

A Unique Case of Neuromyelitis Optica in a Patient with Acquired Immunodeficiency Syndrome: Case Report

Hailey Mair¹ | Joshua Chalkley² | Roman Kassa⁴ | Flavius D. Raslau³ | Ashwini Kini^{5*} | Padmaja Sudhakar^{1,2}

*Correspondence: Ashwini Kini

Address: ¹Department of Ophthalmology, University of Kentucky, Lexington, Kentucky, USA; ²Department of Neurology, University of Kentucky, Lexington, Kentucky, USA; ³Department of Radiology, University of Kentucky, Lexington, Kentucky, USA; ⁴Norton Neuroscience Institute, Norton Healthcare; ⁵Centennial Neuroscience, Tristar Centennial Medical Center

E-mail ✉: ashkini1@gmail.com

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ABSTRACT

Introduction: Neuromyelitis optica (NMO) is an inflammatory, demyelinating central nervous system disorder characterized by concurrence of optic neuritis associated with a lesion in the spinal cord extending over three or more vertebral segments.

Clinical Case: We describe a patient with acquired immunodeficiency syndrome (AIDS) who presented with acute myelopathy and optic neuritis and subsequently was diagnosed with NMO. **Conclusions:** This case highlights the importance of including NMO in the differential diagnosis when an AIDS patient presents with optic neuritis or myelitis. Timely diagnosis of NMO is essential for adequate treatment and recovery.

Keywords: *Neuromyelitis Optica (NMO), AIDS, Demyelinating Disease, Optic Neuritis*

Introduction

Neuromyelitis optica spectrum disorders (NMOSD), previously known as Devic's disease or Neuromyelitis optica (NMO), is an Aquaporin 4 antibody-mediated autoimmune demyelinating disorder of the central nervous system (Sellner *et al.*, 2010). As the name states, permanent vision loss and paraplegia/quadruplegia are the most disabling features of the disease if left untreated. Timely diagnosis and initiation of treatment are important to prevent future attacks that can lead to accumulation of disability. We describe a patient with acquired immunodeficiency syndrome (AIDS) presenting initially as seronegative acute myelopathy with sequential bilateral optic neuritis and was subsequently diagnosed with NMO after a repeat AQP4-IgG antibody was positive. The aim of the article is to raise the awareness

of the medical condition among physicians so as to expedite the workup and diagnosis and initiate treatment in a timely manner.

Case Presentation

A 28-year-old woman presented with difficulty walking due to asymmetric, lower extremity motor weakness with paresthesia for two weeks, constipation and urinary retention. Her past medical history was significant for AIDS (undetectable Human Immunodeficiency Virus (HIV) viral load and CD4 count 585 cells/cm³) diagnosed in 2009 and currently on antiretroviral therapy, herpes simplex virus (unspecified), yeast vaginitis, and atopic dermatitis. She was admitted to the internal medicine service in February 2017. Initial motor exam was significant for asymmetric spastic lower extremity paraparesis (right greater than left, greater proximally), bilateral lower extremity hyperreflexia with crossed adductors, ankle clonus and positive Babinski reflex. Bilateral upper extremity strength was 5/5 with intact reflexes. Sensory exam was significant for sensory level approximately at T7 and loss of vibration and proprioception in bilateral lower extremities. She had an intact mental status, no cranial neuropathy, no afferent pupillary defects, and no ataxia. Differential diagnosis included transverse myelitis secondary to infectious or post-infectious pathology, lymphoma, HIV myelitis, Multiple Sclerosis, NMOSD, Sarcoidosis, and opportunistic infections including Cytomegalovirus, Tuberculosis, and Toxoplasmosis.

An extensive workup was significant for positive Toxoplasmosis IgG (IgM negative), elevated creatinine kinase, low CD4 count, negative serum AQP4 Ab, and an undetectable HIV viral load. A contrast enhanced Magnetic Resonance Imaging (MRI) of head (Fig. 1A, B) showed numerous subcortical T2 white matter lesions, some with enhancement on T1 post-contrast. A contrast enhanced MRI of the full spine (Fig. 1C, D) revealed multiple expansile enhancing cord lesions on T1 post-contrast involving the cervical and thoracic cord with swelling. Chest CT with contrast showed a small right lower lobe pulmonary nodule. Lumbar puncture, completed twice, was significant for lymphocytic pleocytosis (41,000 white blood cells, 87% lymphocytes), elevated proteins (122mg/dL), positive CSF restricted oligoclonal bands with increased IgG synthesis, and negative for cytology and infection panel. Pending definitive diagnosis, she was treated symptomatically for pain and with intravenous ceftriaxone with sulfadiazine and pyrimethamine for possible infection due to her immunocompromised status and positive Toxoplasma IgG titers. IV steroids were deferred at this time due to concern for infection and malignancy.

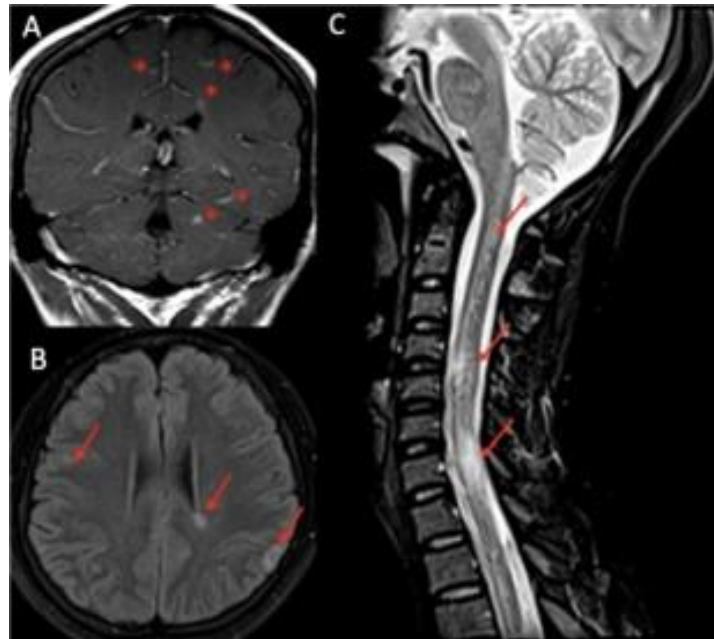


Figure 1: MRI of the brain and spine. Coronal post-contrast T1-weighted (A) and axial Fluid Attenuated Inversion Recovery (FLAIR) (B) images of the brain show T2-hyperintense lesions (asterisks) with corresponding enhancement (arrows) in periventricular, subcortical, and cerebellar regions. Sagittal Short Tau Inversion Recovery (STIR) (C) of the cervical and thoracic spine reveal extensive enhancing lesions throughout the spinal cord.

In the following week, her clinical course progressed, and she developed quadriparesis and sequential optic neuritis over five days. Bedside ophthalmic exam revealed visual acuity of 20/20 in the right eye and light perception in the left eye with a left afferent pupillary defect. Intraocular pressures were within normal range, extraocular movements were full, and the anterior chamber was quiet. Fundus exam revealed bilateral flat optic discs with no retinal lesions. Due to a rapidly progressive clinical course with an inconclusive diagnosis, a brain biopsy was performed and was significant for marked perivascular and parenchymal inflammation with associated macrophages but was negative for malignancy or infection. Echocardiogram showed no vegetations, and CT abdomen and pelvis with contrast revealed no lesions.

The next day, the patient developed a headache, confusion, blurry left eye vision, and left eye pain with extraocular movement, and a repeat imaging and lumbar puncture were performed. Contrast enhanced MRI orbits (Fig. 2) revealed bilateral optic nerve enhancement. MRI head with contrast (Fig. 2) was significant for an interval increase in size and enhancement of several subcortical white matter lesions and a new enhancing lesion in the periventricular region of the right temporal horn. MRI spine (not shown) revealed worsening of cord lesions with patchy intramedullary enhancement and increased cord swelling. Repeat spinal fluid analysis was unremarkable for any new findings.

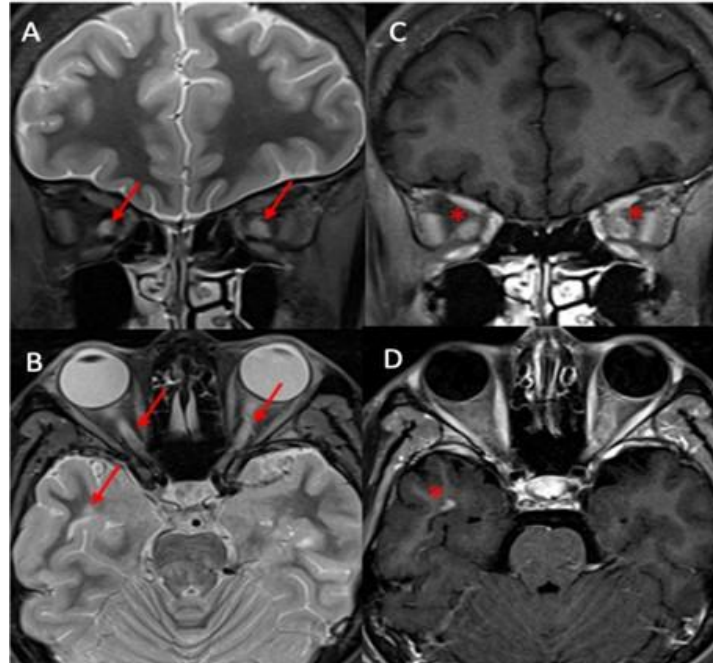


Figure 2: Repeat MRI head and orbits. Coronal (A) and axial (B) Short Tau Inversion Recovery (STIR) and coronal (C) and axial (D) post-contrast T1-weighted images demonstrate extensive T2 hyperintensity of the optic nerves (arrows) with corresponding enhancement (asterisks). In addition, there is a new enhancing lesion in the periventricular region along the right temporal horn.

Due to myelitis and bilateral optic neuritis, treatment with plasmapheresis was started, and two rounds were completed before discontinuing due to an iatrogenic pneumothorax and hemothorax from an indwelling catheter. Her visual acuity decreased to hand motion in the right eye and remained stable at light perception in the left eye. Since extensive workup was negative for infection and malignancy, intravenous methylprednisolone one gram daily for five days was started for treatment of optic neuritis. Repeat AQP4-Ab was positive revealing a diagnosis of NMOSD. She was started on Rituximab infusions inpatient and a steroid taper.

Over the past 5 years, she has continued to follow with neurology and neuro-ophthalmology. She receives Rituximab infusions every six months and has had no relapses. Her most recent neuro-ophthalmology appointment was in April 2023 and neurology appointment was in February 2024. She has had significant neurologic and visual recovery but her vision continues to be reduced in her left eye subjectively. Her most recent visual acuity was 20/30 in right and 20/30 in the left eye with a left afferent pupillary defect and no improvement with glasses. Color vision with Ishihara has improved to 6/14 plates in the right eye and 2/14 plates in the left eye. Contrast sensitivity was reduced bilaterally, and depth perception was poor. Fundus exam was significant for bilateral optic disc pallor, left eye worse than right eye. Humphrey visual fields 24-2 SITA fast of the right and left eye showed stable central scotomas with some peripheral depression (Fig. 3). Optical Coherence Tomography (OCT) retinal nerve fiber layer (RNFL)

showed retinal nerve fiber layer loss and significant bilateral ganglion cell layer loss (Fig. 4). She has had a full motor recovery with motor strength of 5/5 in all extremities with brisk reflexes and downward plantar reflexes bilaterally. Sensation is intact to light touch, temperature, and vibration. Persisting deficits include stable, intermittent paresthesias in her feet bilaterally and occasional fecal incontinence and mixed stress and urge urinary incontinence. She notes no persisting cognitive deficits.

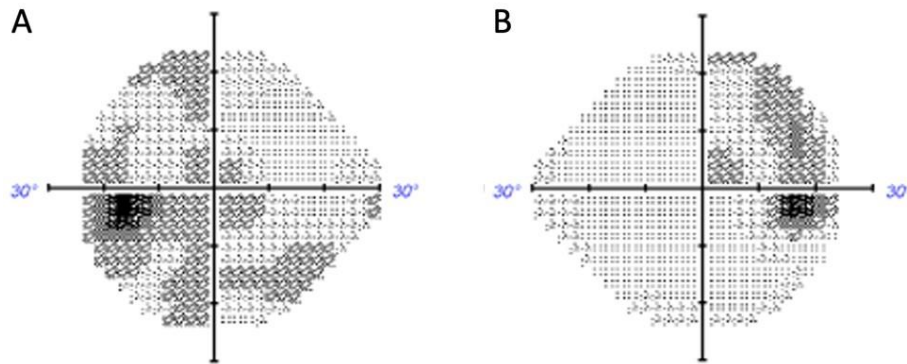


Figure 3: Humphery visual fields left eye (OS) (A) and right eye (OD) (B) showing central scotomas with some peripheral depression.

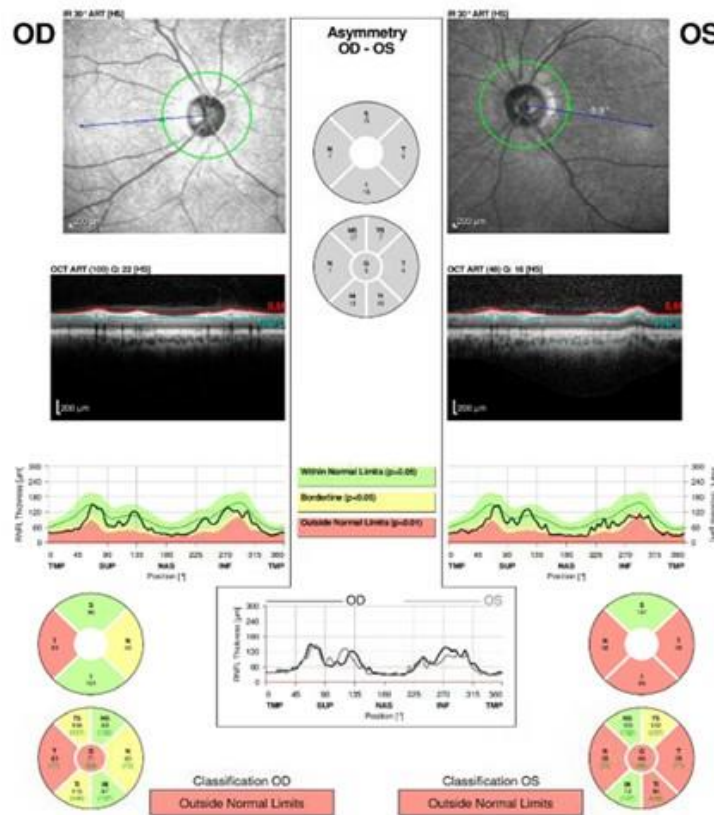


Figure 4: Optical Coherence Tomography (OCT) retinal nerve fiber layer (RNFL) shows significant bilateral retinal nerve fibre loss and was stable from previous tests.

Discussion

NMO can be associated with infectious and immunosuppressive disorders including HIV (Koga *et al.*, 2011) as seen in this case and should be considered in the differential diagnosis. AQP4-IgG antibody can be undetectable in 10-40% of patients (Schmetzer *et al.*, 2021). Two hypotheses are proposed for the pathophysiology of NMO in AIDS patients. The first hypothesis states that T cells infected by a retrovirus, in this case HIV, can induce polyclonal B cell activation and trigger autoimmunity through molecular mimicry. In addition, HIV can increase the permeability of the blood brain barrier and enhance trafficking of infected cells and cytokines. This alteration of the blood brain barrier permits access of NMO-Ab and T cells to the central nervous system (Higuchi *et al.*, 1997). The second hypothesis is that NMO in HIV can be due to a dysregulation of the immune system due to immune reconstitution inflammatory syndrome (IRIS) (Berger *et al.*, 1989; Berger *et al.*, 1992).

NMO is commonly associated with autoimmune diseases and infectious diseases (Berger *et al.*, 1989). There are limited cases of NMO in HIV cases reported in the literature, and the majority of cases result in poor motor and visual outcomes (Blanche *et al.*, 2000). This poor prognosis could be due to HIV, NMO, or due to delay in diagnosis due to the complexity of the medical conditions and immunosuppressed status these group of patients may have. Feyissa, *et al.* (2013) reports two patients who are wheelchair bound due to significant paresthesias despite receiving treatment. In addition, Mathew, *et al.* (2019) reports seven patients with HIV associated NMOSD. The most common clinical presentation was optic neuritis followed by myelitis, and five out of seven patients had poor recovery from the acute attack. In contrast, our patient presentation was myelitis followed by optic neuritis, and she had a positive recovery. Mathew, *et al.* (2019) reports Anti-aquaporin 4 antibody was positive in three of the seven patients. Our patient initially was Anti-aquaporin 4 antibody negative but was positive after retesting. Similar to our patient, no patients had relapses while on immunomodulatory therapy (Mathew *et al.*, 2019). In our case, initial treatment and diagnosis of NMO was delayed due to the combination of the past medical history of AIDS and initially negative AQP4 antibody, the presence of oligoclonal bands in the CSF, and a higher suspicion for infectious and malignancy as the underlying etiology. Fortunately, the patient still made an excellent motor recovery, sensory recovery, and substantial visual recovery.

Conclusions

In summary, repeat testing for NMO should be considered in a patient with AIDS when there is high index of clinical suspicion and presumptive early treatment may be considered to prevent irreversible loss of vision or motor function. The timely diagnosis of NMO is essential for adequate treatment and recovery.

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