Patterns of Gastric Injury
Beyond *Helicobacter Pylori*

Won-Tak Choi, MD, PhD[a], Gregory Y. Lauwers, MD[b,*]

KEYWORDS

• Autoimmune • Collagenous • Eosinophilic • Granulomatous • Lymphocytic • Stomach

Key points

- Non–*Helicobacter pylori* gastritis can be broadly categorized into 4 distinct patterns based on the distribution and nature of inflammation, and other unique features.
- Chronic inflammation in the lamina propria raises consideration for autoimmune gastritis, collagenous gastritis, and lymphocytic gastritis.
- Granulomatous inflammation is associated with Crohn's disease, sarcoidosis, and some forms of infectious gastritis.
- Limited lamina propria inflammation can be seen in the setting of viral infection, caustic gastritis, ulcero-hemorrhagic gastritis, reactive gastropathy, graft-versus-host disease, drug-induced gastritis, and chemoradiation-induced injury.
- Crystal or pigment deposition is present in iron-pilled gastritis, gastric mucosal calcinosis, lanthanum carbonate, and Kayexalate in sorbitol.

ABSTRACT

Gastric biopsies are routinely obtained from patients with symptoms related to the gastrointestinal tract and, as a result, a variety of histologic changes are observed in patients with or without endoscopic evidence of mucosal injury. Although *Helicobacter pylori*–related gastritis is still common, several other patterns of mucosal injury are increasingly encountered. These patterns of injury are classified based on the nature and distribution of inflammation, location of epithelial cell injury, presence of crystal or pigment deposition, and/or other unique features. This article discusses each of these patterns and provides a differential diagnosis for each.

OVERVIEW

Several patterns of gastric injury have been recognized since the identification of *Helicobacter pylori* as a cause of chronic gastritis. Several classification schemes for gastritis have been described, most of which are based on the presence of active (neutrophilic) or chronic (lymphoplasmacytic) inflammation. Herein, we describe a classification system that includes 4 broad groups of non–*H. pylori*–related gastric injury: gastritis with prominent inflammatory infiltrates in the lamina propria, gastritis with granulomatous inflammation, gastritis with focal lamina propria inflammation, and mucosal injury with crystal or pigment deposition.

Disclosure Statement: The authors have nothing to disclose.

[a] Department of Pathology, University of California at San Francisco, 505 Parnassus Avenue, M554, Box 0102, San Francisco, CA 94143, USA; [b] Gastrointestinal Pathology Service, Department of Pathology, Moffitt Cancer Center, 12902 Magnolia Drive, Tampa, FL 33612, USA

* Corresponding author.

E-mail address: Gregory.Lauwers@Moffitt.org

Surgical Pathology ■ (2017) ■–■

http://dx.doi.org/10.1016/j.path.2017.07.003

GASTRITIS WITH PROMINENT INFLAMMATORY INFILTRATES IN THE LAMINA PROPRIA

GASTRITIS WITH LYMPHOPLASMACYTIC INFLAMMATION

Autoimmune Gastritis

Autoimmune gastritis presumably develops from a complex interaction between circulating autoantibodies directed against intrinsic factor and H+/K+ ATPase proton pumps of parietal cells (**Fig. 1**). Progressive destruction of parietal cells leads to lack of intrinsic factor, vitamin B12 deficiency, and hypochlorhydria, as well as iron deficiency due to decreased duodenal uptake. The resultant atrophic mucosa is thin with loss of folds, although patchy preservation of oxyntic mucosa produces a polypoid appearance in early stages of disease.[1] Other abnormalities include low serum pepsinogen I and high serum gastrin concentrations, the latter resulting from hyperplasia of antral gastrin-producing G-cells.

Early histologic features are subtle; patchy lymphoplasmacytic inflammation is centered on oxyntic glands and may be associated with surface foveolar hyperplasia.[2] Fully developed autoimmune gastritis displays dense, diffuse lymphoplasmacytic inflammation with rare eosinophils and neutrophils, predominantly affecting the deep mucosa where it is associated with gland infiltration and damage (**Fig. 2**A). The pit region of the mucosa is relatively spared.[2] Over time, oxyntic glands are replaced by metaplastic epithelium with pseudopyloric, intestinal, and/or pancreatic differentiation (**Fig. 2**B).[2,3] Completely atrophic oxyntic mucosa is composed of metaplastic glands mimicking antral mucosa; a negative gastrin immunostain ensures that a biopsy is from the fundus or body.

Decreased acidity of gastric juices leads to proliferation of G-cells in the antrum that secrete gastrin, resulting in hypergastrinemia. Gastrin is a trophic hormone that stimulates endocrine cells, including enterochromaffin-like (ECL) cells of oxyntic mucosa to proliferate.[2] "Linear ECL-cell hyperplasia" is defined by at least 2 linear groups of 5 consecutive cells lining a gland. "Micronodular hyperplasia" consists of clusters of 5 or more cells bounded by basement membrane and not exceeding 150 μm (ie, approximately the diameter of a gastric gland). Five or more clusters of micronodules are classified as "adenomatoid ECL-cell hyperplasia," whereas "ECL-cell dysplasia" applies to fused micronodules that show loss of basement membrane or span greater than 150 μm in diameter. Linear, micronodular, and adenomatoid ECL-cell hyperplasia have essentially no neoplastic potential,[4] whereas some patients with ECL-cell dysplasia develop well-differentiated gastric tumors (type 1 carcinoid tumors). Of note, even these lesions are associated with a very low risk of progressive disease, especially when compared with type 3 (sporadic) endocrine tumors of the stomach. Autoimmune gastritis with atrophy is also associated with an increased risk of adenocarcinoma.[3]

Syphilitic Gastritis

Gastric syphilis should be considered in high-risk patients who complain of nausea, vomiting, abdominal pain, gastrointestinal bleeding, and/or early satiety. Variable endoscopic findings include diffuse mucosal edema, erythema, multiple erosions and ulcerations, and thickened rugal folds that simulate an infiltrative process.[5] Rare patients develop gastric perforation. Symptoms may wane after a few days of antibiotherapy and, thus, the diagnosis is uncommonly made on biopsies with its true incidence unknown.[5]

Characteristic features include a dense lymphoplasmacytic infiltrate with gland destruction and

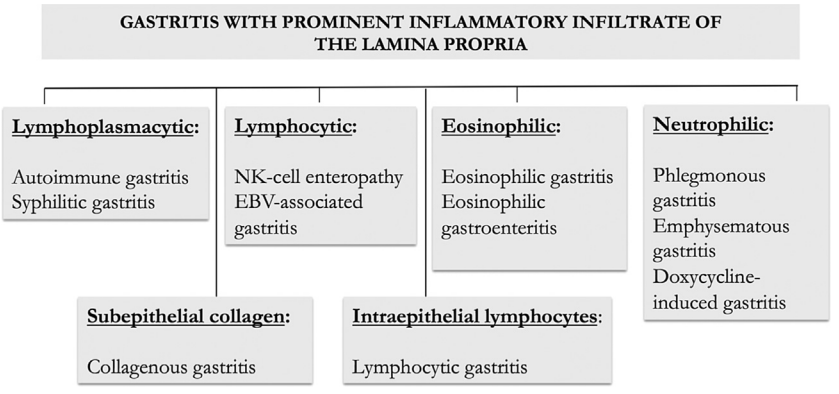

Fig. 1. Differential diagnosis of gastritis with prominent inflammation in the lamina propria.