The Endoscopic Incidentaloma: What to Tell Your Patient with Unexpected Endoscopic Findings: Gastric Intestinal Metaplasia, Silent Ileitis, Carcinoid

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ACG Western Regional Course
January 2015

Unexpected Findings at Endoscopy

• Foreign Bodies
• Masses
• Ulcers
• Varices
• Parasites
• So much more....
Unexpected Findings at Endoscopy

- Gastric intestinal metaplasia
- Silent ileitis
- Carcinoid

Gastric Intestinal Metaplasia

- Intermediate precancerous gastric lesion
- Chronic gastritis → Atrophy → Dysplasia → Adenocarcinoma
- While risk of gastric cancer is increased, absolute risk is low
- Subsets of patients with IM may be at higher risk for progression
Gastric Intestinal Metaplasia

Definition:
Replacement of the surface, glandular and foveolar epithelium in the oxyntic or antral mucosa by intestinal epithelium

Subtypes

- Complete intestinal metaplasia
  - Presence of small intestinal type mucosa
    - Goblet cells
    - Brush border
    - Eosinophilic enterocytes

- Incomplete Intestinal metaplasia
  - Presence of colonic epithelium
    - Multiple, irregular mucin droplets of variable size in the cytoplasm
    - Absence of a brush border
Gastric Intestinal Metaplasia

• Subtypes
  – Limited intestinal metaplasia
    • Confined to one area of the stomach
  – Extensive intestinal metaplasia
    • Involves at least two areas of the stomach
      – Antrum
      – Angularis
      – Body

Gastric Intestinal Metaplasia: Epidemiology

• Incidence varies worldwide
• Increases with age
• Prevalence seems correlated with incidence of gastric cancer
• United States
  – Overall prevalence 19%
    • Caucasians 13%
    • Hispanic/Blacks 50%
• Netherlands
  – Overall prevalence 7%
Gastric IM:  
**Risk Factors**

- Similar to those for gastric cancer
  - *H. pylori* infection
  - High salt intake
  - Smoking
  - Alcohol consumption
  - Chronic bile reflux
- Multistage model for gastric cancer
  - Host genotype and dietary and environmental factors predispose to early pangastric mucosal inflammation
  - Leads to gastric atrophy, IM, dysplasia and then adenocarcinoma

Gastric IM:  
**Clinical Features**

- No symptoms
- Often found incidentally at EGD
- May be associated with gastric achlorhydria
  - Which may lead to SIBO
    - Bloating, flatulence, diarrhea, abdominal discomfort
- Endoscopic appearance
  - Non-specific
  - Sometimes has rough or villous appearance
  - Sometimes thin white mucosal deposits
- Diagnosis
  - Biopsy
**Gastric IM:**
*Evaluating for subtype*

- Important to determine
- Histologic subtype
  - Complete vs. Incomplete
- Extent
  - Limited versus Extensive
- Aids in determination of risk of gastric adenocarcinoma and guides surveillance

*This requires gastric biopsy mapping*
*At least 5 non-targeted gastric biopsies*

**Natural History**

- Metaplastic foci often first appear at antrum/body junction
- Foci enlarge and coalesce
  - Extending into antrum and body
- Atrophic and metaplastic glands replace original glands
  - Normal gastric secretions decrease
- Hypochlorhydria and high circulating levels of gastrin
- Initial metaplastic glands resemble those of small intestine
  - Type 1
- More advanced changes are similar to colonic mucosa
  - Type II, or colonic metaplasia
- Small foci of dysplasia may develop in areas of IM
Cancer risk

- Gastric IM associated with increased risk for cancer
  - Absolute risk is low
- Progression from IM to cancer varies from 0%-10% per year
  - Influenced by virulence of *H. pylori*, environmental factors and host genetics
- Netherlands
  - 61000 individuals with gastric IM
    - Incidence of gastric cancer in 5 years was 0.25%
- More likely to progress with incomplete intestinal metaplasia or extensive metaplasia
  - Spain
    - 478 patients
    - Presence of incomplete intestinal metaplasia 11 fold increase in risk of gastric cancer
    - Presence of family history of gastric cancer associated with 6 fold increase in risk of gastric cancer

Management

Goals
- Decrease risk of gastric cancer in patients with IM by screening and eradication of *H. pylori*
  - Eradication of *H. pylori* appears to reverse histologic changes in many patients with non-atrophic gastritis and atrophic gastritis
  - Eradication of HP does not reverse IM
    - May slow progression to cancer
  - Progression of metaplasia and dysplasia are associated with a decreased burden of *H. pylori* all by themselves
  - *H. pylori* testing with stool antigen or UBT recommended
Management

Goals

– Surveillance for gastric cancer recommended
  • For those with extensive IM
  • For those with incomplete intestinal metaplasia
  • Standard EGD with white light and gastric biopsy mapping
    – Every 2-3 years
  • Generally consistent with ESGE Guidelines (2012)
  – Surveillance may lead to early detection and improved survival
    • No recommendation for surveillance in patients with gastric IM
    • Those at increased risk for gastric cancer (ethnic background, family history) may benefit from screening
      – No interval suggested

• Upper endoscopy with mapping
  – Minimum of five biopsies from body and antrum
  – Additional biopsies from the angularis
  – Separate jars
  – Additional biopsies for endoscopically abnormal areas

• Gastric biopsy mapping essential
  – White light endoscopy does not differentiate atrophic gastritis from IM and more advanced dysplasia
Other Imaging

- **Magnification chromoendoscopy**
  - Generally indigo carmine
  - Inconsistent results
- **NBI**
  - May be useful in a trained individual to detect IM
- **Confocal endomicroscopy**
  - Useful to detect early gastric cancer
  - No data in studies to look for gastric IM

Summary

- Gastric IM characterized by epithelial changes
  - Divided into complete IM and incomplete IM
  - Divided into limited and extensive
- Overall risk of progression to cancer is low in areas of low gastric cancer prevalence (2.5 per 1000 person years)
  - Much higher in people with incomplete or extensive IM
- IM causes no symptoms
  - Detected incidentally on most occasions
Summary

• Diagnosis is made on biopsies
• Evaluation of subtype and extent of metaplasia requires gastric biopsy mapping
• Individuals with extensive or incomplete IM
  – Surveillance EGD and biopsy mapping every 2-3 years
• High risk individuals without incomplete or extensive metaplasia
  – Decision to perform endoscopic surveillance must be individualized
• *H. pylori* should be eradicated

Ileitis

• Crohn’s
• Others
Endoscopic Findings in Crohn’s Disease

- **Aphthous ulcers**
  - Typically small, discrete
  - Deeper ulcers involve entire thickness of wall

- **Cobblestoning**
  - Serpiginous and linear ulcers along longitudinal axis
  - Ulcers are the cracks
  - Normal or inflamed tissue are the stones

- **Skip lesions**
  - Adjacent areas are normal

Crohn’s Mimicry

- **Tuberculosis of the terminal ileum**
  - Narrowed lumen
  - Nodularity
  - Diagnosed by
    - Caseating granulomas (may be deep to biopsies)
    - Positive culture
    - AFB on endoscopic biopsies

- **Other endoscopic features**
  - Grouped ulcers, nodules
  - Destruction of ileocecal valve
Crohn’s Mimicry

Bacteria that can cause ileitis

– Yersinia enterocolitica
– Campylobacter
– Shigella
– Salmonella

Crohn’s mimicry

• Pseudomembranous colitis
  – Small groups of pseudomembranes may look grossly like the aphthous ulcers in Crohn's disease
  – These lesions are typically in the colon
    • On top of mucosa
    • Do not result in ulceration of the underlying tissue
More ileitis

NSAIDs
- NSAIDs associated with a variety of pathologic changes in the GI tract
- Consider NSAID induced disease in small bowel ulcerations or inflammatory changes

Does ileoscopy matter??

- Ileal intubation rates
  - 80%-97%
- Not all suspected to be Crohn’s disease is Crohn’s disease
  - 110 patients with suspected CD on barium exam
  - 48 (or 44%) had a final diagnosis of Crohn’s disease
- Biopsies are critical to establishing diagnoses
  - Target abnormal appearing tissue, polyps, masses
  - Brushings and stool samples may also be helpful
  - Highest diagnostic yield
    - Micro-ulcers (less than 5 mm)
    - Edges of larger ulcers
  - Granulomas to support the diagnosis of CD
    - Only found in 5%-24% of biopsy specimens
Carcinoid Tumors

Carcinoid:
- Well differentiated neuroendocrine tumors
  - Originate in the GI tract, lungs or kidneys/ovaries
- Origin of name
  - Morphologically different from more common GI tract adenocarcinomas
  - Generally less aggressive
- In GI tract
  - Well differentiated neuroendocrine tumors of the luminal GI tract are called carcinoids
  - Those in the pancreas usually referred to as pancreatic neuroendocrine tumors
- Generally rare
  - Increased incidence recently due to improved detection

Carcinoid syndrome

Constellation of symptoms
- Mediated by various humoral factors that are elaborated by tumors
- Flushing and diarrhea
- Generally occurs with metastatic carcinoids originating in the small bowel
Distribution of Carcinoid Tumors

• SEER database (1973-1997)
• GI tract 55%
• Bronco-pulmonary 30%
• In GI tract
  – Small intestine 45% (most common in ileum)
  – Rectum 20%
  – Appendix 16%
  – Colon 11%
  – Stomach 7%

• Since 2000 (screening colonoscopy)
  – Incidence of rectal carcinoids greatly increased

Carcinoids:

Foregut tumors

• Stomach and lung
• 3 types in stomach
• Type 1
  – 70-80% of all gastric carcinoids
  – Associated with chronic atrophic gastritis and pernicious anemia
  – More common in woman
  – Typically
    • Smaller than 1 cm
    • Multiple
    • Polypoid lesions with central ulceration
  – Derived from ECL cells (stimulated by high gastrin levels)
  – Usually diagnosed in patients in their 60s and 70s undergoing EGD for anemia or abdominal pain
  – Generally benign and indolent
  – More likely to be aggressive if greater than 2 cm
Carcinoids: 
Foregut tumors

Stomach

- Type 2
  - Associated with Zollinger–Ellison syndrome
  - Associated with MEN-1
  - Accounts for 5% of gastric carcinoids
  - Arises from ECL cells
    - Stimulated by gastrin
  - Hypergastrinemia produced by a gastrinoma in type 2
  - Often multifocal, usually indolent

- Type 3
  - Sporadic
  - Occurs in absence of atrophic gastritis or MEN 1
  - 20% of gastric carcinoids
  - Most aggressive,
    - Mets to liver in up to 65%

Carcinoids: 
Midgut tumors

Jejunum and ileum

- Increasingly detected at endoscopy and capsule endoscopy
- Since 2000, carcinoids more common in small bowel than adenocarcinoma
- Patients typically in 60s or 70s
- Small bowel carcinoids arise from intraepithelial endocrine cells
- Most commonly located within 60 cm of ileocecal valve;
  - May arise from Meckel's diverticulum
- 25% of patients have more than one
- Most are asymptomatic
  - Found incidentally
- May present as intermittent obstruction
- If symptomatic,
  - Abdominal pain may be due to intussusception, mechanical effect of tumor or mesenteric ischemia
Carcinoids: 
**Appendiceal tumors**

- Most common neoplasm of the appendix
- Discovered in 1/300 appendectomies
  - Usually at the tip of the appendix
- Detected in patients in 40s and 50s
- Most patients asymptomatic
  - Appendiceal carcinoids are submucosal
- Symptoms occur when tumors are large
  - 10% are located at base and can cause appendicitis

Carcinoids: 
**Hindgut tumors**

- Transverse, descending colon and rectum
- Typically non-secretory
- Never associated with carcinoid syndrome, even when metastatic
Colonic Carcinoids

- Typically detected in patients in their 70s
  - During evaluation colonoscopically for diarrhea, abdominal pain, anemia or weight loss
- Incidence of functioning tumors very low
  - Approximately 3%
- Most in right colon (most in cecum)
- No symptoms until these get very large (5 cm or larger)

Rectal Carcinoids

- Generally found incidentally
  - Asymptomatic
- Most commonly diagnosed in people in their 60s
- Rarely can cause
  - Rectal bleeding
  - Change in bowel habits
  - Pain
- Non-secretory in general
  - Therefore, no chance of carcinoid syndrome
Rectal Carcinoids

- Majority are localized at diagnosis (75%-85%)
- Size correlates with likelihood of metastasis
- Size
  - <1 cm    rarely metastatic
  - 1-2 cm   6% metastatic
  - >2 cm    24%, generally mets to liver
- Other poor prognostic features
  - Deep invasion (to muscularis propria or deeper)
  - Lymphovascular invasion
  - High mitotic rate

Management

Gastric carcinoids
  - Type 1 and 2
    - Smaller than 1-2 cm
      - Endoscopic resection
    - More aggressive or numerous
      - Antrectomy
  - Type 3
    - Partial or total gastrectomy with local lymph node resection
Management

Small bowel carcinoids
- Resection of involved small bowel segment and mesentery
- Ampulla of Vater lesions may be more aggressive

Management

Appendiceal carcinoids
- Appendectomy for carcinoids less than 2 cm
- Right hemicolectomy for carcinoids greater than 2 cm and with mesoappendiceal invasion
Management

Colonic carcinoids
- Most non-metastatic lesions managed with
  - Formal partial colectomy and regional lymphadenectomy

Management

• Rectal carcinoids
  - Smaller than 1 cm and confined to mucosa or submucosa
    - Local endoscopic excision
  - 1-2 cm
    - Controversial
    - Must be individualized based on size, mitotic rate, and lymphovascular invasion
  - >2 cm or those that invade past muscularis propria or have regional lymph node mets
    - Surgery (low anterior resection or abdominal perineal resection)
Post-treatment Surveillance

- Gastric carcinoids <2 cm
  - EGD every 6-12 months for 3 years and then annually
- Appendiceal carcinoids <2 cm
  - No surveillance
- Rectal carcinoids <1 cm
  - No surveillance
- Rectal carcinoids 1-2 cm
  - Surveillance proctoscopy at 6 and 12 months