

Gastroparesis as the Sole Presenting Feature of Neuromyelitis Optica

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ABSTRACT

A 33-year-old African-American woman recently diagnosed with severe idiopathic gastroparesis was readmitted for hypoxic respiratory failure secondary to aspiration pneumonia. A fiber-optic endoscopic evaluation of swallow study revealed severe pharyngeal dysphagia. Brain magnetic resonance imaging showed an ill-defined lesion in the posterior aspect of the medulla concerning for a demyelinating process. Serum neuromyelitis optica immunoglobulin G returned positive. Neuromyelitis optica treatment resulted in the patient's clinical improvement. She is currently on a suppressive regimen of intravenous rituximab and is recovering well.

INTRODUCTION

Gastroparesis is characterized by partial paralysis of the stomach, and its cause is often undetermined, although it is sometimes linked to diabetes, collagen vascular disease, neurological disorders, viral illness, surgical complications and drug side effects.^{1,2} Rarely, gastroparesis can result from central nervous system demyelinating diseases such as multiple sclerosis (MS).³⁻⁹ To our knowledge, neuromyelitis optica (NMO), another demyelinating disease, has only been documented as the likely cause of gastroparesis in one case report in the literature.⁴

CASE REPORT

A 33-year-old African-American woman with no prior medical issues was admitted to the hospital with several weeks of intractable nausea, vomiting, and early satiety. The patient denied fever, diarrhea, or sick contacts, and she denied the use of prescription medication or illicit drugs including opiates/opioids. Blood work, including glucose, hemoglobin A_{1c}, electrolytes, thyroid function tests, and β -human chorionic gonadotropin, were all within normal limits. Gastroenterological evaluation with an esophagogastroduodenoscopy showed moderate esophagitis and a 1.5-cm hiatal hernia. Abdominal computed tomography showed no evidence for gastric outlet obstruction. She was discharged on treatment with pantoprazole 40 mg twice a day for 2 weeks, then once daily for 2 weeks, for the esophagitis, as well as erythromycin 250 mg 4 times per day for 5 days and metoclopramide 10 mg 4 times per day as needed for nausea.

Despite appropriate use of the prescribed medications, the patient's gastrointestinal (GI) symptoms worsened, leading to readmission 1 month later. The GI symptoms led to anorexia and an unintended weight loss of 10 kg over 1 month. She also complained of fatigue but denied focal neurological deficits or vision loss. Repeat blood work remained within normal limits, and physical exam was grossly normal. A scintigraphic gastric emptying study showed 95% retention at the end of 4 hours, consistent with severe gastroparesis. A nasojunal tube was placed to optimize her nutritional status, and an outpatient evaluation for gastric pacemaker placement was

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Figure 1. T2-weighted magnetic resonance imaging (MRI) at the level of the cervicomedullary junction showing an ill-defined area of increased signal posterior and lateral to the left, tracking caudally into the region of the vagal nuclei of the medulla, representative of demyelination.



Figure 2. T2-weighted MRI at the cervicomedullary junction 5 months later, showing the lesion volume decreased by 92% and no longer exhibiting signal enhancement, suggesting a regression of demyelination.

planned for the working diagnosis of idiopathic gastroparesis. The patient was discharged with home tube feeding along with pantoprazole 40 mg daily and metoclopramide 5 mg 4 times a day as needed. Within 2 days, the patient returned to the hospital for hypoxic respiratory failure secondary to aspiration pneumonia.

Apart from appearing very fatigued and dyspneic, the physical exam was grossly unremarkable. Neurological exam showed that the patient's visual fields and all cranial nerves, including extraocular muscles, were intact. She exhibited normal strength, tone, and sensation in her extremities, and her reflexes were brisk and equal bilaterally. Babinski sign was absent, and cerebellar testing showed no deficits. A fiberoptic endoscopic evaluation of swallow study revealed severe pharyngeal dysphagia, prompting magnetic resonance imaging (MRI) of the patient's brain and spine that showed an ill-defined lesion in the posterior aspect of the medulla concerning for glioma versus a demyelinating process (Figure 1). Cerebral spinal fluid studies revealed normal opening pressure, cell count and differential, cytology, and no oligoclonal bands. Cerebral spinal fluid NMO-immunoglobulin G (IgG)

was negative. Additional negative lab tests included cerebral spinal fluid venereal disease, anti-voltage gated calcium channel antibodies, striated muscle IgG, serum electrophoresis, serum and cerebral spinal fluid West Nile IgM, electromyography, and anticholinesterase antibodies. Serum NMO-IgG returned positive, prompting the initiation of intravenous methylprednisolone 1 g daily for 5 days. The patient did not improve, so she underwent 5 sessions of plasma exchange. Dysphagia had only modestly improved after steroids and plasma exchange, so a percutaneous endoscopic jejunostomy tube was placed prior to discharge. A modified barium swallow 1 month after discharge showed resolution of dysphagia. The percutaneous endoscopic jejunostomy tube was removed, and the patient has tolerated a regular diet with a 15-kg weight gain 2 months after hospital discharge. MRI of the cervicomedullary junction 5 months after presentation showed the lesion volume decreased by 92% and no longer exhibited signal enhancement, suggesting a regression of demyelination (Figure 2). The patient is currently on a suppressive regimen of intravenous rituximab 1,000 mg with 2 sessions administered 2 weeks apart every 6 months.

DISCUSSION

Intractable nausea and vomiting is a commonly encountered problem in the hospital and outpatient setting. In rare instances, the cause stems from vagal nerve nuclei lesions that, in turn, disrupt autonomic signals necessary to generate the gastric migrating motor complex.^{4,5,8,10} NMO is one autoimmune demyelinating disease that, like MS, has been associated with intractable nausea and vomiting secondary to medullary inflammation.¹¹⁻¹⁴ Unlike MS-induced gastroparesis, however, intractable nausea and vomiting associated with NMO likely stems from inflammation of the area postrema secondary to autoantibodies (NMO-IgG) against the aquaporin 4 (AQP4) protein.^{12,15} AQP4 is the main central nervous system water channel found on the astrocyte cell membrane. While optic nerve and spinal cord injury are classic hallmarks of NMO, intractable nausea and vomiting can precede the onset of neurological deficits by weeks to months.^{12,15,16} This type of presentation comprised 14% of serum NMO-IgG-positive patients based on a database review of NMO-positive cases (10 of 70 NMO cases).¹⁵

The abundance of AQP4 in the area postrema, the emetic reflex center of the medulla, may explain this phenomenon.^{11,12,15} Cases of gastroparesis with or without pharyngeal dysphagia secondary to MS have been well documented.³⁻⁸ These patients typically have radiographic evidence of demyelination at the level of the medulla, raising speculation that gastroparesis results from disruption of vagal nerve nuclei autonomic signals necessary for the gastric migrating motor complex.^{4,5,8,10} Unlike MS-related gastroparesis, a strong link between NMO and gastroparesis has not been established. For example, in one case series, NMO-IgG-positive patients presented with only nausea and vomiting but otherwise exhibited negative gastroenterological studies; in addition, NMO-IgG was found to be negative in the serum of 158 patients with gastroparesis and in the serum of 100 patients with intractable nausea and vomiting that otherwise did not have gastroparesis.¹⁵

One published case report presented gastroparesis preceding fulminant neurological deficits by several weeks in a 10-year-old girl experiencing her second relapse of NMO.⁴ The patient's gastroparesis was attributed to thoracic myelopathy with pure sympathetic dysfunction, based on new lesions seen from T4 to T7. In contrast, our patient's gastroparesis heralded new-onset NMO, not relapse, and our patient's lesions were seen in the posterior aspect of the medulla oblongata. Given that this site of inflammation lines the area postrema and houses the vagal nerve nuclei, it may explain both the nausea/vomiting and the gastroparesis with dysphagia.^{3-8,12,15,16,17} Our patient's symptoms may have been spurred by a combination of autoimmune attack of the AQP4-dense area postrema plus secondary demyelination of vagal nerve nuclei as seen in cases of MS-related gastroparesis. Early

recognition and treatment of NMO can modify the disease's natural course that otherwise renders up to half of untreated patients blind and/or paralyzed within 5 years of onset.¹⁸ Fortunately, the advent of serological markers, specifically NMO-IgG, and more inclusive diagnostic criteria for NMO have made early recognition more feasible.^{19,20}

DISCLOSURES

Author contributions: Both authors contributed equally to the manuscript and share first authorship. A. Salahudeen is the article guarantor.

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