Using Adalimumab to Treat Autoimmune Enteropathy

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ABSTRACT

Autoimmune enteropathy is a rare condition seen in adults with limited therapeutic options available. It manifests with profuse diarrhea and malnourishment. The diagnosis is made through a combination of clinical, serologic, and histologic parameters. The cornerstone of therapy revolves around nutritional optimization and immunosuppression, most commonly in the form of corticosteroids. Alternate therapies, such as antitumor necrosis factor agents, can be considered if there is an inadequate response to steroids. We report a case of autoimmune enteropathy that was successfully treated with adalimumab, a rare treatment for an infrequent disease.

INTRODUCTION

Autoimmune enteropathy (AIE) is a rare condition in adults that is characterized by profuse diarrhea and malnutrition. The diagnosis depends on a combination of clinical, serologic, and histologic characteristics. The mainstay of therapy revolves around nutritional optimization and immunosuppressive medications. The therapeutic options remain few in number given the paucity of reported cases in the literature. We present the second reported case of a patient with AIE who was successfully treated with adalimumab.

CASE REPORT

A 52-year-old man with hypertension, hyperlipidemia, and anxiety presents with a 2-month history of progressive diarrhea, preceded by 2 weeks of nausea. He reports 6 or more watery loose stools per day, including up to 3 times at night, generally precipitated by food intake. Over this 2-month period, he has lost 20 lbs. His stool tests for *Clostridioides difficile*, ova and parasites, and other bacterial pathogens were negative. Upper endoscopy was unrevealing, whereas his colonoscopy showed normal terminal ileal and colonic mucosa with random colon biopsies that were unremarkable. He was treated empirically with oral antibiotics and budesonide as an outpatient.

Two weeks later, he presented to the hospital with worsening diarrhea, weight loss, and inability to tolerate oral intake. On examination, he was ill-appearing with significant cachexia and a body mass index of 20.7 kg/m². His laboratory studies showed hypokalemia, hyponatremia, hypophosphatemia, hypomagnesemia, vitamin D deficiency, and hypoalbuminemia of 1.7 g/dL with an elevated international normalized ratio consistent with nutritional deficiency. He had normal tissue transglutaminase antibody and immunoglobulin levels with an immunoglobulin A of 325 mg/dL, immunoglobulin G of 1,210 mg/dL, and an immunoglobulin M of 106 mg/dL. A small bowel enteroscopy, which appeared grossly normal, revealed biopsies from the duodenum and jejunum that showed marked, near-total villous shortening, crypt hyperplasia, prominent crypt abscesses with focal crypt atrophy, and an absence of intraepithelial lymphocytes, Paneth cells, and goblet cells (Figures 1–3). Antienterocyte immunoglobulin G antibodies were positive. He was diagnosed with AIE based on the clinical, histologic, and serologic findings obtained. The patient was started on total parenteral nutrition and intravenous steroids with an incomplete clinical response. He was subsequently started on infliximab (10 mg/kg) loading while in the hospital. His diarrhea improved, and he was discharged with an oral prednisone taper. As an outpatient, he was tapered off of steroids, completed the infliximab loading phase and started maintenance dosing with complete resolution of his symptoms.

Figure 1. Histological examination of the duodenal bulb showing (A) crypt hyperplasia, subtotal villous shortening and focal acute inflammation with the complete absence of goblet cells, (B) active inflammation and surface foveolar metaplasia, and (C) crypt hyperplasia with marked, near-total villous shortening.

Figure 2. Histological examination of duodenum showing marked, near-total villous shortening, crypt hyperplasia, and focal acute inflammation with the paucity of goblet cells.

A few months later, the patient discontinued his infliximab infusions on his own. He developed recurrent diarrhea and weight loss, for which he underwent a repeat small bowel enteroscopy that showed persistent disease activity on biopsy. He was restarted on infliximab, given his dramatic initial

response. He was premedicated with intravenous hydrocortisone to reduce the risk of antibody formation to infliximab, an intervention supported by previous data in Crohn's disease.¹ However, during his second loading dose, he suffered a severe infusion reaction prompting immediate cessation of the medication. Given his dramatic improvement with initial infliximab administration, we opted to transition him to another anti-tumor necrosis factor agent, adalimumab (induction dosing: 160 mg on day 1, then 80 mg 2 weeks later; followed by maintenance: 40 mg every other week) for control of his disease, which he has tolerated well. Since the initiation of adalimumab, the patient's diarrhea has abated completely. During an in-clinic follow-up, he appeared well, reported formed bowel movements, and gained 30 lbs reaching a new body mass index of 26.3 kg/m² with albumin of 4.6 g/dL. He continues to remain compliant with his subcutaneous injections of adalimumab.

DISCUSSION

AIE is a rare autoimmune gastrointestinal disorder with fewer than 40 adult cases described in the literature to date. Its diagnosis is suspected based on a combination of clinical, serologic, and histologic data. As a part of the diagnostic process, it is imperative to differentiate AIE from key findings seen in other enteropathies, such as celiac disease (Table 1). Clinically, AIE manifests as chronic diarrhea and malabsorption, resulting in

Figure 3. Histological examination of jejunum showing (A) crypt hyperplasia with marked, near-total villous shortening and (B) active inflammation with focal crypt abscess.

Table 1. Key factors differentiating celiac disease from AIE

	Celiac disease	AIE
Clinical	Diarrhea, weight loss, malnutrition	Diarrhea, weight loss, malnutrition
Serology	TTG antibody	Antienterocyte antibody, antigoblet cell antibody
Histology	Villous atrophy, crypt changes, increased intraepithelial lymphocytes	Villous atrophy, cryptitis, lymphocytic infiltration of lamina propria, increased apoptotic bodies, absence of goblet or Paneth cells

AIE, autoimmune enteropathy; TTG, tissue transglutaminase antibody.

significant malnutrition. The characteristic histologic findings are most commonly confined to the small intestine and include villous atrophy, cryptitis, and lymphocytic infiltration of the lamina propria.^{2,3} Antienterocyte and antigoblet cell antibodies may support the diagnosis of AIE but can also be found in other conditions such as inflammatory bowel disease (IBD) and celiac disease.^{4,5} Hence, the criteria noted above should be interpreted together when making the diagnosis of AIE given its overlapping features with other conditions.

The cornerstone to the management of AIE is nutritional optimization and immunosuppressive therapy. However, the optimal immunosuppressive strategy has not been elucidated, given the paucity of reported cases. Most patients are initially trialed on corticosteroids, but often do not have an adequate response, and will ultimately require long-term management with steroid-sparing agents. Medications used for AIE are inspired by therapies for IBD but are not currently approved for this indication. Immunosuppressive medications that have been tried in case reports include azathioprine, 6-mercaptopurine, cyclosporine, tacrolimus, mycophenolate mofetil, and metronidazole, all with variable response rates.^{4,6} A single case also reports the use of vedolizumab for treatment of AIE.⁷ Antitumor necrosis factor agents have gained significant popularity in the treatment of IBD and may have a role in AIE as well. In AIE, infliximab has only been used in a small number of cases, and to our knowledge, there is only one other documented case of AIE being successfully treated with adalimumab.⁸ Despite its infrequent use in patients with AIE, adalimumab is a reasonable consideration when treating this rare condition as it may induce and maintain clinical remission as seen in our patient.

DISCLOSURES

Author contributions: HD Trivedi and SE Shannahan reviewed the literature and wrote and revised the manuscript. M. Morrow

provided the pathology and histological images. MA Peppercorn revised the manuscript. HD Trivedi is the article guarantor.

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