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Research Article

Autoamputation with Band Ligation: Safe and Effective Endotherapy for Small Esophageal and Gastric Subepithelial Lesions

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Abstract

Background: Subepithelial esophageal and gastric lesions comprise a heterogeneous group, some of which harbor malignant potential. Current clinical guidelines are outdated and incomplete regarding the optimal management of subepithelial lesions.

Aims: To evaluate the efficacy and safety of endoscopic ultrasound (EUS)-guided endoscopic band ligation (EBL) for autoamputation of small esophageal and gastric subepithelial lesions.

Methods: We conducted a retrospective review over a seven year period (2006-2013) at a tertiary-care teaching hospital. All patients with esophageal or gastric subepithelial lesions ≤ 10 mm in size treated with EBL with available follow-up were included for analysis.

Results: Forty-three patients with 50 subepithelial lesions ≤ 10 mm of the esophagus or stomach underwent EUS-guided EBL and endoscopic follow-up at our center. Eight patients with 11 esophageal granular cell tumors (GCT) (mean (SD) size 5.8 ± 1.5 mm), 11 esophageal leiomyomas (5.9 ± 1.9 mm), 13 gastric gastrointestinal stromal tumors (GIST) (6.4 ± 1.9 mm), 6 patients with 9 type 1 gastric carcinoids (6.8 ± 1.5 mm), and 5 patients with 6 indeterminate subepithelial lesions (5.7 ± 1.5 mm) were treated with EBL. All lesions were successfully banded with one band with exception of one GIST that would not suction into the banding cap. No serious complications occurred; one patient required dilation of a post-EBL esophageal stricture and one patient had self-limited chest pain.

Conclusions: EUS-guided EBL is a safe, effective method for removal of small superficial esophageal and gastric subepithelial lesions.

Keywords: Ligation; Leiomyoma; Granular Cell Tumor; Carcinoid Tumor; Gastrointestinal Stromal Tumors

Abbreviations

UGI: Upper Gastro Intestinal
GCT: Granular Cell Tumors
GIST: Gastrointestinal Stromal Tumors
ER: Endoscopic Resection

ESD: Endoscopic Submucosal Dissection
EUS: Endoscopic Ultra Sound
EBL: Endoscopic Band Ligation
MP: Muscularis Propria
ECL: Entero Chromaffin-Like
FNA: Fine Needle Aspiration

Introduction

The incidental finding of diminutive subepithelial lesions during upper endoscopy is not uncommon. Subepithelial upper gastrointestinal (UGI) lesions range from benign entities (leiomyoma or pancreatic rest) to lesions with varying degrees of malignant risk (granular cell tumors (GCT), gastrointestinal stromal tumors (GIST), carcinoids) [1] (Table 1).

Table 1. Esophageal and Gastric Subepithelial Intramural Lesions.

Location	No Malignant Potential	Malignant or Malignant Potential
Esophageal	Leiomyoma Lipoma Fibrovascular Polyp Duplication cyst	Granular cell tumor
Gastric	Pancreatic rest Nerve sheath tumor Lipoma Gastric varices Inflammatory fibroid polyp (fibroma)	GIST Carcinoid Glomus tumor Lymphoma Metastasis

Historically, such lesions were managed either with surgical resection or close endoscopic surveillance. Advances in endoscopic therapeutics have resulted in a transition away from potentially morbid surgery towards endoscopic therapy in appropriate candidates. Endoscopic resection (ER) options include lift and cut snare resection, band ligation or cap-assist mucosal resection, or submucosal dissection (ESD) in select centers. The American Gastoenterological Association last published guidelines on the management of gastric subepithelial masses in 2006. Endoscopic surveillance or surgical resection was recommended for glomus tumors and GIST < 3 cm in size; further, surgical resection was recommended for type 3 carcinoids and GIST > 3 cm. However, given the paucity of literature available at that time, a firm recommendation on the management of incidentally detected, small gastric subepithelial lesions could not be made [2,3]. No guidelines exist regarding the management of subepithelial esophageal lesions. Endoscopic ultrasound (EUS)-guided band ligation for purposes of autoamputation can be utilized for removal of small superficial lesions. Endoscopic band ligation (EBL) without resection results in vascular constriction beneath the lesion and eventual sloughing, as the entire lesion is captured above the band. Multiple studies have evaluated ER in the management of these lesions but available literature on EBL is limited. Autoamputation with EBL may confer a lower risk of bleeding and perforation compared to ER or ESD, and is technically easy to perform. We report our single center experience with EUS-guided EBL for autoamputation of diminutive esophageal and gastric subepithelial lesions.

Materials and Methods

A retrospective review of our medical record system was performed to identify patients who underwent EUS-guided EBL of superficial esophageal and gastric lesions over a seven year period (2006-2013). Patient characteristics, clinical history, endoscopic and EUS findings, pathology results, complications, and findings on surveillance endoscopy / EUS were reviewed. Only lesions ≤ 10 mm in size in patients with available follow-up endoscopy at our center were included. The primary outcome measurements were efficacy and safety of EBL.

A leiomyoma was defined as a firm well-defined hypoechoic round or oval lesion arising from the deep mucosal layer (muscularis mucosae) or muscularis propria (MP) of the esophagus. A GIST was defined as a firm well-defined hypoechoic round or oval lesion arising from the deep mucosal layer or muscularis propria of the stomach. Pathologic confirmation was available for all granular cell tumors and gastric carcinoids. Lesions with non-diagnostic pathology arising from the submucosa of the stomach were labeled indeterminate.

Complications were defined as: post-procedural chest and/or abdominal pain necessitating hospital admission, periprocedural or delayed perforation, post-EBL esophageal dysphagia and/or stricture, and post-procedural gastrointestinal bleeding. Index and/or follow-up EUS examinations were performed by 1 of 5 experienced endosonographers at our institution, using a 12 MHz miniprobe (Olympus America Corp, Center Valley, PA), radial echoendoscope (GF-UM20, GF-UM130, GF-UE160-AL5, Olympus America Corp, Center Valley, PA) and/or curvilinear echoendoscope (FG-36 UA; Pentax Medical, Montvale, NJ; GF-UC140P-AL5, Olympus America Corp, Center Valley, PA). EBL procedures were performed using the Speedbander (Boston Scientific Corp, Natick, MA).

This study was approved by the Institutional Review Board of the University of Pittsburgh Medical Center.

Results

A total of seventy-five patients with 82 subepithelial lesions ≤ 10 mm of the esophagus or stomach underwent EUS-guided EBL at our institution from 2006 through April, 2013 (Table 2). Forty-three patients with 50 subepithelial lesions had a follow-up endoscopy at our center and were therefore included for analysis.

Eight patients had 11 biopsy-confirmed esophageal granular cell tumors (GCT) treated with EBL for autoamputation; three

patients had two lesions each. Six lesions were detected in the lower third of the esophagus and 5 in the middle third. By EUS assessment, all lesions were superficial, arising from the deep mucosal (9) or submucosal layer (2). The mean (SD) size was 5.8 ± 1.5 mm as measured by EUS. The sole complication was the development of a mild post-EBL esophageal stricture associated with dysphagia; this was treated with one dilation session. There was no endoscopic evidence of recurrent or residual GCT on follow up EGD and/or EUS.

Eleven patients with 11 diminutive esophageal leiomyomas were treated with EBL for autoamputation. Two lesions were detected at the gastroesophageal junction, 4 in the lower third of the esophagus, 3 in the middle third, and 2 in the upper third. By EUS assessment, 10 lesions arose from the deep mucosa and one from the inner circular layer of the MP (as assessed by a 12 MHz minprobe). The mean (SD) size was 5.9 ± 1.9 mm as measured by EUS. All lesions were successfully ligated with one band. One patient developed self-limited post-procedural chest pain that resolved without intervention; hospital admission was not required. No patients had endoscopic evidence of recurrent or residual leiomyoma on follow up EGD and/or EUS.

Thirteen patients with 13 gastric GISTs were treated with EBL for autoamputation. Seven lesions were detected in the antrum, 5 in the body, and 1 in the cardia. By EUS assessment, 10 lesions arose from the deep mucosa, and 3 from the inner circular layer of the muscularis propria. The mean (SD) size was 6.4 ± 1.9 mm as measured by EUS. With the exception of one lesion that would not suction into the banding device, all lesions were successfully ligated with one band. The lesion that could not be banded arose from the inner circular layer of the muscularis propria and was calcified. There were no complications in this patient group. On follow-up, three patients had evidence of residual GIST at follow-up; one arose from the muscularis propria and two from the deep mucosal layer. All three lesions underwent serial EUS surveillance; one lesion enlarged by 2-3 mm over a 50 month interval and the other two lesions exhibited no change in size at 12 and 36 month follow-up, respectively. These were not rebanded. One other patient was noted to have nodularity at the prior EBL site; it was unclear on EUS if this represented scar or persistent GIST. This lesion was rebanded with negative subsequent follow-up.

Six patients with biopsy-proven Type 1 gastric carcinoids underwent EBL for autoamputation. A total of 9 carcinoids were banded; one patient had two lesions and another patient had three. All lesions were located in the gastric body and arose in histologically-proven atrophic gastritis. By EUS assessment, 4 lesions arose from the deep mucosa and 5 from the submucosa. The mean (SD) size was 6.8 ± 1.5 mm as measured by EUS. All lesions were successfully banded with one band. There were no complications.

Five patients had 6 subepithelial gastric lesions that could not be otherwise characterized. These 6 "indeterminate" lesions arose from the submucosa; four lesions were found in the antrum and 2 in the body of the stomach. Mucosal pinch biopsies were non-diagnostic in all cases. The mean (SD) size was 5.7 ± 1.5 mm as measured by EUS. All lesions were successfully ligated with one band. There were no complications. Two patients had evidence of a nodule at the prior EBL site upon follow-up. It was unclear if these represented scar tissue or persistent lesion. Both lesions were rebanded; one lesion still had a persistent nodule after repeat banding and the other lesion has subsequent follow-up pending.

Discussion

Subepithelial UGI lesions comprise a heterogeneous group which generally harbor little to no malignant potential, especially when diminutive in size. If untreated, these lesions are typically surveyed, which likely results in unnecessary procedures and resultant expense. Current clinical guidelines are incomplete regarding the optimal management of small subepithelial lesions of the UGI tract.

GCTs are mesenchymal tumors of Schwann cell origin [4]. Approximately 10% of GCTs are found in the GI tract, the esophagus being the most common location [5]. GCTs do harbor malignant potential, however malignant transformation occurs in < 2% [6]. Multiple studies have evaluated ER in the management of GCTs. A report of 23 esophageal GCTs found synchronous lesions in 30% of cases, and only 26% exhibited the characteristic yellow appearance. In this study, ER was attempted on 10 lesions <10 mm in size. Resection was histologically complete in 90% and no complications were reported [7]. Another study evaluated the effectiveness of ER in the treatment of 20 consecutive esophageal subepithelial lesions. The average size was 17 mm; 12 were histologically-confirmed GCTs. Eight patients (40%) developed post-ER gastrointestinal bleeding (6 immediate, 2 delayed); all required endoscopic hemostasis [8]. Lee et al reported their experience using band-assisted ER to treat 25 consecutive small (mean size 7.1 mm) esophageal subepithelial lesions. Complete histologic resection was attained in 96% of cases; 14 lesions were histologically confirmed GCTs. No perforations occurred but 4 patients (16%) developed immediate post-ER bleeding and 5 patients (20%) developed self-limited chest pain [9]. In our cohort of 9 patients with 12 GCTs, we found EBL to be technically easy, safe and effective. One patient developed a post-EBL esophageal stricture; this was treated with one dilation session. Further, no residual or recurrent tumor was detected upon follow-up.

Leiomyomas are the most common mesenchymal esophageal tumors, followed by GCTs. A case series of 30 leiomyomas found that the average size associated with symptoms was 5.2 cm [10]. Leiomyomas are generally regarded as benign lesions, however there are rare case reports of malignant transformation to leiomyosarcomas [11,12]. A recent study evaluated 229 patients with esophageal leiomyomas; 118 lesions with a mean size of 7 mm were treated with ER. No complications were reported [13]. In 2004, Sun et al reported their experience with

EBL without electrocautery in the management of 50 esophageal leiomyomas arising from the muscularis propria (mean size 12 mm). On surveillance endoscopy, they found that all 50 lesions sloughed completely with healing observed at a mean of 3.6 weeks. No perforations or hemorrhage was observed but all 50 patients had mild self-limited post-procedural chest discomfort [14]. Our study lends more evidence for the safety and efficacy of EBL in the management of esophageal leiomyomas. All 11 cases were successfully banded, with only one patient experiencing self-limited post-procedural chest pain.

Table 2. Baseline Characteristics.

	Esophageal Granular Cell Tumor	Esophageal Leiomyoma	Gastric GIST	Gastric Carcinoid	Indeterminate Gastric Lesion
Number of Patients	8	11	13	6	5
Number of Lesions	11	11	13	9	6
Age (mean ± SD, years)	47.1 ± 12.7	57.9 ± 11.2	50.1 ± 12.5	64.3 ± 10.5	51.8 ± 12.9
Gender, % Female	75.0	54.5	31.3	21.3	40.0
Lesion Size (max diameter ± SD, mm)	5.8 ± 1.5	5.9 ± 1.9	5.8 ± 1.6	6.8 ± 1.5	5.7 ± 1.5
Anatomic Location	Lower: 6 Middle: 5	GE Jxn: 2 Lower: 4 Middle: 3 Upper: 2	Antrum: 7 Body: 5 Cardia: 1	Body: 2	Antrum: 4 Body: 2
EUS Layer of Origin	M: 9 SM: 2	M: 10 ICMP: 1	M: 10 ICMP: 3	M: 4 SM: 5	SM: 6
Technical Success of Index EBL	11/11 (100%)	11/11 (100%)	12/13 (92.3%)	9/9 (100%)	6/6 (100%)
Complications	1/11 (9.1%)	1/11 (9.1%)	0/13 (0%)	0/9 (0%)	0/6 (0%)
Residual Lesion on Follow-Up	0/11 (0%)	0/11 (0%)	3/13 (23.1%)	N/A	2/6 (33.3%)
Follow-up (mean ± SD, months)	25.9 ± 26.7	16.9 ± 18.0	26.7 ± 13.8	20.5 ± 21.4	24.0 ± 16.2

GISTs are the most common mesenchymal tumor in the GI tract, most frequently found in the stomach. Features suggestive of low malignant risk include size < 5cm, mitotic index < 5/50 per high powered field, and EUS features demonstrating a homogenous, noncystic lesion with a regular border [15,16]. The use of EBL in gastric GISTs arising from the muscularis propria was previously evaluated for lesions ≤ 12 mm in size. Twenty eight of 29 lesions were successfully treated with one band. There was one post-EBL delayed hemorrhage that was treated endoscopically. Despite banding the MP, no perforations developed [17]. However, there are 2 case reports of gastric perforation after EBL of subcentimeter GISTs; both lesions arose from the MP [18]. In our practice, we band GISTs that are superficial (arising from the deep mucosal layer) or arise from the inner circular layer of the MP, and protrude into the submucosal layer. Overall, 13 lesions were banded without any complications. However, we experienced 3 failures. One patient had a GIST arising from the inner circular layer of the MP, which might confer a higher failure rate. The other two lesions were small and arose from the deep mucosal layer; it is unclear as to why these did not slough. It is also possible that residual or persistent lesion seen upon follow up could just represent focal scar tissue, which may appear very similar to a small GIST.

Type 1 gastric carcinoids are the most common type of gastric neuroendocrine tumor and arise from enterochromaffin-like (ECL) cells in the background of atrophic gastritis and a resultant hypergastrinemic state. Despite this well-established association, the incidence of these lesions at the time of diagnosis of chronic atrophic gastritis is only 2.4% [19]. These are typically indolent, well-differentiated lesions with a low incidence of metastasis, especially when < 2 cm in size [20]. Recent studies have demonstrated that regimented endoscopic surveillance with periodic resection of type 1 lesions < 2 cm in size is an effective approach despite the tendency of these lesions to recur [21]. Merola et al recently described their experience with endoscopic surveillance every 6-12 months in 33 patients with type 1 gastric carcinoids; over 65% had multifocal lesions at time of enrollment. After 46 months of follow-up, no patients had developed metastatic disease and there were no deaths. However, 63.6% did exhibit recurrence highlighting the need for ongoing surveillance and retreatment [22]. Our study supports the safety and efficacy of EBL as an endoscopic treatment strategy in type 1 gastric carcinoids.

Six small indeterminate subepithelial lesions arose from the submucosal layer of the stomach and may have represented pancreatic rests or fibromas. Ectopic pancreatic tissue, or pancreatic rests, are benign subepithelial lesions typically found in the gastric antrum [23]. While typically asymptomatic, these rarely cause ectopic pancreatitis and gastric outlet obstruction [24,25]. A recent study by Bain et al showed that band-assisted ER of 19 gastric pancreatic rests was safe; no complications were reported [26]. A drawback of our study is the lack of a definitive histologic diagnosis for most lesions. However, subcentimeter indeterminate subepithelial lesions are generally of little clinical consequence and EBL was effective in the majority of cases.

The differential diagnosis of subepithelial lesions in the esophagus and stomach is heterogeneous with varying degrees of malignant potential; however, when small, the risk of malignant transformation is exceedingly low. It can be difficult to establish a definitive pre-resection diagnosis of these lesions. EUS characteristics alone have been repeatedly shown to be a poor predictor of the true pathologic diagnosis of UGI subepithelial lesions [27-29]. Further, the yield of tunneled "bite-on-bite" biopsies in obtaining a pre-resection pathologic diagnosis in UGI subepithelial lesions is only 30-40% [30]. EUS-fine needle aspiration (FNA) has a much higher yield in the diagnosis of subepithelial lesions; however, its utility is limited in subcentimeter lesions. Buscaglia et al recently found that the additive yield of jumbo biopsies as an adjunct to FNA in subepithelial lesions improved the diagnostic yield over either modality alone; however, even when both methods were combined the overall yield was a modest 67.4% [31]. Again, the yield of this technique in small <10 mm lesions is likely lower. Given the difficulty in securing a pre-resection diagnosis, one

could argue for the resection of all such lesions to eliminate the risk, albeit low, of malignant transformation and the need for continued surveillance. Our study demonstrates that EBL for autoamputation is a safe, effective strategy for the management of multiple esophageal and gastric subepithelial lesions and averts the need for continued endoscopic surveillance in the majority of cases, which is cost saving in the long run. No patient experienced bleeding, which can occur with ER, and EBL is a technique familiar to all endoscopists.

There are several limitations to our study. First, it is retrospective with all the associated limitations of this design. Second, electronic chart review within our hospital network does not include patients admitted to out-of-network hospitals, thus, our findings may underestimate the reported complication rate. Lastly, the specimen is not obtained for pathologic assessment when performing EBL, thus a definitive diagnosis is not possible in many of these lesions. Size also limits this technique, as it is unlikely that lesions > 10 mm can be aspirated into the banding adaptor.

Conclusion

EUS-guided EBL appears to be a safe, effective method for removal of small superficial esophageal and gastric subepithelial lesions. Importantly, EUS-guided EBL for autoamputation may obviate the need for future endoscopic surveillance for the majority of these lesions and prove cost saving in the long run.

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