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Endoscopic Resection of Subepithelial Tumors

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Subepithelial tumors (SETs) are often incidentally found during endoscopic examinations. Endoscopic ultrasonography (EUS) is a good method for differential diagnosis of SETs, but a definite diagnosis cannot be made based on EUS features alone in some cases. Periodic follow-up examinations by endoscopy and EUS remains the recommended management strategy, which involves issues related to patient compliance, cost-effectiveness, and the risk associated with repeated endoscopic procedures and delayed diagnosis of malignancy. Endoscopic resection of the SETs is another technique to treat them as well as to obtain tissue specimens for accurate histologic diagnosis. Herein, a various endoscopic techniques ranging from simple snare resection to endoscopic submucosal tunnel dissection for the management of SETs will be reviewed.

Key Words: Endoscopic resection; Subepithelial; Neoplasms

INTRODUCTION

Subepithelial tumors (SETs) may arise from deep mucosa to serosa depending on the histological type. SETs are mostly asymptomatic lesions with normal overlying mucosa, which are often incidentally found during endoscopic or radiologic examinations (overall frequency 0.3%).¹ Endoscopic ultrasonography (EUS) is a method which has led to a demonstrable improvement of the differential diagnosis of SETs, but a definite diagnosis cannot be done on EUS features alone in some cases, especially for hypoechoic lesions.²⁻⁴ And, although most SETs used to be considered as benign, they do have malignant potential, especially when they originate from the muscularis propria layer such as gastrointestinal stromal tumor (GIST).

In general, a tissue diagnosis may not be necessary for large (>3 cm in diameter) and/or symptomatic lesions that require surgery regardless of the histology.^{4,5} Currently, there are no firm guidelines for the management of small (<3 cm in diameter, <2 cm if GIST is suspected), asymptomatic SETs that origi-

nate from the muscularis propria layer. Periodic follow-up examination by endoscopy and EUS remains the recommended management strategy. However, this approach involves issues related to patient compliance, cost-effectiveness, and the risk associated with repeated endoscopic procedures and delayed diagnosis of malignancy.

There is a growing body of evidence that a pathological diagnosis is necessary for small (<3 cm in diameter), asymptomatic, hypoechoic SETs originating from the muscularis propria on EUS. However, the diagnostic efficacy of current tissue sampling techniques such as EUS-guided fine needle aspiration or EUS-guided trucut biopsy appears to be limited.^{6,7} The use of endoscopic submucosal resection (ESMR) or endoscopic submucosal dissection to resect submucosal lesions is another technique to obtain tissue specimens for accurate histologic diagnosis. Endoscopic resection of lesions arising in the muscularis propria using an insulated-tip electrosurgical knife has also been reported in several small case series. In the present review, a various endoscopic techniques ranging from simple snare resection to endoscopic submucosal tunnel dissection for the management of SETs will be introduced.

STANDARD SNARE RESECTION

SETs which are pedunculated or sessile with less than 1 to 2 cm of base can be resected by using a snare with or without sa-

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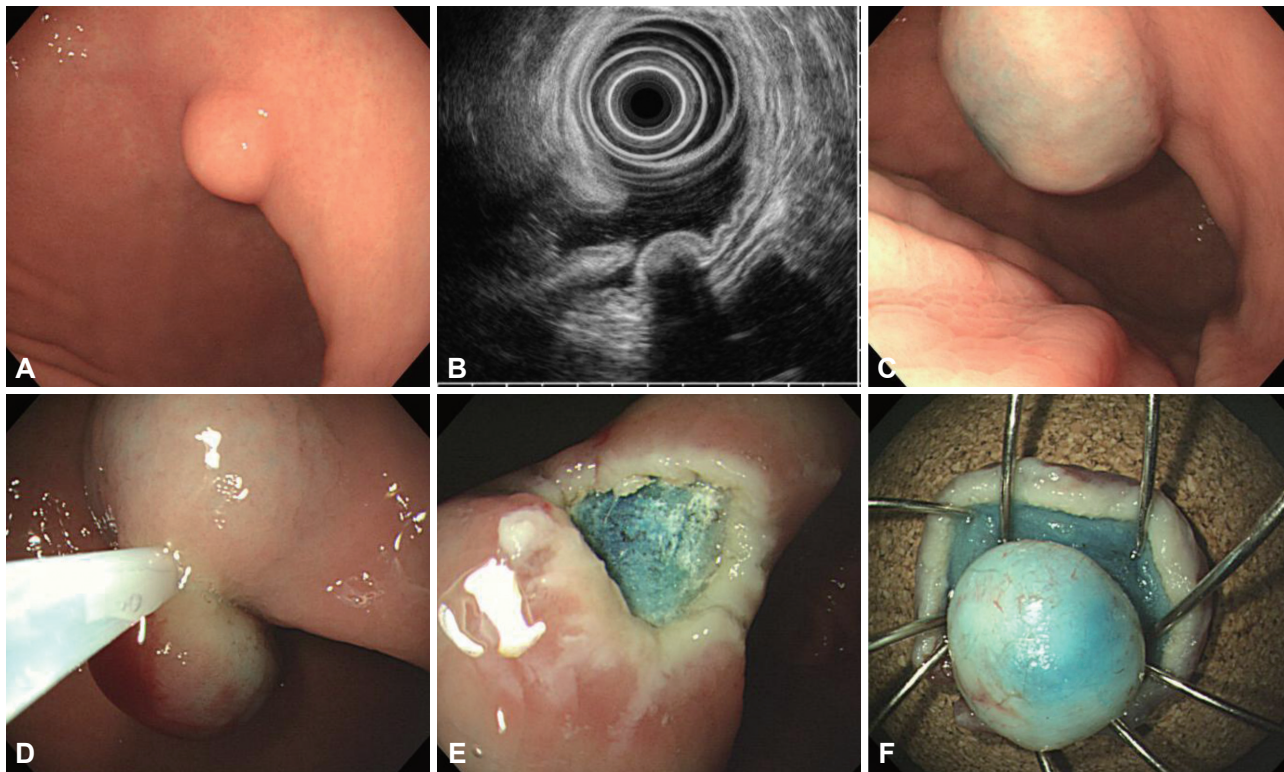


Fig. 1. Standard snare polypectomy of a gastric inflammatory fibrinoid polyp. (A) A subepithelial tumor is observed at the angle. (B) The tumor is hypoechoic and located in the submucosal layer on endoscopic ultrasonography. (C) Submucosal injection is done to elevate the lesion from the proper muscle layer. (D) The tumor is resected by using a snare. (E) The lesion is completely removed. (F) Inner surface of the resected specimen.

line injection with diluted epinephrine (1:100,000) and indigo carmine dye into the submucosal layer using an injection needle (Fig. 1). One series included 45 patients with SETs in various parts of the gastrointestinal tract which were resected with a polypectomy snare with or without assistance of a grasping forceps using a double-channel endoscope.⁸ Kojima et al.⁹ reported their experience with polypectomy of 31 SETs with snare electrocautery and a grasping forceps via double channel endoscope with no perforations and 9% of bleeding rate.

ESMR WITH A LIGATING DEVICE (ESMR-L)

A lifted lesion is aspirated into the ligation device, followed by deployment of the elastic band. Snare resection is performed using blended electrosurgical current, and the resected specimen is then removed by aspiration into the cap or retrieved with a net (Fig. 2). The maximum size of a resectable SET is limited because the diameter of ligation devices is usually between 9 and 11 mm. Wehrmann et al.¹⁰ demonstrated a successful resection of esophageal SETs 13 mm and less in size using ESMR-L. In another series, ESMR-L was performed in all 25 esophageal SETs in less than 10 minutes of procedure time, and the *en bloc* resection rate was 100%. There were no seri-

ous complications such as perforation or massive bleeding.¹¹

ESMR WITH A TRANSPARENT CAP (ESMR-C)

Transparent cap is attached to the distal tip of the endoscope. A crescent shaped snare is positioned into a distal ridge within the cap. A lifted lesion is sucked into the cap thus creating a pseudo-polyp which is immediately captured by closing the prepositioned EMR-snare. Finally the lesion is removed using electrocoagulation. Kajiyama et al.¹² proved that ESMR-C was a safe, effective and less invasive procedure for small esophageal leiomyomas (<2 cm in diameter) derived from the muscularis mucosa.

UNROOFING TECHNIQUE

Lee et al.¹³ evaluated the diagnostic yield and safety of endoscopic partial resection using the unroofing technique in 16 patients with hypoechoic SETs of <3 cm in diameter, originating from the muscularis propria on EUS (14 gastric and 2 esophageal lesions). The overlying mucosa of the SET was removed using an electrosurgical snare with electrical current under minimal aeration to expose the tumor sufficiently (un-

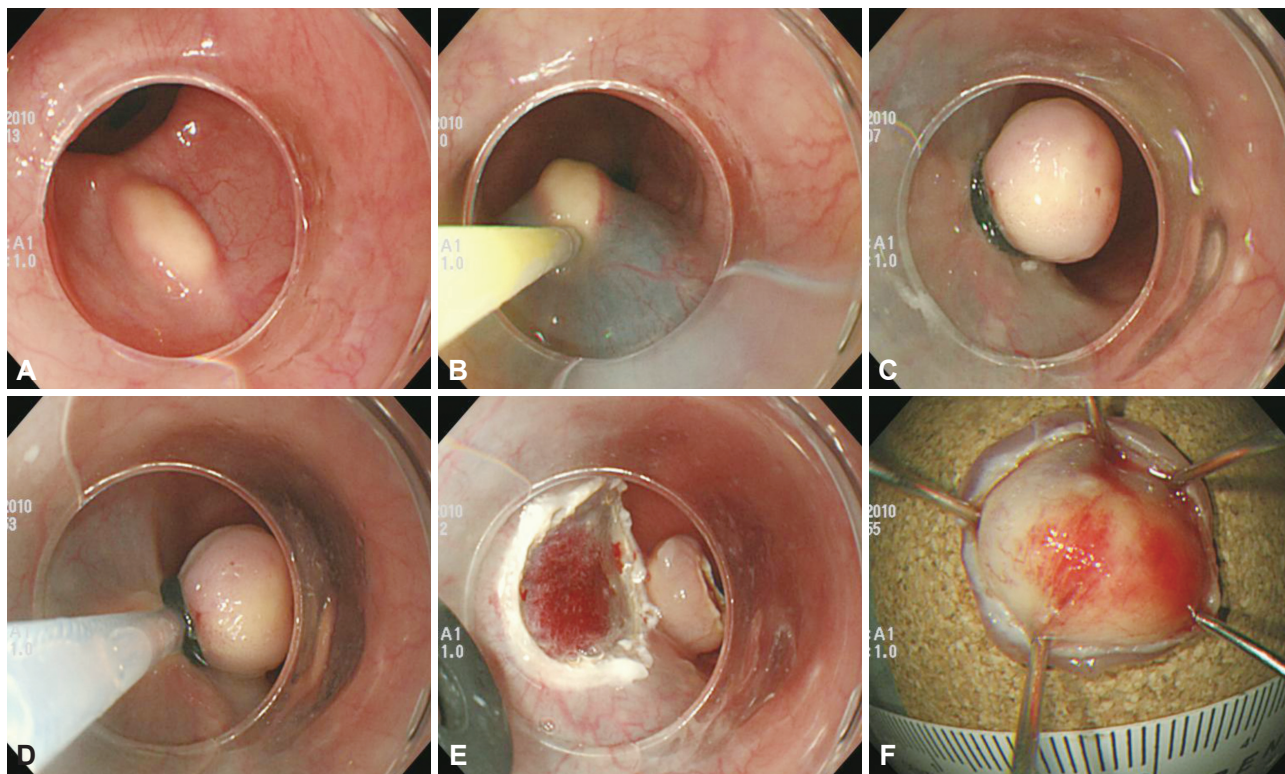


Fig. 2. Endoscopic submucosal resection of an esophageal granular cell tumor with a ligation device. (A) A subepithelial tumor is observed at the lower esophagus. (B) Saline solution with small amount of epinephrine and indigo carmine dye is injected beneath the lesion to elevate it. (C) The lesion is then aspirated into the ligation device, followed by deployment of the elastic band. (D) Snare resection is performed using blended electrosurgical current. (E) The lesion is completely removed. (F) Inner surface of the resected specimen.

Table 1. Main Publications Reporting Success and Complication Rates of Endoscopic Submucosal Dissection for Subepithelial Tumors

First author	Year	No. of cases	Median tumor diameter, mm	Layer origin	Success rate, %	Complication rate, %
Park et al. ¹⁴	2004	15	20.0	MP (11) Non-MP (4)	93	13.3 (1 perforation/ 1 bleeding)
Lee et al. ¹⁵	2006	12	20.7	MP (12)	75	0
Hwang et al. ¹⁶	2009	25	28.7	MP (25)	64	12 (3 perforations)
Shi et al. ¹⁷	2011	30	12.5	MP (30)	93	6.6 (2 perforations)
Bialek et al. ¹⁸	2012	37	25.0	Non-MP (15) MP (22)	100 68	5.4 (2 perforations)
Li et al. ¹⁹	2012	143	17.6	MP (143)	94	4.2 (6 perforations)
Kim GH (unpublished)	2012	41	13.1	Non-MP (34) MP (7)	94 71	2.4 (0 perforation)

MP, muscularis propria; non-MP, wall layers other than muscularis propria.

roofing). Next, the snare grasped the half upper portion of the exposed target lesion and cut the lesion. They showed a high diagnostic yield (93.7%) and no major complications using unroofing technique.

ENDOSCOPIC SUBMUCOSAL DISSECTION USING ELECTROSURGICAL KNIFE

There are a few small case series on endoscopic resection of

SETs originating from the muscularis propria by using an insulated-tip knife (Table 1).¹⁴⁻¹⁹ It must be emphasized that characterization of the layer of origin with EUS is necessary before attempting endoscopic resection because the risk of the procedure, especially perforation, is directly related to the depth of the tumor within the esophageal or gastric wall. It is possible to achieve complete tumor dissection using the insulated-tip knife if the endoluminal SET is loosely adherent to the muscularis propria regardless of their size and shape (Fig. 3). Endoscopic submucosal dissection preserves the in-

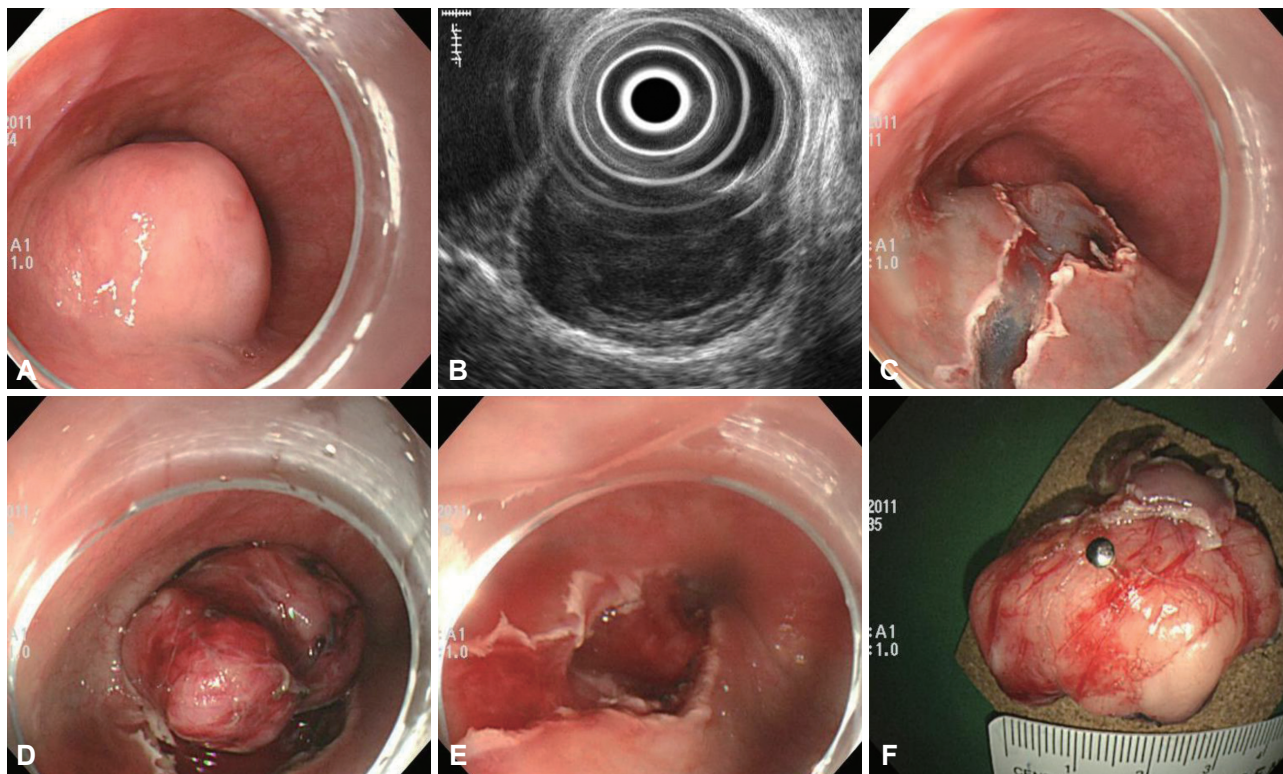


Fig. 3. Endoscopic submucosal dissection of an esophageal leiomyoma using electrosurgical knife. (A) A large subepithelial tumor is observed at the lower esophagus. (B) The tumor is hypoechoic and located mainly in the submucosal layer on endoscopic ultrasonography. (C) After midline incision of overlying normal mucosa, a subepithelial tumor is exposed. (D) Submucosal dissection of the tumor is performed by using an IT-knife. (E) The lesion is completely removed. (F) The resected specimen.

Table 2. Recent Three Publications Reporting Success and Complication Rates of Endoscopic Submucosal Tunnel Dissection for Subepithelial Tumors

First author	Yr	No. of cases	Median tumor diameter, mm	Layer origin	Success rate, %	Complication rate, %
Inoue et al. ²⁰	2012	9	18	MP	78	11 (1 perforation)
Gong et al. ²¹	2012	12	20	MP	100	17 (2 perforations)
Xu et al. ²²	2012	15	19	MP	100	13 (2 perforations)

MP, muscularis propria.

tegrity of the stomach, and shortens patient recovery time.

ENDOSCOPIC SUBMUCOSAL TUNNEL DISSECTION TECHNIQUE

Inoue et al.²⁰ reported a new technique of submucosal endoscopic tumor resection using submucosal tunnel created by the technique of peroral endoscopic myotomy, which was introduced for esophageal achalasia. Following initial mucosal incision approximately 5 cm proximal to the edge of the SET, saline and indigo carmine are injected to create a mucosal bleb. A submucosal tunnel is created by dissecting the submucosal fibers. Submucosal dissection is advanced beyond the distal tumor edge. The SET is dissected from the muscle layer. All muscle bundles that connect to the SET are cut with the triangle-tip knife. The totally mobilized tumor is extracted

from the submucosal space through the mucosal incision. Finally, the mucosal entry is tightly closed with hemostatic clips. Because the overlying mucosal layer is kept intact, this technique may be effective in preventing mediastinitis and peritonitis. In recent three reports about this technique, the success rate was high and the complication rate was acceptable (Table 2).²⁰⁻²²

CONCLUSIONS

The endoscopic resection of SETs has been reported in many series and variety of techniques has been introduced. But the efficacy and safety of endoscopic resection for SETs are not established yet. In all series, follow-up was limited and studies have not included examination of surgical or autopsy specimens to confirm complete resection. Therefore, regular

follow-up is mandatory after endoscopic resection, and wide resection should be considered if an endoscopically resected SET proves to have been incompletely removed and where the histology report shows the tumor to be a GIST with a high risk of malignancy.

Conflicts of Interest

The author has no financial conflicts of interest.

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