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UNMASKING MYELIN OLIGODENDROCYTE GLYCOPROTEIN ANTIBODY-ASSOCIATED DISEASE (MOGAD): CNS DEMYELINATION TRIGGERED BY TNF-α INHIBITION IN A PATIENT WITH ANKYLOSING SPONDYLITIS

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ABSTRACT

Background: Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is a rare but emerging central nervous system demyelinating disorder that can mimic other neurological conditions. The use of TNF-α inhibitors in patients with autoimmune diseases has been linked to central nervous system demyelinating events, but the relationship remains poorly understood.

Case description: We present a 64-year-old male with a history of ankylosing spondylitis previously treated with a TNF-α inhibitor who developed progressive dizziness, ataxia, visual disturbances and cognitive changes. Despite extensive workup, including imaging and cerebrospinal fluid analysis, initial evaluations were inconclusive. MRI was non-diagnostic, and cerebrospinal fluid lacked oligoclonal bands. Ultimately, a serum MOG antibody titre of 1:1,000 confirmed the diagnosis of MOGAD. The patient improved with intravenous corticosteroids and was discharged on a tapering dose of oral prednisone. This case highlights an MRI-negative presentation of MOGAD with strong serologic findings.

Conclusion: This case emphasises the diagnostic challenge of MOGAD in patients with autoimmune backgrounds and neurologic symptoms without clear imaging findings. Clinicians should consider MOGAD in the differential diagnosis when evaluating such patients, particularly those with prior TNF-α inhibitor exposure. Early recognition and treatment with immunotherapy can lead to significant clinical improvement.

KEYWORDS

Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD), TNF-α inhibitors, central nervous system demyelination, autoimmune disease

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LEARNING POINTS

- Clinicians should maintain a high index of suspicion for MOGAD in patients with atypical neurological symptoms, even when MRI findings are negative.
- TNF-α inhibitors may act as potential immunologic triggers for central nervous system demyelination, especially in patients with autoimmune conditions.
- Strong MOG antibody positivity can guide diagnosis in diagnostically ambiguous presentations and warrants the timely initiation of immunotherapy.

INTRODUCTION/BACKGROUND

Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is an emerging central nervous system (CNS) demyelinating disorder that is immunologically distinct from multiple sclerosis and aquaporin-4-positive neuromyelitis optica spectrum disorder (NMOSD). It is characterised by antibodies targeting MOG, a myelin protein expressed on the outermost surface of CNS myelin sheaths and oligodendrocyte processes[1]. The use of TNF-α inhibitors has been associated with an increased risk of both demyelinating and non-demyelinating CNS events, especially in patients with autoimmune conditions. However, whether this association represents a direct effect, or an exacerbation of pre-existing inflammation, remains unclear[2].

Several studies have reported CNS demyelination following TNF-α inhibitor therapy, including agents such as etanercept, infliximab and adalimumab[3,4]. Though the underlying mechanism is not fully understood, TNF inhibition may impair regulatory T-cell function or disrupt cytokine signalling, potentially promoting CNS-directed autoimmunity, particularly in those with underlying immune dysregulation[5]. We present a case of MOGAD that developed in an elderly male with a history of ankylosing spondylitis, highlighting the potential role of TNF-α inhibitors in triggering CNS autoimmune disease.

CASE DESCRIPTION

A 64-year-old Caucasian male with a history of ankylosing spondylitis, asthma, alcohol use disorder (in remission for five months) and depression presented with six months of progressive dizziness, nausea, ataxia, falls, metallic taste, visual disturbances (black spots), confusion and auditory hallucinations. His symptoms began approximately one month after discontinuing adalimumab, which he had taken for 15 years. It had been stopped due to iritis. He experienced intermittent episodes with variable severity, from being bedridden to ambulating with a walker. Most episodes resolved over two weeks, but the current one persisted. He also reported a 40-pound unintentional weight loss over the same period. Six months prior, he was fully independent with activities of daily living. Home medications included disulfiram, naltrexone, bupropion and fluoxetine. Family history was unknown due to adoption.

Previously evaluated by outpatient neurology, he underwent brain and spine magnetic resonance imaging

Description	Result	Normal Range
ANA screen	Negative	Negative
c-ANCA	Negative	Negative
p-ANCA	Negative	Negative
GAD65 antibodies (nmol/l)	0	≤0.02
Deamidated gliadin peptide antibodies, IgG (unit/ml)	<0.4	<15
Deamidated gliadin peptide antibodies, IgA (unit/ml)	1.2	<15.0
Thyroperoxidase antibody (IU/ml)	13.3	<34
Vitamin E (mg/l)	15	5.5–17
Methylmalonic acid (nmol/ml)	0.15	≤0.40
Vitamin B1 (thiamine) (nmol/ml)	156	70–180
Vitamin B6 (µg/dl)	5	5–50
Copper (µg/dl)	119	73–129
Zinc (µg/dl)	70	60–106
C-reactive protein (mg/dl)	1.2	<0.5
Sed rate (mm/hr)	30	0–20
MOG FACS titre	1:1,000	<1:20
NMO/AQP4 FACS	Negative	Negative
Amphiphysin antibodies	Negative	Negative
Anti-glial nuclear antibody (AGNA-1)	Negative	Negative
Anti-Hu (ANNA-1) antibody	Negative	Negative
Anti-Ri (ANNA-2) antibody	Negative	Negative
Anti-Ma2 (ANNA-3) antibody	Negative	Negative
CRMP-5-IgG antibody	Negative	Negative
P/Q-type calcium channel antibodies (nmol/l)	0	≤0.02
Neuronal (V-G) K+ channel antibodies (nmol/l)	0	≤0.02
PCA-1, serum antibody	Negative	Negative
PCA-2, serum antibody	Negative	Negative

Table 1. Comprehensive autoimmune and metabolic workup.

(MRI) and lumbar puncture. Brain MRI at an outlying facility showed subtle medullary enhancement. At the time of admission to our hospital, he was dependent on a walker and wheelchair, and unable to manage daily tasks such as cooking or managing his finances. Notably, he had visited the emergency department recently for abdominal pain; computed tomography (CT) imaging revealed constipation and bladder distention. On examination, he had end-gaze nystagmus and left upper extremity-predominant ataxia. Strength was 4/5 in the right upper extremity, 3/5 in the right lower extremity, 5/5 in the left upper extremity and 3/5 in the left lower extremity. Plantar reflexes were down going, and deep tendon reflexes were 2+ throughout. No dysmetria was observed. A fundus examination was not performed.

Initial laboratory tests, including complete blood count and comprehensive metabolic panel, were unremarkable. Extensive metabolic, autoimmune and infectious workups – including celiac antibodies, vitamins B1, B6 and E, GAD-65, thyroid peroxidase, antinuclear antibody (ANA), antineutrophil cytoplasmic antibodies (ANCA), methylmalonic acid, NMO-IgG, copper and zinc – were all normal *(Table 1)*. Cerebrospinal fluid (CSF) analysis showed elevated protein with a normal IgG index, no pleocytosis and no oligoclonal bands *(Table 2)*. CSF panels for meningitis, malignancy (cytology) and flow cytometry were negative.

A brain MRI on admission showed scattered T2 and FLAIR hyperintensities in periventricular and deep cortical white matter *(Fig. 1)*. An MRI of the face, neck and orbits showed no acute abnormalities. Cervical, thoracic and lumbar spine MRIs revealed moderate foraminal stenosis at C3-4, C4-5 and C5-6 *(Fig. 2)*. This comprehensive workup, alongside normal imaging and CSF analysis, effectively ruled out multiple sclerosis, stroke and other structural spinal pathologies as causes.

A serum MOG antibody titre returned positive at 1:1,000 (normal <1:20), confirming the diagnosis of MOGAD. Neurology diagnosed new-onset MOGAD with neuromyelitis optica features, likely triggered by prior TNF-α inhibitor exposure. The patient received IV methylprednisolone 1 g daily for five days, with improvement in dizziness and ataxia. He was discharged on oral prednisone 60 mg daily with a gradual taper and close outpatient neurology follow-up. A CT of the chest, abdomen and pelvis ruled out malignancy. Weight loss was attributed to poor oral intake due to persistent nausea.

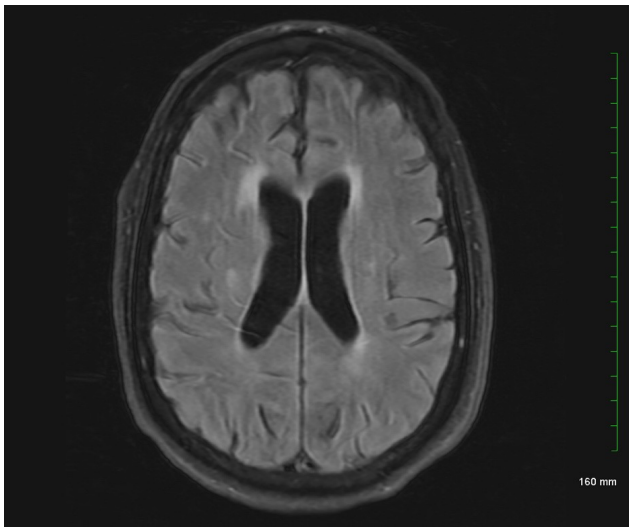


Figure 1. Axial FLAIR MRI of the brain showing scattered hyperintense lesions in the periventricular and deep cortical white matter.

Description	Result	Normal range
IgG index, CSF	0.48	≤0.7
IgG, CSF (mg/dl)	4.2	≤8.1
Albumin, CSF (mg/dl)	33.4	≤27
IgG/albumin, CSF	0.13	≤0.21
IgG, serum (mg/dl)	950	767–1,590
IgG/albumin, serum	0.27	≤0.4
Albumin quotient, CSF/serum	9.54	≤14
Albumin, serum (mg/dl)	3,500	3,500–5,000
CSF oligoclonal bands interpretation (bands)	0	<2
CSF colour	Colourless	Colourless
CSF total nucleated cells	5	0–5
CSF red blood cells	356	0–1
CSF neutrophils	2%	
CSF lymphocytes	77%	
CSF monocytes	21%	
CSF glucose (mg/dl)	43	
CSF total protein (mg/dl)	52	15–45
CSF venereal disease research laboratory	Negative	Negative
CSF N-methyl-D-aspartate encephalitis panel	Negative	Negative

Table 2. CSF immunological and biochemical analysis.

DISCUSSION

This case highlights the importance of maintaining a high index of suspicion for MOGAD in patients with unexplained neurological symptoms, particularly when initial imaging is inconclusive. The case is clinically significant due to its diagnostic complexity, presenting as a subacute, relapsing neuropsychiatric syndrome in an elderly male with a history of ankylosing spondylitis, previously treated with a TNF-α inhibitor. The diagnostic workup required exclusion of several possibilities, including MS and CNS infections, metabolic and paraneoplastic syndromes, and stroke. While the MRI showed no evidence of infarction, CSF analysis without oligoclonal bands was suggestive of an inflammatory

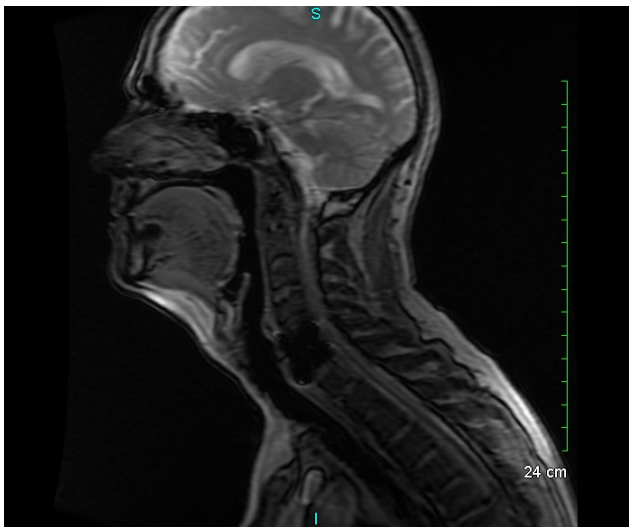


Figure 2. Sagittal T2-weighted MRI of the brain and cervical spine demonstrating no acute demyelinating lesions. Mild to moderate foraminal stenosis is noted at the cervical levels C3–C6.

process distinct from MS. Ultimately, the presence of MOG-IgG antibodies at a titre of 1:1,000 confirmed the diagnosis of MOGAD according to recent consensus criteria[6]. This case underscores the need to consider autoimmune CNS syndromes as potential adverse effects of TNF-α inhibitors. Early diagnosis and prompt initiation of immunotherapy can significantly alter disease trajectory and improve long-term outcomes.

The primary purpose of this report is to emphasise the importance of considering MOGAD as a differential diagnosis in patients presenting with unexplained neurological symptoms, particularly when initial imaging and CSF findings are inconclusive. Our patient experienced a six-month delay in diagnosis despite multiple outpatient evaluations, leading to functional decline. Notably, MOG antibody testing was not performed during the initial workup, and the diagnosis was ultimately confirmed only after high-titre serum MOG-IgG positivity. This case serves as an educational reminder to maintain a low threshold for testing serum MOG antibodies, especially in the context of prior TNF-α inhibitor use, which may serve as an iatrogenic immunologic trigger.

Myelin oligodendrocyte glycoprotein (MOG) is a transmembrane protein located on the outer surface of CNS myelin and is a marker of mature oligodendrocytes. Though it comprises only a small fraction (0.05%) of total myelin, MOG plays potential roles in cell adhesion, microtubule stability and receptor signalling[7]. In MOGAD, pathophysiology involves acute inflammatory attacks in which T cells and MOG antibodies cross the blood–brain barrier. MOG antibodies contribute to disease by opsonising MOG, triggering complement activation and promoting antibody-dependent cellular cytotoxicity. Biomarkers such as myelin basic protein, serum light-chain neurofilaments, glial fibrillary acidic protein and Tau suggest that axonal damage primarily occurs during the initial attack, while relapses are associated with increased myelin injury[8].

According to recently published diagnostic criteria, detection of MOG-IgG using a cell-based assay is central to diagnosing MOGAD. Clinically, MOGAD most often presents with acute disseminated encephalomyelitis (ADEM), optic neuritis or transverse myelitis. Less common manifestations include brainstem or cerebellar involvement and cerebral cortical encephalitis. In the absence of a positive serum MOG-IgG result, diagnosis requires one or more of the above clinical or radiographic features[9].

Acute management of MOGAD typically includes high-dose intravenous methylprednisolone (1,000 mg/day for five days in adults). A slow taper of oral corticosteroids over several months is often recommended to minimise the risk of early relapse[10]. For patients with inadequate response to steroids, plasma exchange (PLEX) is considered as first-line escalation therapy, usually administered every other day for five to seven sessions. Intravenous immunoglobulin (IVIG) can be used as an alternative to PLEX. Long-term treatment options are based on relapse frequency and disease severity, and include azathioprine, mycophenolate mofetil, rituximab, tocilizumab, and intermittent IVIG or corticosteroids[11]. The optimal duration of preventive therapy is not well established and requires further research. Our patient demonstrated clinical improvement after corticosteroid therapy and did not require escalation to PLEX or IVIG. Serial MOG antibody testing may also offer prognostic insight. Patients with transient seropositivity are more likely to experience a monophasic disease course, whereas those with persistent or high titre seropositivity during remission are at higher risk of relapses[12,13].

A similar case of MOGAD coexisting with ankylosing spondylitis was reported by Türk et al., further supporting the association between autoimmune rheumatologic diseases and MOGAD[14]. In addition, literature reports MRI-negative myelitis associated with MOG-IgG antibodies[15]. The most common autoimmune diseases overlapping with MOGAD include anti-NMDA receptor encephalitis and autoimmune thyroid disorders. ANA is the most frequently detected coexisting autoantibody, followed by aquaporin-4 immunoglobulin G (AQP4-IgG). Rarely, MOGAD has been associated with paraneoplastic syndromes and malignancy[16].

In our case, a comprehensive workup effectively ruled out other autoimmune, infectious and paraneoplastic aetiologies. This strengthens the proposed link between TNF-α inhibitor use and CNS demyelinating disease.

CONCLUSION

Our report adds to growing evidence that TNF-α inhibitors may act as potential triggers for MOGAD in susceptible individuals. Given the overlap in clinical presentations and diagnostic ambiguity, clinicians managing patients with autoimmune disorders and TNF-α inhibitor exposure should maintain a broad differential. Our patient presented with MRI-negative myelitis but had a strongly positive serum MOG antibody titre (1:1,000), supporting the diagnosis despite atypical imaging, highlighting a key diagnostic

challenge in MOGAD. Recognition of this disease entity and timely initiation of immunotherapy can lead to substantial functional recovery and improved outcomes. This case reinforces the critical need for awareness of atypical presentations of MOGAD and its potential immunologic triggers, particularly in patients with complex autoimmune backgrounds.

REFERENCES

1. Reindl M, Waters P. Myelin oligodendrocyte glycoprotein antibodies in neurological disease. *Nat Rev Neurol* 2019;**15**:89–102. doi:10.1038/s41582-018-0112-x
2. Kunchok A, Aksamit AJ Jr, Davis JM 3rd, Kantarci OH, Keegan BM, Pittock SJ, et al. Association between tumor necrosis factor inhibitor exposure and inflammatory central nervous system events. *JAMA Neurol* 2020;**77**:937–946. doi:10.1001/jamaneurol.2020.1162
3. Gogulescu A, Blidisel A, Soica C, Mioc A, Voicu A, Jojic A, et al. Neurological side effects of TNF-α inhibitors revisited: a review of case reports. *Medicina (Kaunas)* 2024;**60**:1409. doi:10.3390/medicina60091409
4. Lommers E, Depierreux F, Hansen I, Dive D, Maquet P. NMOSD with anti-MOG antibodies following anti-TNFα therapy: a case report. *Mult Scler Relat Disord* 2018;**26**:37–39. doi:10.1016/j.msard.2018.08.029
5. Mohan N, Edwards ET, Cupps TR, Oliverio PJ, Sandberg G, Crayton H, et al. Demyelination occurring during anti-tumor necrosis factor alpha therapy for inflammatory arthritides. *Arthritis Rheum* 2001;**44**:2862–2869. doi: 10.1002/1529-0131(200112)44:12<2862::aid-art474>3.0.co;2-w
6. Jarius S, Ruprecht K, Kleiter I, Borisow N, Asgari N, Pitarokoili K, et al. MOG-IgG in CNS demyelinating diseases: a multicenter study of 50 patients. *J Neuroinflammation* 2016;**13**:279. doi: 10.1186/s12974-016-0717-1
7. Peschl P, Bradl M, Höftberger R, Berger T, Reindl M. Myelin oligodendrocyte glycoprotein: deciphering a target in inflammatory demyelinating diseases. *Front Immunol* 2017;**8**:529. doi:10.3389/fimmu.2017.00529
8. Corbali O, Chitnis T. Pathophysiology of myelin oligodendrocyte glycoprotein antibody disease. *Front Neurol* 2023;**14**:1137998. doi:10.3389/fneur.2023.1137998
9. 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**:268–282. doi:10.1016/S1474-4422(22)00431-8
10. Ramanathan S, Mohammad S, Tantsis E, Nguyen TK, Merheb V, Fung VSC, et al. Australasian and New Zealand MOG Study Group. Clinical course, therapeutic responses and outcomes in relapsing MOG antibody-associated demyelination. *J Neurol Neurosurg Psychiatry* 2018;**89**:127–137. doi:10.1136/jnnp-2017-316880
11. Cacciaguerra L, Flanagan EP. Updates in NMOSD and MOGAD diagnosis and treatment: a tale of two central nervous system autoimmune inflammatory disorders. *Neurol Clin* 2024;**42**:77–114. doi:10.1016/j.ncl.2023.06.009
12. López-Chiriboga AS, Majed M, Fryer J, Dubey D, McKeon A, Flanagan EP, et al. Association of MOG-IgG serostatus with relapse after acute disseminated encephalomyelitis and proposed diagnostic criteria for MOG-IgG-associated disorders. *JAMA Neurol* 2018;**75**:1355–1363. doi:10.1001/jamaneurol.2018.1814
13. Gastaldi M, Foiadelli T, Greco G, Scaranzin S, Rigoni E, Masciocchi S, et al. NINA study group. Prognostic relevance of quantitative and longitudinal MOG antibody testing in patients with MOGAD: a multicentre retrospective study. *J Neurol Neurosurg Psychiatry* 2023;**94**:201–210. doi:10.1136/jnnp-2022-330237
14. Türk SM, Kotan D, Gönüllü E, Öztürk Z, Karataş D. Case of MOG-IgG-associated disease with ankylosing spondylitis: a rare coexistence. *Turk J Phys Med Rehabil* 2022;**69**:545–548. doi:10.5606/tftrd.2023.9489
15. Yang J, Lee Y-B, Park H-M. MRI-negative myelitis associated with MOG-IgG antibody: a case report and literature reviews. *eNeurologicalSci* 2023;**33**:100481. doi:10.1016/j.ensci.2023.100481
16. Molazadeh N, Bose G, Lotan I, Levy M. Autoimmune diseases and cancers overlapping with myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD): a systematic review. Mult Scler J Exp Transl Clin 2022;**8**:20552173221128170. doi:10.1177/20552173221128170.