"When the wind blows, it hurts" – Neuromylitis Optica presenting with Paresthesias and Allodynia

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Abstract

Patients with Neuromyelitis Optica Spectrum Disorder (NMOSD) and Multiple Sclerosis (MS) often present with similar, nonspecific symptoms. The relationship between the two diseases has long been disputed and their comparable presentation often creates a challenge in diagnosing patients on presentation alone. In this case, we present a patient that has symptoms, imaging, and a physical exam pointing to a likely diagnosis of MS. Further abnormal MRI findings continued high concern for possible early-stage MS. However, cerebrospinal fluid analysis yielded findings that revised the diagnosis to NMOSD. This case is intriguing as it demonstrates the importance of completeness of work up as this in the end changed the management of the patient.

Key words: Neurology, Multiple Sclerosis, Neuromyelitis Optica Spectrum Disorder, and Workup

Neuromyelitis Optica Spectrum Disorder (NMOSD) is a demyelinating disease of the central nervous system (CNS) commonly affecting the optic nerve and spinal cord. Patients have wide variation in presentation but often initially present with optic neuritis. Individuals with this disease are commonly diagnosed during workup for Multiple Sclerosis (MS) due to the commonalities between the two disease presentations. Differentiating NMOSD from MS is important in guiding management, as certain therapies effective in treating MS have shown minimal success in treating NMOSD[11]. In all cases, one must rule out "MS mimickers" or in our case "NMOSD mimickers" such as Syphilis, small vessel vasculopathies, various vitamin deficiencies, and MS. The most specific diagnostic indicator of NMOSD is the presence of IgG antibodies to aquaporin-4 (AQP4-Ab). Originally, NMOSD was thought to be limited to the spinal cord, but brain lesions have been demonstrated to be more common than previously thought[1]. MRI is the ideal imaging modality for locating CNS lesions of demyelinating disease, and laboratory testing includes lumbar puncture analysis for oligoclonal bands and autoantibodies directed at the CNS.

The diagnostic dilemma in question is whether it is more important to be certain that one is correct or to conclude that the evidence points to a specific diagnosis and that "common things are common"[7]. With two clinical events separated by time and space and further evidence on imaging that the lesions appeared demyelinating in nature as they took up gadolinium, the verified McDonald Criteria became the focus of many conversations. Additionally, the presentation with both paresthesia and allodynia is a unique feature not commonly associated with diagnosis of NMOSD. Lastly, this particular case is intriguing as it demonstrates the importance of completeness in the work up which changed the management of the patient.

Case Presentation

A 44-year-old male presented to our community hospital following a neurological clinic appointment. The patient reported two neurological significant events, the first occurred five months prior (in April) and the second

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occurred four months prior (in May) to presentation. In April, he demonstrated a "pinch" in the left arm which radiated down the forearm and into his hand. He felt associated numbness and tingling, described as "hitting your funny bone," with diminished forearm strength. This lasted three weeks until the second event began.

In May, he experienced allodynia of the right flank and right lower extremity. The patient added, "when the wind blows on my leg, it hurts." He noted excruciating pain described as "burning and freezing" simultaneously. He experienced intermittent dizziness, increased fatigue, weakness of the eyebrow muscles on the left side, and minor ptosis on the left side. He denied any vision changes. He noticed a 70% loss of sensation in the glans penis, difficulty sensing urination, and allodynia during sexual intercourse. The patient reported that he had experienced worsening of symptoms under intense stress, on hot days, and when he was engaged in cardiovascular exercises. The team determined that this was very likely Uthoff's phenomenon.

The physical exam revealed mild bilateral ptosis with weakness of the left frontalis muscle. Sensory testing revealed significant allodynia throughout the right sided T4-S2 dermatomes. The patient was positive for Lhermitte's sign with flexion of the neck and positive for McArdle's sign with left-sided wrist extensor weakness.

Investigations

To narrow the differential, the following investigations included a Complete Blood Count, Complete Metabolic Panel, Computerized Tomography of the cervical, thoracic, and lumbar spine, Magnetic Resonance Imaging of the head and cervical region, and Lumbar puncture were obtained. The results of all collected labs are shown in Table 1 and all CSF studies are included in Table 2. The MRI showed a small hyperintensity in the left posterior frontal lobe (Figure 1. and Figure 2.). There was additional concern about a subtle hyper-attenuation in the C6-T1 region of the spinal cord (Figure 3.).

Differential Diagnosis

The patient presents with two different clinical events with the first LUE shooting pain in April and the second RLE severe allodynia in May. Positive physical exam findings of a positive Lhermitte's and positive McArdle's sign have high clinical association with MS diagnosis[2,3]. MRI results revealed an area of hyperintensity in the parietal lobe and hyperintensity in the C6-T1 spinal cord. The lesion in the parietal lobe was interesting, as it did not resemble Dawson's finger projections along the ventricles but rather was located along the periphery of gray-white junction. However, with two areas of damage visible on MRI, the patient was believed to meet the standards set by McDonald Criteria for diagnosis of MS. Following patient discharge, return of CSF results included absence of oligoclonal bands. At this point in time, no treatment had yet been started for MS and the patient had not yet presented for their first appointment as an outpatient. Although this does not specifically rule out a diagnosis of MS, it did raise high suspicion that an alternative explanation may exist. Shortly thereafter, AQP-4 IgG testing yielded positive results, indicating a change in leading diagnosis from MS to the similarly presenting NMOSD.

Treatment

During hospital stay, a regimen of ergocalciferol for 8 weeks duration was started, as well as Nortriptyline 20 mg QHS for pain. Furthermore, QuantiFERON gold testing and JC virus evaluation were performed in anticipation of beginning Disease Modifying Therapy (DMT). The patient was then set up with primary care follow-up with the neurology team.

Outcome and Follow-up

Total duration of inpatient stay was 4 days with initial discharge delayed due to post-LP headache from Dural puncture. Following discharge, the patient returned 2 days later with continued headache at which time Interventional Radiology placed a blood patch. He is currently undergoing trial with disease modifying medications and being followed long-term by the neurology team. At this moment in time, no cure exists for either MS or NMOSD as no remedy is able to reverse the neuronal loss from either disease. In NMOSD, treatment targets acute attack prevention in hopes of decreasing the accumulation of damage from continued attacks. NMOSD patients have shown possible benefit from highly effective disease modifying therapies including Tysabri, Alemtuzumab, and Mavenclad[4]. However, these are shown to have variable efficacy with some cases continuing to progress despite treatment, as well as a high risk of dangerous side effects[4,5]. Some less efficacious treatments aimed at lowering the effects of the complement system on the nervous system are eculizumab, satrilizumab, and inebilizumab. In very hard to control disease (otherwise known as refractory disease), patients are treated with autologous hematopoietic stem cell transplantation[6].

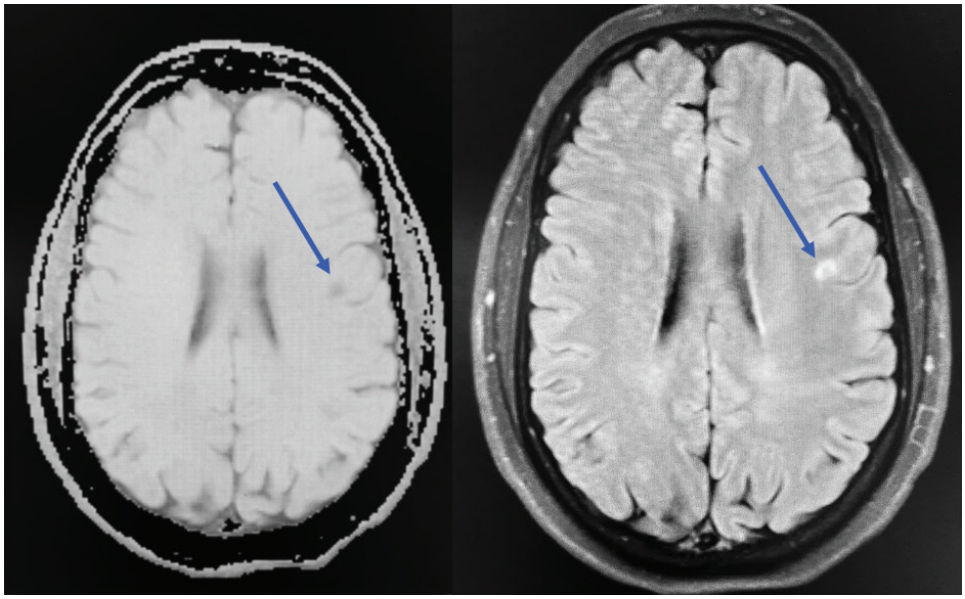

Figure 1: Magnetic Resonance Imaging - Axial images of the lesion in the frontoparietal region with T1 (Left) and T2 Flair (right) with the use of gadolinium contrast.

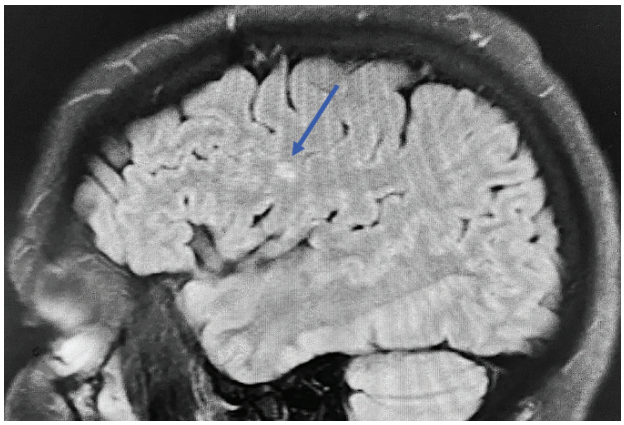

Figure 2: Magnetic Resonance Imaging -Sagittal image of the frontoparietal lesion on T2 Flair with the use of gadolinium contrast.

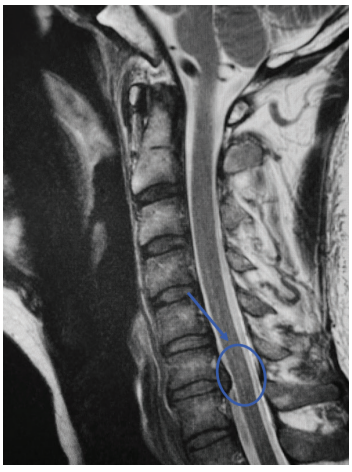

Figure 3: Magnetic Resonance Imaging -Mid-Sagittal Image of the lesion on the C6-T1 Spinal Cord with the use of gadolinium contrast

Test	Result
CMP	Within Normal Limits
CBC	Within Normal Limits
Vitamin D	21.8 ng/mL L
Vitamin B1	116 N
Vitamin B12	491 N
Folate	10 N
TSH	1.7N
T3	2.67 N
T4	0.88 N
TPO Ab	<3 N
Syphilis	Nonreactive
HIV	Nonreactive
CPK	< 10 N
Cocci	Negative
HgbA1C	5.40%
ANA	Negative
ACE	17 N
Lead	<1 mcg N
Copper	72 N
Lyme Ab	Positive
Lyme IgG, IgM	Negative
SPEP	WNL
Bartonella	Negative
ENA	Negative
MMA	136 N

Table 1: Results from Laboratory Analysis

Test	Result
CSF Claricty	Clear
CSF Color	Colorless
Tube # CSF	3
WBC (FLUID)	<3
RBC (FLUID)	<2
NEUTROPHILS (FLUID	16
LYMPHOCYTES (FLUID)	70
MONOCYTES (FLUID)	0
EOSINOPHILS (FLUID)	0
Other Cells	14
Oligoclonal Bands	Negative
Anti-AQP4 IgG	Positive

Table 2: Results from CSF analysis

Discussion

There is danger in jumping to conclusions and making statements that, "common things are common."[7] The true diagnosis was the rarer neuroimmunologic disease - NMOSD. The team initially was leaning toward a diagnosis of MS based on consideration of McDonald criteria and the presence of MRI lesions. NMOSD has been debated to be a subtype of Multiple Sclerosis, but since discovery of the AQP-4 antibody, the two have been considered distinct. This is important, as the treatment of the disease differs - "the devil is in the details". While NMOSD is similar to MS, there are enough differences to necessitate different treatment strategies[8]. One specific study showed 63% of patients with known NMOSD presented with lesions present on head MRI, and of those, 27% subsequently met criteria for MS diagnosis[9] - indicating the need for a complete workup.

This case is of particular interest as the patient did not present with any optic nerve involvement. Proper diagnosis required the team to order the specific anti-aquaporin 4 testing that took weeks for results. Had the team not obtained the AQP4-IgG testing, the patient would have undergone DMT empirically. Treatment for MS includes DMT, whereas NMOSD is typically treated with high-dose glucocorticoids and the effect of other therapies is under continued study[10]. DMT agents that have good clinical data include Tysabri, Alemtuzumab, and Mavenclad[4]. However, these are shown to have variable efficacy with some cases continuing to progress despite treatment, as well as a high risk of dangerous side effects[4,5]. Some less efficacious treatments aimed at lowering the effects of the complement system on the nervous system are eculizumab, satrilizumab, and inebilizumab. In very hard to control disease (otherwise known as refractory disease), patients are treated with autologous hematopoietic stem cell transplantation[6]. While some DMT agents may not have led to a poor outcome, the best course of treatment for this patient required the appropriate diagnosis to ensure that appropriate medical therapy could begin.

Conclusion

This presentation is reflective of the debate of the difference between NMOSD and MS. The patient fit criteria for diagnosis of MS with two lesions separated by time and space. However, the CSF showed absence of oligoclonal bands and positive AQP-4 Ab altering the diagnosis to NMOSD. This case demonstrates the importance of completing the full diagnostic workup, despite simply meeting the criteria for a diagnosis. Our understanding of NMOSD continues to grow and one cannot help but wonder how many patients have been mis-diagnosed with MS due to lack of a complete workup. The hope is that improved testing and treatments become available for each respective disease.

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