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Case Report

Myelin-oligodendrocyte glycoprotein associated optic neuritis: a case report

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ABSTRACT

The role of myelin-oligodendrocyte glycoprotein (MOG) in central nervous system (CNS) myelin and its association with optic neuritis. It emphasizes the importance of early detection and suitable diagnostic investigations for optic neuritis, a condition often linked to multiple sclerosis. A 65-year-old female with MOG-positive CNS demyelination, optic neuritis, and underlying conditions such as hypertension and type 2 diabetes mellitus. The patient's clinical examination, diagnostic test results, and imaging findings are presented, including fundoscopy, 2D Echo, and magnetic resonance imaging (MRI) of the spine. The treatment chart outlines medications administered to the patient. It delves into challenges in identifying optic neuritis, emphasizing the significance of clinical-MRI phenotypes associated with MOG-associated disorders (MOGAD) and reliable laboratory assays for detecting MOG-IgG. It highlights the need for caution in interpreting positive MOG-IgG results and underscores the importance of follow-up for individuals with MOG-IgG seropositivity. The article also discusses various aspects of optic neuritis, including visual field impairments and retinal changes associated with anti-MOG antibodies. It emphasizes the importance of timely and accurate identification of MOGAD through anti-MOG antibody detection. It calls for standardized diagnostic criteria and the refinement of models to enhance understanding and therapeutic approaches for MOGAD. Overall, the article provides insights into the diagnosis, management, and challenges associated with MOG-related disorders.

Keywords: Myelin-oligodendrocyte glycoprotein, Optic neuritis, Anti-MOG antibody, Diagnosis, General medicine, Public health, Neurology, Medical education

INTRODUCTION

In the peripheral and central nervous systems (PNS and CNS, respectively) of vertebrates, immense axons are encased in myelin sheaths that speed up the conduction of action potentials while saving energy needed to sustain ion gradients.[1] The myelin sheath in the PNS is created by spiraling the plasma membrane of the Schwann cell towards the axon, which is then compressed to create the distinctive layered framework of mature myelin. The oligodendrocyte is the myelin-forming cell in the CNS, and the myelin sheath emerges similarly as a spiraled annealing of its plasma membrane. The oligodendrocyte, which is the CNS's myelin-forming cell, produces several proteins, including the myelin oligodendrocyte glycoprotein. Myelin-oligodendrocytes glycoprotein (MOG) is a crucial part of the oligodendrocyte surface membranes, along with myelin basic protein (MBP), proteolipid protein (PLP), and myelin-associated glycoprotein (MAG). These glycoproteins play critical roles in the development, upkeep, and breakdown of myelin sheaths.[2] The myelin-oligodendrocyte glycoprotein (MOG), an insignificantly important component of CNS myelin (0-05%), is expressed in the outer lamella of the myelin sheath.[3] With an extracellular immunoglobulin variable (IgV) domain, a transmembrane hydrophobic domain, a brief cytoplasmic loop, a second hydrophobic area within the membrane bilayer, and a cytoplasmic terminus, MOG is a member of the immunoglobulin superfamily. This superfamily's other members either have a membrane-spanning domain or are

anchored to the surface of the membrane by a glycolipid, making this structure distinct.[4] Optic neuritis, or optic nerve inflammation, is a common cause of acute optic nerve damage in children and adults. Although optic neuritis is usually linked to multiple sclerosis (MS), there are several other possible causes as well. The prognosis and course of treatment for optic neuritis will thus rely on the underlying cause, the length and extent of visual loss, any past injuries, and the effectiveness of previous therapies. The best care for individuals with optic neuritis depends on early detection, suitable diagnostic investigations, and the implementation of successful medications.[5] Optic neuritis often manifests as an aggressive demyelinating condition of the optic nerve, which can be related with multiple sclerosis. Atypical optic neuritis can develop in conjunction with other inflammatory conditions or on its own. Differential diagnosis covers a range of retinal and optic nerve conditions. Visual evoked potentials, CSF analysis, and MRI are examples of diagnostic tests. Optical coherence tomography can reveal retinal axonal loss, which is correlated with indicators of enduring visual impairment. Treatment with high-dose corticosteroids reduces the duration of acute visual impairment but has little effect on the eventual visual result. Atypical types may require extended immunosuppressive regimens.[6]

CASE REPORT

A female patient aged 65 years was admitted to the department of general medicine at Adichunchanagiri Hospital with chief complaints of non-responsiveness to oral commands, decrease appetite, inactive movement of bilateral lower and upper limb, easy fatiguability, and decrease bladder sensation. She was a known case of MOG-positive CNS demyelination associated with optic neuritis, treated with 5 cycles of large volume plasma pheresis and 5 days of intravenous methyl prednisolone and also a known case of hypertension and type 2 diabetes mellitus for 2 years on medication tab. clinidipine and tab. glimeperide respectively.

At the time of visit to the hospital, patient general physical examination was pulse rate – 140 bpm, blood pressure – 100/70mmHg, SpO_2 – 72@ RA, 95% @ 4-6L/O_2, and temperature – afebrile.

Patient systemic examination, at the time of visit – central nervous system: patient is in altered sensorium, GCS – E_4 V_2 M_5, not responding to oral commands and moving only lower limbs spontaneously (Table 1).

Respiratory system – bilateral normal vesticular breath sounds, no added sounds, per abdomen – soft, non-tender, no organomegaly, and bowel sounds heard.

Based on the history and the general examination, the provisional diagnosis was found to MOG associated optic neuritis with type 2 diabetes mellitus and systemic hypertension, suspected case of post COVID atypical pneumonia. Certain investigations were carried out in order to confirm the provisional diagnosis (Tables 2-4).

Table 1: Glasgow coma scale.

Parameters	Right limb	Left limb
Power	UL 1/5	1/5
	LL 4/5	4/5
Tone	Increased	Increased
Reflex	Diminished	Diminished
Plantar	B/L mute	

Table 2: Laboratory investigations.

Test parameter	Result
CRP quantitative (mg/l)	48.9
Electrolytes (mmol/l)	
Sodium	146
Potassium	3.6
Chloride	103
Liver function test	
Total bilirubin (mg/dl)	1.2
Direct bilirubin (mg/dl)	0.3
Indirect bilirubin (mg/dl)	0.90
Total protein (g/dl)	4.9
Serum albumin (g/dl)	2.6
Serum globulin (g/dl)	2.3
SGOT (U/l)	102
SGPT (U/l)	47
Alkaline phosphatase (U/l)	23
D-dimer (mg/dl)	8.85

Table 3: Fundoscopy.

Parame-ters	Right eye	Left eye
Pupil	Pharmacologically dilated	Pharmacologically dilated
Lens	SMC	PCIOL

Table 4: Dilated fundoscopy.

Parameters	Right eye	Left eye
CDR	No glow	Pale-wavy disc with margin clear. Radiating while lesions around the disc. Chorio-retino Atrophic Patch Could not be visualized as the patient was not co-operative.
NCR		
Margin		
AVR		
BGR		
MFR		

Impression- 2° optic atrophy of left eye + myopic fundus of left eye, and right eye – mature cataract.

The 2D echo results indicate the presence of ischemic heart disease, with observed regional wall motion abnormality and hypokinetic local septum. The left ventricular systolic function is nearly normal, with grade 1 LV diastolic dysfunction. Additionally, there is mild mitral regurgitation (MR) and tricuspid regurgitation (TR), accompanied by tachycardia.

The MRI of the entire spine screening reveals a normal-caliber spinal cord with normal signal intensity and no focal lesions. In the cervical spine, there is mild straightening, disc dessicatory changes at multiple levels, and the presence of anterior marginal osteophytes with ligamentum flavum hypertrophy at multiple levels. Specific findings at different levels include diffuse disc bulges, disc osteophyte complexes, and ligamentum flavum hypertrophy. Noteworthy instances include mild spinal canal stenosis at C5-C6, and compression of nerve roots at various levels.

The thoracic spine screening shows no significant abnormalities, while the lumbar spine screening indicates loss of lumbar lordosis, disc dessicatory changes, anterior marginal osteophytes, and grade 1 anterolisthesis of L5 over S1. At L3-L4, L4-L5, and L5-S1 levels, there are diffuse disc bulges with posterior annular fissure, indenting on ventral thecal sac, causing narrowing of bilateral neural foramina without evidence of spinal canal stenosis or nerve root compression.

Based on the investigations and provisional diagnosis, treatment was initiated according to the patient's medical history and allergy history (Table 5).

Table 5: Treatment chart.

Drug	Dose (mg)	Route	Frequency
Meropenem	1000	IV	1-0-1
Linezolid	600	IV	1-0-1
Pantoprazole	40	IV	1-0-0
Enclez	40	Sc	1-0-1
Methyl prednisolone	8	P/O	1-1-1
Azathioprine	50	P/O	1-0-1
Homin		P/O	1-0-1
Dapagliflozin	10	P/O	0-1-0
Optineuron	2 amp in 100 ml NS	IV	1-0-1
Montair LC		P/O	0-0-1
Ecospirin AV	75/20	P/O	0-0-1
Human actrapid		Sc	12-12-10 Units
Dabigatran	110	P/O	1-0-0

DISCUSSION

The challenge in identifying optic neuritis arises from the presence of inflammation, a notable decrease in visual acuity, anomalies in the visual field, and bilateral asymmetric papilledema. To establish a diagnosis of MOGAD, it is essential to have a clinical-MRI phenotype associated with MOGAD and a dependable laboratory assay for detecting MOG-IgG in serum and/or cerebrospinal fluid (CSF). In cases where patients test positive for MOG-IgG and exhibit distinctive phenotypes, caution should be exercised, as the possibility of a false positive result exists, potentially carrying significant therapeutic implications.[7]

Extensive research has demonstrated that individuals maintaining MOG-IgG seropositivity throughout follow-up are at a higher likelihood of experiencing recurrence; hence, emphasizing the importance of early diagnosis, meticulous follow-up, and precise prognostic assessments.[8] The MOG protein's form and glycosylation are crucial for anti-MOG antibody recognition.[2]

In a retrospective analysis involving 135 individuals with acute optic neuritis (ON), Hickman et al identified nine cases where aberrant MRI enhancement occurred in the intracranial optic nerve just anterior to the optic chiasm. Notably, two of these cases exhibited junctional scotomas, indicating a supertemporal visual field impairment in the contralateral eye. The authors concluded that a supertemporal visual field depression in the asymptomatic fellow eye could occasionally result from acute injury to the posterior optic nerve in ON. Consequently, the presence of a contralateral supertemporal visual field defect should not automatically exclude typical ON from the list of potential etiologies.[9]

According to Marignier et al's research, patients commonly exhibit thickening of the peripapillary layer of retinal nerve fibers, likely attributed to optic disc expansion during acute optic neuritis episodes. Subsequently, the peripapillary retinal nerve fiber layer undergoes gradual thinning, with the temporal quadrants experiencing a faster rate of reduction. Notably, optic neuritis associated with anti-MOG antibodies tends to result in less retinal degeneration compared to cases associated with antibodies to aquaporin-4 (anti-AQP4) antibodies. Longitudinal optical coherence tomography, in the absence of fresh clinical attacks, has revealed a decline in the peripapillary retinal nerve fiber layer in affected eyes, without a concurrent change in the combined ganglion cell and inner plexiform layer. This contrasts with the progressive loss observed in optic neuritis caused by anti-AQP4 antibodies or multiple sclerosis. Unaffected eyes have shown thinning in the ganglion cell and inner plexiform layers, indicating subclinical neuroaxonal retinal damage. However, conflicting results about the peripapillary retinal nerve fiber layer have been reported in undamaged eyes, likely attributed to optic nerve inflammation or subclinical chiasm involvement. In our investigation, similar to the MRI paradox, MRI emerges as the primary diagnostic tool for MOGA.[10]

A heightened level of clinical suspicion is crucial due to the diverse clinical characteristics associated with MOGA.

Papilledema and elevated intracranial pressure (ICP) act as two elusive manifestations of MOGA-related diseases. In individuals presenting with elevated ICP and an inflammatory cerebrospinal fluid (CSF) profile, MOGA testing becomes a valuable diagnostic tool. Investigating potential associations between MOGA-related diseases and elevated ICP is imperative for comprehensive clinical assessment.[8]

The current absence of randomized controlled studies for MOGAD necessitates reliance on empirical treatment recommendations, often drawn from prior research. High-dose steroids, in line with their common use in other acquired inflammatory demyelinating diseases, serve as the primary first-line treatment for MOGA-related disorders. Intravenous immunoglobulin represents an alternative treatment strategy, either as monotherapy or in combination with steroids. In cases where steroid treatment proves ineffective, plasma exchange may offer a viable therapeutic option. Notably, our patient exhibited improvement in both clinical and radiological conditions following a significant initial dose of methylprednisolone.[10]

CONCLUSION

The timely and precise identification of MOGAD through reliable anti-MOG antibody detection is crucial for advancing outcomes in the management of this disorder. This not only aids in the early recognition of the condition but also contributes to an enhanced comprehension of the underlying mechanisms that lead to relapses and the progression of disabilities. Moreover, it serves as a foundational step in the formulation and refinement of treatment protocols. Currently, the diagnostic landscape for MOGAD lacks standardized criteria, highlighting the imperative need for the establishment and validation of official diagnostic standards. Once in place, these standards are anticipated to significantly improve diagnostic accuracy and reduce the time taken to confirm a MOGAD diagnosis. Concurrently, the refinement of in vivo and in vitro models is essential to provide more robust evidence elucidating the intricate mechanisms that drive MOGAD, thus contributing to a comprehensive understanding of the disease and informing further advancements in therapeutic approaches.

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