CLINICAL VIGNETTE

Adult Autoimmune Enteropathy

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Case Report

A 38-year-old man presented with a 7-week exacerbation of chronic diarrhea. He had profuse non-bloody diarrhea up to 15 times per day, with undigested food in his stool. His diarrhea was exacerbated with eating, relieved with fasting and would wake him up at night. The patient's chronic diarrhea began in 2005 with three to five bowel movements a day. In 2009, he had an exacerbation of his diarrhea and was admitted, initiated on IV fluids and a gluten-free diet but eventually required TPN due to significant weight loss. Infectious work up including Isosporia, Microsporia, Clostridium difficile, Giardia, ova and parasites, and Cryptosporidium was negative. His TSH, HIV, and Vitamin B12 were normal. The work up for gastrinoma, VIPoma, and pheochromocytoma was negative. Celiac serology showed a positive IgA anti-gliadin antibody; however, pathology showed a duodenum with no Marsh lesions, no histopathologic abnormalities of the mucosa, and no pathologic organisms. A diagnosis of common variable immunodeficiency was contemplated as the patient had decreased IgM and IgG levels (IgG 509 mg/dL [nl 690-1660] and IgM 21 mg/dL [nl 37-318]) and decreased absolute counts for his T-cell subset (CD3 450 /cmm (nl 841-2402) CD4 345 /cmm (nl 355-1426) CD8 105 (nl 255-1090)). As the patient's diarrhea improved on supportive treatment, he was discharged with follow up at Immunology and Allergy clinic as well as GI clinic; however, the patient did not return for follow up.

In 2013, the patient re-presented to our institution after a 7-week exacerbation of his chronic diarrhea. He was unable to maintain adequate oral fluid intake and had required IV hydration at various local emergency departments. His physical exam was notable for signs of cachexia including temporal wasting and interosseous muscle wasting but was otherwise normal. The patient's infectious work up was again negative and his immunoglobulins had normalized. Based on the positive IgA anti-gliadin antibody obtained on the previous hospitalization, transglutaminase antibodies were tested and a push enteroscopy with biopsies of the jejunum was performed. Pathology showed moderate villous blunting and intraepithelial lymphocytes concerning for celiac disease, however, the transglutaminase antibodies were negative. Second generation anti-gliadin antibody and HLA DQ2 and DQ8 were also negative. In the setting of biopsies showing villous blunting and intraepithial lymphocytes with negative celiac serologies, the differential diagnosis included: bacterial overgrowth, protein intolerance, celiac sprue, tropical sprue, and autoimmune enteropathy. Based on the biopsy findings, no laboratory or pathologic evidence of bacterial overgrowth, no history of protein intolerance, no travel history to tropical regions, and negative celiac serologies, the likely diagnosis was adult autoimmune enteropathy. Anti-enterocyte antibodies were negative. The patient was started on prednisone and had full resolution of his diarrhea 12 days later. The frequency of his bowel movements decreased from >15 per day to 2 per day and his stools became more solid on day 12 of treatment. At two week follow up, the patient's weight increased by 13 pounds and his bowel movements continue to be more formed and less frequent. At two month follow up, the patient continued to gain weight and was free of diarrhea.

Discussion

Adult autoimmune enteropathy is a rare autoimmune disease of the gastrointestinal tract characterized by intractable chronic diarrhea, malabsorption, and immune-mediated damage to the intestinal mucosa. Although autoimmune enteropathy is primarily pediatric disease, approximately 30 adult cases of autoimmune enteropathy have been reported in the literature[1]. Often mimicking the clinical and histological manifestations of celiac disease, adult autoimmune enteropathy does not improve with gluten-free diet modifications and is not consistent with celiac HLA serologies and transglutaminase antibodies.

This disease is typically associated with circulating auto-antibodies to the gut mucosa, including anti-

enterocyte or anti-goblet antibodies, but auto-antibodies are not always required for diagnosis according to recently proposed criteria[2]. In the initial description of adult autoimmune enteropathy, self-reactive enteric antibodies were required for the diagnosis[3]. However, as more cases were reported, these antibodies were discovered to have low sensitivity and specificity as they can be present in other autoimmune diseases and immunodeficiency diseases[4,5].

Adult autoimmune enteropathy is treated with steroids[6,7], commonly prednisone and budesonide. Patients who are refractory to corticosteroids have responded to other immunosuppressive therapies like infliximab, rituximab, azathioprine, tacrolimus, cyclosporine, sirolimus, and 6-mercaptopurine[7- 10]. Budesone has the advantage of acting more locally at the gut epithelium due to its low bioavailability thus decreasing the systemic effects.

In this case, the patient was initially ruled-out for common causes of chronic diarrhea and CVID was excluded based on normal levels of immunoglobulins. The patient's clinical symptoms were suggestive of a malabsorptive diarrhea and celiac disease was considered. The biopsy results were suggestive of celiac disease; however, the patient's transglutaminase, celiac HLA type, and second generation gliadin antibodies were negative which was highly suggestive that the patient was not suffering from celiac disease[11]. The serologies for celiac disease are exceptionally sensitive and specific for celiac disease. The IgA anti transglutaminase antibody has a sensitivity and a specificity greater than 95% which is why it is the recommended first test for celiac disease[11]. IgA anti-gliadan antibody has a sensitivity and a specificity greater than 90%[11]. Also, the HLA DQ2 and HLA DQ8 (common celiac HLA haplotypes) are 91% sensitive and 54% specific[11]. but the combination of a negative transglutaminase, a negative gliadin antibody and negative celiac HLA type essentially rules out celiac disease[11]. In this scenario, the differential diagnosis must be expanded to include tropical sprue, protein intolerance, autoimmune enteropathy, and bacterial overgrowth.

This case of adult autoimmune enteropathy highlights the diagnostic challenge of a biopsy suggestive of celiac disease with negative celiac serologies. Many diseases can mimic the symptoms and histological manifestations of celiac disease. It is important for primary care physicians and gastroenterologists to have a familiarity with the diagnosis of adult autoimmune enteropathy as they work through the differential diagnosis of malabsorptive diarrheal syndromes. When the diagnosis of adult autoimmune enteropathy is made, it can lead to successful therapy with corticosteroids.

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