New Treatment Option for Autoimmune Enteropathy: A Rare Case of Intractable Diarrhea Treated with Vedolizumab

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ABSTRACT

Autoimmune enteropathy is an uncommon cause of chronic diarrhea rarely seen in adults. The disease is secondary to an autoimmune process in the gut that leads to villous blunting and subsequent watery diarrhea, abdominal pain, and severe weight loss. The disease has only been described in 37 adults prior to our case, and variable treatment success has been documented with steroids, immunomodulators, and TNF-α inhibitors. This case is the first to show success in treating autoimmune enteropathy with vedolizumab and provides physicians with an additional therapeutic option when limited by a patient’s comorbidities and side effects of other drugs.

INTRODUCTION

Rarely seen in adults, autoimmune enteropathy (AIE) is a condition characterized by chronic diarrhea and malabsorption caused by dysregulated antibody activity in the gut. Symptoms are not improved with dietary modification, and the diagnosis requires evidence of villous blunting on histology. Disease frequently becomes so severe that patients require total parenteral nutrition.1

Because only 37 cases of adult AIE have been cited, there is little data regarding diagnosis and best practices for treatment and management. There are no formal guidelines for AIE treatment, and patients are typically treated with corticosteroids initially, such as prednisone or budesonide.4 However, approximately two thirds of these patients are steroid-dependent or refractory and require additional immunomodulators for maintenance. Therapy with agents including azathioprine, 6-mercaptopurine (6-MP), cyclosporine, tacrolimus, mycophenolate mofetil, sirolimus, and infliximab have all been used with variable responses both clinically and histologically.1,2,5 To our knowledge, adult AIE has not been treated with vedolizumab.

CASE REPORT

A 46-year-old woman with Hashimoto’s thyroiditis, idiopathic cardiomyopathy, and a body mass index of 14 kg/m² presented to clinic with more than 20 years of watery diarrhea and a previous diagnosis of celiac disease with microscopic colitis. However, a strict gluten-free diet provided her no relief. Additionally, this patient lacked typical celiac disease susceptibility HLA genotypes. Stool studies were negative for infectious pathogens. Fecal leukocytes were absent, and a magnetic resonance image was also negative. Colonoscopy was significant for a loss of the normal vascular pattern throughout the colon (Figure 1). Duodenal and colonic biopsies were negative for malignancy but did reveal villous blunting, chronic inflammation of the lamina propria, intraepithelial lymphocytes, and decreased goblet cells (Figure 2). Her laboratory studies revealed a presence of anti-goblet cell antibodies. Therefore, our patient was diagnosed with AIE, now having clinical, histological, and serological support.
Previously the patient had only minimal improvement with budesonide and mesalamine, and each caused her significant lower extremity swelling. After her new diagnosis, she was initiated on high-dose prednisone, which was later tapered with the addition of 6-MP. Even on 6-MP 75 mg daily, our patient reported frequent diarrhea. She had poor tolerance of 6-MP, noting nausea and decreased appetite, and she ultimately developed leukopenia, requiring the daily dose to be reduced to 50 mg. At her next appointment, she was still having significant stool burden, reporting 10–15 watery stools per day with significant pain and bloating. TNF-α inhibitors were contraindicated for our patient due to her cardiomyopathy, so she began treatment with vedolizumab infusions (300 mg every 8 weeks) while continuing 6-MP. After 2 infusions, her abdominal symptoms resolved, and her stool frequency significantly reduced to 5–7 stools per day. Repeat colonoscopy revealed reduced inflammation and only mild congestion, although there was still histological evidence of villous blunting, increased intraepithelial lymphocytes, and decreased goblet cells (Figure 3, Figure 4). Nevertheless, our patient now has a body mass index of 30 kg/m² with plans to taper 6-MP. Her albumin and total serum protein have improved from 2.7 g/dL and 5.8 g/dL to 4.2 g/dL and 6.8 g/dL, respectively. Iron and vitamin D deficiency have both resolved, and she has remained steroid-free without any dietary restrictions. At her last visit, she reported that her stools are more formed and occur with less urgency. Because we believe there is still opportunity for further improvement, particularly on a microscopic level, we are now increasing our patient’s infusion frequency to every 4 weeks.

DISCUSSION
AIE is often misdiagnosed, and patients who are plagued with weight loss, anorexia, and frequent watery bowel movements are often incorrectly treated. Consider AIE in patients with

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**Figure 1.** Endoscopic picture from colonoscopy in 2016 revealing diffusely edematous mucosa.

**Figure 2.** The patient’s 2015 biopsy revealed (A) villous blunting, increased lamina propria lymphoplasmacytic infiltrate, increased epithelial lymphocytes in the duodenum, and absence of goblet cells; and (B) increased lamina propria lymphoplasmacytic infiltrate and an absence of goblet cells in the colon. Patchy neutrophilic cryptitis and a marked increase in intraepithelial crypt apoptosis are also seen.

**Figure 3.** Endoscopic picture taken from the patient’s most recent colonoscopy depicting a less inflamed but still edematous mucosa.
chronic diarrhea and malabsorption that do not improve with changes in diet and have characteristic findings on biopsy. More common disorders with similar presentations such as infection, inflammatory bowel disease (IBD), celiac disease, and microscopic colitis should be excluded as well. \(^4\) Histologic changes are most common in the small intestine and typically include villous atrophy, cryptitis, and lamina propria expansion with lymphocytic infiltration. \(^3\) Of the adult cases seen, approximately 80% of those diagnosed with AIE have a predisposition for autoimmune disease, and more than 90% are positive for anti-enterocyte or anti-goblet cell antibodies. \(^1,2\) Anti-enterocyte or anti-goblet cell antibodies are supportive of the diagnosis but are intentionally excluded from diagnostic criteria because these antibodies have also been reported in patients with IBD and celiac disease and, rarely, even in these patients' relatives. At this time, the positive predictive value of these antibodies and their significance are still unknown. \(^2,4\)

Only 37 cases of adult AIE have been reported in the literature. In our review, monoclonal antibodies, specifically TNF-\(\alpha\) inhibitors, have been used in only 4 of these patients. However, to our knowledge, this is the first case involving the use of vedolizumab or any integrin-binding antibody. Vedolizumab is approved by the FDA for the treatment of both moderate-to-severe ulcerative colitis and Crohn’s disease. TNF-\(\alpha\) inhibitors can worsen cardiac conditions and cause exacerbations in those with reduced ventricular ejection fractions, like our patient. In this case, vedolizumab’s use was extrapolated from its role in IBD therapy. By blocking lymphocyte trafficking in the intestine, vedolizumab controls inflammatory dysregulation that occurs in both IBD and AIE. \(^6\) Successful treatment of AIE with vedolizumab is significant because AIE treatment requires ongoing immunosuppression, and steroid-sparing agents are preferred. \(^5\) In addition, many patients, like ours, have poor or only modest response to steroid therapy. The previously mentioned list of immunosuppressive agents is not without their own side effects and specific contraindications. Furthermore, vedolizumab is generally well-tolerated with gut specificity and remains a therapeutic option when TNF-\(\alpha\) inhibitors are contraindicated, such as in our patient.

Ideally, increased awareness of adult AIE will allow for an increase in appropriate diagnoses of the disease. Thus, while formal treatment guidelines do not yet exist, sharing unique therapeutic successes is critical to best prepare our physicians for these difficult cases.

**DISCLOSURES**

Author contributions: G. Robbins wrote the article and reviewed the literature. J. Tracht and D. Davis reviewed the histology and provided detailed description of the pathology appreciated at each stage. H. Iskandar edited the manuscript, provided the endoscopic images, and is the article guarantor.

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