NEW METHODS

Submucosal tunnel endoscopic resection for extraluminal tumors: a novel endoscopic method for en bloc resection of predominant extraluminal growing subepithelial tumors or extra-gastrointestinal tumors (with videos)

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Background and Aims: The management of subepithelial tumors with a predominant extraluminal growth pattern or extra-GI tumors can be challenging and traditionally requires a surgical resection that is not only invasive but may carry a significant risk of morbidity and mortality. We aimed to assess the feasibility, safety, and efficacy of a novel endoscopic technique termed *submucosal tunnel endoscopic resection for extraluminal tumors* (STER-ET).

Methods: We prospectively enrolled patients who underwent STER-ET for GI subepithelial tumors with a predominant extraluminal growth pattern or extra-GI tumors located at the level of cardia or the proximal part of the lesser curvature of the stomach seen on cross-sectional imaging between January 2016 and March 2017.

Results: Eight patients underwent STER-ET. The mean (± standard deviation) tumor size was 2.8 ± 0.6 cm and 2.3 ± 0.8 cm in longest and shortest dimension, respectively. The average procedure time was 67 ± 4.4 minutes. The rates of curative en bloc resection and en bloc retrieval was 100% and 87.5%, respectively. On final histology, 6 tumors were GI stromal tumors, 1 was a schwannoma, and 1 was a foregut cyst. Five patients had capnoperitoneum during the procedure and required abdominal decompression. One patient had a small mucosotomy successfully treated with a hemostatic clip. There were no major adverse events or deaths. The median length of hospital stay was 3 days. There was no residual tumor on surveillance imaging after a mean follow-up period of 10.0 ± 2.1 months.

Conclusions: STER-ET is a novel technique that appears to be safe and effective in achieving a curative resection for GI subepithelial tumors with a predominantly extraluminal growth pattern or extraluminal tumors in a selected group of patients. However, larger studies are required to validate our finding.

The majority of subepithelial tumors are predominantly asymptomatic and are discovered incidentally during radiologic or endoscopic examinations. There is a wide spectrum of pathologic features of upper GI subepithelial tumors, but the most common mesenchymal tumor originating from the muscularis propria of the GI tract is a GI stromal tumor (GIST).[1-3] GISTs may have a predominant extraluminal growth pattern or may occur outside of the

Abbreviations: CRP, C-reactive protein; EGIST, extra-GI stromal tumor; EUS-FNA, EUS-guided FNA; GIST, GI stromal tumor; HPF, high-power field; NOTES, natural orifice transluminal endoscopic surgery; STER, submucosal tunneling endoscopic resection; STER-ET, submucosal tunnel endoscopic resection for extraluminal tumors.

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GI tract and are termed *extra-gastrointestinal stromal tumors* (EGIST).[4,5] However, in the studies by Agaimy and Wunsch,[5] the authors concluded that the distinction between a true EGIST and GIST with a predominantly extraluminal growth pattern can be difficult and that GISTs may have originated from the outermost muscle layer but may have subsequently lost contact with the muscle layer because of the extensive extramural growth pattern. True EGISTs are rarer and have been reported to be more aggressive compared with GISTs and may arise from the omentum, mesentery, ligaments, liver, gallbladder and retroperitoneal and pelvic organs.[4-7] Given that GISTs typically are resistant to both chemotherapy and radiotherapy, a complete en bloc resection is the only curative treatment option for a non-metastatic lesion.[2]

Traditionally, a wedge surgical resection either by laparotomy or a laparoscopic approach is the only treatment option for GISTs and carries a significant risk of morbidity and mortality.[8-9] With the advancement in endoscopic technology and the discovery of novel endoscopic techniques such as submucosal tunneling endoscopic resection (STER) and endoscopic full-thickness resection, it is now possible for GISTs with a predominant extraluminal growth pattern or extra-GI tumors to be excised curatively by an endoscopic method.[10-13] We previously reported on a case of endoscopic mediastinal tumorectomy by using an endoscopic tunneling technique for extra-luminal tumor resection.[14] Here we describe the first human case series of extraluminal tumor resection by using submucosal tunnel endoscopic resection for extraluminal tumors (STER-ET). This technique was inspired by the STER technique, which used the submucosal space as a working channel to achieve a complete en bloc resection of GI subepithelial tumors with a predominant extraluminal growth pattern or extra-GI tumors. In this study, we assessed the feasibility, safety, and efficacy of this novel endoscopic technique.

METHODS

Patient selection

We prospectively enrolled all consecutive patients who underwent STER-ET for GI subepithelial tumors with a predominant extraluminal growth pattern or extraluminal tumors between January 2016 and March 2017 at Zhongshan Hospital, Fudan Medical University, Shanghai, China. All patients were selected according to the following criteria: (1) a single subepithelial tumor with a predominant extraluminal growth pattern characterized by >90% of the cross-sectional diameter of the tumor located outside of the GI lining, located at the level of the cardia or the proximal lesser curvature of the stomach evident on abdominal CT and EUS; (2) a tumor that was no more than 5 cm in cross-sectional diameter; (3) a non-ulcerated mobile tumor with no involvement of the overlying mucosa on endoscopy; (4) no evidence of metastatic lesions determined by chest and abdominal CT; and (5) the absence of significant cardiorespiratory comorbidities defined as American Society of Anesthesiologists Physical Status Classification System score of $\leq$3. This study was approved by the institutional review board of Fudan University (B2016-019). Written consent was obtained from all patients enrolled in this study. The primary outcome measures were procedure time, tumor size, rate of en bloc resection, rate of en bloc retrieval, procedure-related adverse events, and length of hospital stay. The secondary outcome measures were final histology of the en bloc specimen, leukocytosis, elevated C-reactive protein (CRP) level, and rate of residual tumor on follow-up imaging.

Initial evaluation

Abdominal and chest CT and EUS were used as primary modalities for initial staging and tissue diagnosis. An EUS-guided FNA (EUS-FNA) of the tumors was performed by using a linear array echoendoscope (GF-UE260-AL5; Olympus Optical Co, Ltd, Tokyo, Japan) and a 22-gauge needle (Cook Medical, Winston-Salem, NC, USA or Boston Scientific, Marlborough, Mass, USA) for cytology and cell block analysis.

STER-ET technique

All procedures were performed by 2 experienced endoscopists (P.H.Z., M.D.X.) who had >5 years' experience in advanced endoscopic techniques and had performed >500 cases of endoscopic full-thickness resection and STER. All patients underwent general anesthesia with endotracheal intubation. In this study, a single dose of prophylactic intravenous antibiotic (cefotiam 2 g) was given 30 minutes before the start of the endoscopy and after endotracheal intubation. During the postoperative period, 2 more days of intravenous antibiotics were given. All patients underwent a standard endoscopy (GIF-Q260J; Olympus, Tokyo, Japan) to assess for the presence of a mucosal bulge from extrinsic compression of the tumor to indicate the tumor site. STER-ET was performed by using a standard single-channel endoscope (GIF-Q260J; Olympus) with a transparent hood (D-201-11804; Olympus) fitted onto the tip of the endoscope to improve endoscopic visualization. Other equipment used included an injection needle, a T-type hybrid knife (ERBE, Tuebingen, Germany), an insulated-tip knife (KD-611L; Olympus), a hemostatic forcep (FD-410LR; Olympus), and a high-frequency electrosurgical generator (VIO 200D; ERBE). In addition, a CO_2 regulator (UCR; Olympus) was used during the endoscopic procedure. All STER-ET procedures were performed by using 6 major steps (Fig. 1A-F).

Step 1. When a mucosal bulge was identified, a submucosal injection of a mixture of 100 mL normal saline solution and 1 mL indigo carmine was performed followed by a 2-cm longitudinal mucosal incision made at 5 cm above the