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Neuromyelitis Optica Spectrum Disorder Manifested by Persistent Hiccups and Severe Esophagitis in an Adolescent Patient

*Priya Singh, MD, *†Reinaldo Garcia, MD, and ‡Madhura Y. Phadke, MD

Abstract: Patients with persistent hiccups are often referred to gastrointestinal services. Hiccups lasting greater than 48 hours are classified as persistent, while those lasting longer than 2 months are termed intractable. The etiology of hiccups is broad and can include many organ systems. Here, we present the case of an 18-year-old male patient who presented to the emergency department with an 8-day history of nausea, emesis, and intermittent hiccups. The patient was admitted to the gastroenterology service and underwent workup including esophagogastroduodenoscopy and imaging. Esophagogastroduodenoscopy revealed severe distal esophagitis. He was started on high-dose proton pump inhibitor and sucralfate. During the course of hospital admission, the patient's intermittent hiccups worsened to become constant. Several medical therapies led to little improvement. We initially felt that the esophagitis was the etiology of the patient's symptoms, however, due to ongoing symptoms unresponsive to typical therapy, we obtained a neurological consult. Brain MRI revealed a dorsal medullary lesion. Subsequent work up confirmed the diagnosis of neuromyelitis optica spectrum disorder. Neuromyelitis optica spectrum disorder is a rare, serious, sometimes fatal autoimmune condition of the central nervous system. Early diagnosis and treatment are important predictors of future relapses. Our patient was started on high-dose intravenous steroids with rapid improvement in symptoms. He was discharged home on steroids, proton pump inhibitor and close neurology and gastroenterology follow up. This case outlines the importance of consideration of neurological causes of hiccups or other centrally mediated conditions with gastrointestinal manifestations, even when a concomitant gastrointestinal condition is present.

INTRODUCTION

Patients with intermittent, persistent, or intractable hiccups are often referred to or present to gastrointestinal services, both in the outpatient and inpatient settings. Hiccups lasting greater than 48 hours are classified as persistent, while those lasting greater than 2 months are termed intractable. Here, we present the case of an 18-year-old male patient who presented to the emergency department with an 8-day history of nausea, emesis, and intermittent hiccups.

CASE PRESENTATION

A previously healthy, 18-year-old male patient was admitted to the gastroenterology service for an 8-day history of nonbloody, nonbilious emesis, epigastric abdominal pain, intermittent hiccups, anorexia, and weight loss. The patient had visited several outside emergency departments since symptom onset, during which the patient was thought to have a viral illness and was discharged home with ondansetron and metoclopramide. Just before admission, the patient had a computed tomography scan of the abdomen at an outside emergency department, which showed gas and fluid levels in the small bowel and colon without evidence of obstruction. Additionally, there was no evidence of pancreaticobiliary abnormality or additional luminal pathology.

On admission to our institution, the patient's workup was significant for hypokalemia of 3.1 mEq/L and hypochloremia of 94 mEq/L. He had an otherwise normal comprehensive metabolic panel, normal lipase, normal C-reactive protein, and normal erythrocyte sedimentation rate. Complete blood count showed a monocytosis of 14.8% but was otherwise unremarkable. Urinalysis showed 1+ ketones, 1+ bilirubin, and 4+ urobilinogen. Urine toxicology tests were negative. A streptococcal A antigen and monospot screen were negative. Novel-coronavirus 2019 (COVID-19) polymerase chain reaction testing was negative. An abdominal radiograph and an electrocardiogram were within normal limits. The patient was hemodynamically stable, and his physical examination on admission was unremarkable. He had moist mucous membranes, no oral lesions, abdominal distention, abdominal guarding, or rebound tenderness.

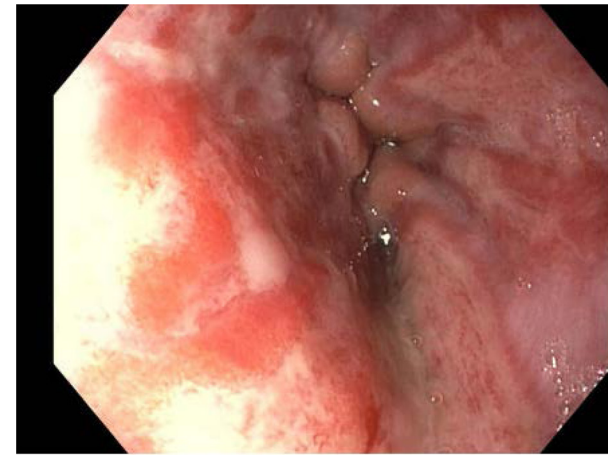

FIGURE 1. Severe distal esophagitis visualized in our patient during esophagogastroduodenoscopy. Note the erythema, friability and superficial linear ulcerations in the distal esophagus.

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From the *Northeast Ohio Medical University, Rootstown, OH; †Division of Pediatric Gastroenterology, Hepatology and Nutrition, Akron Children's Hospital, Akron, OH; and ‡Pediatric Gastroenterology, Hepatology and Nutrition, Stanford University School of Medicine, Palo Alto, CA.
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The authors report no conflicts of interest.
P.S. wrote and revised article. R.G. reviewed and revised article, provided figures, and provided oversight on all areas of article. M.P. wrote and revised article and oversaw all aspects of preparation of article.
Correspondence: Madhura Y. Phadke, MD, Department of Pediatric Gastroenterology, Hepatology & Nutrition, Stanford University School of Medicine, 750 Welch Road, Suite 116; Palo Alto, CA 94304. E-mail: myphadke@stanford.edu.

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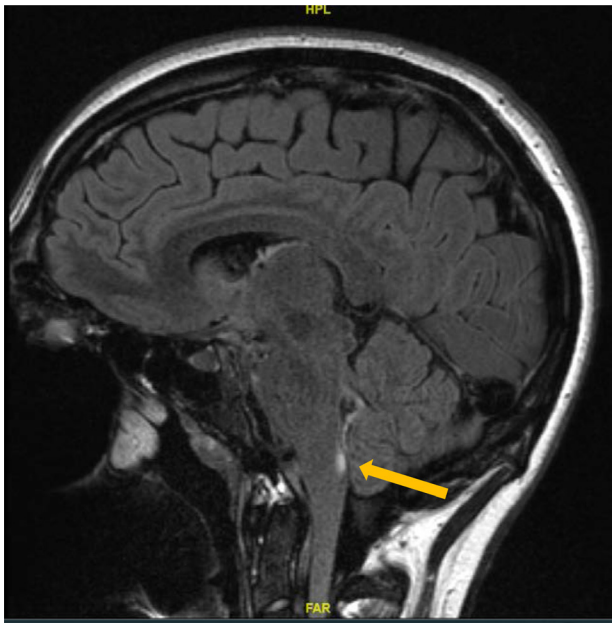

FIGURE 2. MRI scan of the brain in our patient showed a 5.5 mm enhancing dorsal medullary lesion adjacent to the fourth ventricle, a characteristic brainstem lesion in NMOSD. NMOSD = neuromyelitis optica spectrum disorder.

Additionally, a limited neurological exam showed no focal motor or sensory deficits. The patient was not regularly taking any medications at home, and his family medical history was noncontributory to his symptoms.

Our differential diagnoses for this patient primarily focused on infectious or gastrointestinal causes of his symptoms. Although the patient did report general weakness and tingling in the hands, our initial concern for an intracranial abnormality was low due to lack of neurological deficits on physical exam. The patient underwent esophagogastroduodenoscopy the day following admission, which showed severe distal esophagitis (Fig. 1). Esophagogastroduodenoscopy biopsy results showed acute ulcerative esophagitis in the distal esophagus. Infectious/viral testing on the biopsies was negative. The patient was started on a high-dose, intravenous proton-pump inhibitor and sucralfate. His symptoms of nausea and emesis began to improve; however, over the course of the next three days, his previously intermittent hiccups became persistent. A complete abdominal ultrasound and an upper gastrointestinal radiography series were obtained, which were unremarkable. Treatment with metoclopramide, cyproheptadine, and baclofen led to no improvement in symptoms.

Due to worsening hiccups that were refractory to therapy, a Pediatric Neurology consult was obtained. An in-depth, detailed neurological exam revealed ankle contractures, clonus, and diffuse hyperreflexia. A brain and spine MRI was obtained which revealed a 5.5 mm enhancing lesion in the dorsal medulla (Fig. 2). Subsequent work up showed that the patient had autoantibodies which, when combined with the medullary brainstem lesion and cerebrospinal fluid analysis, led to the diagnosis of neuromyelitis optica spectrum disorder (NMOSD). The patient was started on high-dose intravenous steroids with rapid improvement in symptoms. He was discharged home on oral steroids, proton-pump inhibitor, and close Neurology and Gastroenterology follow up.

DISCUSSION

Neuromyelitis optica spectrum disorder is a rare, serious autoimmune condition with significant morbidity and mortality. The disorder is characterized by demyelination and axonal damage that typically involve the optic nerve or spinal cord (1,2). NMOSD is typically associated with autoantibodies that target aquaporin-4, an abundant water channel in the central nervous system (1). This biomarker is present in 70–80% of cases of NMOSD (3). Early diagnosis and treatment of NMOSD are important, as it may lead to improved patient outcomes (3). Patients with NMOSD may present with gastrointestinal symptoms. Area postrema syndrome is a characteristic subtype of NMOSD and occurs when demyelinating lesions are present in the area postrema of the dorsal medulla which may lead to nausea, vomiting, and hiccups (4). Up to 30% of patients with NMOSD present with typical brainstem lesion symptoms (5).

Patients with intractable or persistent hiccups are frequently referred for or present to gastrointestinal services. The differential diagnosis of hiccups is broad, and symptoms may stem from many organ systems (see Table 1) (6). There are case reports in the gastrointestinal literature of hiccups resulting from esophagitis or gastroesophageal reflux disease (7,8). In our patient, our gastrointestinal work-up revealed severe distal esophagitis. Our initial thought process was that the patient's esophagitis was the cause of his hiccups. However, because the patient did not respond to treatment as expected, additional workup was obtained including a Neurology consult and imaging, which led to the final diagnosis. In our patient, the severe esophagitis was more likely a result of several days of nausea, emesis, and intermittent hiccups that led to his hospitalization, rather than the cause of his presentation.

This case outlines the importance of consideration of neurological causes of hiccups or other potentially centrally mediated conditions with gastrointestinal manifestations, even when a concomitant gastrointestinal condition is present. The threshold to obtain neurological input or imaging should be low in patients with nausea and vomiting, in association with hiccups that do not respond to typical treatment as expected.

We would like to thank the patient and his family for graciously providing verbal consent and allowing us to publish this interesting case report.

TABLE 1. This table outlines possible causes of persistent hiccups of both peripheral and central etiologies

	Body system	Possible causes of persistent hiccups
Peripheral etiology	Gastrointestinal	Gastroesophageal reflux disease, hiatal hernia, pancreatitis, abdominal tumor
	Cardiorespiratory	Pericarditis, pneumonia, asthma
	Metabolic	Hyponatremia, hypocalcemia, hypokalemia
Central etiology	Central Nervous system	Vascular lesion, meningitis or encephalitis, tumor, trauma, neuromyelitis optica, multiple sclerosis

Adapted from Steger et al (6).

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