Content available at: https://www.ipinnovative.com/open-access-journals

Indian Journal of Clinical and Experimental Ophthalmology

Journal homepage: www.ijceo.org

Case Report

MOGAD: A novel disease

Tushar Kant Singh[1], **Rakesh Sharma**[1], **Ziaul Haq Yasir**[1]*, **Mukesh Kumar**[2]

[1]*Dept. of Ophthalmology, TS Misra Medical College and Hospital, Lucknow, Uttar Pradesh, India*
[2]*Dept. of Neurology, TS Misra Medical College and Hospital, Lucknow, Uttar Pradesh, India*

ARTICLE INFO

Article history:
Received 07-02-2024
Accepted 27-03-2024
Available online 30-03-2024

Keywords:
MOGAD disease
Optic neuritis
Demyelinating disease
Optic atrophy
Multiple sclerosis

ABSTRACT

Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is an immune-mediated inflammatory neurological disease and a new addition to the demyelinating disorders of the central nervous system(CNS). In MOGAD, specific antibodies (MOG IgG) targeting MOG protein lead to primary demyelination in the CNS, but notably spare astrocytes. The most frequent presentation in children is ADEM and in adult ON. We present a case of 20 year old female who visited our OPD with complaints of diminution of vision with muscular weakness and strain while walking with a history of two similar episodes in the past. The clinical characteristics, laboratory investigation and neuroimaging help in diagnosis. Although the prognosis is generally favorable but severe residual disability can also occur. This underscores the importance of identifying the causes of demyelination on time and prompt treatment of this rather novel disease by judicious use of steroids based on standard protocol resulting in the general well-being of the patient. The present case therefore highlights the need to create awareness of the Clinical-Lab-Imaging characteristics of MOGAD and also suggests the importance of making a detailed multidisciplinary approach into the cause of optic neuritis for better prognosis.

1. Introduction

Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is an immune-mediated inflammatory neurological disease and a new addition to the demyelinating disorder of the central nervous system (CNS).[1] MOG (Myelin oligodendrocyte glycoprotein) is a transmembrane protein (MOG immunoglobulin), that is expressed on the outer lamellae of myelin sheaths and oligodendrocytes in the CNS.[2] MOGAD has now been identified as a separate entity from both multiple sclerosis (MS) and neuromyelitis optica spectrum disorder (NMOSD).[3] Etiologically Demyelinating diseases of the CNS associated with optic neuritis (ON) can be grouped as typical ON due to MS and atypical ON due to MOGAD, NMOSD and idiopathic.[2] MOGAD involves the pediatric population as well as an adult population with varying incidences in different studies.[1,4] MOGAD can produce a spectrum of clinical presentations including optic neuritis (ON), transverse myelitis (TM) and acute disseminated encephalomyelitis (ADEM).[3] ON and TM are the common overlapping presentations among MS, MOGAD and NMOSD but MOGAD doesn't have specific gender involvement and is mostly monophasic course.[1–4]

The most frequent presentation in children is ADEM and in adult optico-spinal.[2–4] In NMOSD, a specific antibody ("AQP4-IgG" or "NMO-IgG) attacks AQP4 water channels in astrocyte foot processes in the CNS(immune astrocytopathy).[2] In MOGAD, a specific Antibody (MOG IgG) targeting MOG protein on myelin sheath leads to primary demyelination in the CNS, but notably spare astrocytes, unlike NMOSD.[2] MS on the other hand is anti-

* *Corresponding author*.
E-mail address: yasir0075@yahoo.co.in (Z. H. Yasir).

https://doi.org/10.18231/j.ijceo.2024.036

AQP4 Ab negative, Anti-MOG Ab negative but Oligoclonal band and MRZ reaction positive in majority of cases.[1–3] Clinical presentation, neuroimaging and laboratory studies can help to differentiate MOGAD from other CNS neuroinflammatory conditions.[2] Identification is necessary to plan therapeutic strategy and to explain the prognosis of disease and autoimmune process.[2,3] MOG-IgG is a core criterion for diagnostic accuracy.[3] Studies have reported that only 6-10% of patients with ON due to MOGAD have final visual acuities worse than 20/200 compared to a third of NMOSD ON patients.[2] MOGAD has a benign course and better recovery compared to MS and NMOSD.[2–4] This underscores the importance of identifying the causes of on time. Therefore, we present a case of optic neuritis due to MOG-autoantibody to highlight the importance of screening and awareness for timely intervention and better prognosis.

2. Case Report

A 20-year-old female presented with the painless, progressive, gradual diminution of vision (DOV) in both eyes (OU) since past 10 days. It was associated with muscle weakness and strain while walking. She gives a history of similar complaints with two such episodes in the past, one in 2017 and another in 2022 for which she was treated by quack doctors in the periphery (Village) and hence no documentation of the incidents could be obtained.

On examination, her visual acuity was 1/60 in the right eye (OD) and Hand Movement in the left eye (OS) with no improvement with pinhole testing. Color vision by Ishihara colour chart was defective OD and could not be assessed OS. Swinging flashlight test revealed relative afferent pupillary defect (RAPD) OS. Extraocular muscle motility was full OU, but the patient reported pain with elevation in OS. Confrontation visual field test results were normal OD and could not be assessed OS. Other external ocular examinations and slit lamp examinations were unremarkable, and IOP measured 12 mmHg OD and 10 mmHg OS with Goldmann applanation tonometry. Dilated fundus examination revealed disc margins were clear with a cup: disc ratio of 0.3 OU. Disc pallor was observed OD and optic atrophy was observed OS. OCT shows generalized thinning in peripapillary RNFL as Nasal < Temporal < Superior < Inferior RNFL OU. (Figure 1). Visual evoked potential showed normal latency OD, prolonged latency OS and reduced amplitude OU (Figure 2). Optic Neuritis was suspected, and an MRI of the brain with and without contrast was performed MRI showed a T2/FLAIR hyperintensity in the bilateral middle cerebellar peduncle, dentate nuclei, dorsal midbrain, pons and medulla, up to cervico-medullary junction most probably due to demyelination (Figure 3). Lumber puncture reported raised protein in CSF. Blood tests hemogram with ESR, C-reactive protein along with KFT, LFT and coagulation profile were within normal limit. ANCA and anti-AQP4 antibody test were negative but MOG(IgG) autoantibody was reported positive. Through these tests a diagnosis of MOGAD was made. In collaboration with the neurology department, the patient was admitted and started on IV Methylprednisolone 1 gram in 250ml normal saline once a day for 3 days according to the Optic neuritis treatment trial(ONTT). Over the course of treatment, the patient's vision improved to 6/60 OD and Finger counting close to face OS and she got symptomatic relief including being able to walk easily by the third day. She was started on Tablet Prednisolone 40mg from the fourth day for the next 11 days.

At the time of discharge on the 14^{th} day, her vision was 6/36 OD and Finger counting close to face OS. She was started on an immunomodulator Tablet Azathioprine 50mg in morning and 25mg in evening for the next one month to reduce chances of recurrence, in collaboration with neurologist. At one month follow up, she reported having no similar recurrence of muscle weakness and difficulty in walking. Her vision had stayed the same at 6/36OD and Finger counting close to face OS. Colour vision had improved to normal OD and could not be assessed OS. IOP was 10mmHg OU. Retinal nerve fibre layer thinning and visual evoked potential were similar as earlier although T2/FLAIR MRI showed signs of re-myelination in the effected regions. Her WBC count was normal, so she was advised to continue on Tablet Azathioprine 50 mg morning and 25 mg evening for next followup visit after 2 months.

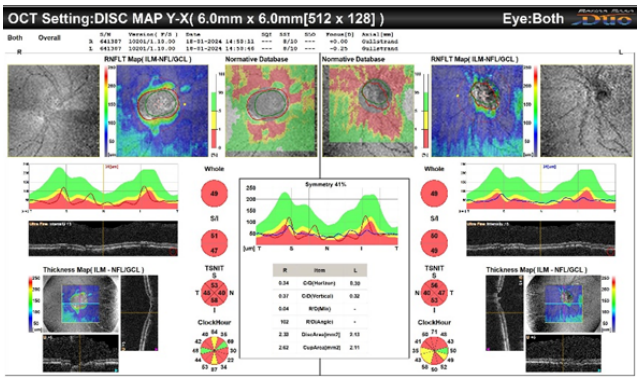

Figure 1: OCT shows generalized thinning in peripapillary RNFL

3. Discussion

MOGAD can easily be confused with other CNS inflammatory diseases such as MS or NMOSD due to overlapping features, but they have a distinct clinical phenotype and prognosis.[1] MOG is a key element of myelin sheath.[5] MOG is present on the outermost myelin sheath layers and oligodendrocyte cell surface.[4] These glycoproteins have roles in the formation, maintenance and disintegration of myelin sheaths.[5] The neuropathological findings of MOGAD are somewhat consistent and most of

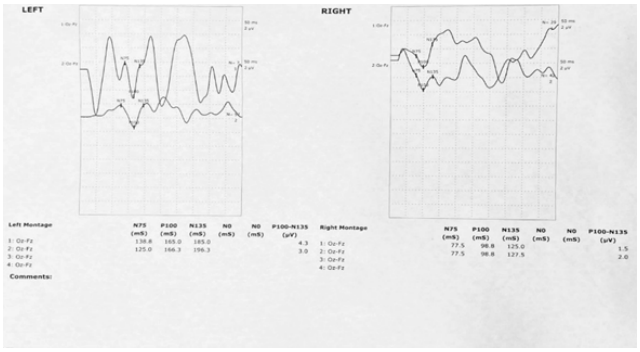

Figure 2: Visual evoked potential showed left eye prolonged latency and reduced amplitude

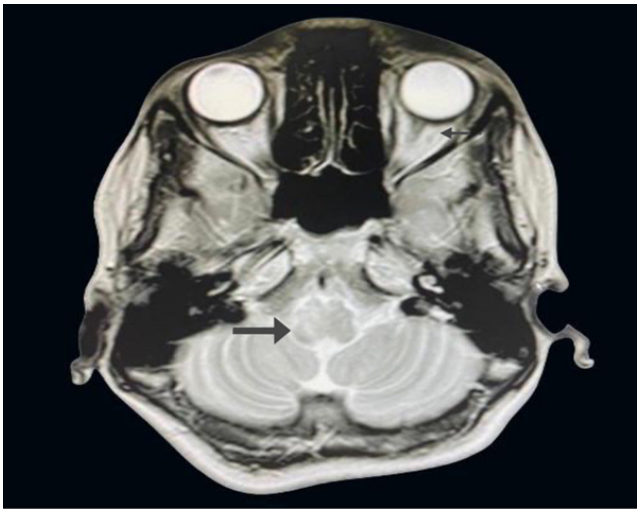

Figure 3: MRI showed a T2/FLAIR hyperintensity in bilateral middle cerebellar peduncle, dentate nuclei, dorsal midbrain, pons and medulla

them reveal MS pattern II lesions with T cell infiltration, IgG deposition and involving complement cascade in demyelination process.[4,6] Thus, upholding an idea about humoral immune pathogenesis of MOGAD.[6] Serum from individuals with MOGAD, when administered in rat models has been confirmed for increasing demyelination and axon loss.[4]

Accurate diagnosis is important because of unique relapse patterns and prognosis for MOGAD.[1] MOGAD has a monophasic clinical course, approximately half of MOGAD patients will experience a recurrence of demyelination, most commonly ON.[7] MOGAD ON has an equal predilection for both genders compared to NMOSD & MS that has females predominance.[2,4] MOGAD can present in children also which is rare for NMOSD.[2] The most common clinical manifestation of MOGAD in children is ADEM and in adults is ON.[7] MOGAD & NMOSD present as bilateral severe vision loss but MS is usually present as a unilateral case.[2] Early studies suggested that MOGAD may have a more favorable prognosis compared with NMOSD and MS.[7] Eye pain is common among all three conditions but seen more frequently with MOGAD ON.[2] Examination of the optic nerve reveals severe edema, in MOGAD ON than in NMOSD ON but MS ON is distinct with no disc edema in majority of cases due to retrobulbar location.[2] OCT peripapillary RNFL thinning is associated with ON, but Nasal pRNFL allows differentiation between MOGAD ON and other ON with the highest accuracy.[8] ON in MAGOD shows enhanced perineural optic nerve sheath extending into orbit, spinal cord H-sign, and T2-lesion resolution over time on MRI.[2,4] In contrast, ON in NMOSD shows enhanced optic nerve that extends towards the optic chiasm and optic pathways.[2] MS ON presents as periventricular white matter lesions not seen with either of the other two conditions.[2] Laboratory testing (MOG-IgG cell-based assays) is more sensitive, especially before initiation of treatment.[3] To confirm MOGAD, we are required to detect Anti-MOG Ab in serum and/or CSF, and the presence of a clinical-MRI phenotype compatible with MOGAD criteria.[4]

MOGAD treatment is debatable due to the lack of randomized controlled trials and existing recommendations for treatment are mostly empirical.[4] MOGAD ON patients tend to recover rapidly with intravenous steroids with better visual outcomes compared to MS ON and less thinning of the peripapillary RNFL, which is not seen with NMOSD ON.[7] Studies have reported that ON secondary to MOGAD has better final visual outcome than NMOSD patients.[2] This guides us in the treatment plan of ONTT for ON secondary to MAGOD that time is of the essence to preserve vision.[7] Immunotherapy appears to successfully mitigate the disease.[1] Azathioprine (AZA) and mycophenolate mofetil (MMF) have an established safety record and display some efficacy as therapeutic strategies for long-term immunosuppression in adult MOGAD patients.[2] Serum MOGAD-IgG titer seropositivity and side effects guide us in deciding the duration of oral steroid tapering and immunosuppressant coverage.[7] Plasma exchange (PLEX) and intravenous immunoglobins (IVIg) are also emerging options for refractory cases.[4]

4. Conclusion

Awareness of the Clinical-Lab-Imaging characteristics of MOGAD is fundamental for prompt diagnosis and treatment. This allows earlier identification and potentially better treatment for best outcomes. The judicious use of steroids along with immunomodulators could help a known case of MOGAD disease in the long term by preventing relapses of demyelination as recovery of vision after each episode is non-binary and a deterioration of visual acuity could hamper the quality of life, as in our case. With this case report, we would like to recommend that every case of recurrent optic neuritis could have this novel and, as in

our case where the conventional test results were negative but autoantibody positive, hence should be treated by a multidisciplinary team of doctors including neurologists. With ever evolving scientific discoveries this case report creates an awareness among the established and budding ophthalmologists to be on their toes about, rather than treating symptoms of optic neuritis, they should find and treat the root cause that in this case would be MOGAD. We would also like to add our investigations and findings regarding this novel disease and add to the existing data about the efficiency of the current treatment paradigm for optimal outcomes.

5. Source of Funding

None.

6. Conflict of Interest

None.

References

1. Longbrake E. Myelin Oligodendrocyte Glycoprotein-Associated Disorders. *Continuum (Minneap Minn)*. 2022;28(4):1171–93.
2. Bhakhri R, Neidermann S, Vivacqua G. Stargardt Disease: a Teaching Case Series. *Optomet Educ*. 2023;49(1).
3. Banwell B, Bennett JL, Marignier R, Kim HJ, Brilot F, Flanagan EP, et al. Diagnosis of myelin oligodendrocyte glycoprotein antibody-associated disease: International MOGAD Panel proposed criteria. *Lancet Neurol*. 2023;22(3):268–82.
4. Sechi E, Cacciaguerra L, Chen JJ, Mariotto S, Fadda G, Dinoto A, et al. Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD): a review of clinical and MRI features, diagnosis, and management. *Front Neurol*. 2022;13:885218.
5. Quarles RH. Myelin sheaths: glycoproteins involved in their formation, maintenance and degeneration. *Cell Mol Life Sci*. 2002;59(11):1851–71.
6. Jarius S, Metz I, König FB, Ruprecht K, Reindl M, Paul F, et al. Screening for MOG-IgG and 27 other anti-glial and anti-neuronal autoantibodies in 'pattern II multiple sclerosis' and brain biopsy findings in a MOG-IgG-positive case. *Mult Scler*. 2016;22(12):1541–9.
7. Chwalisz BK, Levy M. The treatment of myelin oligodendrocyte glycoprotein antibody disease: a state-of-the-art review. *J Neuroophthalmol*. 2022;42(3):292–6.
8. Pakeerathan T, Havla J, Schwake C, Salmen A, Bigi S, Abegg M, et al. Characteristic retinal atrophy pattern allows differentiation between pediatric MOGAD and MS after a single optic neuritis episode. *J Neurol*. 2022;269(12):6366–76.

Author biography

Tushar Kant Singh, Junior Resident https://orcid.org/0009-0004-2247-0422

Rakesh Sharma, Professor https://orcid.org/0009-0001-8344-6897

Ziaul Haq Yasir, Ophthalmologist https://orcid.org/0000-0002-4279-6911

Mukesh Kumar, Neurologist https://orcid.org/0000-0003-1060-5604

Cite this article: Singh TK, Sharma R, Yasir ZH, Kumar M. MOGAD: A novel disease. *Indian J Clin Exp Ophthalmol* 2024;10(1):200-203.