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Systemic Lupus Erythematosus and Neuromyelitis Optica Causing Hypercapnic Respiratory Failure

Authors' Contribution:

Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABCEF 1 **Bianca Dominguez**
ADEF 1 **Sarina Koilpillai**
CDF 1 **Omar Qazi**
ACE 1 **Gerson Quintero**
CE 1 **Mario Madruga**
CEF 2 **Steven J. Carlan** 

1 Department of Internal Medicine, Orlando Regional Healthcare, Orlando, FL, USA
2 Division of Academic Affairs and Research, Orlando Regional Healthcare, Orlando, FL, USA

Corresponding Author: Steven J. Carlan, e-mail: stevecarlan@gmail.com
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Patient: Female, 54-year-old
Final Diagnosis: Systemic lupus erythematosus and neuromyelitis optica
Symptoms: Chest pain • dysphagia
Medication: —
Clinical Procedure: —
Specialty: General and Internal Medicine

Objective: Rare coexistence of disease or pathology
Background: Neuromyelitis optica (NMO) is a rare neurological disease characterized by attacks of transverse myelitis and optic neuritis, contiguous spinal cord lesions on more than 3 vertebral segments on magnetic resonance imaging (MRI), and seropositivity for AQP-4 Ab. The tissue destruction from NMO is immune mediated and results in demyelination and axonal damage. Optic and spinal nerve involvement can eventually lead to blindness, weakness, and altered consciousness, and bladder and bowel involvement in some cases.
Case Report: A 54-year-old Black woman presented with chest pain, dysphagia, generalized weakness, diplopia, and paresthesias in her bilateral feet. A brain MRI revealed an area of hyperintensity in the cervical medullary junction. A diagnosis of NMO was made after the treatment response was poor for systemic lupus erythematosus (SLE) myelitis. She eventually developed acute hypercapnic respiratory failure, became encephalopathic, and was emergently intubated. She was extubated but had poor recovery and was eventually discharged home.
Conclusions: NMO is a rare immune-mediated disease that is often delayed in diagnosis and treatment. Clinical suspicion is important since there is a tendency for the disease to overlap concomitant autoimmune diseases in 25% of cases. Progressive and permanent tissue damage can occur despite the use of high-dose steroids, long-term immunosuppressant agents, immunomodulators, exchange transfusions, and even autologous hematopoietic stem cell bone marrow transplantation.

Keywords: Cardiorespiratory Fitness • Lupus Vasculitis, Central Nervous System • Neuromyelitis Optica

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Background

Neuromyelitis optica (NMO) is a rare neurological disease that was first described in 1894 by Eugene Devic. It was previously known as Devic's disease [1] and thought to be a subtype of multiple sclerosis (MS). With the discovery of anti-aquaporin 4 antibody (AQP-4 Ab), it is now recognized as its own distinct disease entity.

The etiology of NMO is unknown. The disease is characterized by attacks of transverse myelitis and optic neuritis, contiguous spinal cord lesions on more than 3 vertebral segments on magnetic resonance imaging (MRI), and seropositivity for AQP-4 Ab [1]. It is often misdiagnosed because of its protean manifestations, which include blindness, weakness, and spasm in the extremities. Occasionally, bowel and bladder dysfunction and vomiting are present.

NMO is more common in women, has a prevalence of 0.5 to 4.4 per 100 000 people, and the age of onset is typically between 35 and 42 years [2]. NMO is associated with other autoimmune diseases [1] and can occur as a primary autoimmune disorder in patients with existing systemic lupus erythematosus (SLE) [3]. As in autoimmune syndromes, the tissue destruction in NMO is immune mediated, but in this disease the pathophysiological result is demyelination and axonal damage. In NMO, the neural tissue that is damaged is primarily the optic nerve and spine.

We present a case of a patient with SLE and NMO overlap to highlight the importance of correctly diagnosing NMO, particularly in patients with an existing autoimmune disease, as delay of appropriate management can result in adverse patient outcomes in the short and long term.

Case Report

A 54-year-old Black woman with a past medical history of asthma and gallstones presented to the Emergency Department with chest pain, dysphagia, generalized weakness, diplopia, and paresthesias in her bilateral feet. Vital signs on admission were blood pressure of 135/80, heart rate of 69, temperature of 36.8°C, and oxygen saturation (SpO₂) of 99%, with the patient breathing comfortably on room air. No focal neurologic deficits were present on the initial examination. A computed tomography angiography was performed, and she was found to have an acute pulmonary embolism. An echocardiogram revealed a new diagnosis of cardiomyopathy, with an ejection fraction of 35% to 59%. MRI of the brain (**Figure 1**) revealed an area of hyperintensity in the cervical medullary junction, and a full infectious and autoimmune workup was ordered from serum and cerebrospinal fluid studies. Serologic testing

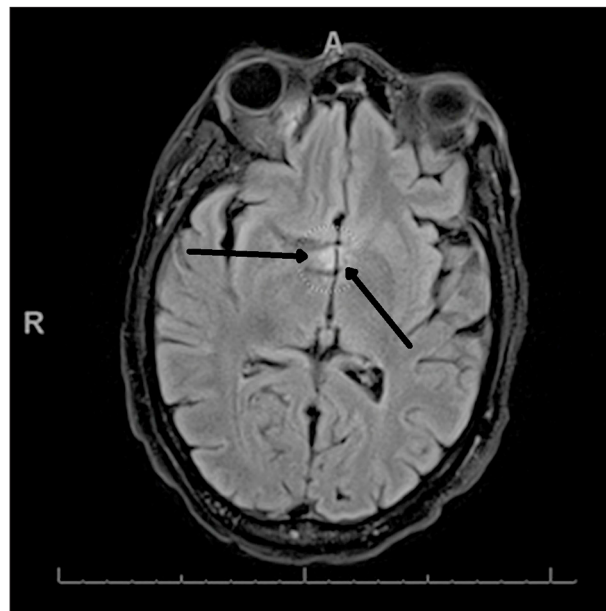


Figure 1. Magnetic resonance imaging of the brain with enhancement at the cervical medullary junction (arrows).

revealed a positive speckled anti-nuclear antibody of 1: 160 and SSA, chromatin, smith-RNP, and dsDNA antibodies, resulting in a new SLE diagnosis. The patient was started on methylprednisolone 1000 mg daily for suspected SLE myelitis, with little improvement in symptoms. The patient began to exhibit increased work of breathing and worsening of her nystagmus. A blood analysis returned positive for AQP-4-Ab, and a diagnosis of NMO was made. The patient was treated with 5 days of plasma exchange then discharged to inpatient rehabilitation on prednisone 40 mg daily. Twenty-five days into her rehabilitation stay, the patient became unresponsive and developed acute hypercapnic respiratory failure. Prior to the acute respiratory failure, the patient did not exhibit any symptoms of an acute asthma exacerbation. Her PCO₂ was 102 on arterial blood gas; she became encephalopathic, was emergently intubated, and was then transferred to the Intensive Care Unit for ventilatory support. Her acute decline did not appear to be related to an underlying asthma exacerbation. She was then started on rituximab infusion and remained intubated for 8 days. Following extubation, she was discharged back to inpatient rehabilitation. Although her respiratory status improved, she had little clinical improvement in her presenting neurological symptoms following the administration of steroids, intravenous immune globulin, plasma exchange, and 2 doses of rituximab. Due to lack of improvement and worsening of findings on a second MRI of the brain, a neuroimmunology specialist recommended starting cyclophosphamide and oral prednisone on a taper, and the patient was ultimately discharged home.

Discussion

NMO-IgG antibodies bind to the water channel aquaporin 4 (AQP4) and are specific to patients with NMO [2]. AQP4 is the most expressed channel in the brain, spinal cord, and optic nerves [4]. Within the brain, AQP4 is located in areas exposed to cerebrospinal fluid on the foot processes of astrocytes at the blood-brain barrier [4]. It is important to highlight that around 1 in 4 patients with AQP4 antibody-positive NMO have a concomitant autoimmune disease, and autoimmune diseases can have overlap in symptoms. In fact, optic neuritis is a feature in NMO but can also be seen in around 30% of patients with SLE myelitis [5]. The overlap among features of SLE, MS, and NMO highlight the importance of using AQP-4 antibodies as a tool in making the proper diagnosis of NMO. Some research also suggests that higher titers of AQP4 antibodies are seen in relapses of NMO and that a decrease in serum titers can be seen following therapy, which may suggest efficacy of certain treatments [6].

Acute treatment of NMO typically begins with the administration of high-dose steroids with methylprednisolone 1 g intravenous for 5 days, followed by oral prednisone 1 mg/kg, then followed by a taper over the course of several weeks. If patients do not improve, plasma exchange is recommended for a duration of 5 days [4]. Long-term immunosuppressant agents, such as mycophenolate mofetil and azathioprine, are used in addition to immunomodulators in the maintenance therapy for the condition [4].

Rituximab has been used as a second-line agent in the United Kingdom, and tocilizumab, methotrexate, cyclophosphamide, intravenous gamma globulin, tacrolimus, and cyclosporine have also been used [4]. Eculizumab, an anti-C5 complement inhibitor, is the only FDA-approved treatment for AQP4-Ab-positive NMO. At present, the medication is used in the prevention of attacks, but its rapid onset of action may suggest the utility of

the therapy in the treatment of acute attacks [7]. Eculizumab has been shown to reduce the rate of relapse by 94% but did not reduce the rate of progression [7].

Parenteral tocilizumab, satralizumab, and off-label use of inebilizumab have also been studied and can be considered as treatment options. Autologous hematopoietic stem cell bone marrow transplantation (AHSCBMT) has been studied in small numbers in refractory cases of NMO and has been associated with clinical and radiologic improvement in addition to improved disability [7]. Immune reconstitution therapy, such as AHSCBMT, may be preferred to long-term immunosuppressive therapies owing to their associated increased risk of infection and malignancy [7].

Conclusions

NMO is a rare entity that has clinical features similar to those of several other neurologic and rheumatologic diseases. Diagnosis of NMO is imperative, as delay in treatment or absence of appropriate treatment can result in the debility in patients. Forty-one percent of AQP4-Ab-positive patients are legally blind in 5 years, and 22% of patients will require the use of a walker 5 years after disease onset [7]. Incorrect treatment of NMO with agents used to treat MS, such as interferon beta or natalizumab, is ineffective and has been associated with exacerbation of NMO symptoms [4,6]. Future research needs to be done to develop better therapies for the acute and maintenance treatment of this disorder.

Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

References:

1. Adawi M, Bisharat B, Bowirrat A. Systemic lupus erythematosus (SLE) complicated by neuromyelitis optica (NMO – Devic's disease): Clinic-pathological report and review of the literature. *Clin Med Insights Case Rep.* 2014;7:41-47
2. Sangani V, Pokal M, Balla M, et al. A case of neuromyelitis optica spectrum disorder with coexisting systemic lupus erythematosus. *J Community Hosp Intern Med Perspect.* 2021;11(4):531-35
3. Tavor Y, Herskovitz M, Ronen G, Balbir-Gurman A. Longitudinally extensive transverse myelitis in a lupus-neuromyelitis optica overlap. *Rambam Maimonides Med J.* 2021;12(1):e0006
4. Huda S, Whittam D, Bhojak M, et al. Neuromyelitis optica spectrum disorders. *Clin Med.* 2019;19(2):169-76
5. Williams JN, Speyer CB, Kreps DJ, et al. Spinal cord syndromes in patients with systemic lupus erythematosus: Differentiating lupus myelitis, neuromyelitis optica, and multiple sclerosis. *Lupus.* 2019;28(14):1656-62
6. Jarius S, Wildemann B. Aquaporin-4 antibodies (NMO-IgG) as a serological marker of neuromyelitis optica: A critical review of the literature. *Brain Pathol.* 2013;23(6):661-83
7. Brod SA. Review of approved NMO therapies based on mechanism of action, efficacy and long-term effects. *Mult Scler Relat Disord.* 2020;46:102538