AOJ Emergency and Internal Medicine

Case Report

Open Access

Double-Seronegative Neuromyelitis Optica Spectrum Disorder Presenting with Acute Flaccid Paraplegia and Bilateral Optic Neuritis

Volume 1 Issue 3 – 2025

Sabyasachi Chowdhury,[1] Vaibhav Agarwal,[2] Jemima Islam,[3] Md. Karimulla Mondal,[4] Anup Kumar Datta[5]

[1]Post Graduate Resident, Department of General Medicine, Institute of Post Graduate Medical Education and Research and SSKM Hospital, Kolkata, West Bengal, India

[2]Post Graduate Resident, Department of General Medicine, Institute of Post Graduate Medical Education and Research and SSKM Hospital, Kolkata, West Bengal, India

[3]Post Graduate Resident, Department of General Medicine, Institute of Post Graduate Medical Education and Research and SSKM Hospital, Kolkata, West Bengal, India

[4]Senior Resident, Department of General Medicine, Institute of Post Graduate Medical Education and Research and SSKM Hospital, Kolkata, West Bengal, India

[5]Assistant Professor, Department of General Medicine, Institute of Post Graduate Medical Education and Research and SSKM Hospital, Kolkata, West Bengal, India

Correspondence: Sabyasachi Chowdhury, Post Graduate Resident, Department of General Medicine, Institute of Post Graduate Medical Education and Research and SSKM Hospital, Kolkata, West Bengal, India. Email abhichoudhury.chowdhury86@gmail.com

Received: November 25, 2025 **Published:** December 19, 2025

Citation: Sabyasachi Ch. Double-Seronegative Neuromyelitis Optica Spectrum Disorder Presenting With Acute Flaccid Paraplegia and Bilateral Optic Neuritis. AOJ Emerg and Int Med. 2025;1(3):45–50.

Abstract

Neuromyelitis optica (NMO) is an autoimmune, demyelinating inflammatory disorder of the central nervous system primarily targeting the optic nerves and spinal cord. The 2015 International Consensus criteria classify patients based on aquaporin-4 antibody (AQP4-IgG) status, with seronegative cases posing diagnostic difficulty because of overlap with other inflammatory and demyelinating conditions. Early recognition is essential, as untreated disease may lead to irreversible neurological disability.

A 30-year-old woman with no comorbidities presented with 15 days of progressive bilateral lower-limb weakness, low back pain, and abdominal distention due to acute urinary retention requiring catheterization. Examination revealed hypotonia of both lower limbs, absent deep tendon reflexes, bilateral extensor plantar responses, and Medical Research Council (MRC) grade 0/5 power throughout. Routine laboratory investigations—including liver and kidney function tests, electrolytes, inflammatory markers, serum proteins, vitamin B12, folate, and urinalysis—were within normal limits.

MRI dorsolumbar spine with whole-spine screening demonstrated longitudinally extensive transverse myelitis. MRI brain and orbit revealed demyelinating changes in the bilateral posterior optic nerves near the chiasm and in the pons. Visual evoked potentials showed prolonged P100 latency, compatible with conduction block. CSF analysis demonstrated lymphocytic pleocytosis, elevated protein, and negative oligoclonal bands. Anti-AQP4 and anti-MOG antibodies were negative. CNS infections, autoimmune encephalitides, systemic autoimmune diseases, sarcoidosis, and paraneoplastic syndromes were excluded based on clinical, biochemical, and radiologic findings.

She received high-dose intravenous methylprednisolone for five days without improvement, followed by seven alternate-day plasma exchange sessions, which led to gradual motor and bladder recovery. She was discharged on tapering oral prednisolone with mycophenolate mofetil.

Seronegative NMOSD may follow a relapsing course with significant long-term disability. Early diagnosis and timely initiation of immunomodulatory therapy are essential to reduce recurrence and improve neurological outcomes. Further refinement of diagnostic modalities is required for better identification of seronegative disease.

Keywords: Neuromyelitis optica spectrum disorder; Longitudinally extensive transverse myelitis; Optic neuritis; Seronegative NMOSD; Demyelinating disorders

Background

Neuromyelitis optica spectrum disorder (NMOSD) is a distinct astrocytopathic inflammatory demyelinating disease that preferentially affects the optic nerves and spinal cord.[1] Diagnostic evaluation relies on the 2015 IPND criteria, which integrate clinical syndromes, MRI characteristics, and AQP4-IgG testing.[1] While AQP4-IgG positivity is seen in most patients, 20–30% remain seronegative[3]. This seronegative population is diagnostically challenging because it overlaps with MOGAD, multiple sclerosis, autoimmune myelopathies, sarcoidosis, and vasculitis.[2,3,4]

Population-based studies show that NMOSD prevalence varies by ethnicity and geography, with higher rates reported in Asian cohorts.[6,7]

Longitudinally extensive transverse myelitis (LETM) is a hallmark feature of NMOSD but may also occur in metabolic, infectious, and autoimmune diseases.[1,5] Bilateral optic neuritis and steroid-refractory myelitis further increase suspicion.[2,9] Seronegative NMOSD may still show aggressive disease with severe relapses and long-term disability.[3,4]

This report highlights an uncommon presentation of double-seronegative NMOSD with simultaneous LETM and optic neuritis, emphasizing the role of careful clinical–radiologic correlation and timely plasma exchange.

Case Description

A 30-year-old married Hindu woman from Shibtala, Howrah, presented with progressive weakness of both lower limbs for 15 days, accompanied by low back pain of the same duration. She also reported abdominal distention with acute urinary retention 15 days earlier, which was relieved by catheterization. She denied trauma, weight loss, diarrhoea, sore throat, recent vaccination or visual loss. A single day of fever preceded the onset of weakness. Her past medical, surgical and drug history was unremarkable, and there was no evidence of envenomation. She was a non-smoker, non-alcoholic, normotensive, euglycemic and euthyroid. She was married with no living issues and no history of abortion. Sleep and appetite were normal, and she reported constipation.

On general examination, she was alert, conscious and cooperative, with mild pallor and no jaundice, cyanosis, clubbing, edema or lymphadenopathy. Neck veins were not engorged. Vital signs were stable, with blood pressure 110/70 mmHg, pulse 88/min, SpO_2 98% on room air and respiratory rate 14/min. Cardiovascular, respiratory and abdominal examinations were within normal limits.

Neurological examination revealed normal higher mental functions and intact cranial nerves. There was generalized muscle wasting involving both upper and lower limbs. The lower limbs were extended at the hip and knee, externally rotated at the hip, with the feet inverted and plantar flexed. Tone was normal in the upper limbs and reduced in both lower limbs. Upper limb motor power showed shoulder abduction, adduction, flexion and extension as 3/5 bilaterally; elbow flexion and extension as 4/5 bilaterally; wrist flexion and extension as 4/5 bilaterally; and hand grip strength as 5/5. Lower limb power was profoundly reduced, with truncal weakness present. Hip flexion, extension, abduction and adduction were 0/5 bilaterally; knee flexion and extension were 0/5; and ankle dorsiflexion and plantar flexion were 0/5 bilaterally. Superficial reflexes revealed preserved corneal reflex but absent abdominal, anal and bulbo-cavernous reflexes, with flexor plantar responses. Deep tendon reflexes showed reduced biceps, triceps and supinator reflexes, with absent knee and ankle jerks and no clonus.

Sensory and cortical modalities were intact. Cerebellar functions were normal, though gait and Romberg's sign could not be assessed. Autonomic system examination was normal, and no meningeal signs were present. Skull and spine examinations were unremarkable.

The overall clinical picture suggested an acute onset symmetrical flaccid paraplegia with bladder and bowel involvement, preserved cranial nerves and intact sensations, indicating a spinal cord lesion. Differential diagnoses considered included acute transverse myelitis, post-viral myelitis, spinal cord stroke, hypokalemic periodic paralysis and thyrotoxic periodic paralysis.

Routine laboratory evaluation showed hemoglobin 9.2 g/dL, total leukocyte count 8900/mm³, differential count N82 L13 M4 E1, platelet count 2.1 lakh/mm³, MCV 102 fL, ESR 50 mm/hr, CRP 66 mg/L, serum sodium 139 mEq/L and potassium 3.8 mEq/L. Urea was 19 mg/dL and creatinine 0.7 mg/dL. Thyroid function tests showed TSH/FT4/FT3 as 2.6 / 1.17 / 1.6. Liver function tests and coagulation profile were within normal limits. MRI dorsolumbar spine with whole-spine screening showed marked diffuse cord swelling from the cervicomedullary junction to the conus, with subtle T2/STIR hyperintensity and minimal patchy enhancement, consistent with longitudinally extensive transverse myelitis (LETM). Based on these findings, possibilities included neuromyelitis optica, multiple sclerosis, infectious myelitis, autoimmune-related myelitis, paraneoplastic myelitis and

metabolic causes such as vitamin B_{12} deficiency.

A lumbar puncture was performed, and treatment was initiated with intravenous methylprednisolone 1 g/day for five days. CSF analysis later revealed colourless clear fluid with 50 cells/mm^3 (all lymphocytes), glucose 39 mg/dL, protein 155 mg/dL and ADA 2.4. Gram stain and ZN stain were negative.

Infectious disease evaluation showed negative VDRL, negative HIV-1/2 IgM/IgG, negative bacterial cultures and a negative neurovirology PCR panel (HSV-1/2, EBV, adenovirus, HHV-6/7/8, CMV, VZV, parvovirus B19, HTLV-1, measles and enterovirus). Autoimmune evaluation showed complement levels C3 174 mg/dL and C4 36.2 mg/dL, with negative dsDNA, MPO, PR3, ANCA, ANA and ANA profile. Serum ACE was 12 U/L.

Serum vitamin B_{12} level was 448 pg/mL, and CECT thorax was normal. Additional CSF assays, including paraneoplastic profile, anti-AQP4 antibody, anti-MOG antibody and oligoclonal band testing, were negative.

During the hospital stay, the patient developed blurring of vision in both eyes. MRI brain and orbit showed signal changes in the pons suggestive of demyelination or metabolic etiology, along with bilateral optic nerve signal alterations consistent with oedema, neuritis or demyelination. Visual evoked potentials demonstrated prolonged P100 latency with low-normal amplitude bilaterally, indicating conduction block and optic nerve demyelination. Fundoscopy confirmed bilateral optic neuritis.

The final diagnosis was seronegative neuromyelitis optica spectrum disorder. After completing five doses of intravenous methylprednisolone, the patient showed no significant clinical improvement and was shifted to oral prednisolone 1 mg/kg body weight. She subsequently underwent seven sessions of alternate-day plasma exchange therapy over 14 days, each session comprising six units of fresh frozen plasma and two units of albumin. After completing plasma exchange, she was initiated on mycophenolate mofetil 1 g/day, and physiotherapy was advised. Treatment response showed return of the bulbo-cavernous and anal reflexes, improvement in lower limb motor power beginning after the third plasma exchange session, and improvement in bladder function allowing catheter removal after one week. Despite neurological improvement, there was no recovery in visual symptoms.

Discussion

This case illustrates the diagnostic and therapeutic challenges associated with seronegative NMOSD. Although AQP4-IgG is highly specific for NMOSD, the absence of both AQP4 and MOG antibodies does not exclude the diagnosis, particularly when characteristic clinical and MRI features are present.[1-3]

Our patient demonstrated LETM, bilateral optic nerve involvement, lymphocytic CSF pleocytosis, and a poor steroid response—features that align with seronegative NMOSD rather than MS, MOGAD, or post-infectious myelitis.[1,2,5,9]

Interpretation and Uniqueness of the Case

This case is notable for several reasons:

- The patient had simultaneous LETM and bilateral optic neuritis while being seronegative for both AQP4 and MOG antibodies, a presentation that is uncommon and diagnostically challenging.
- She developed complete paraplegia with bladder dysfunction despite normal biochemistry and absence of autoimmune markers.
- She demonstrated marked improvement only after plasma exchange, emphasizing that early escalation is crucial in suspected seronegative NMOSD.

Double-seronegative NMOSD is often under-recognized. While some studies show fewer relapses in this group, the initial episodes can be severe and disabling.[3,4] The absence of oligoclonal bands and the presence of LETM favored NMOSD over MS, consistent with published observations.[1,5]

Comparison With Published Literature

Our findings align with established literature:

- LETM spanning three or more vertebral segments is strongly associated with NMOSD and uncommon in MS.[1,5]
- Posterior optic nerve involvement with prolonged P100 latency supports NMOSD rather than MOGAD.[2,9]
- Potential mechanisms for double-seronegative disease include:
  – low-titer undetectable AQP4 antibodies[8]
  – antibodies against currently unknown glial antigens[2]
  – immunopathology overlapping with MOGAD.[2,10]

The patient's marked motor improvement after plasma exchange is consistent with evidence demonstrating that early PLEX is beneficial in steroid-refractory NMOSD.[4]

Conclusion

Seronegative NMOSD should be considered in patients presenting with LETM and optic neuritis despite negative AQP4 and MOG antibody testing. Early recognition, exclusion of mimics, rapid initiation of plasma exchange, and long-term immunosuppression are essential to prevent relapse and disability. This case highlights the importance of aggressive early treatment and the need for improved biomarkers for double-seronegative disease.

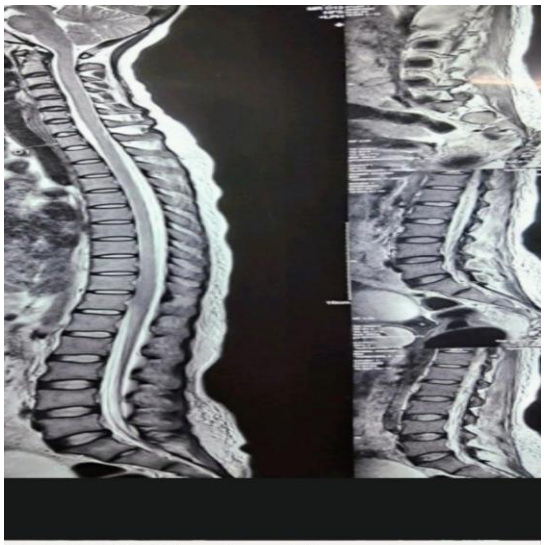

Fig 2. MRI DL Spine shows diffuse cord swelling extending from the cervicomedullary junction to the conus with T2/STIR hyperintensity, consistent with LETM.

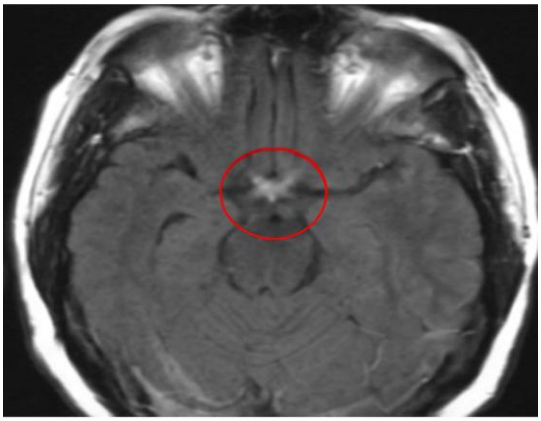

Fig 1 MRI of brain and orbit was suggestive of demyelinating changes in biiateral posterior optic nerves near optic chiasma and pons.

Test	Result
Hemoglobin	9.2 g/dL
TC, DC	8900/mm³, N82 L13 M4
Platelets	2.1 lakh/mm³
ESR, CRP	50 mm/hr, 66 mg/L
Sodium, Potassium	139 mEq/L, 3.8 mEq/L
Urea, Creatinine	19 mg/dL, 0.7 mg/dL
Total Bilirubin, Direct Bilirubin	0.3 mg/dL, 0.1 mg/dL
SGOT, SGPT	27 U/L, 26 U/L
ALP	54 U/L
TSH, FT4, FT3	2.6 µIU/mL, 1.17 ng/dL, 1.6 pg/mL
Vitamin B12	448 pg/mL
CSF Appearance	Clear, colorless
CSF Cell Count	50 cells/mm³, all lymphocytes
CSF Glucose, Protein, ADA	39 mg/dL, 155 mg/dL, 2.4
CSF Gram Stain, ZN Stain	Negative, Negative
CSF Oligoclonal Bands	Negative
AQP4 IgG, MOG IgG	Negative, Negative
Paraneoplastic Panel	Negative
HIV 1/2 IgM/IgG	Negative
CSF Bacterial Culture, VDRL	Negative, Negative
Neurovirology PCR	Negative (HSV-1/2, EBV, Adenovirus, HHV-6/7/8, CMV, VZV, Parvovirus B19, HTLV-1, Measles, Enterovirus)
ANA	Negative
ANCA, MPO, PR3	Negative, <2 IU/mL, <2 IU/mL
dsDNA	<10 IU/mL
Complement C3, C4	174 mg/dL, 36.2 mg/dL
ACE	12 U/L

Patient Consent

Written informed consent was obtained.

Acknowledgement

None.

Conflicts of Interest

We have no conflict of interests to disclose and the manuscript has been read and approved by all named authors.

Funding

None.

References

1. Wingerchuk DM. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. *Neurology*. 2015;85:177–189.

2. Sato DK. Distinction between MOG antibody-positive and AQP4 antibody-positive NMO spectrum disorders. *Neurology*. 2014;82:474–481.

3. Pandit L. Demographic and clinical features of neuromyelitis optica: A review. *Mult Scler*. 2015;21:845–853.

4. Mealy MA et al. Epidemiology of Neuromyelitis Optica in the United States A Multicenter Analysis. *Arch Neurol*. 2012;69:1176–1180.

5. Flanagan E. Short Myelitis Lesions in Aquaporin-4-IgG–Positive Neuromyelitis Optica Spectrum Disorders. *JAMA Neurol*. 2015;72:81–87.

6. Hor JY. Epidemiology of Neuromyelitis Optica Spectrum Disorder and Its Prevalence and Incidence Worldwide. *Front Neurol*. 2020;11:501.

7. Houzen H. Prevalence and clinical features of neuromyelitis optica spectrum disorders in northern Japan. *Neurology*. 2017;89:1995–2001.

8. Jarius S. Preterm infant hippocampal volumes correlate with later working memory deficits. *Brain*. 2008;131:3072–3080.

9. Pache F. MOG-IgG in NMO and related disorders: a multicenter study of 50 patients. Part 4: Afferent visual system damage after optic neuritis in MOG-IgG-seropositive versus AQP4-IgG-seropositive patients. *J Neuroinflammation*. 2016;13:282.

10. Fan S. Comparison of myelin oligodendrocyte glycoprotein (MOG)-antibody disease and AQP4-IgG-positive neuromyelitis optica spectrum disorder (NMOSD) when they co-exist with anti-NMDA (N-methyl-D-aspartate) receptor encephalitis. *Mult Scler Relat Disord*. 2018;20:144–152.