



AGA Clinical Practice Update on Management of Subepithelial Lesions Encountered on Routine Endoscopy: Expert Review

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Introduction

- Subepithelial lesions (SEL) of the GI tract → masses, bulges, or impressions covered with normal-appearing epithelium.
- Originate from muscularis mucosa, submucosa, muscularis propria (MP), or they can be extraluminal.
- Found in 1/300 endoscopies, and two-thirds of SEL are located in the stomach.
- Mostly asymptomatic, but can present with abdominal pain, GI bleeding, or rarely, obstruction.
- Can be non-neoplastic or neoplastic, so diagnosis is imperative.

Diagnosis

- **Endoscopy**
 - Standard biopsies do not get deep enough for dx
- **Forceps biopsy**
 - Bite-on-bite or deep-well biopsy or tunnel biopsy may be done to establish pathologic dx
- **EUS**
 - (1) Characterizes lesion (2) Tissue acquisition
- **EUS-FNA and EUS-FNB**
 - Studies show FNB > FNA for tissue acquisition in SEL
- **Endoscopic Resection Techniques**
 - Non-exposed: No breach of muscularis propria layer
 - Endoscopic Submucosal Resection (ESMR)
 - Submucosal Tunnel Endoscopic Resection
 - Exposed: Breach of MP layer with exposure to extraluminal space
 - Endoscopic Submucosal Dissection (ESD)
 - Endoscopic Full-Thickness Resection

Best Practice Advice

1. **Forceps bite-on-bite or deep-well biopsies or tunnel biopsies** may be done and sometimes establish a pathologic diagnosis of SEL.
2. **EUS → modality of choice** for eval of **indeterminate SEL of the GI tract** (if non-diagnostic tissue by forceps biopsies).
3. **SEL arising from the submucosa → tunnel biopsies** (or deep-well biopsies), **EUS guided fine-needle aspiration (FNA), EUS guided fine-needle biopsy (FNB), or advanced endoscopic techniques** (unroofing or endoscopic submucosal resection).
4. **SEL arising from muscularis propria → sample (FNB or FNA)** to determine whether **GIST or leiomyoma**. Structural assessment and staining → differentiation of mesenchymal tumors and assessing their malignant potential.
5. **Endoscopic resection techniques → for removal of SEL. Should be limited to endoscopists skilled in advanced tissue resection techniques.**
6. **Management of each SEL depends on the size of the lesion, histopathology, their malignant potential, and presence of symptoms.**
7. SEL consistent with a **lipoma or pancreatic rest** on endoscopy and normal mucosal biopsies → **no need for further evaluation or surveillance.**
8. For **SEL arising from muscularis propria** that are **< 2 cm** in size → consider surveillance using EUS.
9. **Gastric GIST > 2 cm** should be considered for **resection.**
10. SEL that are **ulcerated, bleeding, or causing symptoms** should be considered for **resection.**

Common Subepithelial Lesions	Endoscopic appearance	EUS appearance	EUS layer	Histology	
Leiomyoma of the mid-esophagus			Hypoechoic	2nd, 3rd, or 4th	Similar and indistinguishable from GIST. (-) CD117 and (-) CD34 (+) desmin and (+) smooth muscle actin
Lipoma of second portion of the duodenum			Hyperechoic	3rd	Mature adipocytes, relatively uniform in size and lacking cytologic atypia.
Pancreatic rest of the gastric antrum			Hyperechoic or mixed echogenicity	2nd, 3rd, or 4th	Rounded lobules of pancreatic acinar tissue with associated ducts.
Gastrointestinal stromal tumor (GIST) of the gastric fundus			Hypoechoic	4 th (rarely 2nd or 3rd)	Spindle cells, epithelioid cells, or a mixture of both. (+) CD117 and (+) DOG1 (useful if CD117 testing is negative).
Type III gastric carcinoid of greater curvature of the stomach			Mildly hypoechoic or isoechoic	2nd or 3rd	Hyperplasia of ECL cells. Varies depending on the site. Divided into grade G1, G2, and G3, with increasing malignant potential, using mitotic rate (10 hpf) and Ki-67 index (%).