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CASE REPORT | FUNCTIONAL GI DISORDERS

Autoimmune Gastrointestinal Dysmotility in a Patient With HIV Treated With Methylprednisolone and Pyridostigmine

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ABSTRACT

Primary autoimmune gastrointestinal dysmotility is a limited form of autoimmune dysautonomia, driven by antiganglionic autoantibodies (AGAs) against enteric neurons. AGAs are observed in other autoimmune diseases, such as Guillain-Barré syndrome, before the development onset of gastrointestinal symptoms. Here, we report a case of a 57-year-old woman with human immunodeficiency virus, who previously developed Guillain-Barré syndrome, presenting with 6 months of intestinal dysmotility. Diagnosis was made by detecting AGAs to ganglionic acetylcholine receptor, alpha-3 subunit, radiographic evidence of duodenal dysmotility, and exclusion of other causes. The patient received high-dose methylprednisolone with low-dose pyridostigmine, which led to significant improvement of symptoms.

INTRODUCTION

Autoimmune gastrointestinal (GI) dysmotility (AGID) is a limited form of autoimmune dysautonomia targeting the enteric nervous system (ENS). Immune-mediated GI dysmotility is a well-document phenomenon in small cell lung cancer and thymoma, and in systemic autoimmune processes, such as Sjogren syndrome and systemic sclerosis.[1–4] AGID is an immunoglobulin G (IgG)-mediated autoimmune process, caused by antiganglionic autoantibodies (AGAs) targeting the ENS.[5–9] AGAs can be generated during infectious or inflammatory states.[10] Here, we report a case of a patient with human immunodeficiency virus (HIV), who developed AGID several years later.

CASE REPORT

A 57-year-old woman from Uganda with HIV (diagnosed in 2002, last CD4+ 384, viral load undetectable) on Biktarvy presented in 2020 with several months of early satiety and weight loss. Her medical history was notable for portal vein thrombosis complicated by a bleeding duodenal varix managed with cyanoacrylate glue injection. She reported a 15-lb weight loss over 6 months, along with postprandial epigastric pain and emesis. She had no other symptoms, no recent travel, no surgical history, and no relevant family history.

An upper endoscopy revealed 3.5-L fluid in her stomach; the pylorus was widely patent, and the duodenum appeared dilated. Abdominal and pelvic computed tomography showed massive gastric distension and duodenal dilation without a clear transition point (Figure 1). The patient was trialed on metoclopramide and erythromycin with no improvement. She required intermittent nasogastric drainage of 3 L of gastric contents every 3–4 days and was commenced on parenteral nutrition for severe malnutrition. To exclude an obstructing lesion, a small bowel study (enteroclysis) with gastrografin was performed (Figure 2). Imaging studies confirmed impaired duodenal motility, but no obstructive pathology.

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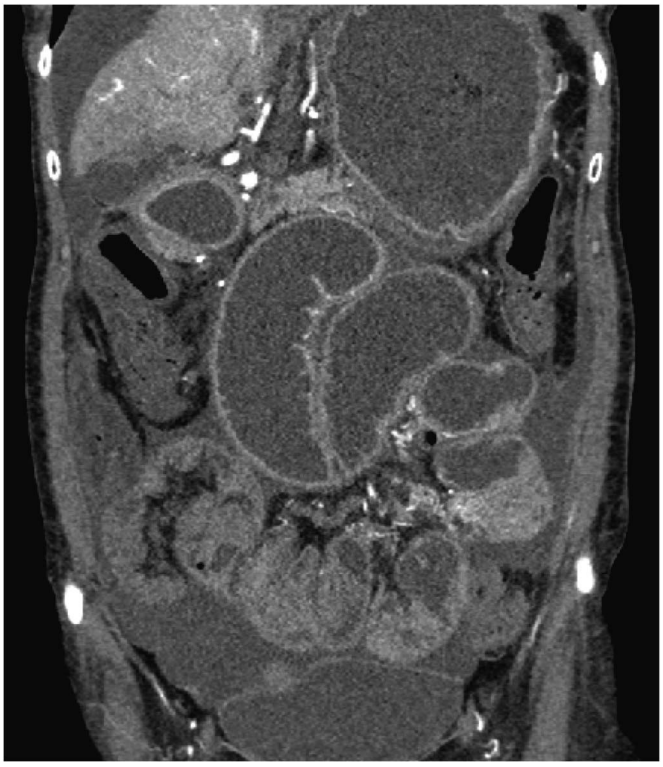

Figure 1. Abdominal and pelvic computed tomography showing distended, fluid-filled stomach and dilated duodenum without transition point.

The patient had normal results for QuantiFERON-release assay, leishmaniasis serum IgG, thyroid-stimulating hormone, hemoglobin A1c, fasting glucose, antinuclear antibody, creatinine kinase, anticentromere, anti-Jo-1, RNA-polymerase III, anti-Ro, and anti-La, and an anti-SCL-70 antibody 0.1 above assay. A duodenal biopsy was notable for inflammation without evidence of parasites, amyloid, or celiac disease. An serum protein electrophoresis and urine protein electrophoresis demonstrated polyclonal gammopathy related to patient's HIV, and a carcinoembryonic antigen, CA 19-9, and α-fetoprotein were negative. Serological evaluation for paraneoplastic autoantibodies (Quest Diagnostics) showed elevated ganglionic acetylcholine receptor (gAChR), alpha-3 subunit (75 pmol/L), and voltage-gated potassium channel (titer 92 pmol/L) AGAs (Table 1).

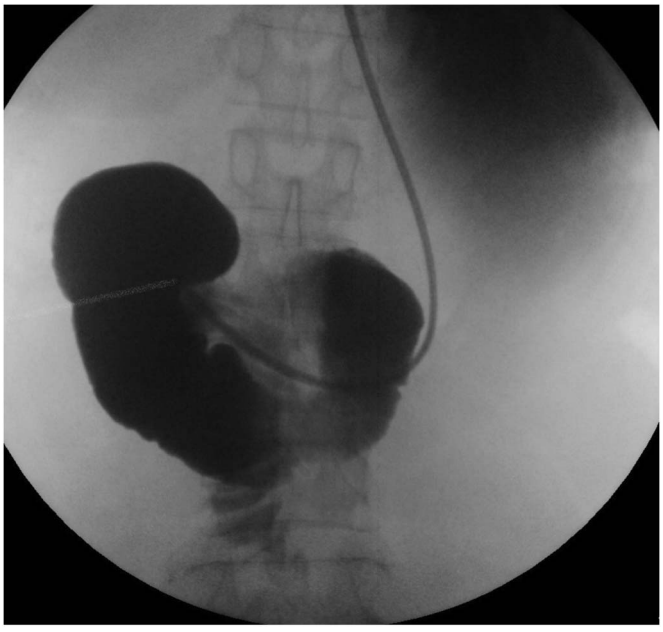

Figure 2. Small bowel contrast study showed impaired duodenal motility without transition point or obstructing mass.

A thoracic computed tomography demonstrated no evidence of thymoma or lung cancer. Based on the clinical and radiographic evidence of GI dysmotility and elevated anti-AChR titers, a presumptive diagnosis of AGID was made. She was started on a 5-day course of 1-g intravenous methylprednisolone with oral pyridostigmine, 30 mg, twice daily. She noticed a significant improvement in her symptoms, no longer required gastric drainage, and was tolerating a normal diet by day 5 of treatment. She was transitioned to 30-mg pyridostigmine 3 times daily and was discharged on day 8 on a normal diet. Two months after discharge, she continues to tolerate an oral diet with mild upper abdominal discomfort, no vomiting, and is maintaining but not regaining her body weight.

DISCUSSION

A growing body of literature supports primary AGID as a distinct dysmotility disorder.[4–9,11] GI motility is a complex neurohormonal process, which requires coordination between the ENS, sympathetic, and parasympathetic nervous systems and the smooth muscles, blood vessels, endocrine cells, epithelium, and interstitial cells of Cajal. Dysregulation at any point can cause GI dysmotility. In AGID, dysmotility results from AGAs targeting the following receptors: gAChR, voltage-gated potassium channel, P/Q-type voltage-gated calcium channel, N-type voltage-gated calcium channel, and glutamic acid decarboxylase.[5] Dysregulation is a presumed IgG-mediated phenomenon with preservation of ganglia[8,9] but reduced neurotransmitter signaling.[9] This is supported by animal models by Meeusen et al and by Lennon et al, who demonstrated anti-gAChR alpha-3 autoantibodies are sufficient and necessary to drive GI dysmotility in mice and rabbits, respectively.[8,9]

AGAs can develop from a number of pathological processes.[10,12] We postulate that our patient's AGID may be related to her HIV infection. Animal models have demonstrated that viruses are sufficient to initiate autoimmune responses targeting enteric neurons.[13] HIV infections, in particular, are strongly correlated with immune activation.[14] Furthermore, a subset of HIV-positive patients will develop GI dysmotility, including both gastroparesis and intestinal dysmotility, which may arise at any time during the course of infection.[15–17] Although some HIV-associated GI dysmotility relates to vagal dysfunction, there is likely a subset that develops AGID, given the association between antiacetylcholine receptor AGAs in HIV-positive patients.[15,17] Of note, the vagally mediated HIV-associated GI dysmotility is not responsive to steroids.[15–17] It is important to

Table 1. Patient antiganglionic antibody panel

Antibody	Result	Reference
VGCC type P/Q Ab	<30 pmol/L	<30 pmol/L
VGKC Ab	92 pmol/L	<80 pmol/L
AChR ganglionic (alpha 3) Ab	75 pmol/L	<53 pmol/L
VGCC type N Ab	<0.30 nmol/L	<0.30 nmol/L

Ab, antibody; AChR, acetylcholine receptor; VGCC, voltage-gated calcium channel; VGKC, voltage-gated potassium channel.

consider that AGID may also arise without identification of a clear, discernable trigger.[10,12,18] Patients may have a genetic predisposition or an unidentifiable environmental exposure that led to AGA development. Therefore, AGID should be considered in the appropriate clinical context.

Recognizing AGID is clinically challenging because AGID is a heterogenous disease, which can affect the GI tract anywhere from the esophagus to anus. Patients may present with achalasia, diffuse esophageal spasm, gastroparesis, small and large bowel dysmotility, and/or anorectal dysfunction.[10,12] Presentation is often subacute, developing over weeks or months. AGID may present with systemic autonomic dysfunction including abnormal pupillary function, anhydrosis, sicca syndrome, orthostatic hypotension, and urinary or sexual dysfunction; however, isolated GI disease is fairly common as seen in our patient.[4–7,10] Given the diverse presentation, AGID should be considered in patients with clinical and/or radiographic GI dysmotility which cannot be explained by an alternative cause. Positive AGAs are supportive, but not specific to AGID[4–7]; however, high AGA titer (ie, >0.5 nmol/L) typically correlates with more advanced disease and systemic dysautonomia.[10,12] Hence, the diagnosis requires exclusion of other common causes of GI dysmotility, including medications, malignant, autoimmune, infiltrative, and infectious causes.

Recognizing AGID is important because patients respond well to immunosuppression. Treatment of AGID is typically combination therapy involving methylprednisolone, intravenous immunoglobulin, plasmapheresis, rituximab, pyridostigmine, or cyclophosphamide.[5,7,19,20] Although there is no standard of care for AGID, immunosuppressive agents typically induce remission.[4–7,13] Therefore, we recommend testing for AGAs in patients presenting with unexplained GI dysmotility with or without clinical features of systemic dysautonomia, especially in HIV-positive patients.

DISCLOSURES

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