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Authors

Zilberstein, Netanel F.
Weiss, Guy A.

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CLINICAL VIGNETTE

Gluten-Sensitive Lymphocytic Gastritis: Two Novel Case Reports and a Review of Literature

Netanel F. Zilberstein, MD[1] and Guy A. Weiss, MD[2]

[1]Rush University Medical Center, Division of Digestive Diseases, Chicago, Illinois
[2]UCLA Celiac Disease Program, David Geffen School of Medicine at UCLA, Vatche and Tamar Manoukian Division of Digestive Diseases, Los Angeles, California

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Abstract

We present two patients presenting with chronic diarrhea who were diagnosed with idiopathic lymphocytic gastritis (LG). Secondary causes of LG, including celiac disease, Crohn's disease, and Helicobacter pylori (H. pylori) infection, were ruled out. A self-initiated gluten-free diet (GFD) led to histologic remission of this condition.

Introduction

Lymphocytic gastritis (LG) is characterized by infiltration of lymphocytes in the gastric epithelium. It is defined histologically by the presence of 25 lymphocytes per 100 gastric epithelial cells.[1] The disease is considered rare, found in less than 1% of gastric biopsies.[1] The clinical features of LG are non-specific and range from asymptomatic to abdominal pain, diarrhea, anemia, dyspepsia or weight loss, as can be seen with other various types of chronic gastritis.[2-4] The etiology of LG may either be idiopathic or secondary to a variety of diseases. The most common secondary causes are celiac disease (CD) and Helicobacter pylori (H. pylori) infection.[2] Other less common etiologies include Crohn's disease, Ménétrier disease, Human Immunodeficiency Virus (HIV), lymphoma, inflammatory polyps, and angiotensin receptor blockers (ARB) such as Olmesartan.[5,6] Secondary LG responds to treatment of the underlying cause; however, there is limited literature on effective treatment modalities for idiopathic LG beyond proton pump inhibitors. We present two novel cases of idiopathic LG that were treated effectively with a gluten-free diet (GFD).

Case 1

A 25-year-old male with immunoglobulin (Ig)A deficiency presented to our tertiary celiac clinic with mild chronic diarrhea for several years. There was no family history of CD or inflammatory bowel diseases. He denied smoking, alcohol use, or use of any medications. Prior serological testing was negative for anti-tissue transglutaminase (tTG) IgA and IgG, and giardia IgA and IgG. Repeat celiac serology also included anti-endomysial antibodies (EMA) and deamidated gliadin peptide (DGP) IgA and IgG, which were all negative. Pancreatic elastase level was normal and fecal calprotecin level was elevated to 192 μg/mg (normal <50). The patient underwent esophagogastroduodenoscopy (EGD) and colonoscopy. EGD demonstrated gastric erythema with biopsies revealing LG (Figure 1). H.pylori staining was negative. Duodenal biopsies showed increased intraepithelial lymphocytes (IEL) without crypt hyperplasia or villous atrophy (compatible with Marsh 1 lesions in a patient with CD). Colonoscopy showed diffuse colonic nodularity, but biopsies only revealed patchy lymphoid nodular inflammation, insufficient for the diagnosis of microscopic colitis and without granulomas to suggest Crohn's disease.

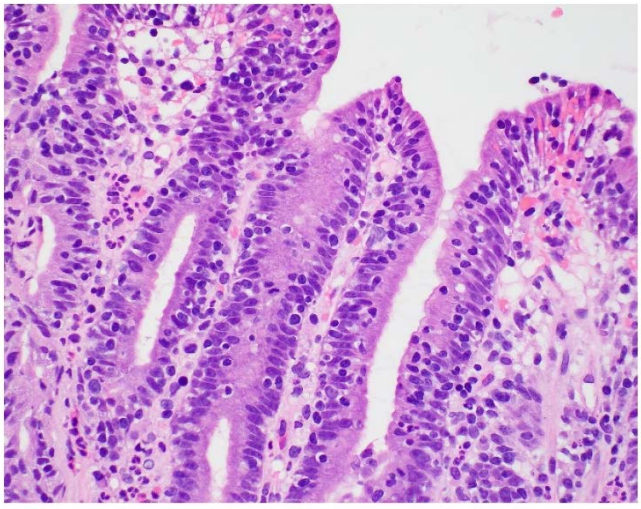

Figure 1. Lymphocytic Gastritis. 200x. Prominent increase in intraepithelial lymphocytes and expanded lamina propria.

In light of his IgA deficiency, which is seen in 2% of CD patients,[7] he also underwent genetic phenotyping, with absent HLA DQ2 and DQ8, excluding the diagnosis of CD. Given his overall unremarkable evaluation, he was diagnosed with idiopathic lymphocytic gastroduodenitis (LGD). He self-initiated a GFD for four months with improved diarrhea.

Several months later, he presented for follow-up with worsening diarrhea despite a GFD. He underwent a lactulose breath test with evidence of small intestinal bacterial overgrowth (SIBO). He was successfully treated with rifaximin with clinical resolution. He continued to adhere to a GFD, and subsequent EGD showed resolution of gastritis and histologic resolution of his LGD.

Case 2

A 20-year-old female with iron deficiency anemia presented to clinic for evaluation of a suspected gluten-associated disorder. She was previously evaluated for a two-year history of chronic diarrhea after international travel. She underwent an unremarkable evaluation, including celiac serology (including tTG IgA and IgG), inflammatory markers like C-reactive protein (CRP), EGD, wireless capsule endoscopy, and colonoscopy. Biopsies were significant for mild reflux esophagitis and LG without H. pylori. Duodenal and ileocolonic biopsies were unremarkable. She was previously trialed on a low fermentable oligo-, di-, and monosaccharides, and polyols (FODMAPs) diet with minimal improvement of her diarrhea. An evaluation at an allergy-immunology clinic concluded no evidence of wheat allergy. On presentation, she was on a GFD for a year following her primary care physician's advice. Celiac genotyping was ordered and was negative; yet, subsequent EGD showed resolution of LG. Despite her adherence to a GFD and histologic resolution of her LG, the patient's diarrhea did not improve.

Discussion

LG is characterized by lymphocytic infiltration of the gastric mucosa and presents with a range of non-specific symptoms. Both patients demonstrated endoscopic and histologic recovery following initiation of a GFD without long-term clinical remission. As idiopathic LG is a diagnosis of exclusion, our patients underwent thorough evaluation to rule out secondary causes.

Since LG is commonly seen in CD, a focus was made to evaluate for this specific comorbidity. Both patients underwent serologic evaluation, which was negative, along with histological examination to assess for seronegative CD.[8] Duodenal biopsies revealed lymphocytic duodenitis in our first case (which can be seen in the rare Marsh 1 CD, also termed mild-enteropathy CD[9]) and were normal in the second case. However, in light of absent CD genes in both cases, the diagnosis of CD was ruled out.

Our first patient was diagnosed with SIBO and was treated appropriately with improvement of his diarrhea, confirming that the diarrhea was not due to his LG. While SIBO is associated with isolated duodenal lymphocytosis, it is not associated with gastric lymphocytosis.[10] Therefore, the treatment of SIBO would not explain the patient's histologic resolution of LG. Similarly, in the second case the patient's histologic findings of LG resolved after initiation of a GFD, but her symptoms did not improve, suggesting that LG may have been an incidental finding. Both cases, therefore, are examples of asymptomatic LG, which is gluten sensitive, in patients without CD or wheat allergy.

In conclusion, to our knowledge these are the first published cases of histological resolution of idiopathic LG following introduction of a GFD. Further studies are required to determine whether a GFD is an effective and definitive treatment of idiopathic LG, and to establish its benefit and the therapeutic goals in asymptomatic patients.

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