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Case Series

Internal Medicine Section

# Clinical Evaluation of Myelin Oligodendrocyte Glycoprotein Antibody Associated Disease- A Case Series

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## ABSTRACT

In recent years, there has been lot of research on Myelin Oligodendrocyte Glycoprotein Antibody (MOG-IgG) associated disease. It's clinical phenotype overlaps with Multiple Sclerosis (MS) and Neuromyelitis Optica Spectrum Disorder (NMOSD), however many questions related to clinical characteristics and pathogenetic role of MOG antibody is still unanswered. Hereby, authors report a case series of nine patients (five females and four males), describing their seropositivity for MOG antibody and clinical characteristics of MOG antibody associated disease. The clinical presentation, radiology, acute treatment and long term management were analysed. The most common presentation was optic neuritis followed by Longitudinally Extensive Transverse Myelitis (LETM). Tab. Azathioprine was most commonly used medicine for disease modifying therapy (long term immunosuppression). The attacks are more severe than MS but recovery is better than antibodies to Aquaporin-4 (AQP4-IgG) seropositive NMOSD.


**Keywords:** Demyelinating, Multiple sclerosis, Neuromyelitis optica spectrum disorder

## INTRODUCTION

In recent years, there has been lot of research on Myelin Oligodendrocyte Glycoprotein Antibody (MOG-IgG) associated disease. Before the cell-based assay transfected with MOG in its conformational form, MOG-IgG were a biomarker of Multiple Sclerosis (MS) [1]. MOG-antibody disease is a separate spectrum of Central Nervous System (CNS) inflammatory demyelinating disease distinct from MS and antibodies to Aquaporin-4 (AQP4-IgG)-seropositive Neuromyelitis optica spectrum disorder (NMOSD) [1].

Myelin oligodendrocyte glycoprotein is a protein expressed over mammalian oligodendrocytes and can elicit demyelinating immune response [2]. The clinical manifestations occur similar to other CNS inflammatory demyelinating diseases. The slight female predominance was reported in the largest clinical series [3]. Preceding prodormal symptoms suggesting infection can occur. The major clinical manifestations are optic neuritis, Longitudinally Extensive Transverse Myelitis (LETM), Acute Disseminated Encephalomyelitis (ADEM) and brainstem demyelinating episode [1]. In paediatric population, ADEM is more common [4]. The episodes are more severe than MS but better recovery than AQP4-IgG-seropositive NMOSD [1].

When classical phenotype of MOG-IgG disease is suspected, antibody testing should be advised. Testing with cell-based assay should be advised and other methodology like Enzyme Linked Immunosorbent Assay (ELISA), western blot or assay using non conformational MOG epitope should be avoided [5].

## CASE SERIES

In the present case series, nine cases presented with CNS demyelinating disease and found positive for MOG antibody and seronegative for AQP4-IgG were included in the study. The patients included were from admitted patients of Department of Neurology or referred patients from Department of Medicine of Sawai Man Singh hospital, Jaipur, Rajasthan, India. In all patients, cell-based assay for both MOG-IgG and AQP4-IgG was advised. Four patients were male and five were females. The patients were adolescents or adults age group with range from 12 to 40 years and mean age of patients was 27.8 years. The most common presentation was optic neuritis followed by LETM. The clinical characteristics of patients, Magnetic Resonance Imaging (MRI) brain and spine, Visual Evoked Potential (VEP), Cerebrospinal Fluid (CSF) findings, acute treatment given, disease modifying treatment, follow-up and recurrences were given in [Table/Fig-1,2].

| Case | Age (in years) and sex | Clinical presentation | MRI of brain and spine | Visual evoked potential p100 latency | Cerebrospinal fluid cells (µL), protein (mg/dL) and sugar (mg/dL) | Acute treatment | Disease modifying treatment | Recurrences (follow-up) and residual symptoms |
|---|---|---|---|---|---|---|---|---|
| 1 | 30 Female | Unilateral (left side) paraparesis with a upper thoracic sensory level (preceding history of delivery of a healthy newborn) | LETM from D8 to conus medullaris | Absent on left eye | 15<br>160<br>61 | 5 days i.v. MPS (no improvement) Followed by 5 cycle of plasma exchange | Azathioprine | No (6 months), residual paresis in both legs |
| 2 | 19 Female | Quadriparesis with a sensory level C3 vertebra (preceding febrile illness) | T2 hyperintensity of cord from C1 to T1 level (LETM) and patchy hyperintensity at T5, T6,T11 and T12 level | Prolonged in both eyes | 50<br>41<br>49 | 5 days of i.v. MPS | Azathioprine | No (6 months) |
| 3 | 12 Female | Unilateral (left side) with preceding unilateral headache | Left optic nerve hyperintensity with enhancement of intraorbital part | Prolonged latency in both eyes (L>R) | 5<br>46<br>106 | 5 days of i.v. MPS | No | No (9 months) |
| 4 | 28 Female | Unilateral (right side) | T2 hyperintensity of right optic nerve | Absent in right and normal in left eye | - | 5 days of i.v. MPS | Azathioprine | Two episodes of optic neuritis before this episode (12 months) |

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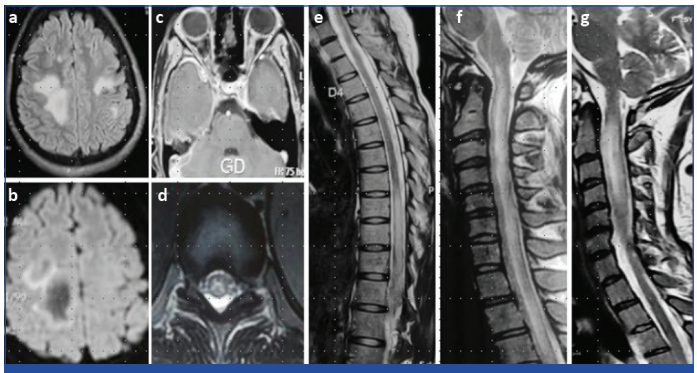
| 5 | 38 Male | Unilateral (left side) | Optic nerve enhancement of intraorbital part | Absent in left and normal in right eye | 15<br>54<br>87 | 5 days of i.v. MPS (no improvement) followed by 5 cycles of plasma exchange | Azathioprine | No (7 months), residual vision loss in left eye |
| 6 | 34 Male | Triparesis (both lower limbs and left upper limb | T2 hyperintense lesion in subcortical white matter of brain showing DWI restriction at rim, short segment myelitis | Normal bilaterally | 10<br>32<br>68 | 5 days of i.v. MPS (no improvement) followed by 5 cycles of plasma exchange | Azathioprine | No (7 months), residual paresis |
| 7 | 35 Male | Triparesis (both lower limb and right upper limb) Cranial nerve palsy (right 5th and left 7th, 9th and 10th ) | T2 hyperintense lesion in subcortical white matter, basal ganglia, pons of brain and C1 to C4 spinal cord) | Prolonged bilaterally | 40<br>36<br>24 | 5 days of i.v. MPS | Azathioprine | No (8 months) |
| 8 | 15 Male | Bilateral | Normal | Prolonged bilaterally | 5<br>50<br>126 | 5 days of i.v. MPS | No | No (10 months) |
| 9 | 40 Female | Unilateral (right side) | Normal | Right eye absent and left eye prolonged | 5<br>34<br>90 | 5 days of i.v. MPS | No | No (8 months) |

**[Table/Fig-1]:** Clinical characteristics of nine patients with MOG antibody disease.
R: Right; L: Left; i.v. MPS: Intravenous methylprednisolone; ON: Optic neuritis; LETM: Longitudinally extensive transverse myelitis; DWI: Diffusion weighted imaging




**[Table/Fig-2]:** a) and b): White matter hyperintensity in T2 FLAIR with its hyperintense rim in DWI imaging of case 6; c): Axial section of T1 image showing enhancement of intraorbital part of optic nerve of case 3; d): T2 axial image at T5 level showing axial H sign in case 2; e): Saggital view of MRI spine showing T2 hyperintensity of cord from D8 to conus medullaris in case 1; f): C1 to T1 in case 2; and g) C1 to C4 in case 7.
Note: In case 8 and 9 MRI brain and spine were normal; DWI: Diffusion weighted imaging

## DISCUSSION

According to previous literature, MOG antibody associated disease accounts for 1.2 to 6.5% cases among all demyelinating syndromes in adults [6]. In previous studies, optic neuritis was the most common presentation [6-8]. Acute disseminated encephalomyelitis is the most common manifestation of Myelin oligodendrocyte glycoprotein antibody-associated disease among <18 years age group [9]. Brain MRI can be abnormal among 50% of cases, regardless of clinical presentation [7]. In optic nerve, anterior part in intraorbital region is described to be most commonly involved while in MRI spine, LETM is the most common presentation but short segment myelitis can be seen in 40% of cases [7].

Out of nine cases, five were females and four were males. Mean age of patients was 27.8 years. This observation is similar to previous literature in which slight female predominance was reported. Similarly, children and young adults are the age groups, commonly affected [3]. The most common presentation was optic neuritis (n=6) in our series as reported in other studies. It was unilateral in five and bilateral in one case (case 8). Though bilateral optic neuritis was seen in one case (case 8), VEP was prolonged or absent in both eyes in five patients, one of these patient (case 7) did not have ocular symptoms. In previous studies, optic neuritis is present in upto 80% patients either on presentation or during course while forty percentages of patients have simultaneous involvement of both eyes [7]. In another study, Lee YJ et al., described optic neuritis was the major phenotype (41-63%) [9]. Brayo P et al., in their series reported optic neuritis in 81% (nine out of 11 cases), it was bilateral in six while unilateral in three cases [8]. The other clinical manifestations in the present study were LETM and cranial nerve palsies other than optic nerve. LETM was observed in four cases and cranial nerve involvement was seen in one case (case 7). Simultaneous optic neuritis with LETM was observed in one case (case 1). In LETM most common involved part was thoracic cord followed by cervical cord. In previous study, spinal cord involvement is seen in 30% cases during presentation and 50% during course [7]. In another case series, it was seen in 18% of cases [8]. The recurrence of symptoms was seen in one case (case 4). This patient was having two episodes of optic neuritis and that was before presenting to us. This case didn't have recurrence after starting immunosuppressive medication. The proportion of patients with a single attack is likely reduced with long-term follow-up [9,10]. In case series by Brayo P et al., it was seen in 64% of cases [8]. The lower recurrence in present case may be due to lower duration (6-12 months) of follow-up. None of the patient developed ADEM like presentation, which was more commonly observed in paediatric age group [4,9].

Visual evoked potential was abnormal in seven patients. It was abnormal bilaterally in five patients. Four of these patients were having symptoms only in one eye. In present case, one of the patients (case 7) didn't have ocular symptoms but abnormal VEP in both eyes. In MRI of brain with orbit the most common pattern was involvement of anterior part (intraorbital part) of optic nerve. This was in accordance to previous literature in which MOG antibody disease have predilection to involvement of anterior part while NMOSD tends to involve posterior part of optic nerve or optic chiasma [4]. Only two patients (case 6, 7) had involvement of white matter in MRI brain in subcortical location and brainstem in the present series. The lesions were large in size as opposed to smaller lesions in MS [Table/Fig-2a and 2b]. In MRI spine involvement of gray matter was common forming axial H sign. In the literature involvement of central gray matter is shown more than white matter in MOG differing it from NMOSD where both gray and white matter typically involve [11].

In 2018 consensus, it has been outlined that MOG antibody should be advised in those patients who presented with one of the classical phenotypes of MOG disease and lack the characteristic of MS. In low probability situation, false positive cases may occur [12]. The testing should be done with one of the cell based assay from blood [12]. In literature, few cases are described having co-existent AQP4-IgG and MOG antibody [6]. Hence, in current case series those patients were selected in which both MOG-IgG and AQP4-IgG were advised and only MOG was positive.

No randomised clinical trials are available to guide treatment for MOG antibody disease; hence, it is largely adopted from management of seropositive NMOSD cases. In acute situation, it has been suggested to use 500-2000 mg i.v. MPs (Intravenous

methylprednisolones) for 3-7 days and plasma exchange is reserved for non responders [13,14]. MOG antibody associated disease is a steroid-responsive condition, and a proportion of patients have early relapses during rapid steroid tapers or shortly after cessation [15]. In our setting, all nine cases received i.v. MPs for 5 days. Six patients showed improvement with i.v. MPs. Three case were not responsive to steroid were offered five cycle plasma exchange on alternative day. At the end of six months, two patients were having residual paresis of limbs while one patient was having incomplete vision recovery.

Disease modifying treatment used in previous studies was monthly injection of i.v. IG, rituximab, mycophenolate mofetil, methotrexate and azathioprine [7,8,13]. There is no consensus about what to use and the duration till when to use. Authors started tab. azathioprine as long term immunosuppressive in six of the presented patients. Three patients with milder presentation or very rapid improvement on methylprednisolone were closely watched. Till now, there are no recurrences at end of 6-12 months of follow-up.

## CONCLUSION(S)

In recent years, a number of immune targets for central nervous system inflammatory demyelinating disease have been identified. MOG antibody disease has become a clear disease entity separated itself from MS and seropositive NMOSD not only from clinico-radiological pattern but also from long term outcome. In the study centre, the authors tested all patients of CNS demyelinating disease with MOG in whom radiology differs from MS. More prospective study and randomised trial are required to better guide for management of MOG antibody disease.

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