Gastric Polyps: Diagnosis and Management

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“I have no relevant relationships requiring disclosure”

- Prevalence of 3.75% (200,000 endoscopies-US)
- Incidental findings (Rare: hemorrhage / outflow obstruction)

Prevalence of gastric polyps

Prevalence of gastric polyp / age

General category     Subtype                          Usual location          Malignant potential
Epithelial          Hyperplastic (and variants)          Antrum and lower body   Low
                    Plastric, jejunal             Body fundus              Low
                    Jejunal                     Body fundus              Low
                    Hyperplastic                Body fundus              Low
Mesenchymal         Inflammatory fibroid polyp          Antrum                  None
                    Others*                    Body fundus              Low to moderate
Neoplastic          Fundic gland polyp               Body fundus              Low
                    Polypoid (adenoma)           Body fundus              Low
                    Neuro-endocrine tumor       Body fundus              Low
Miscellaneous       Cronkhite-Canada                         Unknown                None
                    Xantho (xanthoma)            Unknown                None
                    Gastric heterotopic pancreas  Unknown                Very low

*The risk increases with the size of the polyp.
**The risk is higher in syndromic polyps than in sporadic lesions.
*These include: gastrointestinal stromal tumour (GIST), smooth muscle tumour, gliomma tumour, inflammatory myofibroblastic tumour,
Fundic Gland Polyps

- Oxyntic mucosa
- Sessile: 1-5 mm
- Multiple (40-60%)
- Over time 40-50% are labile

- Sporadic (0.09 to 5% of endoscoped pts; Female +)
- FAP
- Proton pump inhibitors
- GAPPS (Gastric Adenocarcinoma and Proximal Polyposis)

- FAP: inactivating APC / chr 5q allelic loss
- Sporadic: activating β catenin mutation (60%-90%)
Sporadic FGP:
- Dysplasia is rare (1-6%)

Syndromic patients (FAP):
- 25-48% (LGD>HGD [0-12%])
- Only 4 cases of ACA

Goddard AF. Gut 2010;59:1270-1276
- [mean follow-up of 6 years].
  - 54% stable “persisted” (n=13)
  - 33% “regressed” (n=8)
  - 13% “progressed” to HGD/IMC (n=3)

Arnason T. Histopathology 2014,
- [sporadic GED progression rate: LGD: 5-14% and HGD: 24-37%]

Evolution of dysplastic FGP in FAP

- [mean follow-up of 6 years].
  - 54% stable “persisted” (n=13)
  - 33% “regressed” (n=8)
  - 13% “progressed” to HGD/IMC (n=3)

(sporadic GED progression rate: LGD: 5-14% and HGD: 24-37%)

Recommendations:
- Follow q. 2/3 years:
  - Look for large polyps (>1cm)
  - Sample extensively
Key features:

- FG polyposis w/ occasional hyperplastic & adenomatous polyps, sparing the antrum, devt. of intestinal type GCA
- Autosomal dominant inheritance (Incomplete penetrance).
- No colonic polyps
- Point mutations in exon 1B of APC

Mean age: 65yrs - Sessile/pedunculate - Antrum: 60%.

- Multiplicity: 20%
- HP gastritis
- Auto Im. Gastritis
- React. Gastro.
- Others
- Normal

Mucosal background

- Sessile or pedunculated
- Size is variable
Polypoid foveolar hyperplasia

- Thick muscle bands
- Thickened wall vessels
- Cystic glandular dilatation
- Glands in mid zone
- Prolapse variant (of hyperplastic polyp)

208 polypoid lesions reported as hyperplastic polyps

- Polypoid fove. hyperplasia: 49%
- Hyperplastic polyp: 31%
- Prolapse polyp: 20%
Dysplasia: 1.8–16.4%; Carcinoma: 0.3–7.1% (avg 2.1%) (> 2.0 cm)

**Hyperplastic Polyps – Diff. Dx**

<table>
<thead>
<tr>
<th>Inheritance</th>
<th>Juvenile polyposis</th>
<th>Peutz-Jeghers Syndrome</th>
<th>Cowden’s Disease</th>
<th>Cronkhite-Canada Syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gene</td>
<td>SMAD4 or BMPR1A</td>
<td>STK11/LKB1</td>
<td>PTEN</td>
<td>None</td>
</tr>
<tr>
<td>Gastric location</td>
<td>infrequent (15–25%)</td>
<td>25–50%</td>
<td>common</td>
<td>common</td>
</tr>
<tr>
<td>Location of polyp</td>
<td>antrum = body or fundus</td>
<td>random</td>
<td>random</td>
<td>random</td>
</tr>
<tr>
<td>Size of polyp</td>
<td>variable</td>
<td>usually small (&lt;1cm)</td>
<td>usually small (&lt;1cm)</td>
<td>variable</td>
</tr>
<tr>
<td>Lifetime risk of gastric Ca.</td>
<td>15–20%</td>
<td>30%</td>
<td>rare</td>
<td>about 10%</td>
</tr>
</tbody>
</table>

Other differential dx:
- Menetrier’s disease
- Bile reflux: post surgery gastritis
- Gastritis Polyposa Cystica

Diff. diagnosis of hyperplastic polyps is challenging on a superficial pinch biopsies
Juvenile polyps (polyposis)

- Median age of pts presenting with gastric polyps ~40 years
- Rounded and sessile when small but pedunculated with a lobular appearance as they enlarge.

Seta N. The Oncologist 2015; accepted for publication

- No smooth muscle fibers

Peutz-jeghers

Median age of Dx: 16 yrs

- Pits & glands are grouped/packeted; Unremarkable epithelium

Subtle intervening septae of smooth muscle strands
Unremarkable lamina propria
- Increased risk of GI cancer through the hamartoma-adenoma-carcinoma sequence and de novo malignant change.
- Dysplasia is noted in 2-3% of PJ polyps.

**Cronkhite-Canada Syndrome**
- Protein-losing enteropathy.
- Ectodermal changes
- Hamartomatous polyposis.
- (IgG4 related condition?)
- Variable natural history
  - 50-60% mortality
  - Electrolytes imbalance, GI bleeding, opportunistic infections
- Malignant potential~10%

**Gastric Adenoma**
- Nodule of gastric dysplasia:
  "Unequivocal neoplastic (non invasive) process"
- Single in 82% of cases
- 80-90% < 2cm
Architectural/Cytologic Features of Gastric Dysplasia

- Glandular disarray, budding, branching and dilatation
- Nuclear pleomorphism
- High N/C ratio
- Loss of nuclear polarity with pseudostratification
- Lack of differentiation with mucus depletion

Phenotypic Diversity of Gastric Dysplasia

<table>
<thead>
<tr>
<th></th>
<th>Adenomatous</th>
<th>Foveolar</th>
<th>Pyloric</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intestinal CD10</td>
<td>(+) (Apical membrane)</td>
<td>(-)</td>
<td>(+)</td>
</tr>
<tr>
<td>Intestinal MUC2</td>
<td>(+) (Goblet cells)</td>
<td>(-)</td>
<td>(+/-) (glands)</td>
</tr>
<tr>
<td>Intestinal MUC5AC</td>
<td>(-)</td>
<td>(+)</td>
<td>(-)</td>
</tr>
<tr>
<td>Intestinal MUC6</td>
<td>(-)</td>
<td>(+) (glands)</td>
<td>(-)</td>
</tr>
<tr>
<td>Pyloric</td>
<td>(-)</td>
<td>(+) (surface)</td>
<td>(+) (glands)</td>
</tr>
</tbody>
</table>
Polypoid gastric dysplasia, foveolar type

- Cuboidal to low columnar cells,
- Clear/light eosinophilic cytoplasm,
- Round to oval nuclei.

Prevalence of foveolar GED: 22% (Adenomatous: 45%, hybrid 33%) (n=69)

- Foveolar GED is often depressed/flat & associated w/ HGD (p= 0.046).
- HGD associated w/ MUC5AC expression regardless of the type (p=0.026).

<table>
<thead>
<tr>
<th>Grade</th>
<th>Foveolar (n=24)</th>
<th>Intestinal (n=22)</th>
<th>Hybrid (n=14)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HGD (n=25)</td>
<td>15* (63%)</td>
<td>4 (18%)</td>
<td>6 (43%)</td>
<td></td>
</tr>
<tr>
<td>Low grade (n=35)</td>
<td>9 (37%)</td>
<td>18 (82%)</td>
<td>8 (57%)</td>
<td>0.010</td>
</tr>
</tbody>
</table>

* coexistent intramucosal carcinoma in 8 cases

Foveolar differentiation is associated w/ HGD & coexistence of IMC

Pyloric gland adenoma

Valente P; Gastric Cancer 2014

- Foveolar GED is often depressed/flat & associated w/ HGD (p= 0.046).
- HGD associated w/ MUC5AC expression regardless of the type (p=0.026).
Intramucosal adenocarcinoma
High Grade Dysplasia

What we know about PGA
- Older pts (mean age: 70 years)
- Females > males (3:1)
- Oxyntic mucosa
- Autoimmune gastritis +
- FAP (no sex predominance); Lynch Sd
- 53% with HGD (23 cases)
- Pyloric-phenotype (MUC6+, < 30% MUC5AC+)
- GNAS mutation in 48% of cases (none in intestinal & foveolar dysplasia)
- KRAS mutation in 41% of cases

What is new about PGA
- Cardia (8%), antrum (6%), pylorus (3%)
- 27% in AIG but 73% not, w/ 9% in FAP & 36% in normal mucosa
- 55% LGD [average size:1.7 cm] while 37% HGD [avg: 3.4 cm]
- TVA architecture more common in HGD (52%) than LGD
- 51% coexpressed MUC5AC with MUC6 in an intermixed pattern
- Only 7% w/ recurrence at 1 year.
Middle age female

What is your diagnosis?
1. Tubular adenoma
2. Well diff. adenocarcinoma
3. Fundic gland polyp

Chief cells

Parietal cells

MUC6

What is your diagnosis?
1. Tubular adenoma
2. Well diff. adenocarcinoma
3. Fundic gland polyp

H+K+ ATPase

Pepsinogen I

Mixed polyps have been seen

Frequent GNAS and KRAS mutations in pyloric gland adenoma of the stomach and duodenum

Mixed polyps have been seen

GNAS mutation

Histopathology

Chief cell-predominant gastric polyps: a morphologic continuum... Anastomosing glands (95%); Mild atypia (58%); Desmoplasia (16%); Necrosis (8%)

Mixed polyps have been seen

MUC6

MUC5A

Mixed polyps have been seen

MUC6

MUC5A
Gastric polyps: characteristics and management strategies

Table 2  Gastric polyp characteristics and malignant potential

<table>
<thead>
<tr>
<th>Polyp type</th>
<th>Usual number and site</th>
<th>Usual site</th>
<th>Malignant potential of polyp</th>
<th>Malignant potential of background mucosa</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sporadic tubular gland polyp</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pedunculated polypycnoidal glands polyp</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperplasia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Autoimmune</td>
<td></td>
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</tbody>
</table>

Net (Neuroendocrine Tumors) in Autoimmune Gastritis

Types 1-2, 3 are ECL cells tumors

Grade 1 (<2 mitoses x 10 HPF; <2% Ki67 index)
Grade 2 (<20 mitoses x 10 HPF; 3-20% Ki67 index)

Gastric Neuroendocrine Tumors

- Increasing prevalence (? increase in endoscopic examination):
  - 2% of gastric malignancies (0.5% in ‘50)
  - 9% of intestinal neuroendocrine neoplasia (2.4% in ‘50)

<table>
<thead>
<tr>
<th>Type</th>
<th>Background</th>
<th>%</th>
<th>Sex</th>
<th># of tumors</th>
<th>Size</th>
<th>Invasion</th>
<th>Mets/ Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Autoimmune Gastritis ECL-cell hyperplasia</td>
<td>70</td>
<td>F</td>
<td>Multiple (70%)</td>
<td>Small</td>
<td>superficial</td>
<td>&lt;10% Good</td>
</tr>
<tr>
<td>2</td>
<td>MEN-I, ZES, Hyperparathyroidism ECL-cell hyperplasia</td>
<td>5-8</td>
<td>M=F</td>
<td>Multiple (100%)</td>
<td>Small</td>
<td>superficial</td>
<td>10% Good</td>
</tr>
<tr>
<td>3</td>
<td>Sporadic Normal or chronic gastritis but no atrophy</td>
<td>20</td>
<td>M</td>
<td>Single (100%)</td>
<td>Variable</td>
<td>deep</td>
<td>65% Mod/Poor</td>
</tr>
</tbody>
</table>

- Size > 0.5cm
- Submucosal invasion

CHR: CHR, SYN: SYN, CD-56: CD-56
**Type I Gastric NET**  
(Most common)

- Most common type (~70%)
- Predilection for older females
- Associated with autoimmune gastritis
  - Hypo/achlorhydria
  - Hypergastrinemia & antral G-cell hyperplasia
  - Pernicious anemia (subset)
- ECL cell proliferation
- Small and multicentric
- Rare angioinvasion
- Metastases are exceptional
  - LN (5%); Liver mets (2.5%)

**Type II Gastric NET**  
(Least common)

- Associated with ZES/MEN-1 (13-30%)
- Hypertrophic hypersecretory gastropathy
- Hypergastrinemia (gastrinoma associated)
- ECL cell hyperplasia may be present
- Small and multicentric
- Metastases are rare
  - LN (30%); Liver mets (10%)

**Management Type I:**
- > 2cm: high risk of metastases (resection either of the lesion or antrectomy)
- <1cm may remain stable in most cases
- 1-2 cm: ESD (or resection or antrectomy for numerous lesions)

**Inflammatory Fibroid Polyp**

- Benign - Antrum (70%) & ileum (20%)
- Wide age range (mean age 60)
- Intussusception (small bowel)
• Cell of origin: fibroblastic? Myofibroblastic?, histiocytic or dendritic cells?

• cells are (+) for CD34, fascin and calponin, [SMA can be seen].

• c-kit, S100, desmin: negative.

Thank You!