

Case Report

Endoscopic Submucosal Dissection of a Heterotopic Gastric Mucosa in the Stomach: Report of a Case

Yuusaku SUGIHARA, Shin-ei KUDO, Tomokazu HISAYUKI,
Toshihisa HOSOYA, Hideyuki MIYACHI, Haruhiro INOUE
and Shigeharu HAMATANI

Abstract: A 38-year-old man with a submucosal tumor (SMT) at the anterior wall of the pylorus underwent upper gastrointestinal endoscopy. The tumor was 40 mm in diameter with a long stalk extending into the duodenal bulb. In addition, the long stalk had an ulcer with a blood vessel. Removal of this tumor was initially considered to be possible only by distal gastrectomy. However, endoscopic ultrasound (EUS) was subsequently proven to be a reliable investigative procedure for evaluating the lesion. The tumor was characterized by its origin in the second layer, and endoscopic submucosal dissection (ESD) was performed. En bloc resection of a 32×20×40 mm area of tissue with tumor-free lateral/vertical margins was accomplished without complication. Histopathological examination confirmed a heterotopic gastric mucosa. By immunostaining, the neoplasm was positive for MUC6 and negative for amylase and trypsin. In this case, EUS was used to investigate a heterotopic gastric mucosa that originated in the second layer, with no infiltration of the fourth layer under the tumor. Therefore, we performed successful ESD at the appropriate layer.

Key words: heterotopic gastric mucosa, endoscopic submucosal dissection, endoscopic ultrasound

Introduction

Gastric submucosal tumor SMT is a common finding during upper gastrointestinal endoscopy, occurring in approximately 0.36% of routine upper gastrointestinal endoscopies¹⁾. Heterotopic gastric mucosa in the stomach is infrequent in Western countries, but is common in Japan, with an incidence ranging from 11% to 20% of gastrectomy specimens²⁾. Although the etiology of this disease is unknown, it is considered to be a benign disease by nature. However, a few reports have indicated that, although rare, heterotopic gastric tumors in the stomach have the potential for malignancy, with rapid tumor growth or an accompanying ulcer suggestive of carcinogenesis³⁾.

The efficiency of laparoscopic surgery for resecting gastric SMT was previously estab-

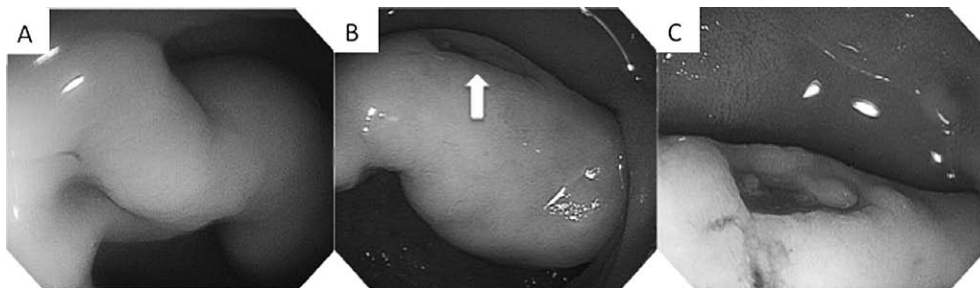


Fig. 1. Endoscopic images of the submucosal tumor (SMT) on admission

An SMT was apparent at the anterior wall of the pylorus. A long stalk could be seen extending from the tumor into the duodenal bulb.

A : Image observed at the stomach showing the long stalk.

B : Image observed at the duodenal bulb showing an ulcer of 5 mm in diameter on the stalk (arrow).

C : Endoscopic imaging showed a blood vessel in the ulcer. Hemorrhaging of the ulcer was a factor considered and hypertonic saline and epinephrine solution (HSE) was injected to stop bleeding.

lished⁴⁻⁶). However, laparoscopic wedge resection is not indicated for tumors located at the esophagogastric junction or near the pyloric ring, and these cases have been traditionally resected using an open approach to ensure negative margins⁷).

In recent years, endoscopic techniques including endoscopic submucosal dissection (ESD) have been developed in Japan for tumor resection. ESD involves circumferential cutting of the mucosa that surrounds the tumor, followed by dissection of the submucosa under the lesion. ESD also enables clinicians to dissect the area under the tumor more completely than is possible with endoscopic mucosal resection (EMR). Indeed, almost any tumor, regardless of size, shape or layer of origin, can be resected en bloc if the appropriate layer to dissect by ESD is determined.

Case Report

A 38-year-old man underwent upper gastrointestinal endoscopy in our institute for severe anemia (hemoglobin: 3.0 g/dL). He had a pulse rate of 137 beats per minute, temperature of 39.1°C, and non-contributory past and family history. On upper endoscopy, he was found to have a submucosal tumor at the anterior wall of the pylorus that was 40 mm in diameter with a long stalk extending into the duodenal bulb. In addition, the long stalk had an ulcer and there was a blood vessel in this ulcer, indicating the possibility of hemorrhaging and prompting immediate injection of the ulcer with mixed hypertonic saline and epinephrine (HSE) to stop and prevent bleeding (Fig. 1). During hospitalization, endoscopic ultrasound (EUS) imaging was performed by the balloon-inflation method.

The submucosal tumor was discovered originating from the second layer of the gastric wall. The fourth layer remained uninfiltated under the tumor. It was therefore decided to remove the tumor by ESD with dissection along the fourth layer (Fig. 2).

ESD was performed under general anesthesia in the operating room. The lesion was first

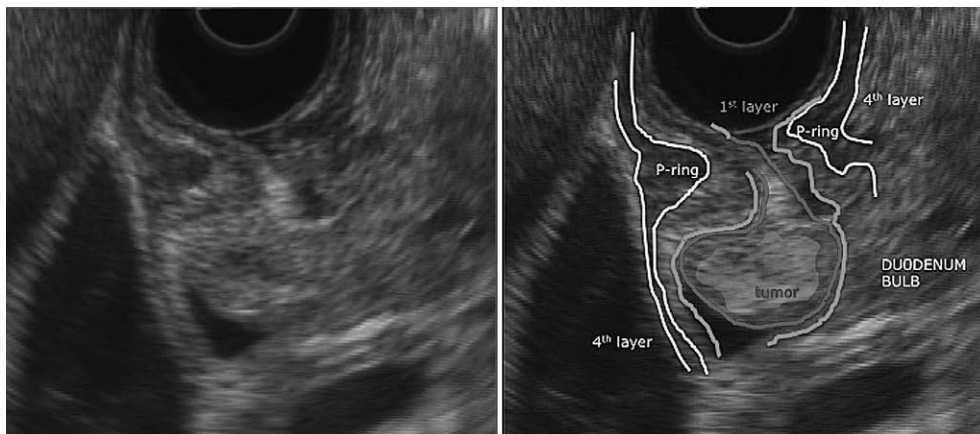


Fig. 2. Endoscopic ultrasound imaging of the submucosal tumor (SMT). The SMT originated in the second layer, with the fourth layer below the tumor remaining intact. This tumor was therefore considered for removal by ESD with dissection along the fourth layer.



Fig. 3. Resected macroscopic specimen. The size of the resected specimen was $32 \times 20 \times 40$ mm. A mucinous gland was found in the submucosal layer under a normal gastric membrane.

lifted by submucosal injection of glycerin into the duodenum bulb. Then, a circumferential incision of the surrounding non-neoplastic mucosa was made using a Flush Knife (Fuji Film, Tokyo, Japan) with a high frequency generator. En bloc resection with tumor-free lateral / vertical margins was accomplished without complication. The resected tumor was $32 \times 20 \times 40$ mm in size. A mucinous gland was found in the submucosal layer under a normal gastric membrane (Fig. 3). Histopathological examination confirmed the diagnosis of heterotopic gastric mucosa. On immunostaining, the neoplasm was positive for MUC6 and negative for amylase and trypsin (Figs. 4, 5).

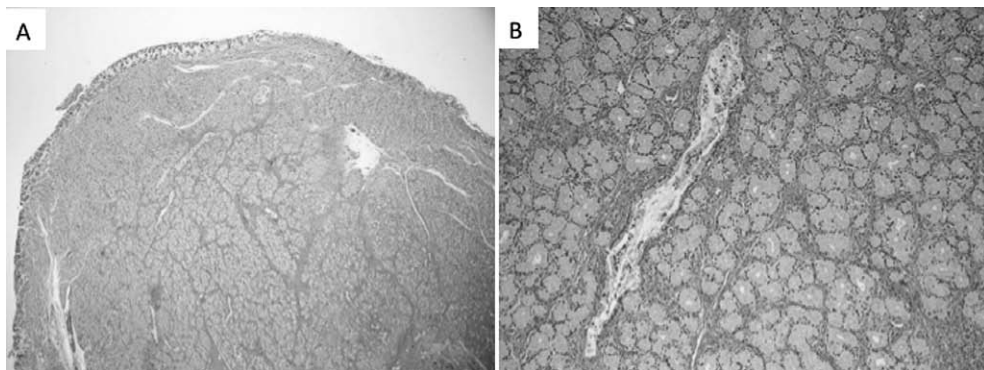


Fig. 4. Microscopic findings by H&E staining

A : The SMT was found in the normal gastric wall (magnification : 12.5×).

B : A normal mucinous gland was also observed (magnification : 100×).

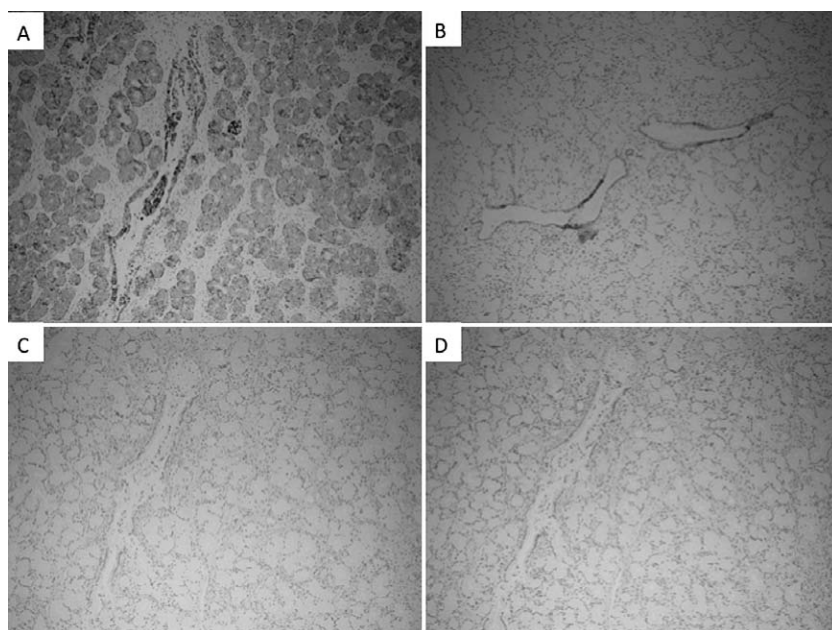


Fig. 5. Microscopic finding by immunostaining

A : The SMT was immunopositive for MUC6.

B : Sporadic positive immunostaining for MUC5.

C and D : The SMT was immunonegative for AMY (C) and TRY (D).

In summary, distal gastrectomy was initially considered in this case because of the patient's severe anemia and because the large size of the SMT made it impossible to remove by polypectomy or endoscopic mucosal resection (EMR). Resection was possible with a minimally invasive procedure, ESD, after determining the appropriate level of the SMT by EUS.

Discussion

In this case, EUS was used to investigate a heterotopic gastric mucosa that originated in the second layer, with no infiltration of the fourth layer under the tumor developing. Therefore, we performed successful ESD at the appropriate layer.

Establishing a definitive diagnosis of gastric SMT based on histological confirmation is relatively difficult, and in most cases an endoscopic biopsy is not possible because of membrane covering the tumor. Even without an accurate pre-treatment diagnosis, open or laparoscopic surgery is thus generally performed to remove SMT. Currently, ESD is used routinely as a diagnostic treatment for SMT of the stomach⁸⁾. In this context, successful ESD relies on predetermining the appropriate layer for dissection. In the present case, EUS was carried out to evaluate the depth and origin of an SMT. As in previous cases, the procedure was successful in determining the appropriate layer in which to dissect the irregularly shaped SMT.

EUS has emerged as a reliable investigative procedure for the evaluation of lesions, especially for gastric SMT, which can be characterized by the layer of origin. The alternative balloon-inflation method is usually used for rapid scanning of submucosal lesions, whereas EUS can scan the five distinct layers that comprise the gastric wall. The two inner layers represent the interface and the muscularis mucosa, while the third, echo-rich layer, corresponds to the submucosal layer. The fourth, echo-poor layer is the muscularis propria, and the fifth, echo-rich layer is the serosa, which is usually not easily distinguishable from the surrounding echo-rich tissue. Scanning the gastric wall is more easily performed in the antrum than in the prepyloric region or the gastric angle, and in such cases, rotating the patient may help to obtain a clearer scan. In general, SMTs are classified into simple cystic, multicystic, and solid cystic tumor types with EUS. The simple cystic tumor type is frequently identified in cysts, and rarely in Brunner's gland hamartomas or in heterotopic gastric mucosa. The multicystic tumor type is commonly identified in lymphangiomas, followed by gastric cystic malformations, hemangiomas, and Brunner's gland hamartomas. The solid cystic tumor type includes duplication cysts, heterotopic gastric mucosa, heterotopic pancreas, myogenic tumors with advanced cystic degeneration, and gastric tuberculomas⁹⁾.

Polypectomy and EMR are treatment modalities that generally use a snare for long stalked tumors to provide easier and more rapid tumor removal than ESD. However, these methods are limited by the size of the tumor that can be resected, and piecemeal resection is unavoidable when the tumor is not diagnosed by biopsy. These methods are also associated with a risk of remnant disease or local recurrence. Indeed, in the present case, biopsy was performed at the initial upper gastrointestinal endoscopy, but the result was only necrotic tissue. EUS-guided fine needle aspiration (EUS-FNA) was also not a suitable method because this SMT was a bleeding tumor and thus there was an increased chance of hemorrhage using EUS-FNA. In the present case, the SMT originated in the second layer,

and not the fourth layer, and it was necessary to dissect the second layer to remove this tumor en bloc for an accurate diagnosis. Polypectomy or EMR would not have been able to completely remove the SMT, thus limiting the diagnostic possibilities.

We used several methods to minimize complications and to obtain clearer views. First, a transparent hood was attached to the tip of the endoscope. Second, to avoid perforation, a glycerin and indigo carmine mixture was injected to achieve higher and more sustained submucosal elevation. Finally, the operator was skilled in ESD and had considerable experience using ESD. Thus, ESD could be safely performed in this patient to remove and diagnose a uniquely shaped gastric SMT.

The etiology of ulcers on heterotopic mucosa is not well established, although it seems reasonable to speculate that the acid and pepsin secretion of such specialized epithelium might be ultimately responsible. The usual initial symptom of these ulcers is bleeding or anemia, and sometimes dysphagia related to scarring and stricture formation¹⁰. An earlier case report showed that an H2 blocker affected bleeding from a heterotopic gastric mucosa in the rectum¹¹. Moreover, proton pump inhibitors have proven helpful in stopping bleeding and reducing inflammation, allowing easier dissection¹².

In conclusion, we investigated a case of heterotopic gastric mucosa originating in the second layer by EUS, and determined that the fourth layer remained uninfiltated under the tumor. Therefore, we performed successful ESD at the appropriate layer.

References

- 1) Papanikolaou IS, Triantafyllou K, Kourikou A and Rosch T: Endoscopic ultrasonography for gastric submucosal lesions. *World J Gastrointest Endosc* **3** : 86–94 (2011)
- 2) Rubio CA and Mandai K: Gastric adenocarcinoma in displaced mucosal glands. *Anticancer Res* **19** : 2381–2385 (1999)
- 3) Sugawara T, Sakuma A, Ouchi A, Kawakami K, Shiiba K, Ebina N and Sato T: Early stomach cancer derived from heterotopic glands — a case report. *Jpn J Cancer Clin* **29** : 1351–1355 (1983)
- 4) Gamal EM, Altorjay A, Szanto I, Garcia J and Kiss J: Laparoscopic wedge resection of the gastric wall for gastric benign tumour. The collaboration of the laparoscopic surgeon and the endoscopist. *Acta Chir Hung* **38** : 167–168 (1999)
- 5) Ke CW, Cai JL, Chen DL and Zheng CZ: Extraluminal laparoscopic wedge resection of gastric submucosal tumors: a retrospective review of 84 cases. *Surg Endosc* **24** : 1962–1968 (2010)
- 6) Lee HH, Hur H, Jung H, Park CH, Jeon HM and Song KY: Laparoscopic wedge resection for gastric submucosal tumors: a size-location matched case-control study. *J Am Coll Surg* **212** : 195–199 (2011)
- 7) Tsujimoto H, Yaguchi Y, Kumano I, Takahata R, Ono S and Hase K: Successful gastric submucosal tumor resection using laparoscopic and endoscopic cooperative surgery. *World J Surg* **36** : 327–330 (2012)
- 8) Hoteya S, Iizuka T, Kikuchi D and Yahagi N: Endoscopic submucosal dissection for gastric submucosal tumor, endoscopic sub-tumoral dissection. *Dig Endosc* **21** : 266–269 (2009)
- 9) Hizawa K, Matsumoto T, Kouzuki T, Suekane H, Esaki M and Fujishima M: Cystic submucosal tumors in the gastrointestinal tract: endosonographic findings and endoscopic removal. *Endoscopy* **32** : 712–714 (2000)
- 10) Sanchez-Pernaute A, Hernando F, Diez-Valladares L, Gonzalez O, Perez Aguirre E, Furio V, Remezal M, Torres A and Balibrea JL: Heterotopic gastric mucosa in the upper esophagus (“inlet patch”): a rare cause of esophageal perforation. *Am J Gastroenterol* **94** : 3047–3050 (1999)

- 11) Murray FE, Lombard M, Dervan P, Fitzgerald RJ and Crowe J: Bleeding from multifocal heterotopic gastric mucosa in the colon controlled by an H2 antagonist. *Gut* **29** : 848-851 (1988)
- 12) Cheli M, Alberti D, Vavassori D, Sonzogni A, Pedretti E and Locatelli G: Heterotopic rectal gastric mucosa : a rare cause of lower gastrointestinal bleeding in children. Case report and review of pediatric literature. *Eur J Pediatr Surg* **17** : 50-54 (2007)

[Received October 24, 2012 : Accepted December 13, 2012]