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Case Report

Laparoscopic resection of a gastrointestinal stromal tumor larger than 5 cm: Report of a Case

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A 46-year-old woman was admitted to our hospital and was diagnosed with a gastric submucosal tumor at the medical examination. Upper endoscopic examination revealed a submucosal tumor in the lower body of the stomach. Abdominal computed tomography (CT) revealed a large tumor of dimensions 51 × 32 mm in the lower body of the stomach with a mixed appearance: a solid part exhibiting a contrast effect and a cystic part exhibiting no contrast. Endoscopic ultrasonic fine needle aspiration biopsy (EUS-FNAB) was performed, and a gastrointestinal stromal tumor (GIST) was diagnosed by immunohistopathological examination. Laparoscopic surgery with five ports was performed for resection. After securing the safety margin the tumor was resected circumferentially using an ultrasonically activated device (USAD). Resection entailed a significant portion of the gastric wall. During surgery, a support yarn hooked in the minor axis direction, and the defect was closed using an automatic suturing device three times. According to the third edition of the GIST clinical practice guidelines, indications for laparoscopic resection of GISTs over 5 cm have been relaxed. It was considered that careful laparoscopic resection would be possible even though this was a large GIST exceeding 5 cm.

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Key words: GIST, Laparoscopic surgery, giant GIST

INTRODUCTION

Gastrointestinal stromal tumor (GIST) is the most common gastric submucosal tumor. Since it does not metastasize via the lymphatic route, surgical resection does not require lymphadenectomy, which makes laparoscopic resection feasible. However, care must be taken during laparoscopic surgery for large gastric GISTs (greater than 5 cm) as inappropriate procedures, such as careless contact of forceps, may result in peritoneal dissemination 1). We report a successful and safe resection of a large GIST exceeding 5 cm.

CASE REPORT

A 46-year-old female presented to our hospital, where she was diagnosed with GIST and admitted. Esophagogastroduodenoscopy revealed a smooth, mildly elevated submucosal tumor located in the lower body of the lesser curvature of the stomach (Figure 1a). The extraluminal component was dominant. Endoscopic-ultrasonic fine needle aspiration biopsy (EUS-FNAB) was performed. Endoscopic ultrasonography revealed the tumor was 52 × 24 mm in size. The internal echo was hypovascular, with a mixed picture of a homogeneous low echo area and a cystic component (Figure 1b). Fine needle aspiration biopsy (FNAB) was performed using a 22G needle.

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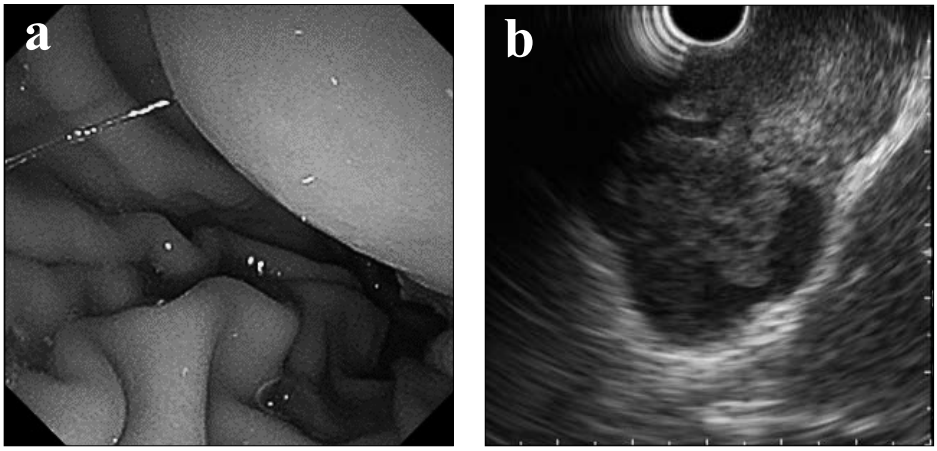

Figure 1: Esophagogastroduodenoscopy revealed a slightly elevated lesion in the lower body and lesser curvature of the stomach (a). Endoscopic ultrasonography (EUS) revealed an irregularly-shaped tumor 52 × 24 mm in size, comprising a hypoechoic part with decreased blood flow and an anechoic part as a cystic component (b).

Microscopic analysis of the biopsy specimen revealed complex growth of intertwined spindle cells with background bleeding. Immunohistochemical findings were positive for c-kit and CD34, and negative for S-100 protein and actin. The specimen was diagnosed as a GIST.

Abdominal CT showed a 47 × 30 mm irregularly shaped mass located in the lower body of the lesser curvature of the stomach. The tumor had a mixed appearance, with a solid part exhibiting a contrast effect and a cystic part exhibiting no contrast effect. Although the tumor was in extensive contact with the pancreatic body, it was decided that there was no pancreatic invasion and only compression. Distant metastasis and lymph node enlargement were not observed (Figures 2a, 2b, and 2c.) Although the tumor was over 5 cm in size, laparoscopic surgery was considered feasible.

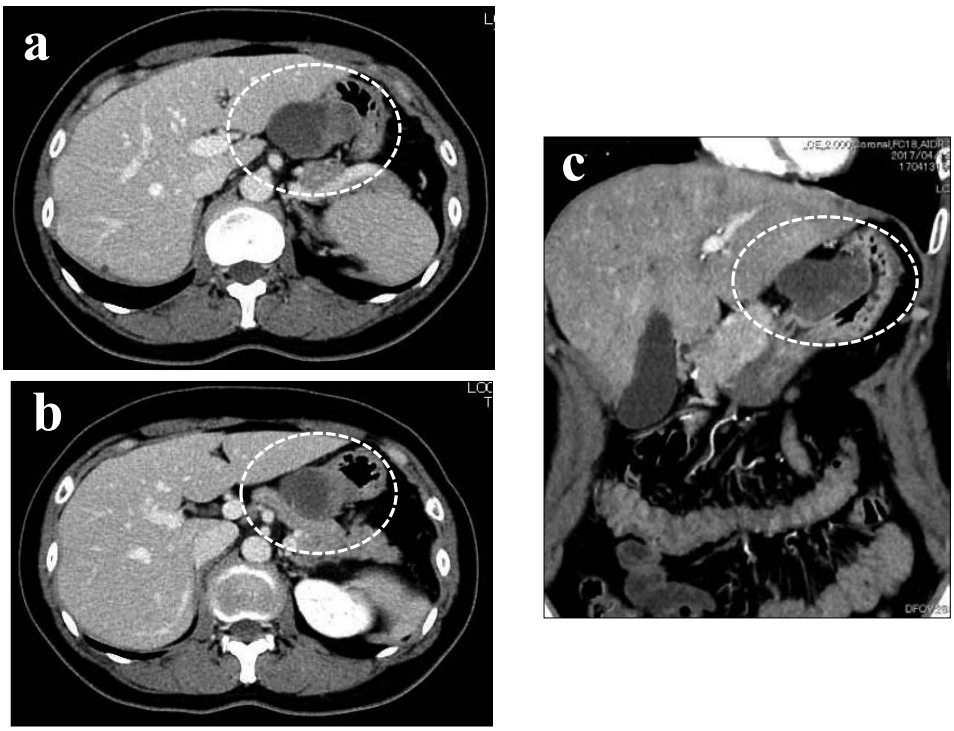

Figure 2: Abdominal CT showed an irregularly-shaped tumor 51 × 32 mm in size consisting of a well-enhanced component and a cystic component demonstrating no enhancement in the lower body and lesser curvature of the stomach. Transitional (a, b) and coronary (c) sections are shown.

Operative findings

During laparoscopy, five ports were utilized to approach the tumor described above (Figure 3a). While assessing the distance to the tumor with the intraoperative endoscope, a small hole was created on the caudal side of the tumor using an ultrasonically activated device (USAD). The margin was secured for oncological safety, so as not to the damage the pseudocapsule of the tumor. The mass was then resected circumferentially (Figure 3b). While the resultant defect in the stomach wall was large (Figure 3c), it was possible to close the wall defect using the automatic suturing device three times, by hanging the support yarn in the direction of the minor axis (Figure 3d). There was also mild deformity of the residual stomach (Figure 3e).

Macroscopic Findings

The resected tumor was 51 × 41 mm in size (Figure 4a). A section of the surface in the minor axis direction showed clear margins around the tumor, consisting of a cystic blood-filled component as well as a solid component (Figure 4b).

Histopathological Findings

The tumor was present in the gastric muscle layer and bleeding was found in the lumen. Immunohistochemical findings were the same as the biopsy specimen, being positive for c-kit and CD34 (Figures 4c and 4d) and negative for S-100 protein and actin consistent with the biopsy specimen diagnosis of GIST. Judging from the tumor size and mitotic count (<1/50 HPF), the tumor was classified as a low-risk GIST. Tumor cells were not exposed at the horizontal and vertical stumps.

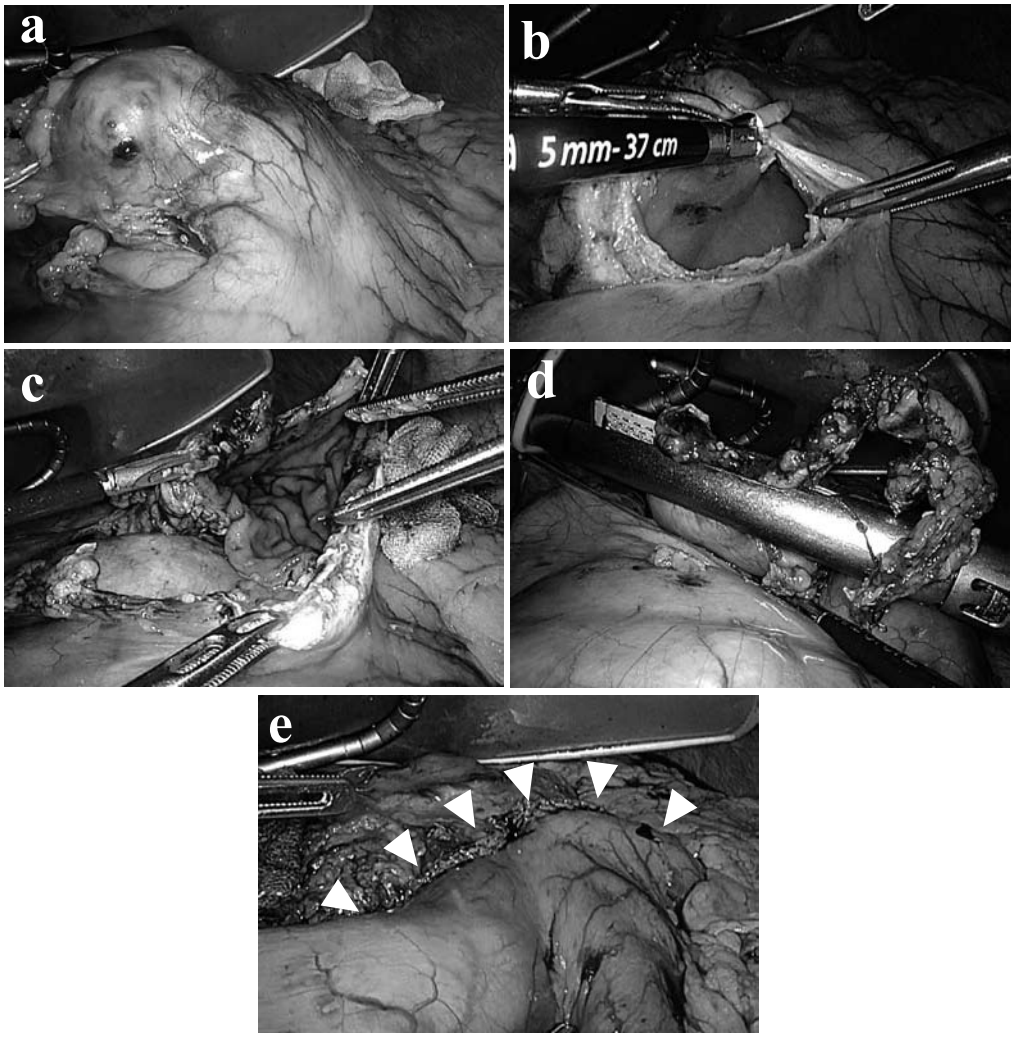

Figure 3: Operative findings: (a) Macroscopic appearance of tumor. (b) The gastric wall was resected ensuring a safety margin using a vessel sealing system. (c) Extensive defect of the gastric wall. (d) Defect was closed by automatic linear stapler. (e) Closure lines of the stomach (white arrowheads point to staple lines).

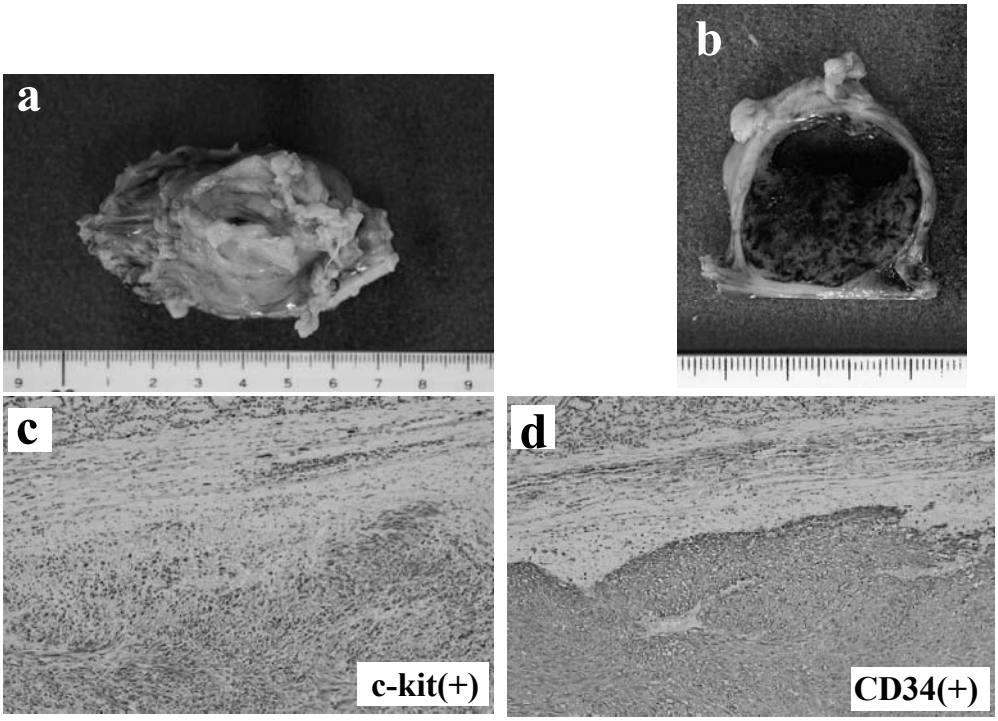

Figure 4: (a) Resected specimen: Resected tumor is 51 × 41 mm in size. (b) Cut surface of tumor in minor axis direction revealing a clear margin, consisting of a blood-filled cystic component as a well as a solid component. (c) Immunohistochemistry c-kit stain positive. (d) Immunohistochemistry CD34 stain positive 10×.

Postoperative Course

The patient's postoperative course was uneventful and there was no delay in gastric emptying following surgery. On the abdominal X-ray taken at discharge, it was confirmed that the staple line spanned more than half of the circumference of the stomach in the minor axis direction (Figure 5).

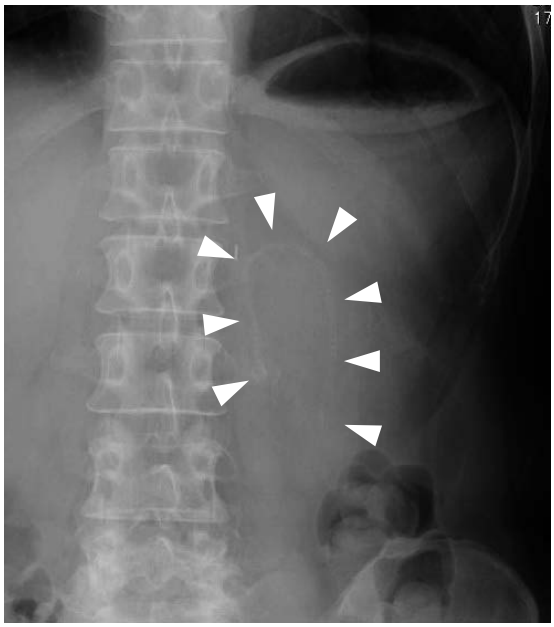

Figure 5: Postoperative abdominal X-ray: staple lines are longer than bisection line in the minor axis direction of the residual stomach (white arrowheads point to staple lines).

DISCUSSION

Gastric submucosal tumors are non-epithelial tumors fairly commonly encountered if small lesions are included, and GIST is considered the most common type of these[2]. GIST derives from the smooth muscle or the muscularis mucosa layers of the gastrointestinal tract, and the developmental forms are classified as intramural, intraluminal, extraluminal, or mixed growth types[3].

GIST is a specific non-epithelial tumor originating from the Cajal-mediated cells that function as pacemaker cells of the peristalsis of digestive tract. The reported occurrence of GIST is highest in the stomach (40-70%), followed by the small intestine (20-30%), and the large intestine (around 10%)[1) 4) 5) 6)].

It is thought that tumorigenesis occurs via continuous activation of the KIT receptor, which triggers downstream cell proliferation/apoptosis inhibiting signal[1) 7)].

CT examination is useful in imaging GIST as it presents as solid lesions that demonstrate various degrees of contrast, and sometimes shows a low absorption range due to necrosis.

EUS commonly reveals continuity with muscle and submucosal layers[3].

For definitive diagnosis, it is necessary to histologically immunostain for KIT and CD34. Tumors testing more than 95% positive for KIT or more than 70-80% positive for CD34 are diagnosed as GIST[8,9].

Treatment guided by the algorithm in the GIST Clinical Practice Guidelines" is recommended[1]. If the diagnosis of GIST is proven on biopsy, surgical resection is recommended, regardless of the size. In many cases, histologic diagnosis cannot be obtained before surgery.

Following resection, adjuvant chemotherapy is considered along with malignancy assessment by risk classification, which combines tumor diameter and mitotic counts of tumor cells. Gene mutations are found in 85% of the c-kit gene (exon 11, 9), about 10% of the PDGFRα gene (exon 12, 18), and are associated with efficacy of imatinib mesylate (Glivec®; tyrosine kinase inhibitor). It is reported that the therapeutic effect of imatinib mesylate is increased by mutation of exon 11 of the c-kit gene and exon 12 of the PDGFRA gene, and decreased by exon 9 of the c-kit gene and mutation of exon 18 (codon 842) of the PDGFRA gene[1,7,8].

Laparoscopic surgery is considered a good option for resection of GIST, as lymph node dissection is not required. However, because laparoscopic surgery uses metallic forceps, peritoneal dissemination may occur due to unexpected contact with the tumor during surgery, so careful and meticulous technique is essential. The second edition of the GIST Clinical Practice Guidelines, recommended laparoscopic surgery for tumors smaller than 5 cm to avoid intraoperative peritoneal dissemination (Grade B). In the third edition of these guidelines, indications for laparoscopic approach have been expanded for laparoscopic gastrectomy if this is feasible for tumors larger than 5 cm[1]. These expanded guidelines are consistent with ongoing improvements in laparoscopic surgical techniques and instruments[10].

The most important aspects of surgical treatment of gastric GIST are considered to be the methods chosen for resection and closure of the stomach wall. A technique combining intraoperative endoscopic and laparoscopic procedures is termed the laparoendoscopic approach (or laparoendoscopic surgery). This approach has been reported in the context of digestive tract and biliary tract disease since the early 2000s as a method of overcoming the respective limitations of the individual procedures[11,12]. Laparoscopy and endoscopy cooperative surgery (LECS), which is a procedure combining an endoscopic submucosal dissection (ESD) technique and laparoscopic surgery, has been reported as a development of this technique[13]. LECS is now widely practiced as it has the advantage of reducing excessive resection of the stomach wall, since ESD is able to set a precise cutting line from the tumor edge.

Resection of intraluminal growth type tumors generally requires the use of an intraoperative endoscope, and these tumors are often excessively stretched mucous membranes. When we performed mucosal incision with monopolar cautery such as an IT knife, the hyper-stretched mucosa was found to be excessively contracted, deviating from the seromuscular layer, which had not yet been separated, and we were concerned about breaching the tumor's pseudocapsule (Figure 6).

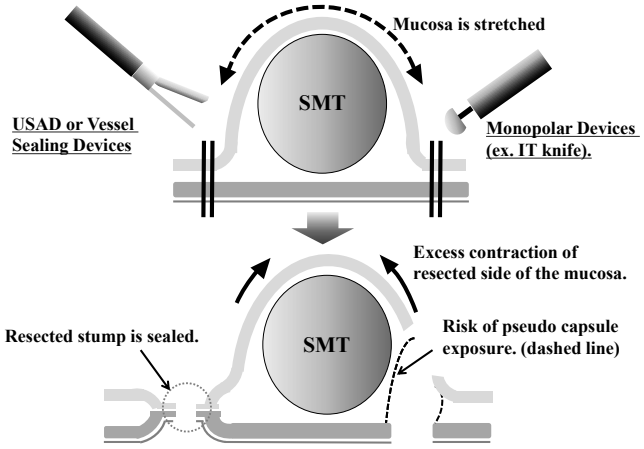

Figure 6: Schematic of the risk of pseudocapsule exposure following gastric mucosal tumor resection. Resection by monopolar instruments (e.g. IT-knife), carries the risk of exposing the pseudocapsule from the resected stump (dashed line) due to excessive contraction of resected side of the gastric mucosa. By contrast, as vessel sealing devices and USAD are able to seal the mucosa and serosa of gastric wall, the risk of pseudocapsule exposure is very low.

ESD is essentially a therapeutic procedure to resect early gastrointestinal epithelial neoplasms by dissecting the submucosal layer. When ESD procedures are used for resection of submucosal tumors, the risk of pseudocapsule exposure must be carefully considered.

In our facility, ESD procedures are used as sparingly as possible for laparoscopic resection of gastric submucosal tumors. When making an incision using monopolar devices, it is necessary to provide a sufficient safety margin so that the pseudocapsule is not exposed even if the mucosa contracts, and/or to close the gastric wall on the tumor's side using continuous full layer suturing.

The safest resection method that does not expose the pseudocapsule is full layer resection from the serosal side using an automatic suturing device. This method has a risk of excessive resection of normal stomach wall in intraluminal

growth type tumors. For resection of intraluminal growth type tumors in our facility, we first confirm the tumor boundary under intraoperative endoscopy and perform the initial incision of the stomach wall at a sufficiently safe site, in accordance with the report of Kakechi et al.[14]. We also take care to resect a sufficient surgical margin under intraoperative endoscopy and make the smallest possible stomach wall incision.

We used the USAD or vessel sealing system as resection devices for the gastric wall. We believe that pseudocapsule exposure can be prevented because these devices are capable of cutting all layers of the stomach wall without slippage.

A wall defect of the stomach is closed using automatic suturing devices (or hand sewn) by hanging up the support yarn, so that a closure line will form in the minor axis direction. The tumor size, developmental pattern, and localization must be borne in mind when choosing the method of excision.

NEWS (non-exposed endoscopic wall-inversion surgery)[15] and CLEAN-NET (Combination of Laparoscopic and Endoscopic Approaches to Neoplasia with Non-exposure Technique)[16] have been reported as novel surgical approaches for gastric submucosal tumor, and these procedures have evolved from the technique of LECS.

These novel techniques were originally devised for epithelial tumors and avoid perforation of the gastric lumen to the abdominal cavity by extension of the submucosal layer. However, when the submucosal layer is extended at the resection of submucosal tumor, there is a possibility that the pseudocapsule may be exposed. Therefore, when operating on submucosal tumor, risk of tumor dissemination must be taken into consideration.

While these novel procedures are considered excellent options, the most important factor is not preservation of stomach wall, but safe resection of the tumor without injury the pseudocapsule.

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