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Published: 2026.XX.XXIntractable Nausea and Vomiting: A Key Feature
of Neuromyelitis Optica Spectrum DisorderAuthors' Contribution:
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Phone: 682-862-9499, e-mail: Jasmine.silva@medicalcityhealth.com
Financial support: This research was supported by HCA Healthcare and/or an HCA Healthcare affiliated entity
Conflict of interest: None declared**Patient:** Female, 22-year-old
Final Diagnosis: Neuromyelitis optica spectrum disorder (NMOSD)
Symptoms: Hiccups • nausea • weakness
Clinical Procedure: Lumbar puncture
Specialty: Neurology**Objective:** Rare disease**Background:** Area postrema syndrome (APS) can present with hiccups, nausea, or vomiting as a neurological presentation of neuromyelitis optica spectrum disorder (NMOSD). However, the diagnosis may be delayed and can result in neurological sequelae that include optic neuritis or myelitis. This report describes the case of a 22-year-old woman with intractable nausea, vomiting, and hiccups due to APS as a clinical manifestation of NMOSD.**Case Report:** A 22-year-old woman presented with a 5-week history of nausea, vomiting, and hiccups. After 3 emergency department visits, a first admission attributed her symptoms to gastroparesis on the basis of a gastric emptying study showing delayed emptying. Symptoms persisted despite antiemetic and prokinetic therapy, and she was readmitted 2 weeks later with new persistent hiccups and progressive bilateral upper-limb weakness. Magnetic resonance imaging (MRI) of the head and cervical spine demonstrated an expansile T2-hyperintense lesion of the dorsal lower medulla and upper cervical cord. Given a high suspicion for a demyelinating attack, plasma exchange and high-dose intravenous corticosteroids were started before serology results returned. Serum aquaporin-4 immunoglobulin G (AQP4-IgG) was subsequently positive, establishing AQP4-IgG-positive NMOSD. Motor function improved after 7 plasma exchange sessions and rehabilitation, and she regained ambulation with a walker.**Conclusions:** This report describes APS as the initial manifestation of NMOSD in a young woman whose intractable nausea, vomiting, and hiccups were first attributed to gastroparesis. NMOSD should be considered when unexplained nausea, vomiting, or hiccups persist beyond 48 hours, since prompt MRI and AQP4-IgG testing allow immunotherapy to begin without delay.**Keywords:** Demyelinating Diseases • Gastroparesis • Nausea • Area Postrema • Neurology • Neuromyelitis Optica • Aquaporin 4 • Case Reports**Full-text PDF:** <https://www.amjcaserep.com/abstract/index/idArt/954044> 2579 — 1 10

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Introduction

Neuromyelitis optica spectrum disorder (NMOSD) is a rare, antibody-mediated inflammatory and demyelinating disease of the central nervous system (CNS) that primarily affects the optic nerves, spinal cord, and brainstem [1,2]. The disorder is defined by 6 core clinical syndromes classified by their anatomical location: optic neuritis, acute myelitis, area postrema syndrome (APS), acute brainstem syndrome, symptomatic narcolepsy or acute diencephalic syndrome, and symptomatic cerebral syndrome [1]. The estimated prevalence of NMOSD is 0.3 to 4.4 per 100 000 population [2]. NMOSD accounts for 1% to 2% of all cases of CNS inflammatory demyelinating disease in the United States and Europe, with multiple sclerosis being far more common [2,3]. Approximately 80% of affected patients are women, and onset most often occurs between 30 and 40 years of age, although the disorder can affect individuals of any age [2,4].

Most patients present with optic neuritis or longitudinally extensive transverse myelitis, producing visual impairment, motor weakness, sensory loss, and sphincter dysfunction [1,2]. Diagnosis follows the 2015 international consensus criteria, which require at least 1 core clinical characteristic together with a positive serum aquaporin-4 immunoglobulin G (AQP4-IgG) assay and the exclusion of alternative diagnoses [1]. AQP4-IgG is detectable in approximately 60% to 90% of patients with NMOSD, and magnetic resonance imaging (MRI) performed with and without gadolinium supports the diagnosis by demonstrating characteristic inflammatory lesions [1,2]. Acute attacks are treated with high-dose intravenous methylprednisolone, with plasma exchange (PLEX) added for severe or corticosteroid-refractory attacks; earlier initiation of PLEX is associated with better recovery [2,5]. Because 80% to 90% of patients follow a relapsing course, long-term relapse prevention with rituximab, azathioprine, or mycophenolate mofetil, or with newer targeted biologic agents, is required [2].

APS results from inflammation of the area postrema, a circumventricular organ in the dorsal medulla that lies outside the blood–brain barrier and is rich in aquaporin-4, making it particularly susceptible to AQP4-IgG [2,6]. Area postrema syndrome is defined as an episode of otherwise unexplained hiccups, nausea, or vomiting lasting more than 48 hours [1]; it is the presenting feature of NMOSD in approximately 10% of patients and occurs at some point during the disease course in 15% to 40% of patients [7,8]. Detection of a lesion in the dorsal medulla on MRI supports the diagnosis, although such lesions are small and may be visible only briefly [9]. Acute treatment is that of any NMOSD attack, with intravenous corticosteroids and PLEX [2,5].

Because gastrointestinal symptoms dominate the presentation, patients with isolated APS are typically evaluated first by

internists or gastroenterologists, and the diagnosis of NMOSD may be delayed until further neurological symptoms emerge [6,9,10]. Ranjan et al described a case of an elderly woman who presented to a gastroenterology clinic with 3 weeks of nausea, vomiting, and hiccups and a normal upper gastrointestinal endoscopy result, and who was subsequently found to be double-seropositive for AQP4 and myelin oligodendrocyte glycoprotein (MOG) antibodies [6]. Raj et al reported a case of a 25-year-old woman with 3 weeks of persistent vomiting and intractable hiccups whose extensive gastroenterological evaluation result was normal, and in whom MRI showed a dorsal medullary lesion despite negative AQP4-IgG and MOG antibodies [10]. The present report describes the case of a 22-year-old woman with intractable nausea, vomiting, and hiccups due to APS as a clinical manifestation of NMOSD.

Case Report

A 22-year-old Hispanic woman with a past medical history of autism spectrum disorder presented with a persistent 5-week history of nausea and vomiting. Prior to this admission, she had presented to the emergency department on 3 separate occasions, with symptoms attributed to a urinary tract infection on 2 visits and viral gastroenteritis on a third. During her first inpatient admission, gastroenterology was consulted; esophagogastroduodenoscopy (EGD) and gastric emptying study were performed, revealing delayed gastric emptying consistent with gastroparesis. She was treated with intravenous metoclopramide and discharged after tolerating oral intake.

She returned 2 weeks later with recurrent nausea, vomiting, and new-onset persistent hiccups. Her mother reported that she had been unable to tolerate solid foods and could only consume liquids. She was again treated with metoclopramide, and nutrition services were consulted; total parenteral nutrition (TPN) was initiated given her moderate protein-calorie malnutrition. Over the course of this hospitalization, her mother noted progressive generalized weakness affecting both upper extremities bilaterally, to the extent that the patient could no longer hold objects such as her phone or perform activities of daily living such as feeding herself or using the restroom independently.

Given the progressive distal muscle weakness and gradual dysphonia, magnetic resonance imaging (MRI) was ordered. The initial scan was non-diagnostic due to severe motion artifact. As the patient continued to deteriorate with worsening flaccid paralysis, neurology was consulted and recommended MRI of the head, cervical spine, and thoracic spine with and without intravenous contrast.

Imaging demonstrated an expansile T2-hyperintense lesion with ill-defined margins and mild heterogeneity involving the

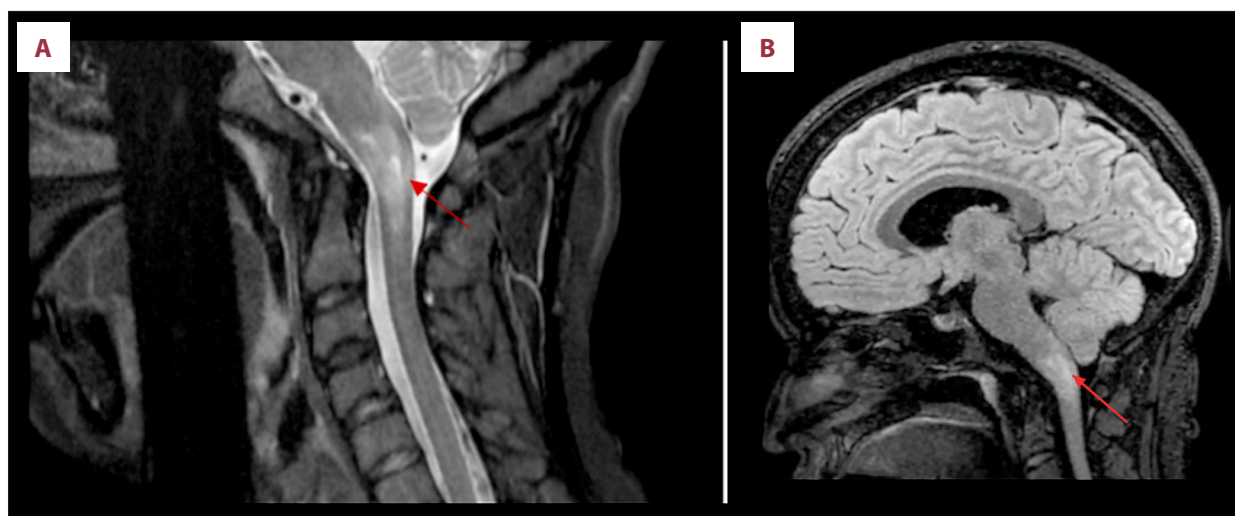


Figure 1. Magnetic resonance imaging (MRI) of the brain and cervical spine in a 22-year-old woman with area postrema syndrome as the presenting manifestation of neuromyelitis optica spectrum disorder. (A) Sagittal T2-weighted MRI of the cervical spine (C-spine), acquired without intravenous contrast, showing an expansile T2-hyperintense lesion with ill-defined margins and mild internal heterogeneity involving the dorsal aspect of the lower medulla and the upper cervical spinal cord, measuring 2 cm in craniocaudal extent (red arrowhead). (B) Midline sagittal MRI of the brain from the same examination, acquired with and without intravenous contrast, showing the cranial extent of the same lesion within the dorsal medulla in the region of the area postrema. On this sequence the lesion was better visualized and measured approximately 3 cm in craniocaudal extent.

dorsal aspect of the lower medulla and the upper cervical cord, measuring 2 cm in craniocaudal extent on the sagittal cervical spine sequence and approximately 3 cm on the brain study, raising concern for a demyelinating process (Figure 1). The location of this lesion in the dorsal medulla, in the region of the area postrema, satisfied the second diagnostic requirement for APS [1]. The patient was transferred to the intensive care unit (ICU), where she underwent a lumbar puncture, and several cerebrospinal fluid (CSF) studies were ordered, including a multiple sclerosis panel with oligoclonal bands, cytology, human T-lymphotropic virus (HTLV)-1/2 testing, angiotensin-converting enzyme (ACE), Lyme antibody with western blot, aquaporin-4 cell-based assay (CBA), CSF glucose, CSF protein, and CSF cell count with differential. Serum studies were also obtained, including sarcoid testing, aquaporin-4 CBA, Sjogren's antibodies, West Nile virus testing, and Lyme titer with western blot. Most of these study results take 4 to 5 days to return. However, because there was high suspicion for a demyelinating condition, the patient was subsequently started on plasma exchange therapy and high-dose corticosteroids. These investigations were undertaken to exclude infectious, granulomatous, neoplastic, and alternative autoimmune causes of a medullary and cervical cord lesion, as required before APS can be attributed to NMOSD [1].

These results returned over the following 4 to 5 days. The cerebrospinal fluid obtained at lumbar puncture (18 mL) was clear and colorless, with 2 white blood cells/microL, no red

blood cells, a protein of 34 mg/dL, and a glucose of 74 mg/dL, all within normal limits. Oligoclonal bands were requested but result were not obtained. A CSF meningitis and encephalitis multiplex polymerase chain reaction (PCR) panel detected no organisms, with *Escherichia coli* K1, *Haemophilus influenzae*, *Streptococcus agalactiae*, *Streptococcus pneumoniae*, *Cryptococcus neoformans/gattii*, cytomegalovirus, herpes simplex virus 2, human herpesvirus 6, human parechovirus, and varicella zoster virus all not detected. Cryptococcal antigen, Lyme PCR, HTLV-1/2 serology, and West Nile virus CSF immunoglobulin G (IgG) were negative, and serum *Treponema pallidum* antibody and human immunodeficiency virus (HIV)-1/2 antibody were non-reactive. Toxoplasma IgG and IgM were both below 3, and *Blastomyces* and *Coccidioides* antibodies were negative.

Angiotensin-converting enzyme was 15 U/L and serum tryptase was 1.3 ng/mL, both within normal limits, providing no support for neurosarcoidosis or a mast cell disorder as a cause of the intractable vomiting. The Sjogren antibody panel was negative, with anti-SSA and anti-SSB antibodies both below 0.2. CSF and serum protein analysis showed a CSF IgG of 2.3 mg/dL against a serum IgG of 917 mg/dL, and a CSF albumin of 14 mg/dL against a serum albumin of 4.1 g/dL, yielding a CSF IgG index of 0.7 and an albumin index of 3. These indices indicate an intact blood-brain barrier without evidence of intrathecal IgG synthesis, a pattern more consistent with NMOSD than with multiple sclerosis, in which intrathecal IgG

synthesis is characteristic. Aquaporin-4 IgG was detected in the cerebrospinal fluid. The absence of pleocytosis and the normal CSF protein do not argue against an acute NMOSD attack, as cerebrospinal fluid analysis in APS is frequently unremarkable [10]. Antibodies to myelin oligodendrocyte glycoprotein (MOG) were not tested in this patient.

The patient received a total of 7 plasma exchange (PLEX) sessions. She became more responsive after the second session, with a stronger voice and the ability to lift both arms off the bed, right more than left. Following completion of PLEX, intravenous steroids were transitioned to an oral steroid taper. Serologic testing of the serum aquaporin-4 CBA ultimately confirmed seropositivity for AQP4-IgG, fulfilling the third diagnostic requirement and establishing a diagnosis of AQP4-IgG-positive NMOSD with APS as its presenting core clinical syndrome [1]. The patient engaged in daily physical therapy and was gradually able to feed herself, grasp objects, and sit upright in bed with assistance. Upon discharge, neurology recommended outpatient follow-up with a neuroimmunologist. The patient was transferred to a skilled nursing facility and subsequently regained the ability to ambulate with the assistance of a walker.

Discussion

This case demonstrates numerous important lessons. First, APS can be the first manifestation of NMOSD in a young adult and can persist for weeks before any neurological sign appears. Second, the presence of an objective abnormality on gastrointestinal testing—here, delayed gastric emptying—can appear to explain the symptoms convincingly and thereby anchor the diagnosis away from the CNS. Third, when the clinical and radiological picture is characteristic, initiating immunotherapy before AQP4-IgG serology returns can limit neurological disability [5].

This case highlights the diagnostic challenges faced with clinical presentation alone for a demyelinating disorder, particularly when neurological deficits appear late. The persistent nausea and vomiting with which the patient presented were less likely due to a urinary tract infection or idiopathic gastroparesis than to APS. The gradual development of neurological deficits in conjunction with an inflammatory medullary lesion on MRI supported the diagnosis of NMOSD [1]. Diagnosis of NMOSD is nearly certain if there is a characteristic first attack and AQP4-IgG antibodies are present [9]. In our case, serology would have taken an additional 4 to 5 days and would have further delayed treatment of a patient who, as is now known, was experiencing an acute NMOSD attack.

Our patient's course both resembles and differs from previously published presentations of APS in instructive ways. As

in the case reported by Ranjan et al, in which an elderly woman presented to a gastroenterology clinic with 3 weeks of nausea, vomiting, and hiccups and a normal upper gastrointestinal endoscopy, and in the case reported by Raj et al, in which a 25-year-old woman underwent extensive and unremarkable gastroenterological evaluation for 3 weeks of vomiting and intractable hiccups, our patient was investigated first for a gastrointestinal cause [6,10]. In all 3 cases the eventual diagnosis rested on the recognition of a dorsal medullary lesion on MRI [6,10]. The cases differ in 2 respects that are relevant to clinical practice. Both previously published cases had a normal gastrointestinal evaluation, whereas our patient had a positive gastric emptying study, which provided an apparently sufficient explanation for her symptoms and plausibly contributed to the longer interval before neuroimaging was obtained. In both of the previously published cases, the patients also remained neurologically well or nearly so at diagnosis and were treated with corticosteroids alone, with symptomatic improvement [6,10]. Our patient, by contrast, progressed to flaccid quadriplegia and dysphonia requiring intensive care and 7 sessions of PLEX in addition to high-dose corticosteroids. Her course therefore illustrates the neurological sequelae that can follow when APS is not recognized early, and supports the addition of PLEX to corticosteroids in severe attacks [5].

The 2 previous published cases also illustrate the range of serological findings in APS. The patient of Ranjan et al was double-seropositive for AQP4 and MOG antibodies, and the patient of Raj et al was seronegative for both yet was still diagnosed with NMOSD on clinical and radiological grounds [6,10]. Our patient was AQP4-IgG seropositive, which is the most straightforward serological scenario, but these comparisons show that a negative AQP4-IgG result does not exclude the diagnosis and should not on its own prompt abandonment of the diagnostic pathway [1].

Confirmation of diagnosis in our case rested primarily on the medullary lesion demonstrated on MRI and positive AQP4 antibody serology. International consensus-based diagnostic criteria for NMOSD require manifestation of 1 or more of the 6 core clinical syndromes, with a positive serum AQP4-IgG test serving as the key distinguishing serologic marker and with exclusion of alternative diagnoses [1]. Notably, detection of a dorsal medullary lesion on MRI is confirmatory for area postrema syndrome, though these lesions are small and visible only briefly [9]. In our patient, the combination of characteristic imaging findings and AQP4 seropositivity established the diagnosis. Treatment response to plasma exchange and high-dose corticosteroids was clinically reassuring and consistent with NMOSD, although treatment response alone is not considered definitive diagnostic proof.

This case demonstrates how a broad symptomatology such as nausea and vomiting can easily mimic other disease processes.

It also demonstrates the need to maintain a broad differential diagnosis when other treatments have failed, including anti-biotics, prokinetics, and antiemetics. This report has limitations. MOG antibodies were not tested, so MOG antibody-associated disease was not formally excluded by serology; however, the patient was seropositive for AQP4-IgG in both serum and cerebrospinal fluid, which establishes NMOSD under the 2015 consensus criteria, and double seropositivity of the kind reported by Ranjan et al is rare [1,6]. Oligoclonal bands were requested but results were not obtained, although the normal CSF IgG index and albumin index indicate an absence of intrathecal IgG synthesis. As these observations derive from a single case, they should be interpreted as illustrative and hypothesis-generating rather than as establishing a definitive diagnostic algorithm or confirming treatment efficacy.

Conclusions

This case report describes the case of a 22-year-old woman in whom persistent nausea, vomiting, and hiccups were initially diagnosed as gastroparesis, with NMOSD only identified after neurological decline prompted further evaluation. Diagnosis was established through the combination of a dorsal medullary lesion on MRI and confirmed AQP4-IgG seropositivity; treatment response to plasma exchange and corticosteroids was clinically beneficial and consistent with the diagnosis.

Clinicians should maintain NMOSD in the differential diagnosis when patients present with unexplained intractable gastrointestinal symptoms, particularly nausea, vomiting, and hiccups persisting beyond 48 hours, especially when neurological signs evolve. In such cases, timely MRI, CSF evaluation, and AQP4-IgG testing are essential to confirming the diagnosis and initiating appropriate immunotherapy without delay.

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Statement

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Consent

Written informed consent was obtained from the patient for their anonymized information to be published in this article. Documentation of written consent can be provided upon request.

AI Disclosure

The authors used the AI tool Claude during the preparation of this manuscript for improving readability of the Background and Discussion sections and restructuring the manuscript to the journal's case report format. The tool was not used to generate, analyze, or interpret clinical data, and it was not used as a source of medical information. All clinical details, imaging findings, and laboratory results were obtained from the patient's medical record by the authors. The authors reviewed and edited all AI-assisted text, verified every reference against the primary source, and take full responsibility for the content and integrity of the manuscript.

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