'I Thought It Was My Diabetes': An Acute Presentation of Neuromyelitis Optica Spectrum Disorder

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ABSTRACT

Neuromyelitis Optica Spectrum Disorder (NMOSD) is an immune-mediated neuroinflammatory disease of the central nervous system. Patients typically present with sensory deficits, weakness, and incontinence. This is a case of a 43-year-old female with diabetes mellitus admitted for acute onset leg weakness and stool incontinence. Spinal MRI imaging revealed transverse myelitis, and her lab work was significant for an anti-aquaporin 4 (AQP4) antibody titer of 1:2,560. Initial treatment consisted of a high-dose steroid taper and plasmapheresis. This unique case illustrates the importance in recognizing delayed presentations of rare neuroinflammatory conditions previously assumed to be a sequela of diabetic neuropathy.

KEYWORDS: NMOSD, Neuromyelitis Optica, transverse myelitis, NMO, Devic's Disease

BACKGROUND

Neuromyelitis Optica Spectrum Disorder (NMOSD) is an immune-mediated inflammatory disease resulting in demyelination, axonal damage, and perivascular lymphocytic infiltrations within the spinal cord and optic nerves.[1] NMOSD has a prevalence of 0.01%, with a predominantly female-to-male ratio of 10:1, though robust epidemiological studies are lacking.[2] We discuss an unusual presentation of NMOSD, where the patient may have had misinterpreted signs and symptoms of the disease years before her initial presentation, illustrating the importance of NMOSD awareness and early intervention.

CASE REPORT

A 43-year-old female with a history of type 2 Diabetes Mellitus (DM) was admitted for acute onset bilateral leg weakness and stool incontinence. Two days prior, the patient reported cervical to mid-back pain, urinary urge incontinence, and an involuntary loss of anal sphincter control. The patient reported similar symptoms one year prior to presentation, which subsequently resolved after being diagnosed with DM and treated with metformin. She had no recent medication adjustments, smoked a quarter pack of cigarettes daily, and did not endorse alcohol or recreational drug use.

On initial presentation, she was afebrile, normotensive, and tachycardic to the 120s. Her physical exam was notable for left lower extremity 2/5 strength to hip flexion, knee flexion and extension, and 4-/5 strength for plantarflexion and dorsiflexion. During an ocular exam, the patient had diminished reactivity to light and accommodation in the left eye as compared to the right. Visual fields were full to confrontation bilaterally. There were no gross abnormalities appreciated on anterior eye exam. Sensation to light touch, crude touch, nociception, and temperature was grossly diminished in the left leg as compared to the right in the L4–L5 dermatomes. Though more pronounced on the left, she had sensory deficits to the umbilicus. There was a positive Babinski sign bilaterally and diminished patellar reflexes on the left. Her initial labs were significant for a WBC of 17.2 x 10^9/L (**Table 1**). Total spine MRI was significant for a segment of patchy enhancement extending from C7 to T10, consistent with transverse myelitis (**Figure 1**). An MRI of her brain without contrast showed T2 FLAIR hyperintensities. A lumbar puncture was performed, and the patient was started on a five-day course of high dose (1,000 mg) methylprednisolone. Neurology was consulted and recommended a broad work-up for the etiology of the transverse myelitis (**Figure 2**). Notable CSF findings included the absence of oligoclonal bands, bloodwork positive for an SSA of 1.6, and a mildly positive ANA titer of 1:40. On hospital day 12, her anti-AQP4 antibody resulted and was positive with a titer of 1:2,560 (**Table 1**).

The positive anti-AQP4 finding suggested a diagnosis of NMOSD, and the patient was started on a two-week 60 mg prednisone taper. Additionally, she underwent five sessions of plasmapheresis over the course of 10 days. In the setting of prolonged steroid administration, she received trimethoprim-sulfamethoxazole for pneumocystis jirovecii (PJP) prophylaxis. Physical therapy was utilized extensively for rehabilitation and pelvic floor strengthening. After 21 days of hospitalization and steroid treatment, the patient noticed significant improvement in her left peripheral vision previously believed to be a chronic complication of her diabetes, strength in her left lower extremity, and sensation. Remarkably, she was able to improve her strength to 3/5 for left hip flexion, and 4/5 for left knee extension prior to discharge to an acute rehabilitation center for further strengthening and initiation of an immunosuppressive regimen (**Figure 3**).

Table 1. Bloodwork results on admission and notable lab findings during hospitalization.

Lab	Result
BMP	
Na+	137 mEq/L
K+	3.8 mEq/L
Cl-	102 mEq/L
HCO3-	23 mEq/L
BUN	26 mg/dL
Cr	1.17 mg/dL
Glucose	67 mg/dL
CBC	
WBC	17.2 x 109/L
Hgb	12.1 g/dL
Hct	36.7%
Plt	349 x 109/L
Infectious	
EBV IgG	16.1 units/mL
HIV, HTLV I/II	NEGATIVE
RPP	NEGATIVE
Enterovirus D68	NEGATIVE
West Nile	NEGATIVE
Borrelia Burgdorferi & Lyme Ab	NEGATIVE
Blood & CSF Cultures	No Growth
Autoimmune	
anti-AQP4	1:2,560
SSA	1.6
ANA (speckled)	1:40
CRP	54.6 mg/dL
ESR	58 mm/hr
SSB	NEGATIVE
Anti-MOG	NEGATIVE
CSF	
CSF oligoclonal bands	NEGATIVE
CSF WBC	Elevated WBC, CSF IgG index
CSF Studies	NEGATIVE VDRL, VZV
CSF Cytology	13 nuc cells, 4% polys

EBV=Epstein Barr Virus, HIV=Human Immunodeficiency Virus, HTLV=Human T-cell Lymphotropic Virus, RPP=Respiratory Pathogen Panel

Figure 1. Spinal MRI showing patchy enhancement of the spinal cord extending from the level of the C7 vertebral body to the T10 level.

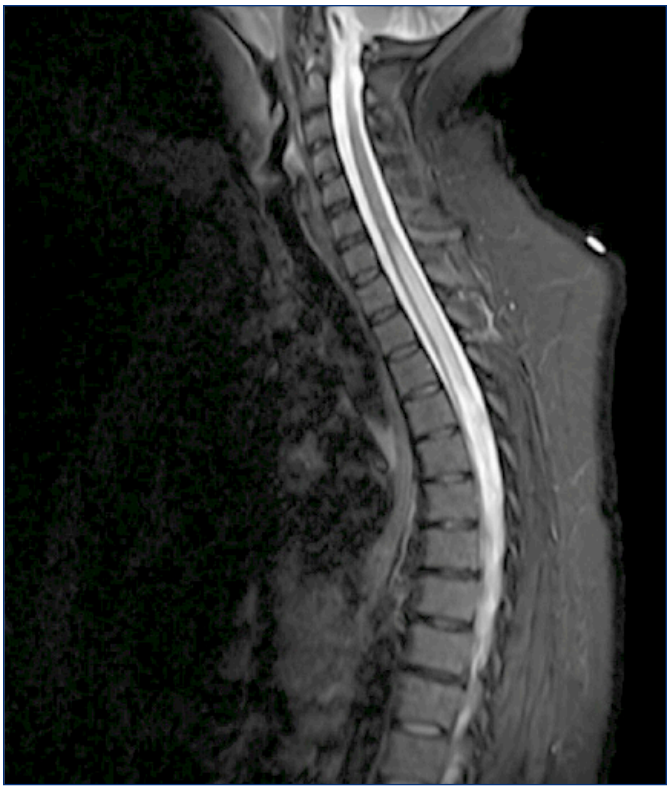


Figure 2. Differential Diagnoses for Transverse Myelitis etiologies[10]

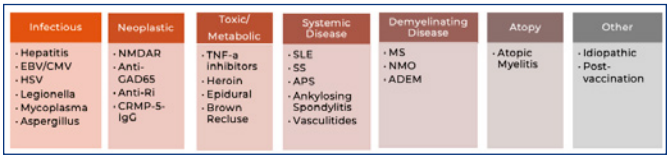
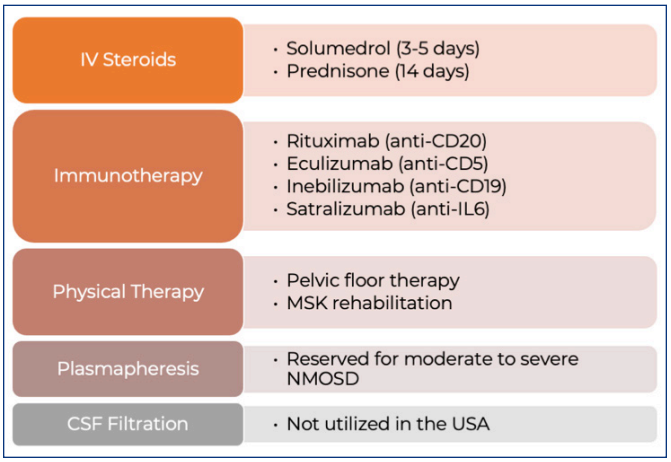


Figure 3. Therapeutic approaches in the treatment of NMOSD[13-15]



DISCUSSION

NMOSD (Devic's Disease) is an inflammatory, relapsing demyelinating syndrome of the central nervous system that preferentially affects the optic nerves and spinal cord. In NMOSD, antibodies target aquaporin-4 (AQP4) channels on the surface of astrocytes, resulting in destruction of the blood-brain barrier. Subsequently, the neuroparenchyma becomes necrotic and loses astrocyte scaffolding.[3] Anti-AQP4 antibodies have been shown to approach 100% sensitivity to NMOSD, though small studies have demonstrated 40% of patients as anti-AQP4 negative.[4,5] There appears to be a strong phenotypic overlap between NMOSD and multiple sclerosis (MS), yet the discovery of anti-AQP4 antibodies, the distinct differences in clinical responsiveness to immunotherapy, and unique histopathologic and imaging features, cements MS as a separate entity from NMOSD.[6] Unlike MS, the demyelination occurring in NMOSD is secondary to the primary immune-mediated destruction of astrocytes, concentrated in the periventricular, periaqueductal grey, and area postrema, creating the possibility for brainstem syndromes like nausea, vomiting, and intractable hiccups.[7]

Patients typically present with optic neuritis and transverse myelitis, with symptoms of acute vision loss, weakness, sensory loss, bowel/bladder incontinence, and leg pain.[8] NMOSD presenting symptoms vary widely, but optic neuritis is present in approximately 35% compared to transverse myelitis in 50% of cases. Specifically for our patient, 10 months prior to presentation, she underwent a dilated fundoscopic exam which revealed left-sided optic disc pallor and thin retinal nerve fibers concerning for optic neuritis. Despite her sequelae of symptoms, it is important to note the classic dyad of optic neuritis and transverse myelitis occurs in only 10% of patients.[9]

Patients with NMOSD have a high predilection for an array of autoimmune conditions.[10,11] Relapses are common and occur in up to 90% of individuals within one to three years of initial presentation; untreated NMOSD can lead to paraplegia, blindness, and even death within five years of the first attack.[12] Recent advancements focus on long-term immunosuppressives such as mycophenolate mofetil, azathioprine, and rituximab, with oral prednisolone for refractory cases.[13] Ongoing clinical trials investigating satralizumab, an anti-IL6 monoclonal antibody, have shown promising results with a reduction in relapses by 70–90%.[14] Similar results also exist with eculizumab, an anti-CD5 monoclonal antibody, and inebilizumab, an anti-CD19 monoclonal antibody.[15]

This presentation of seropositive NMOSD illustrates several important concepts in the management of rare disease. With typical presenting symptoms such as in our patient, it is imperative to first rule out life-threatening conditions like cerebrovascular accident (CVA) or cauda-equina syndrome. Spinal MRI with contrast is important in diagnosis to locate and characterize the degree of transverse myelitis. Our patient developed an AKI after contrast administration, thus further imaging studies including brain MRI had limited diagnostic utility. The lack of MS plaques on MRI, the patient's aggressive onset of sensory deficits, and transverse myelitis of more than three consecutive segments, ultimately made MS less likely. Furthermore, the absence of oligoclonal bands in CSF, as well as high titers of anti-AQP4 antibody, supported a diagnosis of NMOSD in the patient.

Due to the aggressive, relapsing nature of NMOSD, intravenous corticosteroid therapy is commonly the first line treatment for acute attacks. Patients who do not respond promptly to steroids may benefit from plasmapheresis. When not contraindicated, it is important to initiate early steroid administration as preventing acute relapses is the mainstay of treatment compared to preventing progression, unlike in MS.[16] Recent treatment advancements in NMOSD include long-term immunosuppressives such as mycophenolate mofetil, azathioprine, and rituximab.[13]

Despite suggestion of optic neuritis on fundoscopy prior to admission, the lack of orbital sequence studies with contrast during hospitalization precluded the diagnosis. It remained unclear whether the presenting visual deficits were from diabetic retinopathy or acute neuritis from brewing NMOSD. However, given the acute improvement in the patient's vision over the course of her hospitalization, it is most likely that the patient had optic neuritis that improved with an aggressive steroid regimen with superimposed bilateral diabetic retinopathy.

In summary, it is crucial for providers to gather comprehensive histories and neurological exams from patients, particularly those presenting with obvious deficits. In this particular case the localization and onset of symtpoms as well as the patient demographic suggested an autoimmune process over a CVA. Throughout a 24-day hospital course, the patient experienced a remarkable improvement in her visual acuity and leg strength with plasmapheresis and steroids, despite a delayed presentation. Though these symptoms may be commonly misattributed as diabetic retionapthy or neuropathy in patients with DM, it is important to consider that sometimes, something more sinister like NMOSD, may be the culprit.

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Disclosures

The authors have no conflicts of interest to report.

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