

# Endoscopic submucosal dissection for gastric adenomyoma

## A rare entity of 15 cases among 571 patients with gastric submucosal eminence lesions

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### Abstract

Gastric adenomyoma (GA) is a kind of rare gastric submucosal eminence lesions. As the malignant transformation cannot be ruled out, surgery and laparoscopic resection are usually considered. The aim of this study is to evaluate the therapeutic effect and safety of endoscopic submucosal dissection (ESD) for GA.

All of the patients with gastric submucosal eminence lesions who underwent ESD from June 2008 to June 2015 in General Hospital, Tianjin Medical University, China, were identified, and patients with GA, which was confirmed by pathological evaluation, were enrolled for further analysis.

Among the 571 patients who received ESD, 15 cases with uncertain diagnosis before the procedure were finally confirmed as GA. The mean age of these 15 patients was  $46.93 \pm 15.56$  years (range: 18–73). Most of the lesions were located in antrum (12/15 patients), with 2 in the body of stomach and 1 in cardia, respectively. The mean size of the lesions was  $1.47 \pm 0.67$  cm (range: 0.4–3.0). According to the endoscopic ultrasonography, the lesions of 14 patients originated from submucosa and 1 originated from superficial muscularis, totally with mixed echoes changes. En bloc complete resection was achieved in all of the lesions. No perforation, intraoperative bleeding, delayed bleeding, and mortalities occurred. No recurrence or metastasis was found during 1 to 67 months.

ESD appears to be a feasible, safe, and effective treatment for GA with clinical presentation of gastric submucosal eminence lesions.

**Abbreviations:** APC = argon plasma coagulation, CT = computed tomography, ESD = endoscopic submucosal dissection, EUS = endoscopic ultrasonography, EUS-FNA = endoscopic ultrasonography-guided fine-needle aspiration, GA = gastric adenomyoma, PH = pancreatic heterotopia, PPIs = proton-pump inhibitors, SMT = submucosal tumor.

**Keywords:** endoscopic submucosal dissection, gastric adenomyoma, gastric submucosal eminence lesion

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### 1. Introduction

Gastric adenomyoma (GA) is a kind of rare gastric submucosal eminence lesions, which was usually located in antral, pyloric, duodenal, or jejunal location.<sup>[1,2]</sup> GA characteristically consists of glandular/ductular components and smooth muscle bundles.<sup>[3–5]</sup> So far, the youngest patient was a 1-week-old neonate,<sup>[6]</sup> whereas the oldest was even 81 years' old.<sup>[7]</sup> It was first described by Magnus Alsleben in 1903 according to autopsy studies.<sup>[8]</sup> And in 1955, GA was reported again as an individual entity hypothesizing which included aberrant pancreas, Brunner glands, and nondefined myoepithelial growth by Cimmino.<sup>[9]</sup> Since the malignant transformation cannot be ruled out,<sup>[10]</sup> surgery, and laparoscopic resection remains the first-line therapeutic strategies for GA.<sup>[6,11–13]</sup>

Recently, rapid advance in endoscopic technology offers a protocol to implement endoscopic resection without laparoscopic assistant to treat gastric submucosal eminence lesions. Endoscopic submucosal dissection (ESD) has served a critical role in en bloc resection of eminence lesions, which is derived from submucosal and even muscularis propria.<sup>[14–16]</sup> However, to our best knowledge, no comprehensive data are available for the application of ESD for GA. Consequently, we conducted a retrospective study on the patients with gastric submucosal eminence lesions who received ESD between June 2008 and June 2015 to evaluate the feasibility, efficacy, and safety of ESD for GA.

## 2. Methods

### 2.1. Patients

A total of 571 patients with gastric submucosal eminence lesions were administered for further diagnosis and treatment in General Hospital, Tianjin Medical University, China from June 2008 to June 2015 (Table 1). After careful evaluation, ESD was then performed. Among these patients, a total of 15 patients with pathologically diagnosed GA were enrolled in this study. Endoscopic ultrasonography (EUS) and abdominal computed tomography (CT) scan were performed before ESD, to identify the origin of the lesion and clarification of the anatomical structure in the vicinity of the lesions. Demographics, clinical symptoms, pathological characteristics, prognosis, complications, and follow-ups were also reviewed. This study was approved by the institutional review board and ethical committee of General Hospital, Tianjin Medical University. And all of the patients had provided written informed consent for their participation.

### 2.2. ESD technique

ESD was performed by 3 experienced endoscopists of General Hospital, Tianjin Medical University in all patients under anesthesia with propofol. Patients were fasting before the procedure, and underwent the operation in the left lateral decubitus position. ESD procedure was performed by using a single-channel endoscope (GIFQ260J, Olympus). Briefly, several marks were made on the normal mucosa with argon plasma coagulation (APC300, ERBE) surrounding the lesion to indicate safety margins, and a mixture solution of glycerin fructose and methylene blue plus 1:10,000 epinephrine was injected into the submucosal layer to elevate the mucosa. Subsequently, normal mucosa surrounding the marks was incised circumferentially with a hook knife. Using a hook knife or a hybrid knife (JET2, ERBE), the submucosa beneath the lesion was then dissected gradually until the lesion was exposed. To make sure the entire lesions were removed macroscopically, the connective tissue surrounding the lesion was dissected carefully. The lesion was removed when it was completely exposed. And then, APC or hot biopsy forceps (NE6122-G, Endo-Flex GmbH) was used to coagulate small vessels and clips (HX-610-135L, Olympus) were used for hemostasis of big visible vessels if necessary. To reduce the risk of perforation, the wound was closed with several clips in several cases. However, if the bleeding or perforation was out of

control under endoscope, emergency surgery is needed. Other equipments included a transparent cap (MH-593, Olympus), injection needles (NET 2522-G4, Endo-Flex GmbH, Voerde, Germany), snares (NOE 342217-G, Endo-Flex GmbH), grasping forceps (FG-8U-1, Olympus), and high-frequency generator (ICC-200, ERBE).

Patients were asked to fast for the first 48 hours after the operation. Nutritional support was routinely administrated, and proton pump inhibitors (PPIs) were used.

### 2.3. Histopathological evaluations

All specimens were deposited for pathological examination, and all the specimens that were diagnosed as GA were confirmed by an experienced pathologist again. Hypertrophic smooth muscle bundles and glands/ducts that were lined by columnar or cuboidal epithelia were used as characteristic structures in GAs diagnosis.

### 2.4. Follow-up

Endoscopic follow-up was scheduled for all patients. It was performed regularly to view the conditions of wound healing and to exclude any residual or recurrence in the 1st, 6th, 12th month after the initial procedure, then once every year. Lesion residual was defined as GA tissue at the site of previous excision and endoscopic biopsy specimens should be taken. Recurrence was defined as a new lesion after at least 1 negative follow-up endoscope. Abdominal ultrasonography was performed simultaneously, and CT scan was performed when it was necessary.

### 2.5. Statistical analysis

SPSS 18.0 (SPSS Inc, Chicago, IL) statistics software was used for statistical analyses. Quantitative results were expressed as the mean  $\pm$  SD.

## 3. Results

### 3.1. Demographics and pre-ESD evaluation of gastric adenomyomas

A total of 15 (2.63%, 15/571) patients were diagnosed as GA with unclear diagnosis before the procedure. Among these, 5 were males (33.33%) and 10 were females (66.67%), the mean age was  $46.93 \pm 15.56$  years (range: 18–73). Most patients (12) had nonspecific symptoms, including epigastric discomfort, abdominal distension, intermittent abdominal pain, and acid reflux.

According to the EUS before ESD procedure, the mean size of GA was  $(1.47 \pm 0.67)$  cm (range 0.4–3.0 cm), and the lesions of 14 patients originated from submucosa and 1 originated from superficial muscularis. Mixed echoes changes were found at the location of the lesions (Fig. 1). Most of the lesions were located in antrum (12/15 patients), with 2 were found in the body of stomach and 1 was in cardia. Besides, CT scan was also performed and showed the gastric wall incrustation around the lesions, and no metastasis was found in all cases. Demographics, clinical data, and endoscopic characteristics of the patients were summarized in Table 2.

### 3.2. Therapeutic outcomes and complications

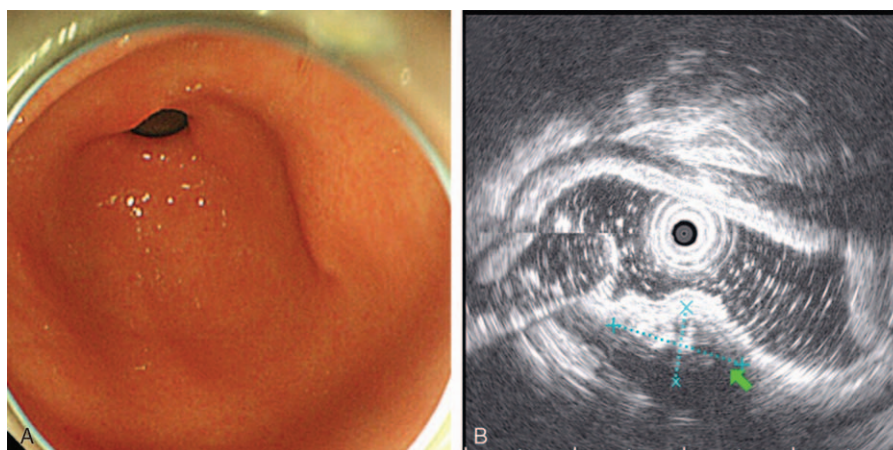
En bloc complete resection was achieved successfully in all of the patients with GA, with duration of procedure of  $88.67 \pm 31.37$

**Table 1**

**All the 571 patients with gastric submucosal eminence lesions received endoscopic submucosal dissection.**

Stomach eminence lesions	Numbers	n, %
Gastrointestinal stromal tumor	195	34.15
Leiomyoma	152	26.62
Chronic inflammation	78	13.66
Heterotopic pancreas	62	10.86
Lipoma	33	5.78
Gastric adenomyoma	15	2.63
Neuroendocrine neoplasm	10	1.75
Schwannoma	6	1.05
Fibroma	6	1.05
Dieulafoy lesion	5	0.88
Other rare gastric submucosal eminence lesions*	9	1.58

\* Other rare gastric submucosal eminence lesions included lymphoma (4), fibromyxoma (2), inflammatory pseudotumor (1), neuroblastoma (1), reduplication of stomach (1).



**Figure 1.** Endoscopic features of gastric adenomyomas. (A) Endoscopic view of a gastric submucosal eminence lesion in the antrum, which was pathologically diagnosed as gastric adenomyoma. (B) Endoscopic ultrasonography showed that the lesion originated from submucosa.

minutes (range: 40–140). The operation time was measured from the time of marking the lesion border to the removal of the lesion. Figure 2 showed the key procedures of ESD for GA.

There was no intraoperative complication, including bleeding, perforation, and episode of GA tissue rupture in all of 15 patients. And no patient underwent other severe complications during the hospitalization, such as fever, delayed bleeding, abdominal pain, nutritional disorder, digestive tract leak, and secondary peritoneal or abdominal infection.

**Table 2**  
**Demographics and clinical data of the 15 patients with gastric adenomyomas.**

Patients	n	%
Sex		
Male	5	33.33
Female	10	66.67
Clinical symptoms		
Epigastric discomfort	6	40.00
Distension	6	40.00
Acid reflux	4	26.67
Abdominal pain	4	26.67
Inappetence	1	6.67
Melena	1	6.67
Location		
Antrum	12	80.00
Body	2	13.33
Cardia	1	6.67
Layer of origin		
Submucosa	14	93.33
Superficial muscularis	1	6.67
Size		
<1 cm	3	20.00
1–2 cm	3	20.00
2–3 cm	9	60.00
Complications		
Perforation	0	0.00
Intraoperative bleeding	0	0.00
Delayed bleeding	0	0.00
Mortalities	0	0.00
Recurrence	0	0.00

### 3.3. Pathological characteristics

Both lateral and deep neoplasm-free margins of the lesions were showed on pathologic examination. The lesions were all characteristically composed of hypertrophic smooth muscle bundles and glands/ducts, lined by columnar or cuboidal epithelia (Fig. 2G).

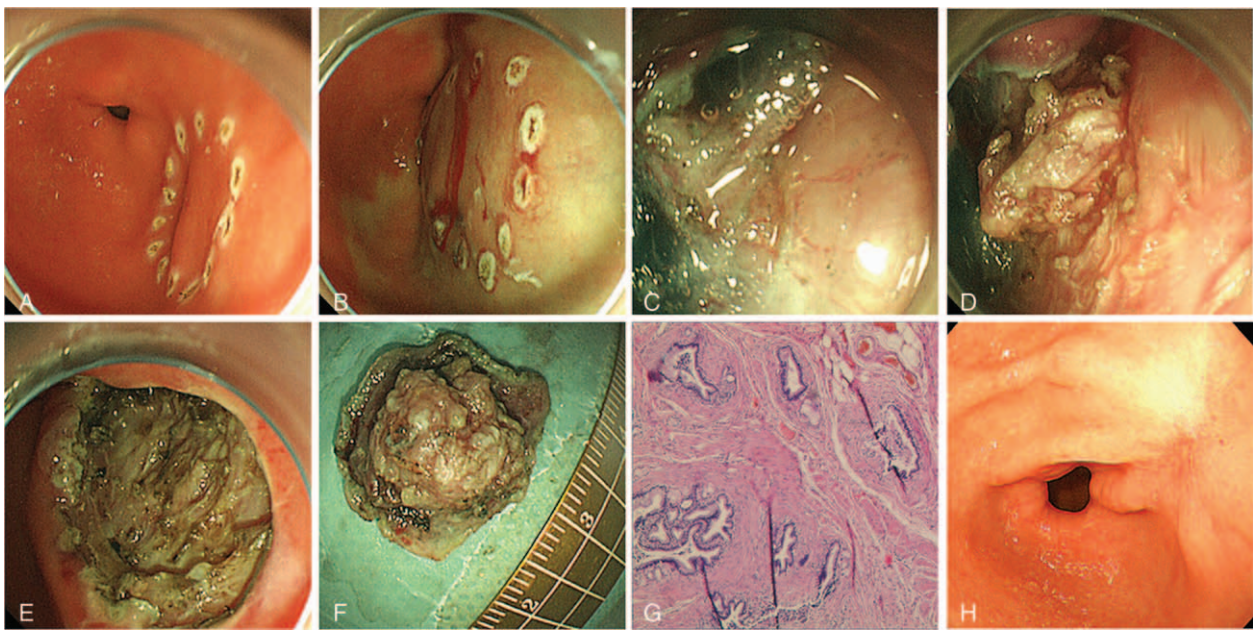
### 3.4. Follow-up outcomes

All the patients were uneventful during the follow-up for 1 to 67 months. The wound of all patients was well healed according to gastroscopy. Abdominal ultrasonography was performed simultaneously. All of the patients recovered well, and no GA tissue residual, local recurrence, or distant metastasis was detected during the study period.

## 4. Discussion

The definition of GA is equivocal. Traditionally, it was considered as a type of pancreatic heterotopia (PH), as the epithelial component resembled those of pancreatic ducts. The PH is classified into 3 types: type I, all the components of the pancreas including ducts, acini, and endocrine islets exist in the lesion; type II, the lesion includes pancreatic ducts and acini; type III, the lesion includes pancreatic ducts and a few acini or dilated ducts only.<sup>[17]</sup> The last subtype of PH was mentioned as GA when the lesions occurred in the stomach.<sup>[18,19]</sup> Moreover, Min et al<sup>[11]</sup> suggested that GA-related smooth muscle disordered proliferation was not considered as a reactive change of misplaced epithelium, but a component of hamartoma without well-differentiated pancreatic tissue. Thus, until recently GA has been regarded as an independent disease.<sup>[11]</sup> However, with different opinions about the histogenesis of these lesions, various other terms have been used, such as myoglandular hamartoma, myoepithelial hamartoma, adenomyomatous hamartoma, and adenomyosis.<sup>[7,10,19–22]</sup>

Malignant transformation potential of GA was controversial. So far, only 1 case report described a case of GA, with gastric adenocarcinoma in its center and implied that malignant transformation of GA was potential.<sup>[10]</sup> As the possibility of malignant transformation of GA still exists, surgery and laparoscopic resection have been considered as the promising



**Figure 2.** Endoscopic submucosal dissection technique and pathological characteristics of gastric adenomyomas. (A) The adenomyoma borders were marked. (B) The mucosa was elevated by a mixture solution of glycerin fructose and methylene blue plus 1:10,000 epinephrine injection. (C) A circular incision was made into the mucosa around the lesion. (D) The adenomyoma was removed from the gastric wall. (E) The wound after adenomyoma resection. (F) The adenomyoma was completely removed. (G) Gastric adenomyoma was characteristically composed of hypertrophic smooth muscle bundles and glands/ducts, lined by columnar or cuboidal epithelia. (H) Endoscopic view of the wound after 2 months' follow-up.

treatment for GA.<sup>[6,11–13]</sup> However, in our cases, we did not find any malignant transformation. There is still no explicit proof in the literature that GA is related to gastric adenocarcinoma. More clinical data are needed to prove this problem.

With the advanced improvement of endoscopic technology and instruments, ESD is extensively employed to treat neoplastic lesions in the gastrointestinal tract and becoming the mainstay with small trauma, few postoperative pain, speedy recovery, low morbidity, short hospitalization, and long-term disease free survival. Although the feasibility and efficacy of ESD for gastric neoplasms have been shown in large series of cases,<sup>[23]</sup> there is no report for evaluation of the application of ESD for GA yet. In this retrospective study, all of the 15 cases among 571 patients with gastric submucosal eminence lesions underwent successful resection via ESD without any complications during the follow-up. Thus, ESD appears to be a feasible, safe, and effective treatment for GA with clinical presentation of gastric submucosal eminence lesions.

Current guidelines suggested that endoscopic ultrasonography-guided fine-needle aspiration (EUS-FNA) is commonly used to diagnose pancreatic solid-cystic lesions. However, EUS-FNA also has the risk of dissemination if there are any tumor cells that come into the needle tract. EUS without FNA remains an important method for nonsurgical diagnosis and classification of submucosal tumors (SMTs) in our clinical work, and owing to the high cost and the potential risks, EUS-FNA for small SMTs is virtually not performed in China. Moreover, FNA procedure for small SMTs is very difficult for the endoscopists to perform. In addition, there seems to be a lack of evidence regarding the optimal strategy in SMTs with a negative EUS-FNA tissue diagnosis, so more prospective trials are urgently needed to answer this question.

Although the results indicated that ESD could be employed to treat GA without recurrence or metastasis in a long time follow-up, our study still had some limitations. First, these case series were from one single center and included a relative small number

of cases because of the rare prevalence. Second, all of the lesions were <3 cm in maximum diameter in our study. Although several studies reported good prognosis of GAs that larger than 3 cm, all of them were treated via surgery but not ESD.<sup>[3,11,13,24,25]</sup> Whether the large lesions have a higher risk of malignant transformation is still unknown, so the therapeutic effect of ESD for larger GAs needs further evaluation in the future studies. In addition, ESD for GA might be a less complicated and less hazardous option, and offer a minimally invasive approach compared to surgery, especially for the patients cannot withstand surgery. Third, ESD for SMTs is controversial, owing to the potential risk of leaving behind residual tissue. In our study, the majority of small SMTs were preoperatively diagnosed as benign tumors, so the patients tended to choose ESD treatment instead of surgery. Although ESD for SMTs is not widely recognized with the potential risk of residual tissue, no recurrence is found during our follow-up period. Fourth, our primary measure of efficacy was endoscopic en bloc (i.e., one-piece) and histological diagnosis by pathologists based on the current references because the exact margins of lesions cannot be measured. However, long-term outcomes and recurrence should be further evaluated.

## 5. Conclusion

Taken together, ESD appears to be an effective, safe, and feasible treatment for GA with clinical presentation of gastric submucosal eminence lesions. However, more multicenter clinical researches with larger sample sizes are necessary to further evaluate the efficacy of ESD for GA.

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## References

- [1] Barbosa IID, Dockerty MB, Waugh JM. Pancreatic heterotopia. *Surg Gynecol Obstet* 1946;82:527.
- [2] Feldmann M, Weinberg T. Aberrant pancreas: cause of duodenal syndrome. *JAMA* 1952;148:893.
- [3] Zhu HN, Yu JP, Luo J, et al. Gastric adenomyoma presenting as melena: a case report and literature review. *World J Gastroenterol* 2010;16:1934–6.
- [4] Erberich H, Handt S, Mittermayer C, et al. Simultaneous appearance of an adenomyoma and pancreatic heterotopia of the stomach. *Virchows Arch* 2000;436:172–4.
- [5] Anami K, Sentani K, Sakamoto N, et al. Infantile adenomyoma subclinically excreted into the patient's diaper. *Pathol Int* 2012;62:532–7.
- [6] Rhim JH, Kim WS, Choi YH, et al. Radiological findings of gastric adenomyoma in a neonate presenting with gastric outlet obstruction. *Pediatr Radiol* 2013;43:628–30.
- [7] Vandelli A, Cariani G, Bonora G, et al. Adenomyoma of the stomach. Report of a case and review of the literature. *Surg Endosc* 1993;7:185–7.
- [8] Magnus-Alsleben E. Adenomyome des Pylorus. *Virchows Arch* 1903;173:137–55.
- [9] Cimmino CV. Gastric adenomyosis versus aberrant pancreas. *Radiology* 1955;65:73–7.
- [10] Kanehira E, Kawaura Y, Ohta Y, et al. Adenomyoma in association with early gastric carcinoma. *Gan No Rinsho* 1990;36:2475–9.
- [11] Min SH, Kim HY, Kim SH, et al. Gastric adenomyoma mimicking gastric duplication cyst in a 5-year-old girl. *J Pediatr Surg* 2012;47:1019–22.
- [12] Kerkez MD, Lekic NS, Culafic DM, et al. Gastric adenomyoma. *Vojnosanit Pregl* 2011;68:519–22.
- [13] Reardon PR, Schwartz MR, Fagan SP, et al. Completely laparoscopic resection of a rare pyloric tumor with laparoscopically sutured gastroduodenostomy. *J Laparoendosc Adv Surg Tech A* 1999;9:147–54.
- [14] Lee IL, Lin PY, Tung SY, et al. Endoscopic submucosal dissection for the treatment of intraluminal gastric subepithelial tumors originating from the muscularis propria layer. *Endoscopy* 2006;38:1024–8.
- [15] Chen X, Cao HL, Wang SN, et al. Endoscopic submucosal dissection for silent gastric Dieulafoy lesions mimicking gastrointestinal stromal tumors: Report of 7 cases—a case report series. *Medicine (Baltimore)* 2016;95:e4829.
- [16] Li QL, Yao LQ, Zhou PH, et al. Submucosal tumors of the esophagogastric junction originating from the muscularis propria layer: a large study of endoscopic submucosal dissection (with video). *Gastrointest Endosc* 2012;75:1153–8.
- [17] Yamagiwa H, Ishihara A, Sekoguchi T, et al. Heterotopic pancreas in surgically resected stomach. *Gastroenterol Jpn* 1977;12:380–6.
- [18] Nakao T, Yanoh K, Itoh A. Aberrant pancreas in Japan. Review of the literature and report of 12 surgical cases. *Med J Osaka Univ* 1980;30:57–63.
- [19] Barnert J, Kamke W, Frosch B. Adenomyoma of the stomach (pancreatic heterotopia)—case report and review of the literature. *Leber Magen Darm* 1985;15:152–6.
- [20] Clarke BE. Myoepithelial hamartoma of the gastrointestinal tract. *Arch Pathol* 1940;30:143–52.
- [21] Lasser A, Koufman WB. Adenomyoma of the stomach. *Am J Dig Dis* 1977;22:965–9.
- [22] Taylor AL. The epithelial heterotopic of the alimentary tract. *J Pathol Bacteriol* 1927;30:415.
- [23] Chung IK, Lee JH, Lee SH, et al. Therapeutic outcomes in 1000 cases of endoscopic submucosal dissection for early gastric neoplasms: Korean ESD Study Group multicenter study. *Gastrointest Endosc* 2009;69:1228–35.
- [24] Chapple CR, Muller S, Newman J. Gastric adenocarcinoma associated with adenomyoma of the stomach. *Postgrad Med J* 1988;64:801–3.
- [25] Kagawa S, Fujiwara T, Nishizaki M, et al. Adenomyoma of the stomach presenting as localized peritonitis. *Dig Dis Sci* 2007;52:3184–7.