Approach to Subepithelial Lesions

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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 & determine appropriate management
Normal Gastrointestinal Wall Layers

Mary Lee Krinsky, DO and Kenneth Binmoeller, MD
Differential Diagnosis

<table>
<thead>
<tr>
<th>Pathology</th>
<th>Muscularis Mucosa</th>
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<th>Muscularis Propria</th>
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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
### GIST Lesion

**Higher risk of malignancy**

- 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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<tr>
<td>Very low</td>
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<td>&lt;5/50 HPF</td>
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<tr>
<td>Low</td>
<td>2-5cm</td>
<td>&lt;5/50 HPF</td>
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<tr>
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<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 eophagus\(^1\)
- IHC staining is negative for CD117, CD34, and s100
  - Positive for desmin and α-smooth muscle actin proteins
- Risk of malignancy is extremely rare\(^1,2\)

Leiomyoma
Leiomyoma

• Management:
  – Surveillance EGD/EUS every 1-2 years\(^1\)
    • 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\(^1\)

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:
  - 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

Pancreatic Rest
Carcinoid Tumor

- Most frequent neoplasm of the small intestine (ileum>jejenum>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**
- Significant Malignant Potential
  - **yes**
    - **Surgery**
  - **no**
    - **Endoscopic Surveillance**

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**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

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