Practical Approach to the Pathologic Diagnosis of Gastritis

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Context.—Most types of gastritis can be diagnosed on hematoxylin-eosin stains. The most common type of chronic gastritis is Helicobacter pylori gastritis. Reactive or chemical gastropathy, which is often associated with nonsteroidal anti-inflammatory drug use or bile reflux, is common in most practices. The diagnosis of atrophic gastritis can be challenging if few biopsy samples are available and if the location of the biopsies in the stomach is not known, such as when random biopsies are sampled in one jar. If the biopsy site is not known, immunohistochemical stains, such as a combination of synaptophysin and gastrin, are useful in establishing the biopsy location.

Objective.—To demonstrate a practical approach to achieving a pathologic diagnosis of gastritis by evaluating a limited number of features in mucosal biopsies.

Data Source.—In this article, we present several representative gastric biopsy cases from a gastrointestinal pathology practice to demonstrate the practical application of basic histopathologic methods for the diagnosis of gastritis.

Conclusions.—Limited ancillary tests are usually required for a diagnosis of gastritis. In some cases, special stains, such as acid-fast stains, and immunohistochemical stains, such as for H pylori and viruses, can be useful. Helicobacter pylori immunohistochemical stains can particularly contribute (1) when moderate to severe, chronic gastritis or active gastritis is present but no Helicobacter organisms are identified upon hematoxylin-eosin stain; (2) when extensive intestinal metaplasia is present; and (3) in follow-up biopsies, after antibiotic treatment for H pylori.

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Gastritis refers to a group of diseases characterized by inflammation of the gastric mucosa. Histologic examination of gastric mucosal biopsies is necessary to establish a diagnosis of gastritis. In clinical practice, the role of the pathologist who evaluates a gastric biopsy for gastritis is to find the cause of gastritis because that will provide direct targets toward which therapeutic measures can be directed. An etiologic classification of gastritis is presented at the end of this section. Comprehensive reviews of gastritis have been published.1,2,3 The goal of this article is to present a practical approach to the diagnosis of the most common types of gastritis encountered in a large practice of gastrointestinal pathology. The reader will be presented several cases representative of typical forms of gastritis; for each case, the reader will be prompted through a series of questions to examine the histologic features of the mucosa, leading to a pattern of answers and to a final diagnosis.

The first question is aimed at determining whether or not there are features of chronic or acute (active) gastritis present. If the biopsy shows chronic gastritis, the following questions should be posed:

1. Are there features of chronic gastritis present? Lymphocytic and plasmacytic inflammatory reaction indicates chronic gastritis.
2. Are there neutrophils in the mucosa? The presence of neutrophils indicate active gastritis.
3. Is there Helicobacter?
4. Is there glandular atrophy? Is intestinal metaplasia present?
5. What is the topography of lesions (predominantly in the oxyntic mucosa of the body and fundus, predominantly in antrum, or involving both locations)?
6. Are there special features (such as granulomas, foveal hyperplasia, viral inclusions)?
7. What ancillary studies are indicated, and what are the results?

Types of Chronic Gastritis

Infectious Gastritis

Helicobacter pylori infection is the most common cause of chronic gastritis. Other forms of infectious gastritis include the following: Helicobacter heilmannii–associated gastritis; granulomatous gastritis associated with gastric infections in mycobacteriosis, syphilis, histoplasmosis, mucormycosis, South American blastomycosis, anisakiasis or anisakidosis; chronic gastritis associated with parasitic infections; and viral infections, such as cytomegalovirus and herpesvirus infection.
Examination of the biopsy material available
Gastral antral mucosa with infections. ma, such as intubation associated mucosal lesions; and vis ischemia and shock; systemic infections; mechanical trauma; uremia; severe stress (trauma, burns, surgery); therapeutic drugs and radiation; acids and alkali in suicide attempts; and alcohol consumption; heavy smoking; cancer chemother apic drugs and radiation; acids and alkali in suicide attempts; uremia; severe stress (trauma, burns, surgery); ischemia and shock; systemic infections; mechanical trauma, such as intubation associated mucosal lesions; and viral infections.

Case 1
A 60-year-old man underwent esophagogastroduodenoscopy. A biopsy of gastric antrum was submitted to pathology to rule out _H pylori_. The histologic findings are shown in Figure 1, A through C.

Findings.—Examination of the biopsy material available gives the following answers:
1. Are there features of chronic gastritis? Yes. The gastric antral mucosa shows expansion of the lamina propria by chronic inflammatory cells, consisting of plasma cells and small lymphocytes, predominantly located toward the luminal aspect of the mucosa, a pattern that is suggestive of _H pylori_ infection.
2. Are there neutrophils in the mucosa? Yes. Therefore, this represents active gastritis. This is a mild form of active gastritis.
3. Is there _Helicobacter_? Yes. Hematoxylin-eosin (H&E) examination reveals diagnostic _H pylori_ bacterial forms in the surface mucus layer in close proximity to the apical aspect of surface epithelial cells.
4. Is there glandular atrophy? The biopsy sample available is not adequate for evaluation of atrophic gastritis; multiple biopsies, including samples of gastric body, are necessary for adequate evaluation of glandular atrophy. Is there intestinal metaplasia? Yes.
5. What is the topography of lesions? The chronic gastritis in this case involves, at minimum, the gastric antrum; it is advisable to obtain biopsy samples of both gastric antrum and body for a better evaluation of gastritis, as recommended by the updated Sydney guidelines for classification of gastritis.
6. Are additional special features present? No.
7. Are special stains recommended? No.

Diagnosis.—Gastric antral mucosa with _H pylori_-associated chronic gastritis, mildly active, and focal intestinal metaplasia.

_H PYLORI-_ASSOCIATED CHRONIC GASTRITIS

The _Helicobacter_ species consist of gram-negative rods that infect the gastric mucosa. _Helicobacter pylori_ bacteria are 3.5 μm long and are generally comma-shaped or have slightly spiral forms. _Helicobacter heilmannii_, a rare agent of chronic gastritis, is a 5- to 9-μm-long bacterium, with a characteristic tightly corkscrew-shaped, spiral form. _Helicobacter pylori_ infection usually is acquired during childhood, persisting as chronic gastritis if the organism is not eradicated. During progression of gastritis over the years, the gastric mucosa undergoes a sequence of changes that may lead to glandular atrophy, intestinal metaplasia, increased risk of gastric dysplasia and carcinoma, and mucosa-associated lymphoid tissue lymphoma, reported as extranodal, marginal zone, B-cell lymphoma in the World Health Organization classification. _Helicobacter pylori_ infection is associated with the histologic pattern of active and chronic gastritis, reflecting the presence of neutrophils and mononuclear cells (lymphocytes and plasma cells) in the mucosa, respectively. The term _active gastritis_ is preferred to _acute gastritis_ because _H pylori_ gastritis is a long-standing chronic infection with ongoing activity. Lymphoid aggregates and lymphoid follicles may be observed expanding the lamina propria, and rare lymphocytes may enter the epithelium. _Helicobacter pylori_ organisms are found within the gastric mucus layer that overlays the apical side of gastric surface cells, and lower numbers are found in the lower portions of the gastric foveolae. _Helicobacter pylori_ may be found within the deeper areas of the mucosa in association with glandular cells in patients on acid blockers, such as the commonly used proton pump inhibitors.

_Helicobacter pylori_-associated gastritis can display different levels of severity. The severity of _H pylori_ gastritis activity may be indicated in a pathology report as mild (rare neutrophils seen), moderate (obvious neutrophils within the glandular and foveolar epithelium), or severe (numerous neutrophils with glandular microabscesses and mucosal erosion or frank ulceration). _Helicobacter pylori_-associated chronic gastritis can manifest as a pangastritis involving the area from the pylorus to the gastric body and cardia, or it may predominantly involve the antrum. Patients with gastric ulcers generally have antral-predominant gastritis, whereas pangastritis,
or at least multifocal gastritis, is more common in patients with gastric carcinoma. The latter generally have significant intestinal metaplasia and gastric oxyntic glandular atrophy coexisting in the background stomach. It is important to make a pathologic diagnosis of atrophic gastritis because gastric atrophy is associated with increased risk of gastric cancer.15,16 Patients with chronic atrophic gastritis may have up to a 16-fold increased risk of developing gastric carcinoma, compared with the general population.15,17

When large numbers of \textit{H pylori} are present in the mucosa, the identification of typical organisms is generally possible on H&E stains. However, there are cases of chronic active gastritis with features suggestive of \textit{H pylori} gastritis in which the organisms are not detected. Several special stains have been extensively used to help identify \textit{H pylori} organisms in the gastric mucosa, including modified-Giemsa, Genta, thiazine stains, and immunohistochemistry against \textit{Helicobacter} antigens. The selection of the special stain used is largely dependent on preferences related to individual practices. Although, overall, no major differences in sensitivity and specificity have been reported, studies have recommended immunohistochemical stains in a subset of cases.18,19 In our practice, we prefer to use immunohistochemical stains for detection of \textit{H pylori} if organisms are not found on H&E stains in the following cases: (1) if moderate to severe chronic gastritis or any grade of active gastritis is present but no \textit{Helicobacter} organisms are identified on H&E; (2) when extensive intestinal metaplasia is present because \textit{H pylori} density is reduced in areas of intestinal metaplasia; and (3) during follow-up biopsies after antibiotic treatment for \textit{H pylori}. \textit{Helicobacter helmanii} may cause similar pathology, and the treatment is similar to \textit{H pylori}.5

**Case 2**

A 45-year-old man is seen to rule out \textit{H pylori}. He presents with a history of Crohn disease. The histologic findings are shown in Figure 2.

**Findings.**—Examination of the biopsy material results in the following pattern of answers:

1. Are there features of chronic gastritis? Yes. The gastric antral mucosa shows expansion of the lamina propria by chronic inflammatory cells, consisting of admixed plasma cells and small lymphocytes, throughout the thickness of the mucosa.

2. Are there neutrophils in the mucosa? Yes, with an occasional glandular abscess; therefore, there is active gastritis. Of note, the active gastritis has a patchy distribution.

3. Is there \textit{Helicobacter}? No. Examination with H&E stain does not reveal such bacterial forms. Immunohistochemical stain is performed.

4. Is there atrophy? The biopsy sample available is not adequate for evaluation of atrophic gastritis because the biopsy material is only from the gastric antrum; multiple gastric body biopsies are necessary for adequate evaluation of glandular atrophy. There is no intestinal metaplasia.

5. What is the topography of lesions? The chronic gastritis involves, at minimum, the gastric antrum.

6. Are additional special features seen? No. Although in a case of Crohn disease gastritis, epithelioid granulomas may be present; in this case, no granulomas were seen.

7. Are special stains recommended? Yes. \textit{Helicobacter pylori} immunohistochemical stain, which is helpful in cases where Crohn disease is suspected because the absence of \textit{H pylori} organisms in chronic active gastritis is consistent with Crohn disease. The \textit{H pylori} immunohistochemical stain in this case is negative.

**Diagnosis.**—Gastric antral mucosa with chronic active gastritis, moderately active, patchy. No \textit{H pylori} organisms are identified by H&E or immunohistochemistry. Note: These features are consistent with Crohn disease-associated gastritis.

**CROHN DISEASE—ASSOCIATED GASTRITIS**

The hallmark histopathologic features of Crohn disease—associated gastritis are the presence of patchy, acute inflammation with possible gastric pit or glandular abscesses, commonly with a background with lymphoid aggregates. Recent studies20 reported the presentation of gastritis in patients with Crohn disease as a focally enhanced gastritis, characterized by small collections of lymphocytes and histiocytes surrounding a small group of gastric folds or glands, often with infiltrates of neutrophils. In severe cases, there may be diffuse inflammation in the lamina propria, with variable glandular loss, fissures, ulcers, transmural inflammation, and fibrosis. Noncaseating epithelioid granulomas may be present in about one third of cases of Crohn disease gastritis but are often not seen, at least in part, because of limited tissue sampling.

When granulomas are identified, the differential diagnosis includes other forms of granulomatous gastritis. There are infectious and noninfectious causes of granulomatous gastritis. Noninfectious diseases represent the usual cause of gastric granulomas and include Crohn disease, sarcoidosis, and isolated granulomatous gastritis. Sarcoid-like granulomas may be observed in cocaine users, and foreign material is occasionally observed in the granulomas. Sarcoidosis of the stomach is usually associated with granulomas in other organs, especially the lungs, hilar nodes, or salivary glands. A diagnosis of idiopathic, iso-
Examination of the biopsy material results

Gastric oxyntic mucosa with gastric body to rule out pachygyria (hematoxylin-eosin, original magnification x10). The histologic findings are shown in Figure 3, A and B.

Figure 3. Helicobacter pylori–associated atrophic gastritis. A, Chronic active gastritis involving the gastric oxyntic mucosa with glandular atrophy (hematoxylin-eosin, original magnification x10). Inset shows rare neutrophils in the glandular epithelium (white arrows). B, Immunohistochemical stain for Helicobacter pylori shows a small area with organisms attached to the surface epithelium. Insets show individual Helicobacter bacteria (thin arrows) with characteristic elongated, slightly spiral S shape or clusters of packed bacteria (thick arrowhead) closely adherent to the surface of epithelial cells. Immunohistochemical stains are useful in cases such as this one, when H pylori organisms are closely associated with the surface epithelial cells making it difficult to ascertain the characteristic bacterial morphology on hematoxylin-eosin stains (original magnification x40).

lated, granulomatous gastritis is rendered when known entities associated with granulomas are excluded.

Case 3

A 60-year-old man presents with a nodularity of the gastric body to rule out H pylori. Esophagogastroduodenoscopy with biopsy of the nodular areas was performed. The histologic findings are shown in Figure 3, A and B.

Findings.—Examination of the biopsy material results in the following pattern of answers:

1. Are there features of chronic gastritis? Yes.
2. Are there neutrophils in the mucosa? Yes. There are neutrophils in the mucosa, representing active gastritis.
3. Is there Helicobacter? No. Examination with H&E stain does not reveal H pylori bacterial forms. Immunohistochemical is performed.
4. Is there atrophy? Yes. There is a reduced number of oxyntic glands in the biopsy. There is no intestinal metaplasia.
5. What is the topography of lesions? The chronic gastritis involves, at minimum, the gastric body.
6. Are additional special features seen? No.
7. Are special stains recommended? Yes. Helicobacter pylori immunohistochemical stain, which is positive.

Diagnosis.—Gastric oxyntic mucosa with H pylori–associated chronic active gastritis and glandular atrophy, moderate. No intestinal metaplasia is identified. Helicobacter organisms are identified by immunohistochemistry.

ATROPHIC GASTRITIS

Several publications, including those reporting the Sydney system and the updated Houston classification of gastritis, have proposed criteria for the evaluation of atrophic gastritis. Interobserver variability is significant, especially in the evaluation of antral atrophy. Recent advances that appear to decrease the interobserver variation in the assessment of gastric atrophy have been reported. Atrophy is more accurately assessed after resolution of severe inflammation of the mucosa; therefore, if there is H pylori gastritis, the infection should be eradicated before atrophy is definitively evaluated. When marked inflammation is present, a diagnosis of indefinite for atrophy may be offered, especially if there is no intestinal metaplasia.

The recommended definition of atrophy is the loss of appropriate glands, and atrophy can be scored according to the degree of severity as mild, moderate, or severe. In this definition, intestinal metaplasia represents a form of atrophy described as metaplastic atrophy (or gastric glandular atrophy with intestinal metaplasia).

Gastric atrophy is usually associated with intestinal metaplasia. However, in limited endoscopic biopsies, intestinal metaplasia might not be sampled, whereas the mucosa shows definitive atrophy. Usually gastric atrophy and intestinal metaplasia occur on a background of chronic gastritis, hence the term atrophic gastritis.

Sampling of the mucosa for evaluation of atrophy and gastritis is generally adequate by using the 5 biopsies recommended by the Sydney system, including 2 biopsies from the antrum, 2 from the corpus or body, and 1 from the incisura angularis. It is essential for the pathologist to have a means of determining the specific site in the stomach where a biopsy is sampled from because specific topography of atrophy characterizes the different types of atrophic gastritis. In atrophic gastritis associated with H pylori, glandular atrophy and intestinal metaplasia involve both the gastric antrum and body, whereas in autoimmune atrophic gastritis, the disease is essentially restricted to the gastric body. Ideally, the precise location is indicated by the endoscopist, and the biopsies from different sites are submitted in separate containers. However, using special stains can help the pathologist determine the location of the biopsy fragments received. This approach is exemplified in case 5.

Gastric atrophy and intestinal metaplasia are associated with increased gastric cancer risk, but unlike the intestinal metaplasia of Barrett syndrome, no specific recommendations for surveillance have been established in the United States, although published data in other populations have suggested a benefit. In that study, patients with...
Examination of the biopsy material results

Gastric oxyntic mucosa with chronic active gastritis (Figure 4, B), show a linear pattern of synaptophysin-positive cells. Immunohistochemical stains for synaptophysin and gastrin are performed. The linear arrays of synaptophysin-positive cells represent enterochromaffin-like cell hyperplasia. Enterochromaffin-like cell hyperplasia occurs in response to hypergastrinemia that results from hypochlorhydria associated with gastric oxyntic cell atrophy.

6. Are additional special features seen? No.
7. Is immunohistochemical stain for \(H. pylori\) positive? No.

**Diagnosis.**—Gastric oxyntic mucosa with chronic active gastritis and glandular atrophy, severe. No intestinal metaplasia is identified. No \(H. pylori\) organisms are identified. Note: These features are most suggestive of autoimmune gastritis.

**AUTOIMMUNE ATROPHIC GASTRITIS**

This form of gastritis (reviewed in Sepulveda et al\(^1\) and Capella et al\(^\ast\)) is caused by antiparietal cell and anti-intrinsic factor antibodies and presents as a chronic gastritis with oxyntic cell injury, and glandular atrophy essentially restricted to the oxyntic mucosa of the gastric body and fundus. The histologic changes vary in different phases of the disease. During the early phase, there is multifocal infiltration of the lamina propria by mononuclear cells and eosinophils and focal T-cell lymphocyte infiltration of oxyntic glands with glandular destruction. Focal mucous neck cell hyperplasia (pseudopyloric metaplasia), and hypertrophic changes of parietal cells are also observed. During the florid phase, there is increased lymphocytic inflammation, oxyntic gland atrophy, and focal intestinal metaplasia. The end stage is characterized by diffuse involvement of the gastric body and fundus by chronic atrophic gastritis associated with multifocal intestinal metaplasia. In contrast to the gastric body, the antrum is spared. Recently, a distinct form of autoimmune gastritis, characterized by atrophic pangastritis, was reported in a small group of patients with systemic autoimmune disorders.\(^2\,3\)

Autoimmune gastritis is a relatively rare disease but represents the most frequent cause of pernicious anemia in temperate climates. The risk of gastric adenocarcinoma was reported to be at least 2.9 times higher in patients with pernicious anemia than in the general population, and there is also an increased risk of gastric carcinoid tumors.

**Case 4**

Esophagogastroduodenoscopy of a 60-year-old man shows gastritis. The pathologist needs to rule out \(H. pylori\) and gastric atrophy. The gastric site of the biopsy is not specified. Figure 4, A through C, represents the histologic findings.

**Findings.**—Examination of the biopsy material results in the following pattern of answers:

1. Are there features of chronic gastritis? Yes.
2. Are there neutrophils in the mucosa? Yes. There are neutrophils in the mucosa; therefore, there is a component of active gastritis.
3. Is there \(H. pylori\)? No. Examination with H&E stains do not reveal \(H. pylori\) bacterial forms. Immunohistochemical stain is performed.
4. Is there atrophy? If the biopsy is from gastric oxyntic mucosa then there is atrophy, however, if the specimen is from the antrum, it may represent chronic gastritis without atrophy. There is no intestinal metaplasia.
5. Are special stains recommended? Yes. Immunohistochemical stains for synaptophysin and gastrin are performed. Immunohistochemical stains for synaptophysin (Figure 4, B), show a linear pattern of synaptophysin-positive cells, whereas the gastrin stain is negative. Because gastrin is negative, the biopsy is not from the gastric antrum (G cells are characteristically located in the antrum and pylorus), and therefore, it can be established that the biopsy is of oxyntic mucosa with reduced oxyntic glandular profiles, establishing a diagnosis of atrophy. The linear arrays of synaptophysin-positive cells represent enterochromaffin-like cell hyperplasia. Enterochromaffin-like cell hyperplasia occurs in response to hypergastrinemia that results from hypochlorhydria associated with gastric oxyntic cell atrophy.
6. Are additional special features seen? No.
7. Is immunohistochemical stain for \(H. pylori\) positive? No.

**Diagnosis.**—Gastric oxyntic mucosa with chronic active gastritis and glandular atrophy, severe. No intestinal metaplasia is identified. No \(H. pylori\) organisms are identified. Note: These features are most suggestive of autoimmune gastritis.

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Autoimmune gastritis is a relatively rare disease but represents the most frequent cause of pernicious anemia in temperate climates. The risk of gastric adenocarcinoma was reported to be at least 2.9 times higher in patients with pernicious anemia than in the general population, and there is also an increased risk of gastric carcinoid tumors.

**Case 5**

A 47-year-old woman presents with a history of celiac disease. Esophagogastroduodenoscopy was performed, with biopsy of gastric antrum. The pathologist needs to rule out \(H. pylori\). Figure 5, A and B, illustrates the histologic findings.

**Findings.**—Examination of the biopsy material results in the following pattern of answers:

1. Are there features of chronic gastritis? Yes. There are large numbers of intraepithelial lymphocytes.
2. Are there neutrophils in the mucosa? No.
3. Is there \(H. pylori\)? No. Examination with H&E stains do not reveal \(H. pylori\) bacterial forms. Immunohistochemical stain is performed.
4. Is there atrophy? If the biopsy is from gastric oxyntic mucosa then there is atrophy, however, if the specimen is from the antrum, it may represent chronic gastritis without atrophy. There is no intestinal metaplasia.
5. Are special stains recommended? Yes. Immunohistochemical stains for synaptophysin and gastrin are performed. Immunohistochemical stains for synaptophysin (Figure 5, B), show a linear pattern of synaptophysin-positive cells, whereas the gastrin stain is negative. Because gastrin is negative, the biopsy is not from the gastric antrum (G cells are characteristically located in the antrum and pylorus), and therefore, it can be established that the biopsy is of oxyntic mucosa with reduced oxyntic glandular profiles, establishing a diagnosis of atrophy. The linear arrays of synaptophysin-positive cells represent enterochromaffin-like cell hyperplasia. Enterochromaffin-like cell hyperplasia occurs in response to hypergastrinemia that results from hypochlorhydria associated with gastric oxyntic cell atrophy.
6. Are additional special features seen? No.
7. Is immunohistochemical stain for \(H. pylori\) positive? No.

**Diagnosis.**—Gastric oxyntic mucosa with chronic active gastritis and glandular atrophy, severe. No intestinal metaplasia is identified. No \(H. pylori\) organisms are identified. Note: These features are most suggestive of autoimmune gastritis.

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**Case 5**

A 47-year-old woman presents with a history of celiac disease. Esophagogastroduodenoscopy was performed, with biopsy of gastric antrum. The pathologist needs to rule out \(H. pylori\). Figure 5, A and B, illustrates the histologic findings.

**Findings.**—Examination of the biopsy material results in the following pattern of answers:

1. Are there features of chronic gastritis? Yes. There are large numbers of intraepithelial lymphocytes.
2. Are there neutrophils in the mucosa? No.
3. Is there \(H. pylori\)? No. Examination with H&E stains do not reveal \(H. pylori\) bacterial forms. Immunohistochemical stain is performed.
4. Is there atrophy? If the biopsy is from gastric oxyntic mucosa then there is atrophy, however, if the specimen is from the antrum, it may represent chronic gastritis without atrophy. There is no intestinal metaplasia.
5. Are special stains recommended? Yes. Immunohistochemical stains for synaptophysin and gastrin are performed. Immunohistochemical stains for synaptophysin (Figure 5, B), show a linear pattern of synaptophysin-positive cells, whereas the gastrin stain is negative. Because gastrin is negative, the biopsy is not from the gastric antrum (G cells are characteristically located in the antrum and pylorus), and therefore, it can be established that the biopsy is of oxyntic mucosa with reduced oxyntic glandular profiles, establishing a diagnosis of atrophy. The linear arrays of synaptophysin-positive cells represent enterochromaffin-like cell hyperplasia. Enterochromaffin-like cell hyperplasia occurs in response to hypergastrinemia that results from hypochlorhydria associated with gastric oxyntic cell atrophy.
6. Are additional special features seen? No.
7. Is immunohistochemical stain for \(H. pylori\) positive? No.

**Diagnosis.**—Gastric oxyntic mucosa with chronic active gastritis and glandular atrophy, severe. No intestinal metaplasia is identified. No \(H. pylori\) organisms are identified. Note: These features are most suggestive of autoimmune gastritis.
stain does not reveal *H pylori* bacterial forms. Immunohistochemical is performed.

4. Is there atrophy? No. There is no glandular atrophy and no intestinal metaplasia.

5. What is the topography of lesions? The chronic gastritis involves, at minimum, the gastric antrum.

6. Are additional special features seen? Yes. The specific features in this biopsy include a characteristic intraepithelial lymphocytosis. Immunohistochemical stain for CD3 is positive, highlighting a population of T lymphocytes in the mucosa and, typically, many intraepithelial lymphocytes.

7. Are special stains recommended? Yes. Immunohistochemical stain for *H pylori*, which is negative.

**Diagnosis.**—Chronic gastritis with increased intraepithelial T lymphocytes. No *Helicobacter* organisms are identified. Note: These features are consistent with lymphocytic gastritis—associated with celiac disease.

**LYMPHOCYCTIC GASTRITIS**

Lymphocytic gastritis is a type of chronic gastritis characterized by marked infiltration of the gastric surface and foveolar epithelium by T lymphocytes and by chronic inflammation in the lamina propria. A diagnosis can be rendered when 30 or more lymphocytes per 100 consecutive epithelial cells are observed, and the counts are recommended in biopsies from the gastric corpus. The endoscopic pattern is, in some cases, described as varioliform gastritis. The cause of lymphocytic gastritis is usually unknown, but some cases are seen in patients with gluten-sensitive enteropathy/celiac disease and in Ménétrier disease. Smaller numbers of intraepithelial lymphocytes can also be seen in *H pylori* gastritis, but the diagnosis of lymphocytic gastritis should be reserved for cases with marked intraepithelial lymphocytosis in the absence of active *H pylori* gastritis. Lymphocytic gastritis can be observed in children but is usually detected in late adulthood, with average age of diagnosis of 50 years.

**Case 6**

A 75-year-old woman presents after esophagogastroduodenoscopy. Gastric antrum shows gastritis; the pathologist is asked to rule out *H pylori*. The histologic findings are shown in Figure 6.

**Findings.**—Examination of the biopsy material results in the following pattern of answers:

1. Are there features of chronic gastritis? There is minimal chronic gastritis.

2. Are there neutrophils in the mucosa? No.

3. Is there *Helicobacter*? No. Examination of H&E stains does not reveal *H pylori* bacterial forms.

4. Is there atrophy? No. There is no atrophy or intestinal metaplasia.

5. What is the topography of lesions? The chronic gastritis involves, at minimum, the gastric antrum.

6. Are additional special features seen? Yes. There are diagnostic special features, including foveolar hyperplasia with a corkscrew appearance of the foveolae. The foveolar epithelium shows reactive cytologic features, including reduced cytoplasmic mucin. The lamina propria shows congestion and smooth muscle hyperplasia, with prominent muscularization of the most superficial mucosa.

7. Are special stains recommended? No ancillary tests are performed.

**Diagnosis.**—Gastric antral mucosa with features consistent with reactive gastropathy. No *H pylori* organisms are identified.

**CHRONIC, REACTIVE (CHEMICAL) GASTROPATHY**

Chronic reactive gastropathy (also know as chemical gastropathy) is very common in current clinical practice. The mucosal changes are usually more prominent in the prepyloric region, but they may extend to involve the oxyntic mucosa. The usual underlying causes include chronic bile reflux and long-term NSAID intake. The histopathologic features include mucosal edema, congestion, fibrovascular hyperplasia in the lamina propria, and foveolar hyperplasia with a corkscrew appearance in the most severe forms. The foveolar epithelium characteristically shows reactive nuclear features and reduction of mucin. The epithelial changes occur with little background chronic inflammation. However, if there is erosion of the mucosa, superficial neutrophils may be present. Erosive gas-
Gastritis (Figure 7, A) can present clinically as acute gastritis, often associated with NSAID intake.

The features associated with bile reflux are typically found in patients with partial gastrectomy, in whom, the lesions develop near the surgical stoma. However, alterations induced by bile reflux also affect the intact stomach. A recent study reported altered mucin expression in reactive gastropathy, including aberrant expression of MUC5Ac in pyloric glands. Evaluation of mucin-expression patterns can be useful to support a diagnosis of reactive gastropathy; however, additional studies are warranted to validate this potential application of mucin immunohistochemistry.

Case 7

A 45-year-old woman presents with a history of bone marrow transplant. Esophagogastroduodenoscopy shows gastric erosion. The histologic findings are represented in Figure 7, B.

Findings.—Examination of the biopsy material results in the following pattern of answers:

1. Are there features of chronic gastritis? Yes. The sample of gastric mucosa reveals mucosal erosion with granulation tissue and associated chronic and acute inflammation.
2. Are there neutrophils in the mucosa? Yes. There are superficial neutrophils in the mucosa, but they are limited to the area of mucosal erosion.
3. Is there Helicobacter? No. Examination with H&E stain does not reveal such bacterial forms.
4. Is there atrophy? No. There is no atrophy or intestinal metaplasia.
5. What is the topography of lesions? Away from the areas of erosion, there is no evidence of gastritis; therefore, the location of the biopsy is not contributory in this case.
6. Are additional special features seen? Yes. There are special features including enlarged cells, arousing suspicion of cytomegalovirus inclusions in the granulation tissue.
7. Are special stains recommended? Yes. Immunohistochemical stain for cytomegalovirus reveals rare but characteristic viral inclusions (not shown).

Diagnosis.—Gastric antral mucosa with erosion and cytomegalovirus inclusions, consistent with cytomegalovirus-associated gastritis.

CYTOMEGALOVIRUS GASTRITIS

Cytomegalovirus infection of the stomach is observed in patients with underlying immunosuppression. Histologically, intranuclear eosinophilic inclusions and smaller intracytoplasmic inclusions in enlarged cells are characteristic. A patchy, mild inflammatory infiltrate is observed in the lamina propria. Viral inclusions are present in endothelial or mesenchymal cells in the lamina propria and may be seen in gastric epithelial cells. Severe activity may result in mucosal ulceration.
COMMENT

Most types of gastritis can be diagnosed with H&E stains. To reach a determination of etiology and a specific diagnostic entity, a limited list of questions can be used to evaluate the histopathology of gastric biopsies, which can lead to a pattern of answers that corresponds to a specific diagnosis of the most common types of gastritis. Although not ideal, the diagnosis of gastritis can be reached from limited biopsy material, even when the location of the biopsy is not indicated. If the biopsy site is not known, immunohistochemical stains for synaptophysin and gastrin can help determine the biopsy location, permitting a specific diagnosis of atrophic gastritis type. Helicobacter pylori immunohistochemical stains can be particularly useful when moderate to severe chronic gastritis or any active gastritis is present but no Helicobacter organisms are identified on H&E stains, when extensive intestinal metaplasia is present, and to evaluate follow-up biopsies after antibiotic treatment for H pylori.

At the end of the day, there are a number of cases with a diagnosis of chronic inactive gastritis, generally mild, for which a specific etiology cannot be determined by histopathologic examination alone. This may be accounted for by limited tissue sampling, nonspecific focal, mild, chronic inactive gastritis associated with various systemic disorders, or as yet uncharacterized forms of gastritis.

References


Archives of Pathology & Laboratory Medicine and Archives of Ophthalmology will publish a joint theme issue on ophthalmic pathology in August 2009. Articles on diagnostic procedures, pathologic mechanistic pathways, and translational research in retinoblastoma, melanoma, lymphoma, orbital, and adnexal tumors in ophthalmic pathology will have the best chance for consideration in this theme issue. Manuscripts must be submitted no later than February 1, 2009 for consideration in the joint theme issue. All submissions will undergo our usual peer review process.

Important: When submitting a manuscript for this theme issue, be certain to mention this in both the cover letter and the Comment section within the AllenTrack submission system.

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