NEUROMYELITIS OPTICA SPECTRUM DISORDERS PRESENTING AS AREA POSTREMA SYNDROME (APS)

ARABELLE ABELLARD MD[1,2], MELVIN D WICHTER MD[2]
UNIVERSITY OF ILLINOIS AT CHICAGO[1]/ADVOCATE CHRIST MEDICAL CENTER[2]

UIC UNIVERSITY OF ILLINOIS AT CHICAGO

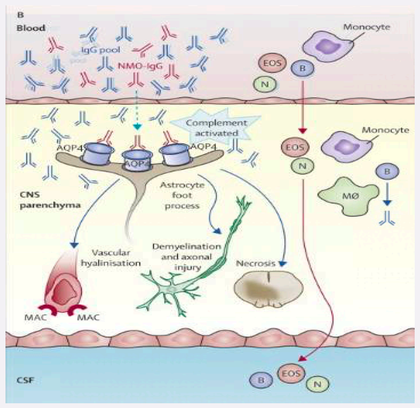
Advocate Christ Medical Center
Inspiring medicine. Changing lives.

Learning Objectives

1. Learn about neuromyelitis optica spectrum disorders (NMOSD).
2. Recognize the importance of including neuromyelitis optica spectrum disorders (NMOSD) in the differential diagnosis of a patient presenting with intractable nausea and vomiting.

Introduction

This case aims to emphasize the importance of including neuromyelitis optica spectrum disorders (NMOSD) in the differential diagnosis of a patient presenting with intractable nausea and vomiting because early diagnosis will allow for prompt initiation of treatment. NMOSD are more common in females and may be overrepresented in people of African ancestry and Asians. They are immune-mediated diseases that cause demyelination and axonal injury in the central nervous system (CNS). They can affect the optic nerves and the spinal cord, causing optic neuritis and transverse myelitis, respectively.

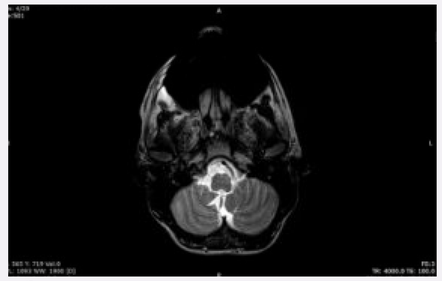


1A

Image shows NMO-IgG binding to aquaporin 4 channels in the central nervous system. Complement activation leads to increase tissue permeability, injury, necrosis and demyelination.

Case Presentation

A 46-year-old African American female with no significant past medical history presented to her local emergency department on two occasions for persistent nausea and non-bloody, non-bilious acute vomiting. She denied fevers, chills, abdominal pain, diarrhea or constipation. Each time, she was sent back home from the ED on anti-emetics. Her persistent symptoms prompted her to seek additional medical help at a tertiary medical center. While hospitalized, she complained of bilateral lower extremity tingling and lower extremity muscles weakness which quickly progressed to involve her upper extremities. She then developed hyporeflexic, flaccid quadriplegia with paresthesia, muscle spasms, bladder and bowel dysfunction and decreased discriminative touch, proprioception and vibration sense in all extremities. CT scan brain was negative. Brain and spine MRI showed cervical lesions with a long segment of intramedullary T2 signal changes measuring 4 cm in length beginning at the upper cervical spine at the C2-C3 levels and extending up to the lower brainstem-medulla region. High dose of intravenous (IV) steroids was initiated with resolution of her nausea and vomiting. She continued to remain alert, without aphasia and respiratory failure. Slit-lamp eye exam was unremarkable. Optic nerves were intact on imaging. CSF analysis showed lymphocytic pleocytosis with WBC of 765 cells/uL (96% lymphocytes), elevated protein, positive NMO-IgG antibody (or anti-aquaporin 4 Antibody or AQP4 antibody), positive Epstein-Barr virus (EBV) on polymerase chain reaction. Plasma serology revealed positive EBV IgG, but negative EBV IgM. Paraneoplastic panel and comprehensive infectious and autoimmune workups were otherwise unremarkable. A diagnosis of transverse myelitis secondary to NMOSD was made. She underwent five sessions of plasmapheresis and was continued on a maintenance dose of prednisone after seven days of high intensity daily IV steroids. She also received 2 weeks of ganciclovir without noticeable improvement. However, mild improvement was noted on imaging and physical exam after initiation of rituximab. She received two infusions of 1000 mg of rituximab two weeks apart to be followed by maintenance dosing every 6 months. Repeat MRI showed interval decrease of abnormalities in the cervical region. She was able to shrug her shoulders and move her left wrist again, but her lower extremities remained paralyzed. She was discharged to a rehabilitation facility.



1B

MRI image showing hyperintense T2 lesion in the area postrema

Discussion

The etiology is not well understood, but it is believed to be auto-immune related and mainly mediated by the humoral immune system (B-cells). Until the discovery of the antibody against the water channel protein aquaporin-4 (AQP4), NMOD were thought to be a subtype of multiple sclerosis (MS). The area postrema in the dorsal medulla, close to the fourth ventricle, can be attacked by NMO-IgG antibodies that bind to AQP4 water channels in that region and cause nausea and vomiting as seen in our patient. Our patient had met at least two of the six clinical core diagnostic criteria. Although she did not have optic nerve involvement at the time of diagnosis, she did have a long segment of upper cervical spinal cord lesions that extended into the medulla on T2-weighted MRI, CSF pleocytosis, and positivity for the CSF NMO antibody.

In the acute phase, NMOSD are treated with IV steroids and plasma exchange therapy. However, early initiation of long-term immunosuppression with rituximab, an anti-CD20 monoclonal antibody that targets B- cell mediated humoral immunity, leading to plasma cell precursors depletion, prevents attacks and causes a decrease in relapses.

Conclusion

Patients presenting with unexplained intractable nausea and vomiting should raise suspicion for area postrema syndrome, an early manifestation of NMOSD. Our patient's CSF was positive for EBV based on PCR results, and serum IgG was positive, while IgM was negative. Although some studies have suggested a potential link between EBV and MS through immunological alterations, positive CSF EBV results should be interpreted with caution. The relationship between EBV and NMOSD is uncertain at this time.

References

1. Wingerchuk DM, Banwell B, Bennett JL, et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. *Neurology.* 2015;85(2):177-189. doi:10.1212/WNL.0000000000001729
2. Waters PJ, McKeon A, Leite MI, et al. Serologic diagnosis of NMO: a multicenter comparison of aquaporin-4-IgG assays. *Neurology.* 2012;78(9):665-669. doi:10.1212/WNL.0b013e318248dec1
3. Weinshenker BG, Wingerchuk D. Neuromyelitis Spectrum Disorders. Mayo Clinic Proceed. 2017 April; 92(4): 663-679. doi:10.1016/j.mayocp.2016.12.014
4. Glisson CC. Neuromyelitis optica spectrum disorders. In: González-Scarano F, Dasje JF, ed. UpToDate 2019.www.uptodate.com. Accessed November, 2019.
5. **Figure 1A:** Wingerchuk D, Lennon VA, Lucchinetti CF, et al. The spectrum of neuromyelitis optica. Lancet Neurology. 2007 Sept 1;6(9):805-815.
6. **Figure 1B:** Hau L, Kállay K, Kertész G, et al. Allogeneic haematopoietic stem cell transplantation in a refractory case of neuromyelitis optica spectrum disorder. Multiple Sclerosis and Related Disorders. Elsevier B.V. 2020;42:A102110