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### Pearls and Oysters: MOG-AD Meningoencephalitis with Holocord Gray Matter Predominant Myelitis

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**Abstract**

Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) has been implicated in a wide range of central nervous system encephalitis and myelitis presentations. We present a previously healthy 16-year-old female who presented with acute onset headaches that rapidly progressed to encephalopathy, flaccid paraparesis, lower extremity hyperreflexia, and urinary retention. Serial MRI brain and total spine imaging demonstrated evolving diffuse supratentorial leptomeningeal enhancement and holocord gray matter restricted T2 bright lesion without enhancement. CSF was markedly inflammatory with MOG antibody positive >1:10000. The patient improved after empiric steroids, plasma exchange and IVIG.

**Pearls**

- MOGAD is among a limited set of pathologies that can acutely and concurrently affect all levels of the CNS.
- The presence of hyperreflexia can suggest other acute myelopathies over acute flaccid myelitis (AFM).
- MOGAD can present with dramatic CSF pleocytosis and elevated opening pressure.

**Oy-sters**

- MRI findings may lag behind symptom development in MOGAD; consider repeating imaging if initially negative.
- The owl/snake eyes and H signs exist on a spectrum of gray matter myelopathies not limited to AFM, ischemia, or compressive lesions. Their presence should prompt consideration of demyelinating disorders such as MOGAD and NMOSD.

## Case report

An athletic 16-year-old female with history of chronic sinus “problems” presented with two weeks of progressive refractory headaches. She attributed her symptoms to “sinus headaches” which initially improved with oral steroids, but headaches returned one week later with associated gait “wobbliness.” She therefore presented to the emergency department where her exam was notable for nuchal rigidity. An initial brain MRI with and without contrast was normal (not shown). A lumbar puncture (LP) demonstrated 550 white blood cells (WBCs) (91% neutrophils), 20 red blood cells (RBCs), glucose of 44 (serum 84), and protein of 112 mg/dl. She received antibiotics and dexamethasone empirically for meningitis, which were discontinued after meningitis PCR panel (Biofire Diagnostics, Salt Lake City UT) and cultures returned negative.

On hospital day seven she developed transient hip pain followed by ascending paraparesis and urinary retention. Repeat MRI brain and total spine with and without contrast on hospital day nine demonstrated subtle leptomeningeal enhancement (Figure 1:A-C), but no cord lesions (spinal images not available). Repeat LP demonstrated an opening pressure of 33mmHg. On hospital day ten she developed confusion and was transferred to our tertiary care children’s hospital. Her transfer exam was notable for bradycardia down to 49 beats per minute, nuchal rigidity, intermittent encephalopathy, left upper extremity myoclonus, lower extremity weakness (0/5 on the left and 1/5 on the right), diffuse 3+ deep tendon reflexes with 3-4 beats of ankle clonus bilaterally, diminished sharp discrimination in the bilateral lower extremities, and urinary retention. Fundoscopy was negative for papilledema. Repeat contrasted MRI brain and total spine on hospital day twelve demonstrated resolution of sulcal CSF signal non-suppression (Figure 1: D,E) and a holocord, gray matter predominant, T2 hyperintensity without contrast enhancement extending from the cervicomedullary junction to lumbosacral junction (Figure 2: A-C). Continuous EEG demonstrated frontal intermittent rhythmic delta activity. Repeat LP revealed an opening pressure of 15mmHg, 290 WBCs (65% lymphocytes), 0 RBCs, glucose of 55 (serum 100), and protein of 100. Oligoclonal bands, flow cytometry and cytology were negative. An extensive infectious evaluation for viral causes, including Enterovirus D68 (EV-D68), fungal, mycobacterial and arthropod-born illnesses, was negative. Rheumatologic workup was notable for a negative ENA, ANA titers of 1:320, indeterminate p-ANCA, normal complement 3 and 4 levels, and negative dsDNA.

The patient received a 5-gram course of IV methylprednisolone followed by an oral taper. Her encephalopathy improved; however, given persistent weakness and high suspicion for an antibody-mediated process, she underwent seven plasma exchange procedures. After procedure three, previously drawn serum myelin oligodendrocyte glycoprotein (MOG) IgG returned positive (1:10,000). Aquaporin-4 (AQP4)-IgG was negative. Given her high MOG-IgG titer and severe presentation, she was started on monthly IV immune globulin. After two weeks of inpatient rehabilitation she had a mildly wide-based gait and intermittent urinary incontinence, which improved at one year follow-up. Repeat MOG-IgG one month after initial testing remained elevated (1:1,000). Follow-up MRI brain and spine with and without contrast three months after discharge demonstrated partial resolution of her spinal lesion and normal brain (Figure 1:F, Figure 2:D,E).

## Discussion

MOGAD is an inflammatory demyelinating disorder of the central nervous system which presents with broad phenotypic diversity. Characteristic presentations include acute disseminated encephalomyelitis (ADEM), transverse myelitis (TM), and/or optic neuritis (ON). However, multifocal, brainstem syndromes, unilateral or diffuse cortical encephalitis, meningitis, and leukodystrophy-like presentations have also been described<sup>1</sup>. Attacks are often preceded by an infectious prodrome, such as the sinusitis reported in our patient<sup>2</sup>. The disease course may be monophasic or relapsing, with a monophasic course being reported in greater than 80% of pediatric MOGAD cases<sup>3</sup>.

ADEM is the predominant phenotype in children, while myelitis is more common in adults<sup>1</sup>. Our patient presented with non-ADEM meningoencephalitis and myelitis, which is a rare phenotype<sup>4</sup>. In an observational study looking at 116 pediatric patients with MOGAD-IgG positivity, only 8% had myelitis with concurrent brain MRI abnormalities and 11% had myelitis with ON<sup>5</sup>. Another study reviewed 54 pediatric/adult patients with MOG-IgG associated myelitis, finding 22% had a multifocal presentation (17% with ADEM and 5% with ON)<sup>2</sup>. Typical brain MRI findings in MOG-IgG associated ADEM include predominance of cortical and deep gray matter T2/FLAIR lesions, the locations of which are variable<sup>4</sup>. Bilateral thalamic lesions are commonly seen in pediatric patients with MOG-associated ADEM<sup>1,6</sup>. Leptomeningeal enhancement is also a distinct phenotype in MOGAD<sup>7,8</sup>. Longitudinally extensive transverse myelitis (LETM) is a common presentation of MOGAD<sup>7</sup>. TM alone has a broad differential, including sarcoidosis, paraneoplastic myelopathy, idiopathic TM, MS, NMOSD with AQP4Ab, AFM, and MOGAD<sup>9</sup>. Relative to alternative demyelinating diagnoses such as NMOSD or MS, MOG-Ab positive TM tends to involve T2 signal abnormality restricted to the gray matter<sup>2</sup>. This pattern of gray matter predilection presents itself as a T2 sagittal line and axial “H” sign<sup>4,7</sup>.

The initial spinal MRI was normal for our patient; however, repeat imaging demonstrated myelitis (Figure 2:A-C). Similarly, her initial brain MRI was normal, and serial imaging demonstrated only subtle incomplete FLAIR sulcal fluid non-suppression with corresponding leptomeningeal enhancement (Figure 1:A-C). This discordance between the severity of clinical presentation and MRI findings is not uncommon. Initial normal neuroimaging should not rule out an inflammatory demyelinating process such as MOGAD when there is high clinical suspicion, as studies have shown that the first brain MRI can be normal in up to 55% of patients with cerebral involvement<sup>6</sup>. Pediatric patients with spinal involvement had abnormal initial spinal MRI only 27% of the time<sup>6</sup>. If initial imaging is normal, follow up imaging is crucial when clinical suspicion for an inflammatory process is high.

Our patient’s clinical picture was severe, with development of lower extremity paralysis and autonomic dysfunction. Involvement of the conus in MOG-IgG related TM leads to higher risk of long term autonomic and motor disability<sup>10</sup>. Despite the severity of presentation, her three-month follow-up imaging demonstrated resolution of her brain MRI abnormalities and near resolution of her MRI spine abnormalities. This radiologic improvement at follow up is typical of MOGAD<sup>11</sup>.

Any diagnosis of acute CNS dysfunction should raise the suspicion for infectious etiologies such as West Nile virus, varicella zoster virus (VZV), herpes simplex virus (HSV), human T-lymphocytic virus (HTLV), or human immunodeficiency virus (HIV), in addition to seasonal viruses<sup>9</sup>. Given our patient’s presentation of TM with acute flaccid paralysis and MRI finding of spinal cord lesions restricted to the

gray matter tract, acute flaccid myelitis (AFM) secondary to a viral etiology was an important diagnostic consideration<sup>12</sup>. With recent outbreaks of EV-D68 associated AFM (2014, 2016, and 2018), appropriate testing for this pathogen was indicated. As MOGAD can meet clinical criteria for and mimic AFM<sup>2</sup>, distinguishing between these two diagnoses is key for appropriate management and prognosis<sup>9</sup>. The exam informs the distinction between MOG-associated TM and AFM; whereas AFM leads to areflexia, asymmetric flaccid weakness, and lack of sensory involvement, MOGAD typically presents with hyperreflexia, symmetric weakness, and sensory involvement as was evident in our patient. In addition, our patient's encephalopathy prompted concern for MOGAD, as cerebral involvement would be unexpected in AFM.

Without randomized clinical trials, treatment of MOGAD is guided by observational studies and expert consensus<sup>13</sup>. MOG-IgG titers may take several days to return; therefore, empiric treatment must be initiated promptly when clinical suspicion is high to minimize residual symptoms<sup>14</sup>. The recognition of clinical, MRI, and CSF patterns of MOGAD is therefore paramount. Expert opinion recommends the use of high-dose IV corticosteroids in management of the acute phase<sup>6,13</sup>. For severe cases or cases refractory to treatment with steroids, plasma exchange and IVIG may be used<sup>9,13</sup>. While most pediatric cases are monophasic and respond well to acute therapies, relapsing disease can increase the risk of long-term neurologic deficit<sup>3,14</sup>. Some reported factors associated with pediatric relapsing disease include persistent MOG-IgG positivity, older age, and ON phenotype<sup>14</sup>. In one prospective cohort study of pediatric MOGAD patients, relapse was more common in those with persistent seropositivity over a median of four years (56%) versus those who had seronegative status (31%)<sup>3</sup>. No consensus exists on maintenance therapy in MOGAD; however, maintenance immunotherapy has been shown to reduce relapse, with IVIG associated with the lowest annualized relapse rate in one large multicenter study<sup>15</sup>. As our patient presented with high MOG-IgG titers, severe presentation, and poor initial recovery of her paraparesis and encephalopathy, she met criteria for a severe phenotype. Therefore, the decision was made to continue monthly IVIG for 2 years of treatment followed by clinical reevaluation and repeat titers, per EU pediatric MOG consortium consensus treatment guidelines<sup>14</sup>.



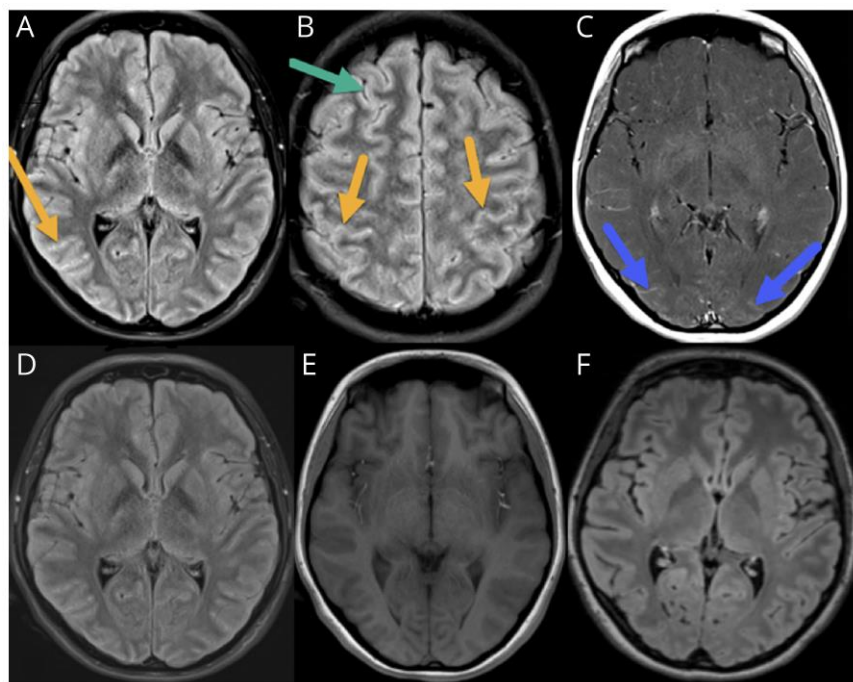
## References

1. Cobo-Calvo Á, Ruiz A, D'Indy H, et al. MOG antibody-related disorders: common features and uncommon presentations. *J Neurol*. 2017;264(9):1945-1955. doi:10.1007/s00415-017-8583-z
2. Dubey D, Pittcock SJ, Krecke KN, et al. Clinical, Radiologic, and Prognostic Features of Myelitis Associated With Myelin Oligodendrocyte Glycoprotein Autoantibody. *JAMA Neurol*. 2019;76(3):301-309. doi:10.1001/jamaneurol.2018.4053
3. Waters P, Fadda G, Woodhall M, et al. Serial Anti-Myelin Oligodendrocyte Glycoprotein Antibody Analyses and Outcomes in Children With Demyelinating Syndromes. *JAMA Neurol*. 2020;77(1):82-93. doi:10.1001/jamaneurol.2019.2940
4. Baumann M, Bartels F, Finke C, et al. E.U. paediatric MOG consortium consensus: Part 2 - Neuroimaging features of paediatric myelin oligodendrocyte glycoprotein antibody-associated disorders. *Eur J Paediatr Neurol EJPN Off J Eur Paediatr Neurol Soc*. 2020;29:14-21. doi:10.1016/j.ejpn.2020.10.002
5. Armangue T, Olivé-Cirera G, Martínez-Hernández E, et al. Associations of paediatric demyelinating and encephalitic syndromes with myelin oligodendrocyte glycoprotein antibodies: a multicentre observational study. *Lancet Neurol*. 2020;19(3):234-246. doi:10.1016/S1474-4422(19)30488-0
6. Wynford-Thomas R, Jacob A, Tomassini V. Neurological update: MOG antibody disease. *J Neurol*. 2019;266(5):1280-1286. doi:10.1007/s00415-018-9122-2
7. Fadda G, Alves CA, O'Mahony J, et al. Comparison of Spinal Cord Magnetic Resonance Imaging Features Among Children With Acquired Demyelinating Syndromes. *JAMA Netw Open*. 2021;4(10):e2128871. doi:10.1001/jamanetworkopen.2021.28871
8. Wang J, Qiu Z, Li D, et al. Clinical and Imaging Features of Patients With Encephalitic Symptoms and Myelin Oligodendrocyte Glycoprotein Antibodies. *Front Immunol*. 2021;12:722404. doi:10.3389/fimmu.2021.722404
9. Wang C, Greenberg B. Clinical Approach to Pediatric Transverse Myelitis, Neuromyelitis Optica Spectrum Disorder and Acute Flaccid Myelitis. *Child Basel Switz*. 2019;6(5):E70. doi:10.3390/children6050070
10. Bruijstens AL, Breu M, Wendel EM, et al. E.U. paediatric MOG consortium consensus: Part 4 - Outcome of paediatric myelin oligodendrocyte glycoprotein antibody-associated disorders. *Eur J Paediatr Neurol EJPN Off J Eur Paediatr Neurol Soc*. 2020;29:32-40. doi:10.1016/j.ejpn.2020.10.007

11. Sechi E, Krecke KN, Messina SA, et al. Comparison of MRI Lesion Evolution in Different Central Nervous System Demyelinating Disorders. *Neurology*. 2021;97(11):e1097-e1109. doi:10.1212/WNL.00000000000012467
12. Wang C, Narayan R, Greenberg B. Anti-Myelin Oligodendrocyte Glycoprotein Antibody Associated With Gray Matter Predominant Transverse Myelitis Mimicking Acute Flaccid Myelitis: A Presentation of Two Cases. *Pediatr Neurol*. 2018;86:42-45. doi:10.1016/j.pediatrneurol.2018.06.003
13. Marignier R, Hacoheh Y, Cobo-Calvo A, et al. Myelin-oligodendrocyte glycoprotein antibody-associated disease. *Lancet Neurol*. 2021;20(9):762-772. doi:10.1016/S1474-4422(21)00218-0
14. Bruijstems AL, Wendel EM, Lechner C, et al. E.U. paediatric MOG consortium consensus: Part 5 - Treatment of paediatric myelin oligodendrocyte glycoprotein antibody-associated disorders. *Eur J Paediatr Neurol EJPn Off J Eur Paediatr Neurol Soc*. 2020;29:41-53. doi:10.1016/j.ejpn.2020.10.005
15. Chen JJ, Flanagan EP, Bhatti MT, et al. Steroid-sparing maintenance immunotherapy for MOG-IgG associated disorder. *Neurology*. 2020;95(2):e111-e120. doi:10.1212/WNL.00000000000009758

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Figure 1: Brain MRI images

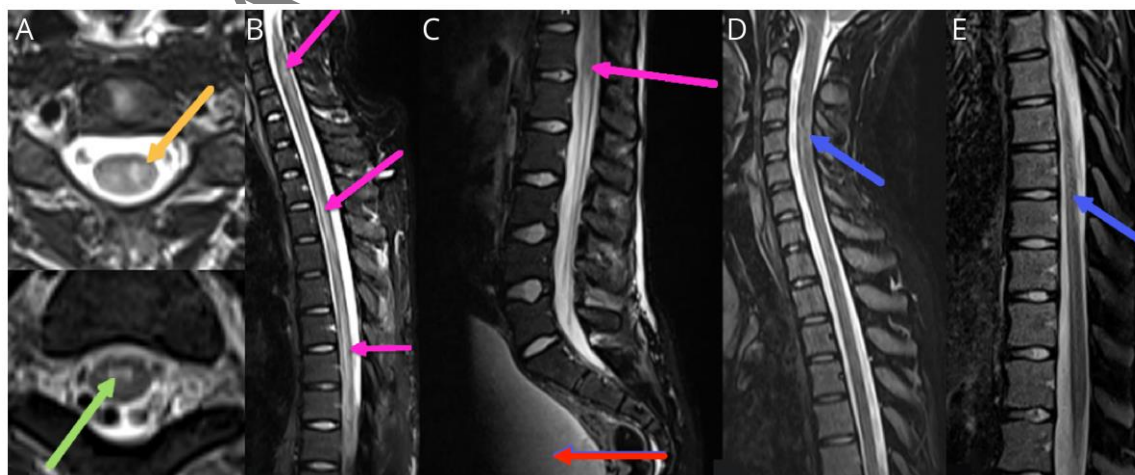


Axial MRI brain images from hospital day 9 obtained at the community hospital including (A,B) FLAIR sequence showing areas of incomplete sulcal fluid suppression (orange arrows) with normal CSF suppression (green arrow) and (C) axial post-contrast T1 showing corresponding subtle leptomeningeal enhancement (blue arrows).

Axial MRI images from hospital day 12 obtain at the tertiary children's hospital including (A) FLAIR sequence (D) and post-contrast T1 (E) demonstrate normal brain imaging with resolution of sulcal CSF signal non-suppression.

Axial MRI FLAIR imaging at three months follow up (F) without abnormal signal.

Figure 2: Spinal cord MRI images



MRI spine images from hospital day 12 including (A) Axial T2 showing areas of diffuse, multifocal, patchy intramedullary grey matter predominant T2 prolongation (orange arrow) and



*“snake eyes sign” (green arrow) from the cervicomedullary to the lumbosacral junction and (B, C) Sagittal T2/STIR view demonstrating longitudinally extensive holocord lesion (pink arrows), as well as distended neurogenic bladder (C. red arrow).*

*Follow-up sagittal T2/STIR MRI spine at three months (D,E) showing partial improvement of lesion.*

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