A CASE REPORT

Autoimmune Enteropathy: An Uncommon Presentation

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INTRODUCTION

Diarrhea is a common gastrointestinal complaint, with infection, irritable bowel syndrome, inflammatory bowel disease (IBD) and malabsorption syndromes (such as lactose intolerance and celiac disease) being the most common etiologies. We report a case of a 70-year old male with a two-month history of profuse, watery diarrhea. An abdominal computerized tomography (CT) scan on initial presentation revealed pneumatosis intestinalis. Extensive workup that included enteroscopy and colonoscopy revealed histology suggestive of autoimmune enteropathy. Anti-enterocyte antibodies confirmed the diagnosis. Although rare, autoimmune enteropathy (AIE) represents an important consideration in the differential diagnosis of intractable diarrhea in adults.

Presentation

A 70-year old male with a history of resected Meckel’s diverticulum and acid reflux was admitted for profuse, frequent, watery diarrhea and hypotension. Two months prior, he had presented to an outside hospital with similar symptoms including mild abdominal pain; he was found to be severely dehydrated with associated acute kidney injury. At that time, a computed tomography (CT) of the abdomen and pelvis revealed pneumatosis intestinalis of the small intestine and colon. Due to his presentation and CT findings, the patient underwent an exploratory laparotomy. There was no evidence of ischemia, perforation or necrotic bowel noted during laparotomy. Subsequent colonoscopy at the outside hospital was normal. However, random biopsies were suggestive of lymphocytic colitis for which the patient was discharged on budesonide therapy along with total parenteral nutrition (TPN). He presented to our hospital with ongoing intractable diarrhea despite compliance to his medication therapy.

At the time of presentation, he endorsed greater than 15 watery stools per day with nocturnal symptoms. A gluten-free and lactose-free diet failed to improve his symptoms. He had lost nearly 20 pounds in the last two months. He denied recent travel or sick contacts. He had no history of autoimmune disease as well as no family history of gastrointestinal or autoimmune disease. He had a longstanding smoking history but denied alcohol or drug use.

Vital signs were all within normal limits. On physical exam, his findings were only significant for a deconditioned gentleman as well as rectal exam showing peri-anal excoriations. Laboratory studies demonstrated a normocytic anemia, elevated
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Again demonstrated pneumonitis intestinalis of the small intestine and colon (Figure 1).

Given his non-response to budesonide therapy, and in consideration for an alternative diagnosis, the decision was made to undergo upper enteroscopy and repeat colonoscopy. Esophagogastroduodenoscopy (EGD) and upper enteroscopy findings were normal and random biopsies of the duodenum and jejunum were taken. The colonoscopy showed boggy, edematous appearing mucosa. Random biopsies of the colon were taken as well.

Small bowel biopsies all indicated moderate to severe villous blunting, with marked lamina propria infiltrate (plasma cells and lymphocytes) (Figure 2). No goblet or paneth cells were identified. There was marked crypt apoptosis. Colon biopsies exhibited active colitis with preserved crypt architecture. Markedly increased crypt apoptosis was again demonstrated (Figure 3). No goblet or paneth cells were visualized.

Serum Anti-Enterocyte IgG antibodies were present in elevated titers and demonstrated positive linear periapical staining of the enterocytes and staining in the goblet cells. Anti-enterocyte IgA antibody also demonstrated positive linear periapical staining of enterocytes in elevated titers.

When the diagnosis of autoimmune enteropathy was established, he was placed on intravenous methylprednisolone. Shortly after, he was started on TPN for nutritional support. The patient began responding positively to intravenous steroids on the third day of treatment, resulting in a decrease in frequency and volume of bowel movements. As he clinically improved, he was transitioned to oral prednisone and discharged with a steroid taper for outpatient gastroenterology follow-up.

Discussion

Autoimmune enteropathy is a rare cause of intractable diarrhea in children and an even rarer cause in adults.

It is best defined as a presentation of chronic diarrhea, malabsorption, with specific small intestinal histologic features and is typically confirmed by the presence of circulating auto-enteric antibodies. Extraintestinal manifestations may include hypothyroidism, nephrotic syndrome, autoimmune hemolytic anemia, and rheumatoid...
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arthriti sei. A lack of response to a gluten-free diet or other dietary exclusions is also described, as is a predisposition to other autoimmune diseases. The disease was first described in 1982 in London in a 15 month-old child with protracted diarrhea and weight loss. Since that time, only a handful of adult cases of AIE have been reported with the largest case series from Mayo Clinic Rochester comprising of 15 patients. 

AIE is histologically characterized by findings including: villous blunting, increased mononuclear inflammation in the lamina propria, lymphocytic infiltration into deep crypt epithelium with a relative decrease of surface lymphocytosis (< 40 lymphocytes per 100 epithelial cells), as well as the presence of increased crypt apoptotic bodies. Mononuclear infiltrates are comprised of both plasma cells and lymphocytes. Colon histopathology shows similar histologic abnormalities to those seen in the small bowel. Gastric biopsies not uncommonly demonstrate an autoimmune atrophic gastritis as well. CT findings are typically non-diagnostic. This is the first known case to report the findings of pneumatosis intestinalis in autoimmune enteropathy.

The presence of anti-enterocyte or anti-goblet cell antibodies is supportive of the diagnosis of AIE, although the detection of these antibodies has been described as “observer dependent.” The significance of circulating auto-enteric antibodies in regards to pathology has not been fully delineated. Akram et al. did not show association between the clinical course, intestinal histology, and the type of circulating auto-enteric antibodies.

While anti-enterocyte antibodies have not been reported in celiac disease and inflammatory bowel disease, anti-goblet antibodies have been reported in patients with chronic inflammatory bowel disease, as well as in their asymptomatic first-degree relatives. Despite concerns regarding their sensitivity and specificity, anti-enterocyte antibodies aid in establishing a diagnosis of AIE in cases with protracted diarrhea and malabsorption.

Much of the pathophysiology behind autoimmune enteropathy is unknown, but some studies have pointed to a deficiency or dysfunction in CD4+ and CD25+ regulatory T cells which are involved in the down-regulation of a variety of bodily immune responses. Mutation in the FOXP3 gene (forkhead box p3) in T cells, for instance, has been found in inherited forms of autoimmune enteropathy such as the rare X-linked recessive disorder of early childhood known as IPEX (immunodysregulation polyendocrinopathy enteropathy X-linked) syndrome.

Scarce data exists regarding epidemiology, disease course, and treatment options for AIE. Anecdotal experience guides a number of treatment decisions including use of corticosteroids as well as immunosuppressive drugs such as azathioprine, cyclophosphamide, tacrolimus, cyclosporine and infliximab. In a retrospective study, over half of the patients responded to steroid therapy. However, two-thirds of these patients either became steroid-dependent or refractory requiring additional immunomodulating or biologic therapy for maintenance of remission.

CONCLUSION

Autoimmune enteropathy represents a rare and important consideration in the differential diagnosis of intractable diarrhea in adults. It should be especially sought out in cases of malabsorption and small bowel villous atrophy not responding to a gluten-free diet. This disorder may also be considered in patients presenting with pneumatosis intestinalis when other common causes have been excluded. Treatment can be challenging and often requires both nutritional support with immunosuppressive medications.

References