



Retrospective Study

Endoscopic resection using band ligation for esophageal SMT in less than 10 mm

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originated from the submucosa.

METHODS: From May 2009 to September 2014, after medical chart and endoscopic ultrasonography report review, a total of 15 esophageal tumors located in the submucosal layer were resected by EMR-B. Previous symptom, location, pathology, complete resection rate, incidence of complications, incidence of minor complication, size, length of procedures time and follow up months were evaluated. To evaluate local recurrence at the resection site, periodic follow-up endoscopic examination was undertaken in all of the patients. The first endoscopic examination was performed about 6 mo after the endoscopic resection. Thereafter, the endoscopic follow up were scheduled annually.

RESULTS: The mean age was 50.3 ± 9.67 years. The mean tumor size was 6.93 ± 3.15 mm and most of the lesions size was between 5-10 mm in diameter (10/15, 66.6%). In all patients, endoscopic *en bloc* resection was achieved. In one patient, the vertical margin was involved. The mean procedural time was 8.86 ± 3.66 min. In all patients, no evidence of severe complications such as perforation or bleeding occurred. Minor complications such as chest pain (2/15, 13.3%) and heartburn (3/15, 13.3%) were reported but they symptoms were controlled by proton pump inhibitors, ulcermin and/or analgesics. Histologic assessments of the removed specimens revealed 10 granular cell tumors (66.6%), 4 leiomyomas (16.6%) and one lipoma (6.6%). No recurrence was observed during the mean follow up period of 45 ± 3.5 mo (range: 5-64 mo).

CONCLUSION: EMR-B might be considered safe and effective for the diagnosis and treatment of lesions measuring less than 10 mm in diameter.

Key words: Band ligation; Endoscopic mucosal resection; Esophagus; Submucosal tumor; Ultrasonography

Abstract

AIM: To evaluate the safety and feasibility of endoscopic resection using band ligation (EMR-B) for the diagnostic and therapeutic removal of tumors located in the esophageal subepithelial region having

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Core tip: In cases of esophageal tumors originating in the submucosal layer, we consider that endoscopic resection may be necessary if esophageal biopsy results are non-conclusive. Endoscopic resection using band ligation is effective for diagnosis and treatment of lesions measuring less than 10 mm in diameter.

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INTRODUCTION

With the increased use of routine endoscopy for health checks in Korea, the frequency of identifying asymptomatic incidental esophageal subepithelial tumors is increasing. Although most of such small tumors are clinically insignificant, some which have originated from the submucosal layer, identified by endoscopic ultrasonography (EUS), have malignant potential^[1-3]. For example, granular cell tumor, carcinoid tumor, gastrointestinal stromal tumor and lymphoma could be found in the submucosal layer^[4,5]. Therefore, it is essential to distinguish between benign and malignant, or potentially malignant, tumors.

Recently, EUS has been demonstrated to apparently provide an advantage over endoscopy in the diagnosis of tumors beneath the mucosal layer, and can differentiate intramural lesions from extrinsic compression. For intramural lesions, EUS can determine the exact size, layer of origin, echogenicity and margin with surrounding structures^[6]. However, the EUS only predicted the correct histologic diagnosis in 43% of cases and was dependent on the operator's experience^[6-9]. Ultimately, histologic confirmation should be obtained whenever possible. But, the diagnostic yield of simple endoscopic biopsy for subepithelial tumor is low. Where the endoscopic "bite on bite" technique is used in esophageal submucosal tumors, the diagnostic yield is 14%-42% in some reports, but there was a high risk of bleeding requiring endoscopic intervention in about 2.8% of cases^[10,11].

Conventional endoscopic mucosal resection (EMR) can usually be used for superficial gastrointestinal neoplasms confined to the mucosal layer and esophageal submucosal tumors less than 10 mm in diameter. However, complete histologic resection is not always easy to achieve using EMR for tumors located in the submucosal layer, which results in frequent involvement of the resection margin. Recently, in the case of small tumors of less than 10 mm in diameter

and located in the submucosal layer, EMR using a band-ligation device (EMR-B) showed a high complete resection rate^[12].

This study aimed to evaluate the safety and feasibility of EMR-B for diagnostic and therapeutic removal of tumors located in the esophageal subepithelial region having originated from the submucosa.

MATERIALS AND METHODS

From May 2009 to September 2014, after medical chart and EUS report review, a total of 18 hypoechoic mass lesions in the esophageal submucosa, defined by EUS, were found. After exclusion of cystic and vascular lesions by EUS, endoscopic biopsies had been performed in these patients; however in nine patients negative pathologic results were obtained. After appropriate exclusions, 15 of the 18 patients underwent EMR-B at Pusan National University Yangsan Hospital in Korea during the study period. The data was collected prospectively, but the data analysis was done retrospectively. This study was reviewed and approved by the Institutional Review Board at Pusan National University Yangsan Hospital. Written informed consent was obtained from all the patients prior to EMR-B. The procedures were performed under conscious sedation (intravenous administration of midazolam and/or meperidine) by two endoscopists (Choi CW and Kim HW) with > 5 years of experience in performing therapeutic endoscopy (including endoscopic submucosal dissection). For sedation, 2.5 mg of midazolam and 12.5 mg of meperidine were initially administered and another dose of 2.5 mg of midazolam and 12.5 mg of meperidine were injected at endoscopist's discretion when required.

All patients were examined by endoscopy and EUS before the endoscopic resection. For EUS, the UM3R ultrasonic mini-probe (UMP, 20 MHz; Olympus, Tokyo, Japan) was used. Indications for endoscopic resection were as follows: measured tumor size < 10 mm in diameter, hypoechoic lesions, hard mass, and confined to the submucosal layer as assessed by the EUS catheter probe (Figure 1).

There is a general consensus that solid tumors in the submucosal layer (hypochoic lesions on EUS) are to be removed. However, EMR-B is not recommended for cystic or vascular lesions because they have a tendency to rupture during band ligation. For EMR-B, a model GIF-H260 single-channel endoscope (Olympus) was inserted into the esophagus. After careful inspection, a solution (10% glycerin plus 5% fructose in 0.9% saline diluted 1:100000 with epinephrine-normal saline solution and mixed with a small amount of indigo carmine) was injected submucosal layer around the lesion to lift it off the muscle layer. A single-channel endoscope with a band ligation device attached to its tip was reinserted into the esophagus. The lesion was then aspirated into the ligator device, followed by deployment of the elastic band. Snare

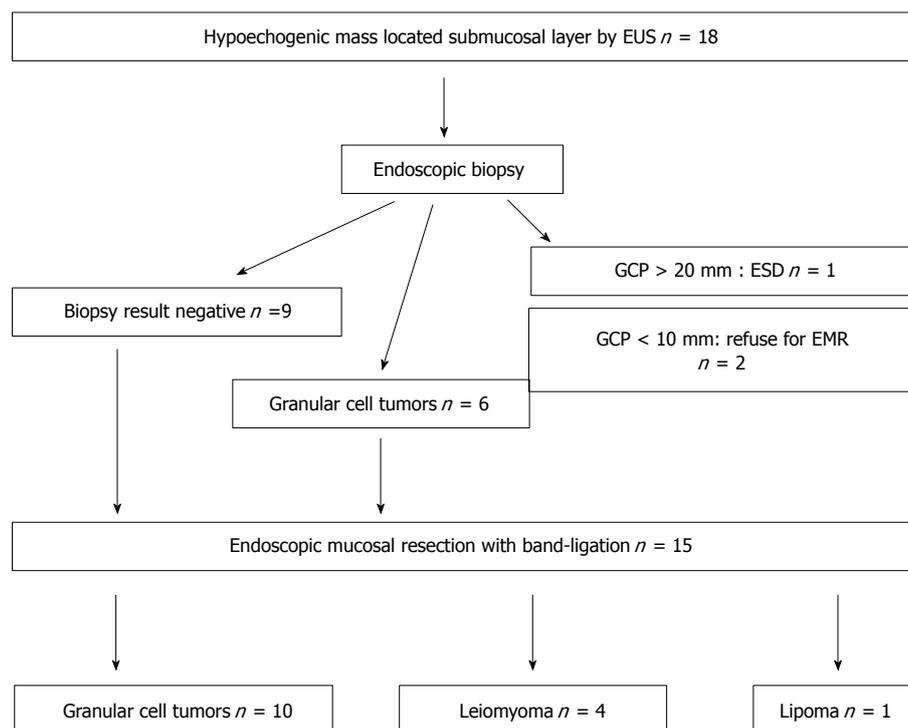


Figure 1 Flow chart of endoscopic treatment for esophageal tumor located in the submucosal layer by endoscopic ultrasonography. EUS: Endoscopic ultrasonography; GCP: Granular cell tumor; EMR: Endoscopic mucosal resection; ESD: Endoscopic submucosal dissection.

resection was performed below the band by using an Endocut Q current (effect 3, cut duration 2, cut interval 5), which was generated using a VIO300D electro-surgical unit (ERBE, Tuebingen, Germany) (Figure 2).

The specimens were carefully evaluated histopathologically in slices at 2 mm intervals, with the microscopic evaluation including histopathologic type, depth of invasion, and lateral and vertical resection margins. *En bloc* resection was defined as endoscopic resection of the entire lesion in a single piece. Complete resection was defined as being unable to identify tumor cell tissue microscopically at the resection margin.

To evaluate local recurrence at the resection site, periodic follow-up endoscopic examination was undertaken in all of the patients. The first such endoscopic examination was performed about 6 mo after the endoscopic resection. Thereafter, the endoscopic checkups were scheduled annually.

(10/15, 66.6%) (Table 2).

Endoscopic results and follow up

In all patients, endoscopic *en bloc* resection was achieved. In one patient, the vertical margin was involved, but during the follow up period of 48 mo, no evidence of local recurrence was found in spite of no additional treatment being given. The mean procedural time was 8.86 ± 3.66 min. No evidence of severe complications such as perforation and bleeding (including delayed bleeding after hospital discharge) occurred. Minor complications such as chest pain (2/15, 13.3%) and heartburn (3/15, 20.0%) were reported but they symptoms were controlled by proton pump inhibitors, ulcermin and/or analgesics. Histologic examination revealed 10 granular cell tumors (66.6%), four leiomyomas (16.6%) and one lipoma (6.6%) (Table 3). No recurrence was observed during the mean follow up period of 45 ± 3.5 mo (range: 5-64 mo).

RESULTS

Characteristics of patients and lesions

During the study period, a total of 15 esophageal tumors located in the submucosal layer were resected by EMR using band ligation. Table 1 shows the details of patients' information and endoscopic and pathologic results. The mean patient age was 50.3 ± 9.67 years. The locations of lesions were equally distributed. The mean tumor size was 6.93 ± 3.15 mm, and most of the lesions were between 5 and 10 mm in diameter

DISCUSSION

Recently, due to the increased use of high resolution endoscopy and routine health checkups, esophageal subepithelial tumors have been detected more frequently and referred to academic hospitals for EUS. Although EUS plays an integral part in evaluating such tumors, its accuracy in delineating the layer of origin and making a specific diagnosis is limited and subject to the operator's experience. Usually, after excluding lipomas, vascular lesions or cysts by

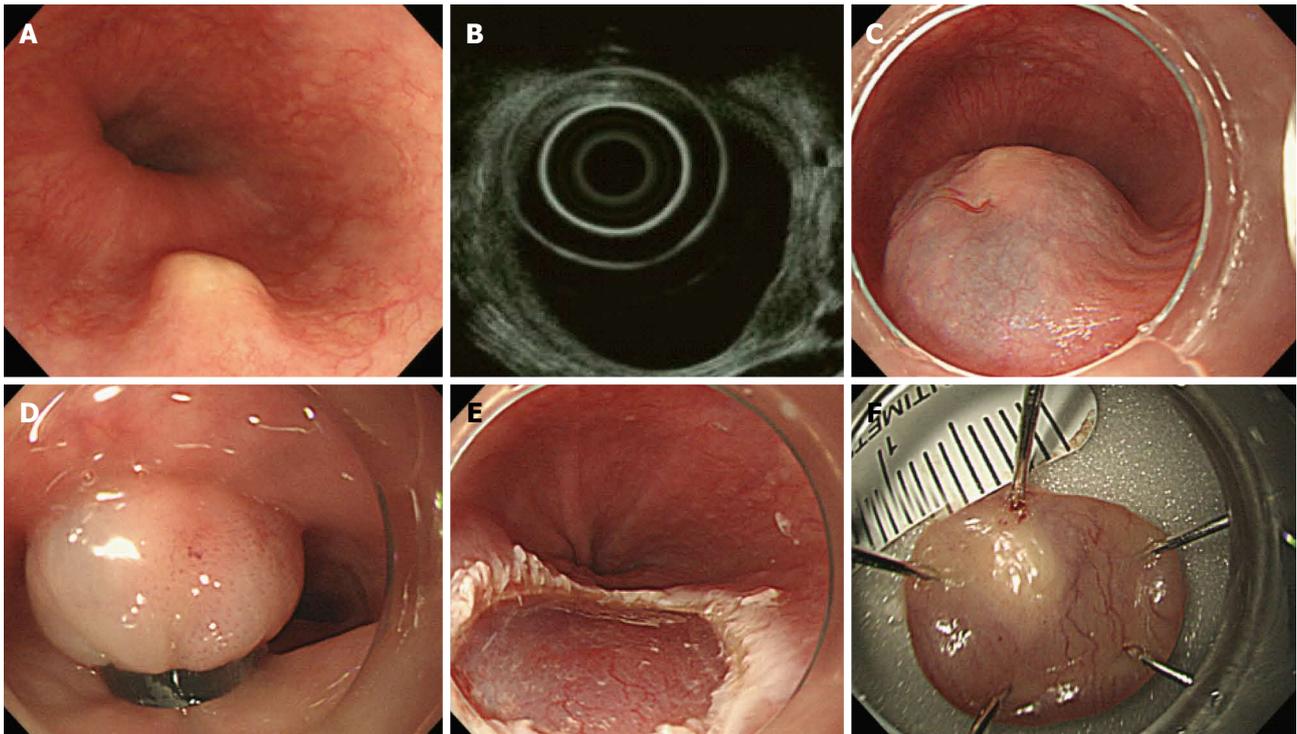


Figure 2 Endoscopic mucosal resection using band-ligation. A: Endoscopic view of esophageal granular cell tumor; B: Endoscopic ultrasound showed a hypoechoic lesion in the submucosal layer; C: Submucosal injection was performed; D: The tumor was ligated with the elastic band after submucosal solution injection; E: Ulcer after resection; F: Resected specimen.

Table 1 Summary of clinicopathologic features and treatment outcome in 15 patients underwent endoscopic resection using band ligation for esophageal submucosal layer tumor

No.	Gender	Age (yr)	Pathology	Symptoms	Location	Procedure time (min)	Complication	Minor complication	Size (mm)	En bloc resection	Margin status	Follow-up (mo)	Outcomes
1	M	54	GCP	None	Middle	10	No	Chest pain	8	Yes	LM (-)/VM (+)	64	No recur
2	F	52	GCP	None	Upper	4	No	No	7	Yes	LM (-)/VM (-)	46	No recur
3	M	44	GCP	Reflux	Lower	7	No	No	8	Yes	LM (-)/VM (-)	41	No recur
4	M	52	Lipoma	None	Lower	17	No	No	7	Yes	LM (-)/VM (-)	41	No recur
5	F	31	Leiomyoma	None	Upper	7	No	Hot burn	13	Yes	LM (-)/VM (-)	25	No recur
6	M	46	GCP	Heartburn	Middle	10	No	Chest pain	7	Yes	LM (-)/VM (-)	20	No recur
7	M	57	GCP	None	Lower	8	No	Chest pain	7	Yes	LM (-)/VM (-)	17	No recur
8	F	42	GCP	Epigastric pain	Upper	8	No	No	2	Yes	LM (-)/VM (-)	17	No recur
9	F	46	GCP	None	Upper	10	No	No	9	Yes	LM (-)/VM (-)	12	No recur
10	M	58	GCP	Epigastric pain	Middle	15	No	No	4	Yes	LM (-)/VM (-)	5	No recur
11	F	48	GCP	Globus	Lower	9	No	No	12	Yes	LM (-)/VM (-)	43	No recur
12	F	44	Leiomyoma	None	Middle	5	No	No	6	Yes	LM (-)/VM (-)	43	No recur
13	F	70	Leiomyoma	None	Middle	5	No	No	7	Yes	LM (-)/VM (-)	45	No recur
14	F	46	GCP	None	Lower	12	No	No	1	Yes	LM (-)/VM (-)	12	No recur
15	F	65	Leiomyoma	None	Upper	6	No	Hot burn	6	Yes	LM (-)/VM (-)	45	No recur

GCP: Granular cell tumor; LM: Lateral margin; VM: Vertical margin.

EUS, gastrointestinal subepithelial tumors apparently originating from the submucosal layer need pathologic confirmation^[13]. To achieve this, simple endoscopic biopsy was the first approach used. However, the diagnostic yield with the use of this simple biopsy technique from the luminal side, even with the “bite on bite” technique, is limited (less than 38% diagnostic rate), although the use of jumbo forceps increases the yield to about 60% but at the expense of an increased

incidence of bleeding that requires endoscopic hemostasis in a third of patients^[14,15].

Although the conventional EMR technique for biopsy of gastrointestinal submucosal tumors is a simple procedure, this technique is sometimes associated with margin involvement and crush injury of the resected specimens, which leads to difficulty in pathologic evaluation and often necessitates additional surgical intervention. To overcome these shortcomings, EMR-B

Table 2 Characteristics of patients and tumors *n* (%)

Characteristics	Values
Age, yr (mean ± SD)	50.3 ± 9.67
Sex, male	6 (40)
Tumor location	
Upper esophagus	5 (33.3)
Middle esophagus	5 (33.3)
Lower esophagus	5 (33.3)
Tumor size, mm (mean ± SD)	6.93 ± 3.15
Tumor size, mm	
> 10	2 (13.3)
5-10	10 (66.6)
< 5	3 (20.0)

GCP: Granular cell tumor; LM: Lateral margin; VM: Vertical margin.

Table 3 Clinical outcomes of endoscopic resection using band ligation *n* (%)

Characteristics	Values
Endoscopic complete resection	15 (100)
pathologic complete resection	14 (93.3)
Lateral margin	15 (100)
Vertical margin	14 (93.3)
Procedure time, min (mean ± SD)	8.86 ± 3.66
Major complication	
bleeding	0 (0)
perforation	0 (0)
Minor complication	
Hot burn	2 (13.3)
Chest pain	3 (20.0)
Recurrence on follow up	0 (0)
Pathologic outcomes	
Granular cell tumor	10 (66.6)
Leiomyoma	4 (16.6)
Lipoma	1 (6.6)

has been described as an effective assessment and treatment modality^[16]. It is known that EMR-B is safe to remove the subepithelial tumor in the submucosal layer less than 10 mm on any sites of digestive tract.

With EMR-B, tumors can be frontally viewed with a hood attached to the endoscope and lifted sufficiently by endoscopic suction. In this way, undamaged circular resected specimens can be obtained and EMR-B provides a deeper resection margin compared with conventional EMR^[16]. In the present study, the *en bloc* resection rate and complete pathologic resection rate were 100% and 93.3%, respectively. In addition, no serious complications such as perforation or delayed bleeding occurred.

According to our research results, most of the tumors were granular cell tumors^[17-21]. Although the natural history of granular cell tumor is unclear, most such tumors are known to have a benign clinical course. However, approximately 1.5%-2.7% of cases have malignant potential^[17,20,22,23]. On endoscopy, a granular cell tumor presents as a submucosal lesion that is gray-white to yellowish in color. On EUS, it appears as a sub-mucosal homogeneous hypoechoic mass with well-defined margins^[24,25].

No generally accepted management of his tumor has yet been established because the precise natural course of the lesion is unknown. Nevertheless, several authors recommend endoscopic resection as a safe and effective treatment option^[26,27].

This study had several limitations. First, because this was a retrospective study, there may have been a potential bias when retrospectively reviewing the outcome of the endoscopic resection. Secondly, all of the endoscopic procedures were performed by two skilled endoscopists who had had more than 5 years of therapeutic endoscopic experience at academic hospitals. Thirdly, this study was based on a limited experience at a single center. In conclusion, in cases of esophageal tumors originating in the submucosal layer, we consider that endoscopic resection might be necessary if esophageal biopsy results are inconclusive. After exclusion of cystic and vascular lesions by EUS, EMR-B might be considered safe and effective for the diagnosis and treatment of lesions measuring less than 10 mm in diameter.

COMMENTS

Background

After exclusion of cystic and vascular lesions, the pathologic diagnosis of an esophageal tumor originating in the submucosa is necessary. However, endoscopic ultrasonography (EUS) is not conclusive and the diagnostic yield from esophageal simple biopsy is low. This study aimed to evaluate the safety and feasibility of endoscopic resection using band ligation (EMR-B) for the diagnostic and therapeutic removal of tumors located in the esophageal subepithelial region having originated from the submucosa.

Research frontiers

This study aimed to evaluate the safety and feasibility of EMR-B for the diagnostic and therapeutic removal of tumors located in the esophageal subepithelial region having originated from the submucosa.

Innovations and breakthroughs

According to our research results, EMR-B is recommended for the solid tumor of less than 1 cm from the submucosal layer of origin, except for cystic or vascular lesion in our endoscopy center.

Applications

Although majority of the tumors originated from submucosal layer are benign, tumors with malignant potential such as neuroendocrine tumors or lymphoma may be found as subepithelial tumor originated from submucosal layer. Such as, if gastrointestinal subepithelial tumors originated from submucosal layer are suspected by EUS, endoscopic resection is recommended.

Terminology

For EMR-B, endoscope was inserted into the esophagus. After careful inspection, a solution was injected submucosal layer around the lesion to lift it off the muscle layer. A single-channel endoscope with a band ligation device attached to its tip was reinserted into the esophagus. The lesion was then aspirated into the ligator device, followed by deployment of the elastic band. Snare resection was performed below the band.

Peer-review

This study aimed to evaluate the safety and feasibility of EMR-B for diagnostic and therapeutic removal of tumors located in the esophageal subepithelial region having originated from the submucosa. The results are interesting and may represent a effective for the diagnosis and treatment of lesions measuring less than 10 mm in diameter.

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