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Lymphocytic Gastritis in A Patient with Microscopic Colitis: A Case Report

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Lymphocytic Gastritis in a Patient With Microscopic Colitis: A Case Report☆

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Abstract

Lymphocytic gastritis (LG) is a rare form of gastritis characterized by lymphocytosis in the gastric mucosa, while microscopic colitis (MC) is the chronic inflammatory disease of the large intestine with lymphocytic or collagenous colitis as two distinct histologic forms. These lymphocytic disorders of the gastrointestinal tract (GIT) have various associations, commonly gluten-sensitive enteropathy, *Helicobacter pylori* infection and while others are less commonly associated. We report a case of a 24-year-old patient with concomitant lymphocytic gastritis and microscopic colitis diagnosed via histopathologic analysis of tissue specimens from stomach and colon. The presence of a lymphocytic disorder in GIT should prompt workup for associated disorders. There is also an association between lymphocytic disorders of the lower GIT with the upper GIT, and vice versa. Endoscopy is important to diagnose comorbid lymphocytic conditions, and subsequently, guiding treatment.

Keywords: Lymphocytic gastritis, Microscopic colitis, Gastritis, Comorbid lymphocytic disorders

1. Introduction

Initially described by Haot et al. in 1986, LG is a histologic pattern of injury characterized by intraepithelial lymphocytosis in the gastric surface epithelium and chronic inflammation in the lamina propria.[1] LG is a rare form of gastritis, seen on less than 1% of gastric biopsies and between 1% and 8% of patients presenting with dyspepsia.[2] LG has been associated with other etiologies, with the most common being gluten-sensitive enteropathy (GSE) in 38% of cases and *Helicobacter pylori* (*H. pylori*) infection in 29% of cases. Less common associated etiologies include lymphoma, NSAID use, microscopic colitis, and idiopathic.[3–5]

MC is a chronic inflammatory disorder of the large intestine. The two types of MC are lymphocytic colitis and collagenous colitis, which differ in histologic characteristics.[6] The etiology of MC is poorly understood, but it has been associated with other autoimmune conditions such as GSE, diabetes, thyroid dysfunction and psoriasis.[7] Among these associations, MC has been most linked with GSE. Studies have shown that about 4% of patients with MC have GSE.[8] Other lymphocytic disorders of the GIT have been associated with MC including lymphocytic esophagitis, lymphocytic gastritis, and duodenal intraepithelial lymphocytosis.[9]

This study reports a case of concomitant lymphocytic gastritis and microscopic colitis diagnosed in a 24-year-old male. The aim of this study is to demonstrate that any lymphocytic disorder of the lower GIT should prompt suspicion and evaluation for a related disorder affecting the upper GIT and vice versa. Endoscopy is crucial in diagnosing the comorbid occurrence of different lymphocytic disorders, and subsequently directing treatment against them.[9]

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2. Case description

A 24-year-old male with anxiety, Raynaud's syndrome, and undifferentiated connective tissue disorder presented with a two-year history of cramping abdominal pain associated with loose stools and bloating to the gastroenterology clinic. The patients' bowel movements were irregular, ranging from multiple loose stools daily to multiple formed stools daily, to no stool on certain days. He denied blood or mucus in his stools. He was taking omeprazole, which was continued. The patient's home medications of meloxicam and hydroxychloroquine were held given concern this was possibly contributing to his GI symptoms, however despite stopping these medications his symptoms persisted. Further work-up including celiac panel, stool analysis for ova and parasites, *Clostridioides difficile*, *Giardia duodenalis*, and fecal leukocytes, were unremarkable.

The patient underwent an esophagogastroduodenoscopy (EGD) and colonoscopy (CSC) with multiple biopsies obtained. EGD showed normal appearing mucosa in the esophagus, stomach and in the second part of duodenum and no gross lesions were seen. Similarly on CSC, the mucosa in the terminal ileum and the entire colon was normal and no gross lesions were identified. Biopsies revealed inflammation throughout the GI tract. The histologic sections of the stomach biopsy showed lymphocytic gastritis with numerous intraepithelial lymphocytes (Figure 1). An immunohistochemical stain for Helicobacter organisms were negative. Duodenal biopsy revealed mucosa with borderline increase in intraepithelial lymphocytes, but with preserved villous architecture. Colon biopsy revealed mucosa with patchy intraepithelial lymphocytosis, suggesting lymphocytic (microscopic) colitis (Figure 2). The patient was prescribed budesonide treatment for 2 months with a subsequent taper. On follow-up the patient reported that his symptoms initially resolved however shortly after

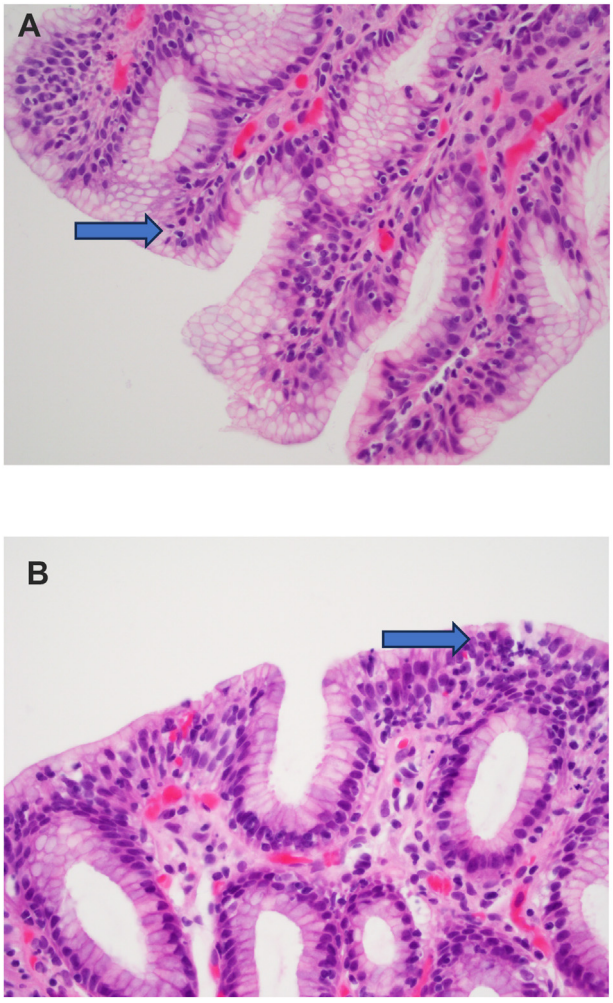

Fig. 1. A & B: Stomach biopsy shows a lymphocytic gastritis pattern with increased intraepithelial lymphocytes (blue arrows).

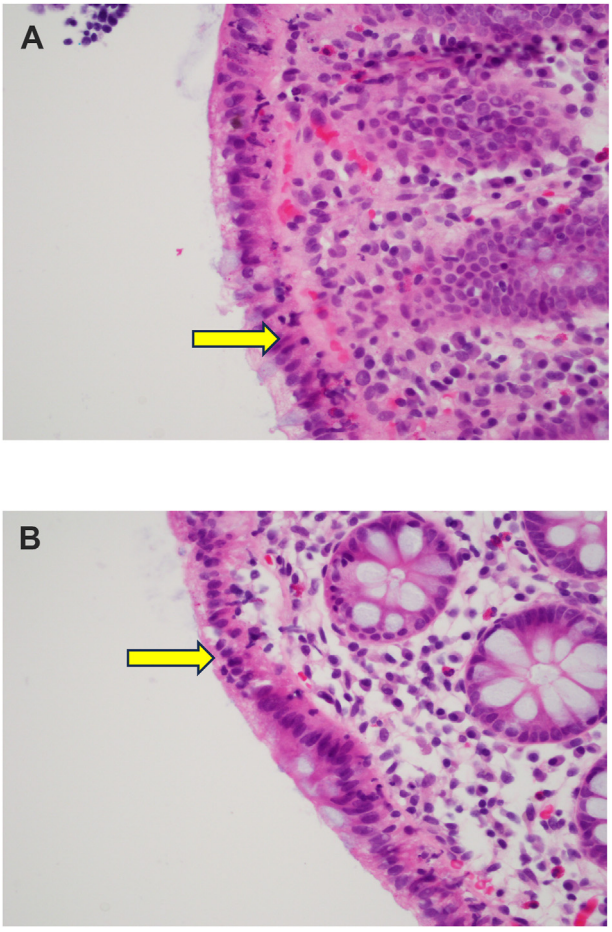

Fig. 2. A & B: Increased intraepithelial lymphocytes (in patches) are seen on the colon biopsy (yellow arrows).

noted a return in his symptoms. He was subsequently prescribed a retrial with budesonide for 2 months, and upon follow-up, reported improved symptoms along with formed stools.

3. Discussion

LG represents a histologic pattern of injury that can result from many causes. LG mainly affects adults, with a peak incidence in the sixth decade of life, and affects males and females equally.[10,11] Clinical symptoms include abdominal pain, dyspepsia, diarrhea, anorexia, recurrent vomiting, weight loss, and iron deficiency anemia.[11-13] Of the known associated conditions, the relationship of LG with GSE and *H. pylori* infection have been studied the most. The pathogenesis of LG is poorly understood, but it is thought to be caused by an atypical immune response to luminal agents, such as gliadin (gluten protein) and *H. pylori*, in genetically predisposed individuals.[14] One study showed that 7 out of 10 patients with LG had the human leukocyte antigen (HLA) DQ2 haplotype, which is present in about 95% of patients with GSE, which points to a common pathophysiologic mechanism.[11]

LG is diagnosed when there are at least 25 intraepithelial lymphocytes per 100 epithelial cells on gastric mucosal biopsy, with increased chronic inflammation in the lamina propria. Almost all intraepithelial lymphocytes are CD3 and CD8 positive.[15] Histologically, LG typically involves the entire stomach, but there are topological differences in intraepithelial lymphocytosis as well as morphological differences based on the etiology. Studies demonstrate that LG associated with GSE is antral-predominant, while LG associated with *H. pylori* is body-predominant.[16] Glandular micro-abscesses have been seen in cases with *H. pylori,* but not in cases associated with GSE and NSAID injury.[5] Yip et al. revealed a pan-gastric pattern of injury due to NSAID use.[17] Genta et al. found that LG associated with MC had no significant topological preference of gastric lymphocytosis.[15]

MC is a chronic inflammatory disease of the large intestine, that typically affects the older population and has a greater prevalence in females. The predominant symptom is chronic, watery, non-bloody diarrhea that can be accompanied by abdominal pain, fecal urgency, and incontinence. The two types of MC are lymphocytic colitis and collagenous colitis, which differ in histologic characteristics on biopsy.[6] Lymphocytic colitis is diagnosed if there are more than 200 intraepithelial lymphocytes per 100 enterocytes, mild mononuclear proliferation in the lamina propria, surface destruction, and normal subepithelial collagen. Collagenous colitis is diagnosed if there is thickened and irregular subepithelial collagen, with or without inflammatory cells and small vessels, mild mononuclear proliferation in the lamina propria, surface destruction often with epithelial detachment, and intraepithelial lymphocytosis.[9]

Previous studies have shown an association between MC with GSE. Studies have shown that there is a possible etiology that explains the frequent comorbid relationship between MC and GSE. Both conditions have an increased presence of HLA-DQ2 and have T1-helper cell mucosal cytokine involvement.[18,19] Similar to the pathogenesis of LG, the pathophysiology of MC is presumed to involve atypical immunological reactions to luminal agents in patients with genetic predisposition.[20]

Analysis by Sonnenberg et al. further revealed that all types of lymphocytic disorders of the upper GIT, such as lymphocytic esophagitis, lymphocytic gastritis, and duodenal intraepithelial lymphocytosis, were significantly more common in patients with MC, compared to patients without MC. LG was 15 times more likely in patients with MC, and GSE was 6 times more likely in patients with MC, compared to the overall study population. Between the two subtypes of MC, the comorbid existence of another lymphocytic disorder was higher in patients with lymphocytic colitis compared to collagenous colitis.[9] Our report has similar findings, i.e., lymphocytic microscopic colitis along with lymphocytic gastritis. Additionally, one can also make a case for microscopic enteritis (formerly known as duodenal lymphocytosis or lymphocytic duodenitis) as a borderline increase in intraepithelial lymphocytes was noticed on duodenal biopsy specimen, in the setting of co-presence of LG and MC in our patient report.

Therefore, incidental finding of any lymphocytic disorder in the lower GIT should prompt evaluation for a related disorder in upper GIT and vice versa. This will help guide the treatment plan.[9] Studies have shown that LG may act as a self-limited condition. In the 11-year span of the study, Genta et al. found that 80% of subjects showed no histopathological evidence of LG within a year of follow-up. However, this study was limited by the lack of information on whether these patients' received treatment or cleared LG naturally.[15] Other studies point to LG resolution following treatment of their underlying etiology. For example, Hayat et al. reported that in subjects with histologically confirmed *H. pylori* and LG, *H. pylori* eradication treatment with a 1-week course of omeprazole, clarithromycin, and metronidazole resulted in improved symptoms and reduction in the number of intraepithelial lymphocytes.[11] In clarithromycin triple therapy, the

two different antibiotics work through bacteriostatic and bactericidal effects to overcome antibiotic resistance by the bacteria, while the proton pump inhibitor reduces gastric secretions, which promotes mucosal healing.[21] Jevon et al. found that in patients with GSE and coexisting LG on histology, gluten-free diet led to resolution of gastric and small intestinal lymphocytosis. The theory is that without any gluten in the patients' diet there is no maladaptive immune response to the protein to result in intestinal destruction and inflammation.[22] Therefore patients diagnosed with MC as well as GSE should be treated with a gluten-free diet. For cases of MC with no known etiology there are many medication options including antidiarrheals, bismuth subsalicylate, mesalamine, cholestyramine, and budesonide. Among these therapies, oral budesonide shows the best evidence for efficacy. Budesonide is a potent glucocorticoid, with weak mineralocorticoid activity, that has a wide range of anti-inflammatory effects in the intestines. By binding to glucocorticoid receptors in the cytoplasm, budesonide inhibits expression of pro-inflammatory genes (i.e., TNF-alpha, interleukin-2 gene) and promotes expression of anti-inflammatory genes (i.e., interleukin-10 gene). Budesonide also has a high hepatic first-pass metabolism therefore causing a local response, with minimal adverse systemic effects. Relapsing MC cases are treated with budesonide as well.[23]

4. Conclusion

In conclusion, a histopathologic diagnosis of a lymphocytic disorder in the GIT should raise level of suspicion for a comorbid condition in another part of the GIT. The associations among lymphocytic disorders in the upper and lower GIT suggest a common etiology, which can help guide the patient's treatment. Topographic findings in the gastric mucosal biopsy may also help give direction to the underlying etiology. Future studies using molecular and immunologic markers may be beneficial to gain further knowledge on the underlying pathophysiology of these associations.

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None to disclose.

Informed consent

Obtained. IRB approval available upon editor's request.

Data availability

All the essential data is included in the draft.

Author contributions

Saba Ahmed MD: Primary Author. Case description and literature review, and referencing.

Jewel Estrella MS-3: Data Collection and contributed to discussion.

Khaleeq Siddiqui MD: Contributed to discussion, review and editing.

Fahad Malik MD: Conception of the article, review and editing.

Karen Avgush MD: Final Review and editing, literature review.

Yasir Ahmed, MD: Supervised the entire process, from drafting the initial manuscript to finalizing the draft. Literature search, figures' description, referencing, and review and editing and final draft for publication.

Conflict of interest

None.

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