Objectives

- Review the epidemiology and pathology of the major subepithelial lesions in the GI tract
- Discuss various approaches to the diagnosis and management of these lesions
Background

• Subepithelial lesions are frequently encountered
  – ~1% of EGD procedures diagnose a subepithelial lesion
  – ~13% of lesions are malignant at diagnosis
  – Many lesions are benign, but have malignant potential

• Most lesions are discovered incidentally

• Most likely symptom is anemia and/or GI bleeding
  – Other symptoms include abdominal pain and obstruction


Background

• M:F ratio=1; most patients >50 years old

• CT/MRI/US usually not sensitive enough to detect and characterize most subepithelial lesions

• EUS is able to:
  – Differentiate extramural compression from intramural growth
  – Determine layer of origin
  – Accurately measure size
  – Evaluate for regional lymphadenopathy
  – Obtain tissue
  – Help to determine appropriate management
Normal Gastrointestinal Wall Layers

Differential Diagnosis

<table>
<thead>
<tr>
<th>Pathology</th>
<th>Muscularis Mucosa</th>
<th>Submucosa</th>
<th>Muscularis Propria</th>
<th>Serosa</th>
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<tr>
<td>GIST</td>
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<tr>
<td>Leiomyoma</td>
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<tr>
<td>Lipoma</td>
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<tr>
<td>Granular Cell Tumor</td>
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<td>Pancreatic Rest</td>
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<tr>
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<td>Fibroid lesion</td>
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Differential Diagnosis

GIST Lesion

- Originate from the interstitial cells of Cajal (MP layer)

- Gain of function mutation in KIT gene → activation of the c-kit protein (tyrosine kinase receptor)¹

- IHC staining is positive for CD117 in 95% cases (corresponds to c-kit activation)

- All have malignant potential

GIST Lesion

• Higher risk of malignancy\textsuperscript{1-3}
  – Lesion size >3cm on EUS
  – Intestinal (jejunum) >> gastric lesions
  – Mitotic rate >5-10/50 HPF

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<tr>
<th>Risk of Malignancy</th>
<th>Size</th>
<th>Mitotic Count</th>
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<td>&lt;5/50 HPF</td>
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<td>Low</td>
<td>2-5cm</td>
<td>&lt;5/50 HPF</td>
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<tr>
<td>Moderate</td>
<td>&lt;5cm</td>
<td>6-10/50 HPF</td>
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<tr>
<td>High</td>
<td>&gt;5cm</td>
<td>&lt;5/50 HPF</td>
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<tr>
<td></td>
<td>&gt;5cm</td>
<td>6-10/50 HPF</td>
</tr>
<tr>
<td></td>
<td>Any size</td>
<td>&gt;10/50 HPF</td>
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GIST Lesion

• Management:
  – Symptomatic lesions: surgical resection*
  – Asymptomatic, large lesions (>2cm): surgical resection*
  – Asymptomatic, small lesions (<2cm):
    • Annual EGD/EUS for surveillance vs. surgical resection

*Simultaneous referral to medical oncologist for consideration of adjuvant therapy with Imatinib (Gleevec®) for high risk lesions

Leiomyoma

• Originate from the MP layer (occasionally MM layer)

• Most common location is the mid-distal eosophagus

Leiomyoma

Management:

- Surveillance EGD/EUS every 1-2 years
  - For asymptomatic, small lesions (<1-2cm)

- Surgical resection
  - Symptomatic, enlarging, structural changes during surveillance

- Endoscopic resection
  - Small lesions (<2cm) arising from the MM layer on EUS exam

Lipoma

• Fatty tumors arising from the SM layer
• Most commonly occur in the colon and gastric antrum
• Positive "pillow sign" 98% specific for lipoma
• Essentially no malignant potential
• Characteristic EUS features
• Jumbo biopsies often reveal yellow, adipose tissue


Granular Cell Tumor

• GCTs are of Schwann cell in origin
• Arise from the MM or SM layer
• Most GI tract GCTs are located within the esophagus
• Risk of malignancy is extremely low
  – ~2-4% at time of diagnosis; all >4cm in size

Granular Cell Tumor

• Management:
  – Small lesions (<1cm) • annual EGD exam
  – Large lesions (>2cm) • surgical resection
  – Intermediate lesions (1-2cm) • surveillance EGD exams vs. endoscopic resection


Pancreatic Rest

• Prevalence of 1-2% in autopsy studies
• 90% located in the stomach; mostly gastric antrum
• Symptoms present in minority of patients:¹
  – Ulceration and pain
  – Pancreatitis
  – Bleeding
  – Gastric outlet obstruction
  – Dysphagia
• Characteristic central umbilication on endoscopy
• Arise from the SM layer on EUS
• Essentially no malignant potential

Carcinoid Tumor

- Most frequent neoplasm of the small intestine (ileum>jejunum>duodenum)$^1$
  - Small bowel accounts for 25% of all carcinoids

- Slight female predominance (M:F ratio=1:1.6)

- Originate from mucosal layer and penetrate deep

- Gastric carcinoids account for 9% of all carcinoids$^2$
  - 3 subtypes of gastric carcinoids
  - Varying levels of malignant potential

Gastric Carcinoid Tumors

- Type I: associated with atrophic gastritis, pernicious anemia and hypergastrinemia
  - Low malignant potential

- Type II: associated with MEN 1, Zollinger-Ellison Syndrome, and hypergastrinemia
  - Intermediate malignant potential

- Type III: sporadic form, normal gastrin levels
  - High malignant potential


Management of Gastric Carcinoid Tumors

- Type I and II lesions (hypergastrinemia):
  - Endoscopic resection for small lesions, <1-2cm
  - Surgical resection for large lesions, or multiple lesions (>5)
  - Consideration or surgical antrectomy or fundectomy
    - Removal of G-cells or ECL cells, respectively
  - Surveillance EGD every 6-12 months

- Type III lesions (normal gastrin levels):
  - Surgical resection with lymph node dissection

Rectal and Duodenal Carcinoid Tumors

**Management of rectal tumors:**
- Small lesions (<1cm), confined to SM: endoscopic resection
- Large lesions (>2cm), or invasion to MP layer, or regional lymph node involvement: surgical resection
- Intermediate lesions (1–2cm), confined to SM: endoscopic vs. surgical resection

**Management of duodenal tumors:**
- No guidelines exist for non-ampullary tumors
- Reasonable to adopt the same approach to rectal lesions


**Algorithm for the Approach to Subepithelial Lesions**

**EGD**
- Biopsy overlying mucosa
- Estimation of lesion size

**Lesion<1cm**
- Repeat EGD in 1 year

**Lesion>1cm**
- EUS
  - Characterize the lesion
  - Evaluate for signs of malignancy
  - Tissue acquisition for definitive Dx

**Growing in size, Or >1cm**
- Yes: Methods of Tissue Acquisition
- No

**Methods of Tissue Acquisition**
- EUS-FNA\(^1\), or EUS-FNB (core needle)
- Tunneled, jumbo biopsy forceps\(^2\)
- Unroofing, enucleation, other techniques\(^3,4\)
- Endoscopic resection

**Significant Malignant Potential**
- Yes: Surgery
- No: Endoscopic Surveillance