Submucosal Endoscopic Tumor Resection

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Gastric subepithelial tumor (SET) is an incidental finding during esophagogastroduodenoscopic examination, which usually shows protruding intra-luminal mass covered with normal mucosa.\(^1\) Gastric SETs contain all tumors which are originated from mesenchyme, vessels or neurons, including benign (i.e. leiomyoma, cyst, fibroma, lipoma, lymphangioma, hemangioma) or malignant tumors (i.e. leiomyosarcoma, lymphoma, fibrosarcoma and melanoma), and epithelial neoplasms originated from epithelial layer are excluded. Most of gastric SETs are considered as benign behavior, however, some SETs especially from muscularis propria layer may have malignant potential, and should be carefully followed up. For example, gastrointestinal stromal tumor (GIST) is one of the most common intra-luminal gastric SET, and known to show malignant behavior in 10 ~ 30% of cases.\(^2,3\) Recent National Comprehensive Cancer Network (NCCN) guideline states that GISTs which are less than 2.0 cm in the longest diameter and do not have suggesting findings of malignancy by endoscopic ultrasonography (EUS) such as irregular border, cystic spaces, ulceration, echogenic foci and heterogeneity, might be considered as endoscopic surveillance for 6 to 12 months intervals.\(^4\) However, previous studies reported that up to 3.7% of small GISTs which were less than 2.0 cm and showed benign findings by EUS finally classified as high risk group due to high mitotic index (MI) larger than 10/50 high power field (HPF).\(^5\) Thus, if gastric SETs originated from muscularis propria layer are not definitely diagnosed as benign lesions such as lipoma by EUS, endoscopic removal of SETs for pathologic confirmation may be necessary for optimal diagnosis and treatment.

Open abdominal surgery or laparoscopic wedge resections have been mainstay for resection of gastric SETs, however, as technical advancement and clinical experiences are achieved, endoscopic procedures are now being introduced for removal of gastric SETs.\(^6-8\) These procedures have been being progressed from classical methods such as snare polypectomy or incisional enucleation to standard procedures such as endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD) and more advanced and novel techniques such as endoscopic submucosal tunnel dissection (ESTD) and endoscopic full-thickness resection (EFTR). Among them, standard ESD method has been reported as feasible and safe method for resection of gastric SETs. This technique includes following steps: 1) round mucosa incision around tumor; 2) direct dissection of the submucosal layer beneath the tumor under direction vision; and 3) complete \textit{en bloc} resection and safe retraction of specimen.\(^9\) However, SETs originated from muscularis propria layer are difficult to resect completely by ESD,
and risk of perforation tends to increase. Recent studies reported that gastric SETs originated from muscularis propria layer removed by ESD showed 73 ~ 94% of complete resection rate, however, perforation rate was up to 15%.10-12 For effective dissection of muscularis propria layer, endoscopic muscularis dissection (EMD) has been introduced as a modification of ESD. This technique is distinguished from ESD method by the following characteristics: 1) longitudinal mucosal incision rather than round; 2) complete dissection as deep as muscularis propria at the base of the tumor by electrical dissection of blunt dissection to separate the tumor from the muscularis propria; and 3) closure of mucosal defect using hemoclips.13 Liu et al reported that complete resection rate was 97%, but perforation was also as high as 13%, even though all of them were conservatively managed without surgery.13

Both ESD and EMD techniques have a disadvantage for relatively high risk of perforation in case of SETs originated from muscularis propria. Recently, peroral endoscopic myotomy (POEM) has been introduced for endoscopic treatment modality of refractory achalasia, and this procedure is now being applied for resection of SETs originated from deep layer in muscularis propria. This method has the following major procedures: 1) creation of submucosal tunnel from 5 cm above the tumor; 2) dissection of the tunnel; 3) dissection of the tumor from the muscularis propria layer; 4) closure of mucosal entry using hemoclips.14 Inoue et al15 firstly reported nine case series of esophageal or cardiac SETs originated from muscularis propria layer by ESTD technique, and all but two huge SETs larger than 6.0 cm achieved complete resection without major complications such as perforation. Another pivotal study reported that 18 case series of gastric fundal SETs originated from muscularis propria were resected using ESTD method, by creating mucosal entry at distal esophagus and tunneling across cardia. Mean size was 21 mm (range 8-50), all tumors were completely resected and one case of pneumoperitoneum was conservatively managed without rescue surgery.16 We experienced six cases of antral or cardiac SETs originated from muscularis propria, and all of them achieved en bloc resection by ESTD method.17 More clinical experiences are necessary and clinical outcomes need to be evaluated in the near future.

For successful resection of larger SETs originated from muscularis propria layer, EFTR method is also being introduced nowadays. Zhou et al18 firstly reported 26 cases of gastric SETs originated from muscularis propria using EFTR without laparoscopic assistance. This method consists of following procedures: 1) circumferential mucosal incision around tumor; 2) dissection at muscularis propria layer to exposed tumor; 3) additional dissection serosa layer to intentionally create perforation; 4) removal of tumor including surrounding muscularis propria and serosa layer using snare; and 5) closure of wall defect by hemoclips. In this study, mean size of the tumor was 28 mm (range 12-45) and no major complication occurred during procedure. However, this procedure needs highly advanced endoscopic technique, and still raises the skepticism about the resection of larger SETs and closure of wall defect, the latter can lead serious complication such as peritonitis after procedure. To overcome above shortcomings, laparoscopy-assisted EFTR (LAEFR), or hybrid natural orifice transluminal surgery (NOTES) is also being introduced. This method also consists of circumferential mucosal incision and dissection at muscularis propria layer to exposed tumor, however is different from EFTR by the following characteristics; 1) endoscopic full thickness resection including muscularis propria and serosa layer around the 2/3 ~ 3/4 circumference; 2) laparoscopic resection of remaining 1/3 ~ 1/4 circumference; and 3) laparoscopic closure of gastric wall defect. This method has several advantages over laparoscopic surgery alone in that resection margin can be easily assessed and several SETs located in pylorus, cardia or esophagogastric junction also can be removed by endoscopic guidance. Furthermore, this method seems to be superior to ESTD or EFTR without lap-
endoscopic assistance considering larger SETs which are usually unresectable by both methods. Several Japanese studies demonstrated that gastric SETs located in proximal stomach or intra-luminal protruding SETs were successfully resected without major complications, and their mean size were ranging 38 ~ 46 mm, which were larger than those by ESTD or EFTR without laparoscopic assistance.19,20

In conclusion, benign gastric SETs cannot be distinguished entirely from those with malignant potential by EUS or conventional esophagogastroduodenoscopy. Thus, even small SETs \(\leq 2.0\) cm, especially if they are originated from muscularis propria and have suggestive findings of GIST, need to be resected and pathologically confirmed in selected cases. Several standard methods such as EMR or ESD have been performed for complete resection of gastric SETs, and novel procedures such as ESTD or EFTR are now being developed. Furthermore, LAEFR might be an alternative option for overcoming limitations of endoscopic procedures only.

References