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Nodular Lymphoid Hyperplasia: A Rare Find Underscores Individualized Medicine

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Background	A 28-year-old woman undergoing endoscopy was found to have a carpet-like distribution of innumerable 2 to 10 mm polyps within the visualized duodenum.
Summary	Our patient was undergoing esophagogastroduodenoscopy (EGD) as part of the routine evaluation for bariatric surgery. This presentation was initially thought to be a rare duodenal manifestation of familial adenomatous polyposis (FAP). Several polyps were biopsied, along with mucosal samples from her stomach and esophagus. The results demonstrated reactive lymphoid follicles within the duodenum, characteristic of nodular lymphoid hyperplasia (NLH). The patient was also found to demonstrate histologic evidence of *H. pylori* infection.
Conclusion	Nodular lymphoid hyperplasia is characterized by innumerable polyps composed of reactive lymphoid follicles within the duodenum. We report an instance of adult NLH associated with concurrent *H. pylori* infection. NLH rarely manifests in adults and has been suggested to precede mucosa-associated lymphoid tissue lymphoma. Surveillance by regularly visualizing the upper GI tract removes the Roux-en-Y as an approach for bariatric surgery.
Key Words	nodular lymphoid hyperplasia; familial adenomatous polyposis; duodenitis; *Helicobacter pylori*; mucosa-associated lymphoid tissue; germinal center hyperplasia
Abbreviations	NLH: Nodular lymphoid hyperplasia CVID: Common variable immune deficiency FAP: Familial adenomatous polyposis EGD: Esophagogastroduodenoscopy *H. pylori: Helicobacter pylori* MALT: Mucosa-associated lymphoid tissue

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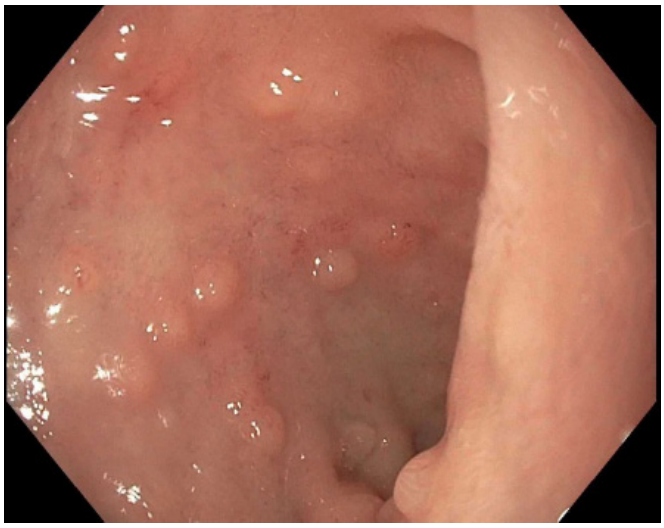
Case Description

Among the various responsibilities of the gastrointestinal tract is the sampling of luminal contents and reaction to potential threats. In children, hypertrophy of mucosa-associated lymphoid tissue (MALT) after exposure to certain viral antigens may appear as numerous nodules along the duodenal mucosa. This is attributed to a relatively immature adaptive immune system and is seldom seen in adults.[1] We reported a rare instance of nodular lymphoid hyperplasia (NLH) found incidentally on esophagogastroduodenoscopy (EGD) in an adult.

Our patient is a 28-year-old female with a history of class III morbid obesity (BMI 56), polycystic ovarian syndrome, iron deficiency anemia, and vitamin D insufficiency. She presented for EGD as part of the routine pre-operative evaluation for bariatric surgery. At every encounter, she denied acid reflux/heartburn, post/pre-prandial nausea, epigastric pain, and indigestion. We proceeded with endoscopy using the Olympus TJFQ180V duodenoscope.

After unremarkably visualizing the esophagus and stomach, the duodenum demonstrated a remarkable carpet-like distribution of 2 to 10 mm polyps (Figure 1). Biopsies were taken of the lesions, stomach, and distal esophagus. With familial adenomatous polyposis (FAP) as the working diagnosis, our patient was scheduled for a colonoscopy which proved unremarkable, demonstrating a grossly normal appearing colonic mucosa.

Figure 1. Initial EGD Visualizing Second Part of Duodenum with Many Sub-Centimeter Nodules. Published with Permission

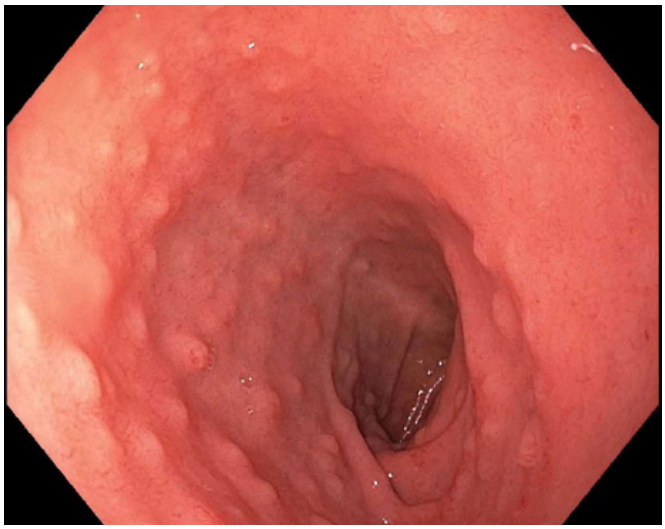


The EGD biopsy/pathology report read:

1. Duodenum: Chronic duodenitis with reactive lymphoid follicles;
2. Stomach: Chronic active gastritis with organisms morphologically consistent with Helicobacter pylori;
3. Distal Esophagus: Active esophagitis with focally up to 40 eosinophils per high power field.

The patient was diagnosed with *Helicobacter pylori* (*H. pylori*) gastritis and subsequently prescribed omeprazole, amoxicillin, metronidazole, and clarithromycin, a standard eradication therapy. An EGD performed a month later confirmed the successful eradication of *H. pylori* infection, but the duodenal mucosa retained its ominous morphology (Figure 2).

Figure 2. Follow-Up EGD Visualizing Second Part of Duodenum with Many Sub-Centimeter Nodules. Published with Permission



The Roux-en-Y gastric bypass (RYGB) procedure has proven superior to the sleeve gastrectomy in diabetic populations and for relieving reflux symptoms, and thus was the initial operation of choice for this patient.[2] In the RYGB, the proximal 10% of the stomach is divided, leaving a 30-50 cc gastric pouch and a separated gastric remnant. The gastric pouch is then anastomosed to the jejunum (this is the Roux limb). The Roux limb, which is between 100 and 150 cm in length, is then anastomosed to the biliopancreatic limb, combining to form the common channel. In comparison, sleeve gastrectomy involves resecting a large crescent-shaped section of the stomach from the fundus to

the antrum, preserving the gastroduodenal junction. The RYGBs resultant anatomic rearrangement prevents traditional endoscopic visualization of the biliopancreatic limb. Considering this, we decided to shift course to a sleeve gastrectomy as the potential progression of NLH to lymphoma warrants regular surveillance of the upper GI tract. She was scheduled for a repeat EGD a year after the operation.

Discussion

NLH is a condition with unknown etiology marked by the appearance of many sub-centimeter nodules distributed along the GI tract (most commonly the small intestine). While it may appear at any age, it is more common in children and very rare in adults. NLH alone does not have well-defined symptomatology and often is an incidental finding on EGD. The chronic inflammatory state present in the duodenum may cause chronic diarrhea, intestinal bleeding, and abdominal pain.[3]

There is little literature concerning this condition in adults, but etiology has been suggested as divisible into either immune deficiency or immune hyperstimulation. The immune deficiency state in question is one of an adaptive immunity defect. Common variable immune deficiency (CVID) has often been present in reported instances of NLH.[4] In CVID, there is a maturational defect of the plasma cells that occupy germinal centers within lymphoid tissue. Those germinal centers within the mucosa of the duodenum then begin to hypertrophy as plasma cell precursors accumulate in an attempt to compensate for functional inadequacy. This ultimately may result in the hyperplastic nodular lymphatic tissue characteristic of NLH.

Conversely, some suggest repetitive stimulation of an adequate GI immune system leads to reactive hyperplasia of lymphatic follicles. This theory is supported by the apparent association between NLH and *H. pylori* infections. Khuroo et al. identified a relatively large cohort of individuals (40 patients; 23 male, 17 female) displaying NLH and prospectively followed them for five years.[5] EGD identified patients with NLH during workup for epigastric pain, vomiting, and weight loss. Remarkably every patient was concurrently infected with *H. pylori*.

Further strengthening the connection, a significant resolution in the appearance of NLH followed the effective eradication of the infection. Their patients with resistant infections did not show substantial change. Curiously, iron deficiency anemia was a secondary finding in their entire cohort, as it was in our patient.

Malignancy is the greatest concern upon discovery of NLH as the appearance has been linked to lymphoma and may be a pre-malignant lesion disorder, transitioning into MALT lymphoma.[3] There is little data to support the rate of transition nor an established protocol for monitoring these patients. Our bariatric procedure recommendation was adjusted to allow easy duodenal visualization and surveillance of her small intestine, given the sparsity of consensus.

Conclusion

NLH presents as the remarkable appearance of many sub-centimeter lymphatic nodules projecting into the lumen of the duodenum, sparing the bulb and often extending no further than its distal border. The condition may follow infection in children, but it is exceedingly rare in adults. Though not well characterized, literature regarding the condition has suggested a relation with or progression to lymphoma. The findings influenced our choice of bariatric procedure to facilitate future monitoring anatomically.

Lessons Learned

Addressing weight to the implications of unknown factors is an exercise of experience and education demonstrated in the break from algorithmic medicine that is a physician's judgment call. A fluid approach to a rigid outcome is key when accounting for rare findings in clinical decision-making, underscoring the importance of individualized medicine.

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