Seronegative Neuromyelitis Optica Spectrum Disorder: An Unusual Presentation of Acute Brainstem Syndrome

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Patient: Female, 27-year-old
Final Diagnosis: Acute brainstem syndrome • seronegative neuromyelitis optical spectrum disorder
Symptoms: Dysphagia • dysphonia • hoarseness • vomiting
Medication: —
Clinical Procedure: —
Specialty: —

Objective: Unusual clinical course
Background: Neuromyelitis optica (NMO) is an autoimmune, demyelinating, inflammatory disorder affecting the central nervous system, mostly targeting optic nerves and the spinal cord. NMO spectrum disorder (NMOSD) is a newly revised nomenclature in which new diagnostic criteria have been developed, including serological testing of serum aquaporin-4 immunoglobulin G (AQP4-IgG) antibodies. Results of a negative antibody will group the patient in a seronegative subgroup.

Case Report: We describe the case of a 27-year-old female who presented to our hospital with new onset of sudden unexplained vomiting, dysphagia, dysphonia, and food regurgitation. Extensive investigations were done and brain magnetic resonance imaging (MRI) showed a small nonspecific area of signal abnormality in the right dorsal medulla. Aquaporin-4 antibodies were negative, and the patient was diagnosed with seronegative NMOSD with acute brainstem syndrome after meeting the diagnostic criteria. The patient’s condition improved after steroids administration.

Conclusions: We report an unusual presentation of seronegative NMOSD presenting with acute brainstem syndrome.

MeSH Keywords: Aquaporin 4 • Brain Stem • Dysphonia • Neuromyelitis Optica • Vomiting

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**Background**

Neuromyelitis optica (NMO) is considered a rare, autoimmune, inflammatory and demyelinating disease targeting the central nervous system. Previous NMO diagnostic criteria include involvement of the optic nerves and the spinal cord, but more or less central nervous system manifestations might be present [1]. Neuromyelitis optica spectrum disorder (NMOSD) is a newly revised nomenclature, where recent studies developed new diagnostic criteria which included serological testing of serum aquaporin-4 immunoglobulin G antibodies (AQP4-IgG).

Diagnostic criteria of NMOSD with AQP4-IgG requires at least 1 core clinical characteristic or magnetic resonance imaging (MRI) finding related to optic neuritis, acute myelitis, area postrema syndrome, acute brainstem syndrome, diencephalic, or cerebral syndromes. For the diagnosis of NMOSD without AQP4-IgG, more comprehensive clinical requirements with additional neuroimaging findings are needed [1]. The literature supports that AQP4-Ab testing is important in establishing the diagnosis of NMOSD; however, results showing negative antibodies will group the patients in a seronegative subgroup [2].

The presence of brainstem symptoms with the involvement of area postrema might contribute to the presentation of unexplained nausea and vomiting and mostly associated with medullary lesions on the brain MRI [3].

**Case Report**

A 27-year-old female, who had papillary thyroid cancer with a status of post total thyroidectomy with bilateral neck dissection and radioactive iodine, presented to our hospital complaining of hoarseness of voice, vomiting, dysphagia, and food regurgitation that started 4 days before her presentation. Her symptoms occurred after an upper respiratory tract infection and were gradual in onset.

The patient reported an episode of change in voice after her thyroidectomy, which was done 4 years prior, that resolved a few days later. She had no allergies and denied taking any home medications. She reported a history of 2 abortions both in her first trimester. Her history was negative for smoking tobacco, drinking alcohol, or drug abuse. Her travel history was insignificant. The patient was admitted, and the endocrine surgeon evaluated her and confirmed that her symptoms were not related to her previous thyroid surgery since her computed tomography (CT) scan was unremarkable for any active changes.

On general examination, the patient was alert and oriented to time, person, and place.

On head and neck examination, her throat was congested without tonsillar enlargement or presence of exudates; an endoscopy showed vocal cord paralysis and pooling of saliva. Dysphonia was noticed and described as hypernasality.

The cranial nerve examination showed equal and reactive pupils bilaterally, full extraocular movements with no diplopia, pain, or nystagmus, and normal facial sensation without facial weakness; the uvula was deviated to the left and gag reflex was absent when stimulating the soft oropharynx, the tongue was central with no atrophy. The rest of the examination was unremarkable. The patient was given a single dose of dexamethasone 8 mg intravenous (IV) and ceftriaxone 1 mg IV.

Further workup was done to investigate possible gastroenterology, neurology, and autoimmune causes. Modified barium swallow test was performed, and mild pharyngeal dysphagia was seen by mild to moderate residues in valleculae and pyriform possibly due to weak muscle contraction. No aspiration or penetration was observed with all tested consistencies. A primary Speech Pathologist was consulted, and a special diet was recommended to the patient. A lumbar puncture was performed, and results are shown in Table 1.

The autoimmune workup was significant for increased anticardiolipin IgM and increased IgG (all subsets), aquaporin-4 antibodies, antinuclear antibody, oligoclonal bands (OCBs), and paraneoplastic panel were all negative.

The CT head and neck scans were unremarkable for any lesions, while the MRI of the brain showed a small nonspecific area of signal abnormality in the right dorsal medulla (Figure 1), and a

| **Table 1. Results of lumbar puncture.** |
|-----------------------------------------|
| **Color** | **Colorless** |
| RBC | 2 cells/µL |
| WBC | 14* cells/µL |
| Lymphocytes | 96 cells/µL |
| Monocytes | 3 cells/µL |
| Appearance | Clear |
| Neutrophils | 1 cells/µL |
| Oligoclonal bands, CSF | Negative |
| Glucose, CSF | 3.18 mg/dL |
| Protein, CSF | 342 mg/dL |
| IgG, CSF | 48 mg/dL |
| CSF culture and Gram | Negative |

RBC – red blood cells; WBC – white blood cells; CSF – cerebrospinal fluid (CSF); IgG – immunoglobulin G.
2.4 mm area of hypoenhancement in the pituitary gland which might represent a small incidental microadenoma.

The patient was treated with prednisone 50 mg orally for 5 days, and she showed improvement in her voice and swallow. She was discharged with neurology follow-up in the outpatient clinic.

Discussion

Our patient presented with unexplained vomiting, dysphagia, dysphonia, and food regurgitation. MRI of the brain showed the presence of a small nonspecific area of signal abnormality in the right dorsal medulla; and cerebrospinal fluid (CSF) showed negative AQP4-IgG. These findings met the diagnostic criteria of NMOSD without AQP4-IgG [1]. Two cases reported in 2016 and 2019, one a patient complaining of lower limbs numbness, weakness, blurred vision, and urinary retention, and the other case a patient complaining of lumbar pain, bilateral ataxia, central facial palsy, ophthalmoparesis, and urinary retention. Both cases had an absence of aquaporin-4 antibodies; the diagnosis of NMOSD was established in the presence of multiple core clinical characteristic and MRI findings [2,4]. A case of isolated brainstem syndrome with an unusual presentation was reported in 2019, the diagnosis of NMOSD was established after the detection of elevated levels of AQP4-IgG, and the presence of hyperintense lesion identified at the lower medulla on MRI brain [5]. In 2015, a case of pediatric NMO with muscle and lung involvement in addition to central nervous system disease was reported, which suggests that multiple systems can be involved in NMO including non-infectious pulmonary findings [6]. Another report suggested that miscarriage of pregnancy might be related to anti-aquaporin-4 antibodies, however, more studies are needed to assess and confirm this relationship [7]. Intractable nausea and vomiting are related to area postrema (AP) syndrome which can be the first sign of NMO when neurological signs and symptoms are not present. Early diagnosis following complete history and physical examination and early treatment are important factors that can lead to better prognosis [8]. In 2012, a case of anorexia and weight loss with positive aquaporin-4 antibody and MRI lesions in the medulla, pons, and thalamus was suggested to be part of NMOSD due to AP involvement [9].

Other studies have reported the efficacy of immunosuppressive therapy in reducing NMOSD activity and preventing future attacks. In many neurologic diseases, including NMOSD, low dose oral corticosteroids have been used. Oral prednisone has also been used as a co-medication during the first few months of therapy with azathioprine, a purine analog that has antiproliferative and immunosuppressive effects that works as an anti-metabolite and reduces lymphocytes differentiation. Other studies have described significant improvement of the disease after rituximab and mycophenolate mofetil administration [10]. Plasma exchange has been suggested as a rescue treatment for patients with severe symptoms not responding to steroids [11].

Conclusions

This report discussed the case of a 27-year-old female who presented to our hospital with unexplained vomiting, dysphagia, dysphonia, and food regurgitation. On examination, a deviated uvula and absent gag reflex were observed. MRI of the brain showed a small nonspecific area of signal abnormality in the right dorsal medulla. CSF was negative for AQP4-IgG, confirming the diagnosis of seronegative NMOSD with acute brainstem syndrome. This is an unusual presentation of seronegative NMOSD which is limited specifically to acute brainstem symptoms in the absence of optic neuritis and transverse myelitis symptoms that will contribute to the few cases reported in the literature.

Conflict of interest

None.
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