Case Presentations:
Gastric Polyps and The
Company They Keep - Gastritis

Elizabeth Montgomery, MD
Department of Pathology
Johns Hopkins Hospital
Baltimore MD

Stomach!

- We will begin with a whirlwind tour of the things that we can encounter in gastric biopsies and then review cases with differential diagnosis

First, a few pitfalls
A Few Benign Pitfalls

- Crushed mucosa with sloughed mucous neck cells
- Erosive gastritis/gastropathy including iron pill gastritis
- “Signet cell change”
- Gastric Xanthoma

Pitfall – erosive gastropathy – note that the reparative glands respect the muscularis mucosae border.

Pitfall - Iron pill gastritis with reactive changes.
Pitfall - Iron pill gastritis with reactive changes

Pitfall - "signet cell change" in ischemic columnar mucosa; cells lose their cohesion and slough into the lumen whilst "rounding up"
Pitfall - "signet cell change" in ischemic columnar mucosa; cells retain E-Cadherin expression

Remember that "signet cell change" is very different from the in situ signet ring cell cancers in patients with CDH1 (the gene encoding for e-cadherin) germline mutations.
Pitfall – crushed mucosa with prominent mucus neck cells – note the sloughed single cells are not within lamina propria but "floating" and seen in gland lumina.
Pitfall – crushed mucosa with prominent mucus neck cells – note the sloughed single cells are seen in gland lumina – oil immersion (bad idea)

The real thing – signet cell carcinoma - the bad cells are firmly in the lamina propria so not seen in the lumina

Gastric xanthoma
Gastric xanthoma, PAS

Mucosal calcinosis – seen in patients with renal failure or other disorders of calcium metabolism such as parathyroid adenomas
Sarcina ventriculi Patient with diabetes and slow gastric emptying – note exudate and organisms at low power.
Sarcina ventriculi gastritis

- Gram positive, anaerobic, sugar-fermenting bacterium, *S. ventriculi* was first observed in the human stomach in 1842 by Goodsir. Readily found in soil and is known to cause a similar type of gastric injury in animals.
- Delayed gastric emptying and carbohydrate stasis in association with acidic gastric juices may provide an ideal culture medium.

Sarcina Ventriculi gastritis

- Studied patients all had underlying delayed gastric emptying (one had a bezoar) from diabetic neuropathy, narcotic use, and pyloric stenosis secondary to malignancy.
- The organism may simply colonize pre-existing lesions but there are too few cases to draw firm conclusions as to whether the organism is truly a pathogen.
- Packets of 4, 8 or more cells with characteristic flattening.

Packets of 4, 8 or more cells with characteristic flattening.

Lymphocytic gastritis – Most common association – Celiac disease followed by H. Pylori

Collagenous Gastritis

- Associated with various autoimmune diseases in both children and adults
- We have seen it associated with medications (eg Benicar/Olmesartan)
- Early studies proposed 2 clinicopathologic subtypes:
  - (1) children (18 y of age or younger) presenting with severe anemia, nodular gastric mucosa, and isolated gastric disease; and
  - (2) adults with chronic watery diarrhea that is associated with diffuse collagenous involvement of the gastrointestinal tract.

Collagenous gastritis – poorly understood and sometimes resolves by itself – presents with watery diarrhea just like collagenous colitis.

Collagenous gastritis in gastric body. Is something missing (you betcha – parietal cells).
Collagenous gastritis associated with autoimmune gastritis – chromogranin stain showing enterochromaffin-like (ECL) cell hyperplasia
Granulomatous gastritis – pattern – can be Crohn’s disease but always requires correlation with clinical findings.

Cytomegalovirus gastritis – note that the EPITHELIAL cells are often affected in the stomach.

Cytomegalovirus gastritis – the monocyte-rich inflammation can mimic a lymphoma.
Russell body gastritis – usually a curious incidental finding and only sometimes associated with plasma cell disorders.

Syphilis Gastritis

- Not well studied and correlation with HIV status is not well established in the literature (which consists mostly of case reports)
- The key is that it tends to present in young adults with diffuse erosive gastritis or lesions that mimic carcinoma and lymphoma
Vintage images of syphilis gastritis courtesy of the late Jack Yardley
Epstein Barr Virus Gastritis
Epstein-Barr virus gastritis – mimics lymphoma

EBV in situ hybridization
EBV gastritis – note nuclear hybridization in the exuberant mixed lymphoid infiltrate

Measles gastritis

Measles gastritis
And now a whirlwind of things we encounter on biopsies..... Some rare and some common

Case 1

• A 68 year old woman with dyspepsia underwent upper endoscopy and had some gastric biopsies.
• The endoscopist thought the mucosa was atrophic and also saw a polyp.
Diagnosis, Case 1

• Autoimmune gastritis
• Hyperplastic polyp

Esophagus, Stomach, and Duodenum: Normal Anatomic Outlines and Relationships

Normal Antral Mucosa with Gastric Lumen (LUM), Foveolae (FOV), and Antral Glands (AG) Indicated
Normal Oxyntic Mucosa with Foveolae (FOV), Parietal Cells (PC), and Chief Cells (CC) Indicated

Major Endocrine Cell Types of the Stomach and Their Products - Immunostain Demonstrations

A few Comments on *Helicobacter pylori* Gastritis
Two Australians win Nobel Prize in Medicine
Awarded for work on peptic ulcer disease

Prevalence of Helicobacter pylori Infection in Developing vs. Developed Countries

*UNIDENTIFIED CURVED BACILLI IN THE STOMACH OF PATIENTS WITH GASTRITIS AND PEPTIC ULCERATION*

BARRY J. MARSHALL    J. ROBIN WARREN
Department of Gastroenterology and Pathology, Royal Prince Alfred Hospital, Sydney, New South Wales
Consequences of H. pylori infection

- Many are asymptomatic
- “dyspepsia”
- Peptic ulcer
- Atrophy and intestinal metaplasia of mucosa
- Increased risk for intestinal type adenocarcinoma
- MALT lymphoma
- ?? Link to autoimmune gastritis

Chronic Active H. pylori Gastritis with Neutrophils (PMN's) in Gland

Duodenal and “Pre-Pyloric” Ulcers
Eradication of *H. pylori* in Recurrent Duodenal Ulcer

![Graph showing probability of remission over weeks after treatment](image)

Benign Gastric Ulcer - Lesser Curve, Transitional Zone

![Image of gastric ulcer](image)

Environmental Metaplastic Atrophic Gastritis

- Associated factors:
  - *H. pylori* infection
  - Dietary: High salt; smoked foods; nitrates; poor fruit and vegetable intake
  - Others:
    - Smoking

NEJM 328: 308-312, 1993
H. Pylori associated Metaplastic Atrophic Gastritis
(Stemmermann’s Technique; stained for alkaline phosphatase)

Carcinoma in Environmental Metaplastic Atrophic Gastritis (EMAG)

Effect of eradication of Helicobacter pylori on incidence of metachronous gastric carcinoma after endoscopic resection of early gastric cancer: an open-label randomised controlled trial.
Autoimmune gastritis

Metaplastic Atrophic Gastritis (MAG)  
Autoimmune vs. H. pylori Types

Autoimmune  H. pylori

Autoimmune vs. Environmental  
Metaplastic Atrophic Gastritis

Autoimmune  H. Pylori
Autoimmune MAG (AMAG)

- **Etiology/Pathogenesis:**
  - Autoimmune-induced damage
  - Inherited predisposition
  - Parietal cell antibodies
  - Intrinsic factor antibody
  - *H. pylori* organisms usually absent

- **Pathology:**
  - **Body (ONLY)**
    - DIFFUSE METAPLASIA; mucosa thin
    - Loss of oxyntic glands ("atrophy")
  - **Antrum** - NO METAPLASIA; hyperplasia
  - **Endocrine**
    - G-cell hyperplasia
    - ECL cell hyperplasia
Oxyntic Mucosa: Autoimmune Metaplastic Atrophic Gastritis (AMAG) - Intestinal and Pyloric Metaplasia

Autoimmune MAG (AMAG) Clinical Correlations

- Achlorhydria or marked hypochlorhydria
- B-12 malabsorption
- Serum gastrin - high levels
- Gastric cancer: risk increased
- Gastric ulcer: not a problem (no acid!)

We used to think this was a Northern European disease but it is equal opportunity. Female prevalence holds regardless of race.

Hyperplastic Polyps

- Hyperplastic polyps may arise anywhere in the stomach
- Slight preference for the antrum
- 20% multiple
- Considered to be non-neoplastic lesions (though many molecular alterations reported)
- It is unusual for hyperplastic polyps to arise in normal stomachs.
Hyperplastic Polyps - Associations

- Most strongly associated with atrophic gastritis of either autoimmune or environmental (e.g., *Helicobacter pylori*-associated) types
- post-antrectomy state
- chemical/reactive gastropathy
- following therapy for gastric antral vascular ectasia ("watermelon stomach").
Hyperplastic Polyps and Autoimmune Gastritis

- Extensively documented association.
- Autoimmune gastritis is suggested histologically when biopsies show corpus-predominant gastritis, glandular atrophy, and intestinal metaplasia.

Antrum – 68 yo woman
Multiple Gastric Carcinoids

Case 2

- A partial gastrectomy was performed for a “cancer” in a 55 year old woman with a history of type 1 diabetes (so an autoimmune “diathesis”)
Type 1 carcinoid arising in gastric body of 50+ woman with history of type 1 diabetes

The flat oxyntic mucosa surrounding Type 1 carcinoid

ECL cell hyperplasia

Intestinal metaplasia

(pseudo)pyloric metaplasia
When Does It Stop Being ECL Cell Hyperplasia and Become Carcinoid?

- Extensive literature on hyperplasia-dysplasia-neoplasia – no practical value
- Some use a cut-off of 0.5 mm as “carcinoid”
- Our definition – if the endoscopist sees a nodule it’s a carcinoid
- It is pointless to measure minute lesions – they never hurt the patients... even as full fledged carcinoids

Some Issues

- Many pathologists don’t know how to diagnose autoimmune gastritis/pernicious anemia pattern
- Many internal medicine/family practice colleagues have no idea that they need to give their patients vitamin B12 when the diagnostic line in the pathology report says “autoimmune gastritis” and think their patients have uncomplicated iron deficiency anemia -the high gastric pH does not allow for iron absorption
- Many surgery colleagues want to perform aggressive resections for such tumors
Another Type 1 carcinoid of the gastric body. There is no background oxyntic mucosa.

Type 1 carcinoid, Chromogranin stain. Note the ECL cell hyperplasia in the background.

Type 1 carcinoid -
We avoid doing ki-67 stains in Type 1 carcinoids since they are essentially always indolent and results such as this one don’t mean anything - metastases are rare for type 1 carcinoids and deaths are exceptional.

Time to Talk About Type 2 Carcinoid
Slide A is from the duodenum and slide B is from the stomach. What syndrome can you dream up to explain these findings?
A, gastrin stain

B, gastrin stain
Diagnosis – Zollinger-Ellison Syndrome with a duodenal gastrinoma and a gastric carcinoid tumor/WDNET of ECL cell type
Type 3 Gastric NET

- No autoimmune backdrop, no Zollinger Ellison (no gastrinoma)
- In other words, no hypergastrinemia
- More aggressive than type 1 with about a third dying of disease and metastases in about 70%
- *(metastases are rare for type 1 and deaths are exceptional)*
- data poor on type 2 but they are indolent
For this lesion, we need more information to subtype it – if we know it's antral then it is type 3

Another Type 3 carcinoid in a patient with normal serum gastrin. The background is normal oxyntic mucosa. This lesion is spindly and reminiscent of a gastrointestinal stromal tumor.

A spindled type 3 carcinoid
Type 3 carcinoid – note the intact parietal cells

Type 3 carcinoid – and others – pitfall alert – note weak AE1/3

Type 3 carcinoid – Cam 5.2 saves the day...
Type 3 carcinoid – Chromogranin stain – No ECL cell hyperplasia in adjoining mucosa

True high grade gastric neuroendocrine lesions can also be very rarely encountered and are most often metastases from the lung; this was primary in the antrum.

Mitoses in this small cell carcinoma are easy to find.
This is a synaptophysin stain.

What Do We Need to Assure?

• Be sure you know how to diagnose autoimmune gastritis!!!! Many pathologists do not know how.
• Clinicians do not know what it is – we have begun to report “autoimmune gastritis/pernicious anemia pattern”
• We see autoimmune gastritis in about 2% of our gastric biopsies “in house” at Johns Hopkins – if this diagnosis is never in your path reports you are not recognizing the pattern and the patient needs you to!
• Think of autoimmune gastritis when the biopsy of body looks like antrum with “bottom-heavy” inflammation.

Sample report

• Gastric body (biopsy): Autoimmune gastritis/pernicious anemia pattern

• Note: These patients are prone to both iron deficiency anemia and pernicious anemia (the high gastric pH interferes with iron absorption) as well as various epithelial neoplasms. Correlation with serum gastrin and studies of vitamin B12 levels may be of interest.
Follow-Up of Autoimmune Gastritis

- European societies have endorsed gastric surveillance every 1-3 years in autoimmune gastritis patients
- US Societies have yet to do so. The data supporting the European guidelines are weak

Case 3

- Large gastric body polyp in a 72 year old woman with long history of autoimmune gastritis
• 2.7% of all gastric polyps
• Adults (73±12.8 years),
• Women (75%).
• In stomach, mostly in body (64%), often found in patients with autoimmune gastritis (36%).
• Some showed transition to adenocarcinoma

• Now known to have GNAS* mutations, both sporadic and syndromic examples (familial adenomatous polyposis), which they share with oxyntic gland adenoma/chief cell adenoma.

*guanine nucleotide-binding protein (G protein), alpha subunit*
• **Table 1** Location of pyloric gland adenoma (PGA) throughout the gastrointestinal tract based on a recent analysis of 373 patients with PGA in Bayreuth including 90 cases that were published elsewhere.
  - Duodenum 2.7%
  - Bulb 8.3%
  - Antrum 3.8%
  - Corpus 54.1%
  - Cardia 17.4%
  - Oesophagus (in Barrett's) 2.4%
  - Remaining stomach BII 3.4%
  - Rectum 1.1% (4 cases)
  - Papilla of Vater 0.8%
  - Pancreatic duct 0.3%
  - Bile duct 1.4%
  - Gall bladder 4.3%
  - Bil, Billroth II.

• **Table 2** Distribution of pyloric gland adenoma cases in Baltimore at Johns Hopkins Hospital.
  - Duodenum 14.8%
  - Bulb 10.0%
  - Antrum 2.6%
  - Corpus 37.0%
  - Cardia 13.2%
  - Oesophagus (in Barrett's) 2.6%
  - Papilla of Vater 1.5%
  - Pancreatic duct 3.7%
  - Gall bladder 15.3%

• Vieth M, Montgomery EA. Some observations on pyloric gland adenoma: an uncommon and long ignored entity! J Clin Pathol 2014

Pyloric gland adenoma – Ki-67
Pyloric gland adenoma – MUC 6

Pyloric gland adenoma, MUC5AC

Pyloric gland adenoma
Zone of intramucosal carcinoma (invasion of the lamina propria)
Consequences of Autoimmune Gastritis

- Atrophy of oxyntic mucosa
- Pernicious anemia
- Gastric adenomas (either intestinal or pyloric type since these types of metaplasia are found)
- Type 1 carcinoid tumors (from ECL cell hyperplasia)
- Hyperplastic polyps
- Adenocarcinomas

Thank you