



Clinical Improvement With Pyridostigmine in a Patient With Acetylcholine Receptor Antibody-Associated Autoimmune Gastrointestinal Dysmotility

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ABSTRACT

Autoimmune gastrointestinal dysmotility (AGID) is a rare form of limited autoimmune dysautonomia caused by autoantibodies against the enteric nervous system. Our patient was a 53-year-old man with 1 year of bloating, intolerance of oral intake, and recurrent ileus. Esophageal manometry showed aperistalsis and hypotensive lower sphincter, consistent with scleroderma esophagus. However, because the patient had no other sequelae of this disease, AGID was considered. Serologic evaluation revealed ganglionic acetylcholine receptor autoantibodies. Treatment with pyridostigmine led to resolution of symptoms. Early recognition of AGID should be considered when manometry shows scleroderma esophagus in patients without other evidence of systemic sclerosis.

INTRODUCTION

Autoimmune gastrointestinal dysmotility (AGID) is a rare form of limited autoimmune dysautonomia that occurs as an idiopathic or paraneoplastic process.¹⁻³ AGID is caused by autoantibodies against the enteric nervous system and can affect every level of the gastrointestinal (GI) tract.¹ Patients present heterogeneously with GI dysmotility symptoms including poor oral intake due to dysphagia, unrelenting abdominal bloating, nausea and vomiting, and constipation.⁴ Several types of autoantibodies have been identified against plasma membrane cation channels, including neuronal voltage-gated calcium channels, acetylcholine receptor (ganglionic and muscle), and neuronal voltage-gated potassium channels.³ Epidemiologic and prevalence data of AGID have not yet been established because reporting of AGID is limited to case series.⁴

CASE REPORT

A 53-year-old man with a history of well-controlled type 2 diabetes presented with 1 year of progressive postprandial abdominal bloating, nausea, and vomiting. Over the course of the year, the patient had undergone extensive workup with upper endoscopy, colonoscopy, magnetic resonance enterography, and computed tomography (CT) angiography, all of which had been unrevealing. The patient had been hospitalized multiple times for ileus and the inability to tolerate oral intake. CT imaging during one of these episodes showed pneumatosis intestinalis (Figure 1). Given the numerous hospitalizations for ileus, the patient underwent diagnostic laparoscopy, which revealed no evidence of mechanical obstruction.

At the time the patient presented to our institution, he had lost 65 pounds and was no longer tolerating oral intake. As a result, he had developed severe hypovitaminosis, peripheral neuropathy, hypoalbuminemia with resultant peripheral edema, and profound motor weakness, consequentially requiring a wheelchair for ambulation. He was started on total parenteral nutrition (TPN) and referred for urgent esophageal impedance manometry, which showed evidence of failed peristalsis per the Chicago Classification 4.0 criteria (distal contractile integral <100 mm Hg/s⁻¹/cm⁻¹) (Figure 2). In the upright position, manometry showed that gravity essentially emptied the esophageal lumen with time, consistent with a lack of outflow



Figure 1. A computerized tomography scan showing dilated loops of small bowel with pneumatosis cystoides intestinalis.

obstruction and a hypotensive lower esophageal sphincter (Figure 3). The patient was placed on alternating metoclopramide and erythromycin, with minimal improvement of symptoms.

Manometry findings were believed to be consistent with scleroderma esophagus; however, because the patient had no laboratory (negative anti-Scl70/topoisomerase 1, anti-centromere, and anti-RNA polymerase II) or clinical evidence to support this diagnosis, the Mayo Clinic Paraneoplastic Autoantibody Panel was sent and returned positive for the presence of ganglionic acetylcholine receptor (AChR)

antibody (0.06, normal <0.02) and neuronal voltage-gated calcium channel antibody (0.06, normal <0.03). Diagnosis of AGID was made. Because AGID is often a paraneoplastic phenomenon, CT of the chest, abdomen, and pelvis was performed and returned negative for occult malignancy. Given the presence of ganglionic AChR antibody, he was started on the acetylcholinesterase inhibitor, pyridostigmine at 60 mg twice daily. The patient had dramatic improvement in symptoms leading to increased oral intake and weight gain with weaning of TPN and subsequent resolution of neuropathy, vitamin deficiencies, and return of the ability to ambulate without assistance.

DISCUSSION

AGID is a relatively new entity, first described in the literature in the early 2000s.⁴ We present a case of a patient who developed chronic intestinal pseudo-obstruction secondary to AGID. This case report highlights the possible severity of AGID and need for specific diagnosis to provide targeted treatment. Although our patient's symptoms were severe and largely limited to the upper GI tract, AGID seems to occur on a spectrum varying in severity and location of hypomotility symptoms.

To the best of our knowledge, this is the first case to describe a patient with AGID with manometry findings consistent with scleroderma, which is characterized by esophageal aperistalsis and reduced lower esophageal sphincter tone. Although systemic sclerosis often has GI manifestations, isolated GI tract scleroderma without any laboratory findings is incredibly rare. Thus, knowledge of AGID was

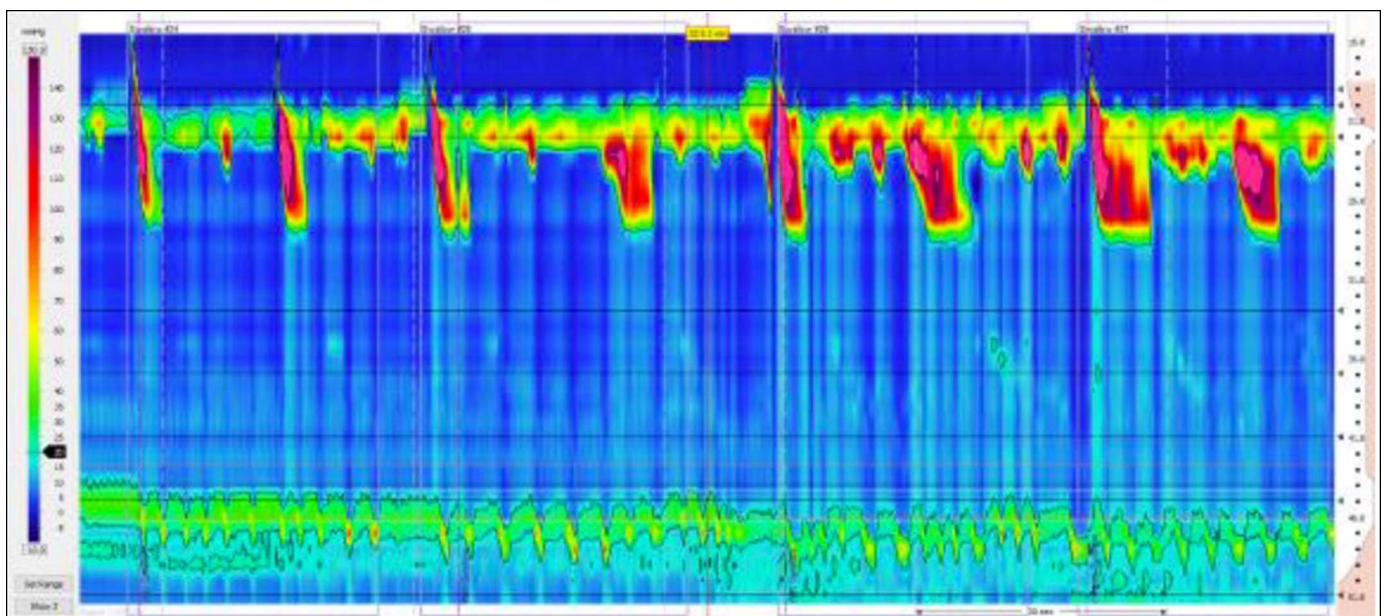


Figure 2. High-resolution esophageal impedance manometry showing the complete absence of smooth muscle motor function. Pressure observed at the gastroesophageal junction is due to vascular compression and respiratory pressure.

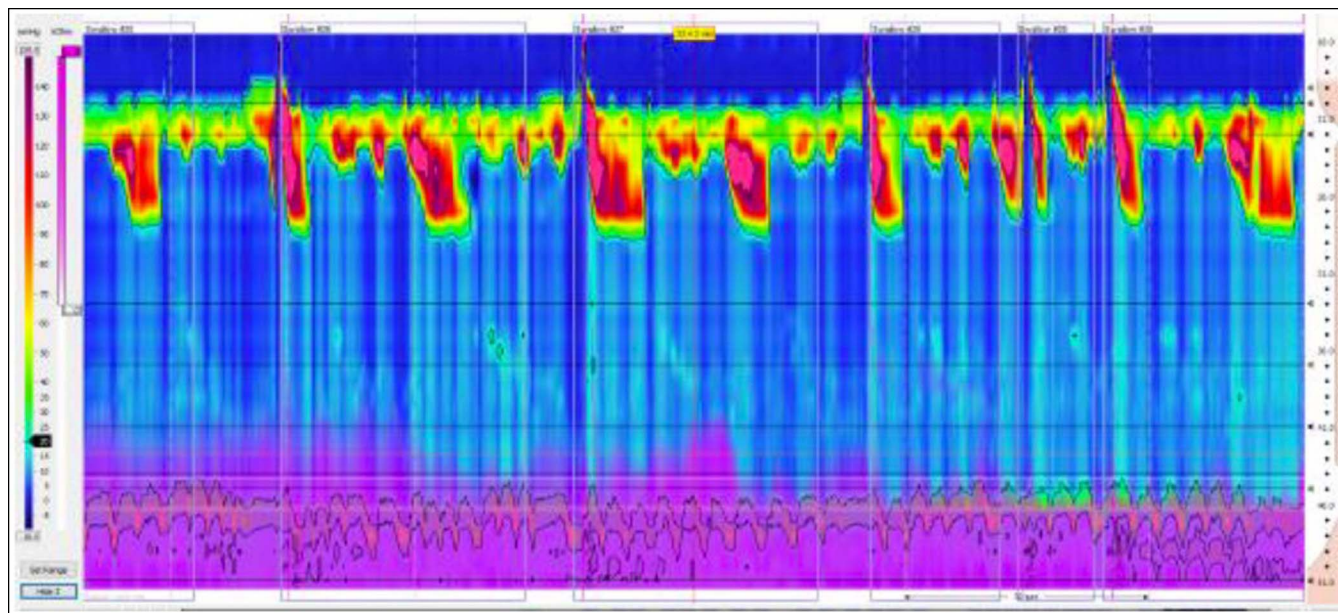


Figure 3. Esophageal manometry with the patient in an upright position showing emptying of the esophageal lumen with time consistent with a hypotensive lower esophageal sphincter.

imperative. Of the patients previously described in the literature with AGID and esophageal dysmotility, most were found to have findings more consistent with achalasia and increased lower esophageal sphincter tone.^{1,5}

Our patient showed dramatic and rapid improvement with the use of pyridostigmine. The use of pyridostigmine to treat AGID has been described in a case report by Pasha et al⁶ in 2006 in a patient with severe isolated gastroparesis found to have AGID with an antibody profile identical to that of our patient. Pyridostigmine, an acetylcholinesterase inhibitor, is mostly commonly known for its use for the treatment of myasthenia gravis, an autoimmune disorder characterized by muscle weakness due to antibodies against nicotinic AChR at the neuromuscular junction.⁷ Pyridostigmine has been used for the management of myasthenia gravis for over 60 years and is considered a well-tolerated and safe option.⁷ Treatment options for AGID are not well defined however. Several therapy options have proven efficacious including corticosteroids, intravenous immunoglobulin (IVIg), and plasmapheresis.^{4,8-10} Although pyridostigmine provides symptomatic relief and does not modify the underlying immune process, we chose to avoid immunomodulator therapy given the reassuring safety profile and cost of pyridostigmine as compared with other treatment options.

Early recognition of AGID as a rare cause of GI dysmotility is crucial for timely diagnosis and prevention of complications, such as severe protein calorie malnutrition. This diagnosis should be considered in patients with symptoms of GI hypomotility without an identifiable cause. Our case also highlights the importance of considering this diagnosis in patients with

esophageal dysmotility with manometry findings consistent with scleroderma esophagus who lack other evidence to support this diagnosis.

DISCLOSURES

Author contributions: All authors gave final approval of the version to be published and agreed to be accountable for aspects of the work. S. Sekhri acquired the data and is the article guarantor. S. Sekhri and P. Beniwal-Patel designed the data and drafted the work. S. Sekhri, B.Massey, and P. Beniwal-Patel analyzed the data and edited the work.

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Informed consent was obtained for this case report.

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REFERENCES

1. Dhamija R, Tan KM, Pittock SJ, Foxx-Orenstein A, Benarroch E, Lennon VA. Serologic profiles aiding the diagnosis of autoimmune gastrointestinal dysmotility. *Clin Gastroenterol Hepatol*. 2008;6(9):988-92.
2. Lennon VA, Sas DF, Busk MF, et al. Enteric neuronal autoantibodies in pseudoobstruction with small-cell lung carcinoma. *Gastroenterology*. 1991;100(1):137-42.
3. Flanagan EP, Saito YA, Lennon VA, et al. Immunotherapy trial as diagnostic test in evaluating patients with presumed autoimmune gastrointestinal dysmotility. *Neurogastroenterol Motil*. 2014;26(9):1285-97.

4. Nakane S, Mukaino A, Ihara E, Ogawa Y. Autoimmune gastrointestinal dysmotility: The interface between clinical immunology and neurogastroenterology. *Immunol Med*. 2021;44(2):74–85.
5. Mukaino A, Minami H, Isomoto H, et al. Anti-ganglionic AChR antibodies in Japanese patients with motility disorders. *J Gastroenterol*. 2018;53(12):1227–40.
6. Pasha SF, Lunsford TN, Lennon VA. Autoimmune gastrointestinal dysmotility treated successfully with pyridostigmine. *Gastroenterology*. 2006;131(5):1592–6.
7. Maggi L, Mantegazza R. Treatment of myasthenia gravis. *Clin Drug Invest* 2012;31(10):691–701.
8. McMillan HJ, Srinivasan J. Achalasia, chronic sensory neuropathy, and N-type calcium channel autoantibodies: Beneficial response to IVIG. *Clin J Gastroenterol*. 2010;3(2):78–82.
9. Weinkauff C, McPhillips S, Krouse R, Levine I. Autoimmune gastrointestinal paralysis: Failure of conventional treatment without immunomodulation. *Case Rep Surg*. 2014;2014:1–4.
10. Greenburg DL, Mo CC, Hemmer PA. IVIG for thymoma-associated pseudo-obstruction: report of successful treatment. *Eur Neurol*. 2007;58(2):116–7.

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