CLINICAL VIGNETTE

Helicobacter pylori and Lymphocytic Gastritis: Cause and Effect?

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Case

A thirty-one-year-old male presented to gastroenterology with two years of chronic epigastric abdominal pain, diarrhea and weight loss. His symptoms had worsened in over six months prior to his initial visit. He reported 1-2 formed bowel movements/day at baseline. Since developing symptoms, he now averages 3-4 loose stools/day, associated with cramping pain and nausea without emesis or anorexia. His weight at initial consultation was 152lbs. His primary care physician started omeprazole with no improvement. Serologic blood and stool testing returned negative for celiac serologies and infectious stool studies: C diff, stool Cx, ova & parasites and *H. pylori*. However, his fecal calprotectin was elevated. Upper endoscopy and colonoscopy appeared normal. Pathology from random gastric biopsies were consistent with lymphocytic gastritis. He was treated with prednisone 40mg followed by a taper over the course of a month with symptoms improving by 90%. His weight increased to 166lbs by the end of the taper. After completion of the prednisone taper, his symptoms began to recur. He had a second upper endoscopy 2 months after the first. Gastric mapping was performed during the second endoscopy. Pathology from the gastric mapping showed diffuse evidence of lymphocytic gastritis in all the biopsies as well as presence of *H. pylori*. He was then treated with triple therapy, but symptoms began to recur 2 days after completing the antibiotics.

Discussion

Helicobacter pylori (*H. pylori*) is a common infection seen in about 1/3 of Americans and ½ of the global population. It is considered to be a level 1 carcinogen. It causes chronic active gastritis in 80% of patients who harbor the bacteria.[1] *H. pylori* is also known to induce gastric intestinal metaplasia leading environmental atrophic gastritis, gastric carcinoids (neuroendocrine tumors) and gastric adenocarcinoma through the correa cascade pathway. However, any relationship between *H. pylori* and lymphocytic gastritis (LG), remains poorly understood.

Lymphocytic gastritis is a condition in which there is an increased number of intraepithelial lymphocytes (IEL) 25 per 100 gastric epithelial cells and foveolar epithelial cells.[2] This is in comparison to the definition of "chronic active gastritis" which is what is typically seen with *H. pylori* gastritis. Chronic active gastritis is defined as the presence of 4-7 intraepithelial cells per 100 gastric epithelial cells. Chronic active gastritis related to *H. pylori* also has a specific pattern with a high neutrophilic infiltrate which is not seen in LG.[3] Lymphocytes seen in LG typically show CD3+ and CD8+ phenotypes.[3]

Lymphocytic gastritis is much rarer than *H. pylori* or atrophic gastritis. Is has been reported in 1-5% of chronic gastritis cases during upper endoscopy. Endoscopically, lymphocytic gastritis will often appear endoscopically as normal. Sometimes endoscopically visual signs of LG can range from mosaic patterns or in more severe cases with erosions, ulcers or polyps. Lymphocytic gastritis is generally seen in patients during their 5-6th decades of life. Typical symptoms of lymphocytic gastritis include: upper abdominal pain, vomiting, weight loss and dyspepsia.

Studies report an association between *H. pylori* and LG ranging from 0-27%. Nielsen et al. reported no *H. pylori* associated with LG. This retrospective study involved 56 patients, with only 2 testing positive histologically for both LG and *H. pylori*. Nine of the LG patients without *H. pylori* had positive serologies for *H. pylori*. Whitney et al hypothesized that *H. pylori* infection evolves from an acute infection with a neutrophilic infiltrate to a chronic inflammatory condition with a lymphocytic infiltrate.[4] Thus, LG may be an immunological reaction to an *H. pylori* antigen or specific virulence factor as opposed to the infection with bacteria itself. One theory currently suggests that there is a relationship between *H. pylori* and LG and the elusive relationship , is because the incidence of *H. pylori* has been declining since the *H. pylori's* discovery and eradication.[5] Another theory suggests immunohistochemical staining of gastric biopsies is not as sensitive as serologies or breath testing due to sampling error.[6] In contrast, there is a relationship between LG and celiac disease (CD). This association is thought to be related to HLA DQ2: DQB1*0201 seen in CD patients.[2] In Nielsen's study 36% (19/54) of LG patients were found to have CD. Other studies have cited a 10-38% association between LG and CD. The rate for positive celiac serologies in LG patients was also found to be much higher than *H. pylori* rate in LG patients. In patients with CD and LG, adhering a gluten free diet was found to improve both conditions by lowering the IEL count. In a similar fashion Makienen et al similarly found treating patients with LG with standard triple therapy also resulted in tremendous reduction in IEL count and clinical symptoms.[7]

Conclusion

Currently the relationship between *H. pylori* infection causing lymphocytic gastritis remains in question. Our patient tested histologically negative for *H. pylori* on his initial endoscopy but then tested positive on a follow up endoscopy following a course of corticosteroids. Perhaps the initial lack of finding *H. pylori* was due to sampling error as many fewer gastric biopsies were taken on the initial endoscopy. Alternatively, the prednisone immunosuppression may have unmasked the *H pylori*. Although the patient responded favorably to both corticosteroids and triple therapy (amoxicillin + clarithromycin + omeprazole), he continues to have relapsing symptoms with cessation of either therapy. Despite negative duodenal biopsies and celiac serologies he should be screened for HLA mutations associated with Celiac disease and *H. pylori* stool antigen should be checked following completion of triple antibiotic therapy to rule out resistant *H. pylori*. In conclusion, LG does not appear to be distinct clinicopathology entity but rather a morphological change in gastric mucosa due to a variety of potential etiologies.

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