelt ED, Wong YY, Ketelslegers IA, Hamann D, Hintzen RQ. Neuromyelitis optica spectrum disorders: comparison of clinical and magnetic resonance imaging characteristics of AQP4-IgG versus MOG-IgG seropositive cases in the Netherlands. *Eur J Neurol*. 2016;23(3):580–7. [PubMed: 26593750]
11. Kim SM, Woodhall MR, Kim JS, Kim SJ, Park KS, Vincent A, et al. Antibodies to MOG in adults with inflammatory demyelinating disease of the CNS. *Neurology(R) neuroimmunology & neuroinflammation*. 2015;2(6):e163. [PubMed: 26516628]
12. Hoftberger R, Sepulveda M, Armangue T, Blanco Y, Rostasy K, Calvo AC, et al. Antibodies to MOG and AQP4 in adults with neuromyelitis optica and suspected limited forms of the disease. *Mult Scler*. 2015;21(7):866–74. [PubMed: 25344373]
13. Hyun JW, Woodhall MR, Kim SH, Jeong IH, Kong B, Kim G, et al. Longitudinal analysis of myelin oligodendrocyte glycoprotein antibodies in CNS inflammatory diseases. *J Neurol Neurosurg Psychiatry*. 2017;88(10):811–7. [PubMed: 28684532]
14. Ramanathan S, Mohammad S, Tantsis E, Nguyen TK, Merheb V, Fung VSC, et al. Clinical course, therapeutic responses and outcomes in relapsing MOG antibody-associated demyelination. *J Neurol Neurosurg Psychiatry*. 2018;89(2):127–37. [PubMed: 29142145]
15. Sepulveda M, Armangue T, Sola-Valls N, Arrambide G, Meca-Lallana JE, Oreja-Guevara C, et al. Neuromyelitis optica spectrum disorders: Comparison according to the phenotype and serostatus. *Neurology(R) neuroimmunology & neuroinflammation*. 2016;3(3):e225. [PubMed: 27144216]
16. Jurynczyk M, Tackley G, Kong Y, Geraldes R, Matthews L, Woodhall M, et al. Brain lesion distribution criteria distinguish MS from AQP4-antibody NMOSD and MOG-antibody disease. *J Neurol Neurosurg Psychiatry*. 2017;88(2):132–6. [PubMed: 27951522]
17. Sato DK, Callegaro D, Lana-Peixoto MA, Waters PJ, de Haidar Jorge FM, Takahashi T, et al. Distinction between MOG antibody-positive and AQP4 antibody-positive NMO spectrum disorders. *Neurology*. 2014;82(6):474–81. [PubMed: 24415568]
18. Ramanathan S, Reddel SW, Henderson A, Parratt JD, Barnett M, Gatt PN, et al. Antibodies to myelin oligodendrocyte glycoprotein in bilateral and recurrent optic neuritis. *Neurology(R) neuroimmunology & neuroinflammation*. 2014;1(4):e40. [PubMed: 25364774]
19. Kitley J, Leite MI, Kuker W, Quaghebeur G, George J, Waters P, et al. Longitudinally extensive transverse myelitis with and without aquaporin 4 antibodies. *JAMA neurology*. 2013;70(11):1375–81. [PubMed: 23999580]
20. Ogawa R, Nakashima I, Takahashi T, Kaneko K, Akaishi T, Takai Y, et al. MOG antibody-positive, benign, unilateral, cerebral cortical encephalitis with epilepsy. *Neurol Neuroimmunol Neuroinflamm*. 2017;4(2):e322. [PubMed: 28105459]
21. Hamid SHM, Whittam D, Saviour M, Alorainy A, Mutch K, Linaker S, et al. Seizures and Encephalitis in Myelin Oligodendrocyte Glycoprotein IgG Disease vs Aquaporin 4 IgG Disease. *JAMA Neurol*. 2018;75(1):65–71. [PubMed: 29131884]
22. Polat I, Yis U, Karaoglu P, Ayanoglu M, Ozturk T, Guleryuz H, et al. Myelin Oligodendrocyte Glycoprotein Antibody Persistency in a Steroid-Dependent ADEM Case. *Pediatrics*. 2016;137(5).
23. Montcuquet A, Collongues N, Papeix C, Zephir H, Audoin B, Laplaud D, et al. Effectiveness of mycophenolate mofetil as first-line therapy in AQP4-IgG, MOG-IgG, and seronegative neuromyelitis optica spectrum disorders. *Mult Scler*. 2017;23(10):1377–84. [PubMed: 27885065]

24. Kim SH, Kim W, Li XF, Jung IJ, Kim HJ. Repeated treatment with rituximab based on the assessment of peripheral circulating memory B cells in patients with relapsing neuromyelitis optica over 2 years. *Arch Neurol*. 2011;68(11):1412–20. [PubMed: 21747007]
25. Waters P, Woodhall M, O'Connor KC, Reindl M, Lang B, Sato DK, et al. MOG cell-based assay detects non-MS patients with inflammatory neurologic disease. *Neurology(R) neuroimmunology & neuroinflammation*. 2015;2(3):e89. [PubMed: 25821844]
26. Papais-Alvarenga RM, Neri VC, de Araujo EAACR, da Silva EB, Alvarenga MP, Pereira A, et al. Lower frequency of antibodies to MOG in Brazilian patients with demyelinating diseases: An ethnicity influence? *Multiple sclerosis and related disorders*. 2018;25:87–94. [PubMed: 30056361]
27. Pache F, Zimmermann H, Mikolajczak J, Schumacher S, Lacheta A, Oertel FC, et al. MOG-IgG in NMO and related disorders: a multicenter study of 50 patients. Part 4: Afferent visual system damage after optic neuritis in MOG-IgG-seropositive versus AQP4-IgG-seropositive patients. *J Neuroinflammation*. 2016;13(1):282. [PubMed: 27802824]
28. Fernandez-Carbonell C, Vargas-Lowy D, Musallam A, Healy B, McLaughlin K, Wucherpfennig KW, et al. Clinical and MRI phenotype of children with MOG antibodies. *Mult Scler*. 2016;22(2):174–84. [PubMed: 26041801]
29. Misu T, Sato DK, Nakashima I, Fujihara K. MOG-IgG serological status matters in paediatric ADEM. *J Neurol Neurosurg Psychiatry*. 2015;86(3):242. [PubMed: 25136054]
30. Ketelslegers IA, Van Pelt DE, Bryde S, Neuteboom RF, Catsman-Berrevoets CE, Hamann D, et al. Anti-MOG antibodies plead against MS diagnosis in an Acquired Demyelinating Syndromes cohort. *Mult Scler*. 2015;21(12):1513–20. [PubMed: 25662345]

Highlights

- MOG antibody disease is an emerging entity that yet needs to be characterized.
- Although previously thought to be a monophasic disease, relapsing course is a common presentation among such patients.
- Sensitivity to steroid use and withdrawal is a unique feature.
- Clinical presentation involves mainly optic nerves, although brain and spine can be affected as well.
- The encephalopathic presentation is more common among such patients and might help in its distinction from MS and AQP4 NMOSD.

Figure 1.A:

A case with positive MOG antibody, 1.B. MOG antibody negative subject (AQP4 positive), 1.C. MOG antibody low and high positive controls.

Table 1.

Summary of the epidemiologic and clinical characteristics of the cohort.

Characteristic	Number (Percentage)
Sex	
Female	16 (69.5)
Race	
Caucasian	13
African/American	5
Latino	1
Other	4
Age	
Mean	42.6 years
Median	44 years
Range	7–72 years
Age at onset	
Mean	37 years
Median	39 years
Range	3.5 – 66 years
EDSS	
Mean	1.9
Median	1.5
Range	0 – 4
Number of relapses	
Mean	4
Median	4
Range	1 – 18
Autoimmune disease	
Thyroid disease	5 (19.2%)
Ulcerative colitis	1 (3.8%)
Presentation at disease onset	
Optic neuritis	11(47.8%)
ADEM- like	5 (21.7%)
Transverse myelitis	4 (17.4%)
ON + TM	1 (4.3%)