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Using endoscopy to minimize the extent of resection in the management of giant GISTs of the stomach

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ABSTRACT

INTRODUCTION: The stomach is the most common site for GISTs. Wide local resection to achieve negative margins is the standard of care. Giants GISTs requiring extensive resection are usually managed with neo-adjuvant therapy followed by partial or total gastrectomy.
PRESENTATION OF CASE: We present a case report of a giant GIST on the lesser curvature of the stomach. Neo-adjuvant therapy was administered. Intra-operative endoscopy was used to reduce the extent of gastric resection.
DISCUSSION: Simultaneous intra-operative endoscopy demonstrated a 2 mm fistula on the lesser curvature of the stomach. A stapler was used to encompass the mass and the fistulous opening. A frozen-section showed clear margins and the endoscope was used to perform an air-leak test. The patient recovered without complications.
CONCLUSION: Intra-operative endoscopy can reduce the extent of gastric resection for large GISTs while maintaining the oncologic principles of negative margins and minimal tissue handling.

1. Introduction

Gastrointestinal stromal tumors (GISTs) account for 85% of mesenchymal neoplasms affecting the gastrointestinal tract [1]. They are believed to originate from the interstitial cells of Cajal that regulate gastrointestinal motility [2]. Approximately 80% to 95% of GISTs harbor mutations in the KIT gene and 5% have gain of function mutations in the platelet derived growth factor receptor – alpha [3]. GISTs are located primarily in the stomach (60% to 70%) and are usually discovered incidentally [4]. They are more likely to become symptomatic as they increase in size and can present with pain, bleeding, spontaneous rupture, or a palpable mass [5]. The malignant potential of GISTs is not easy to predict and depends on variables such as size, location, and mitotic activity [6].

The gold standard for the management of GISTs is surgical excision with negative margins. Wide resection margins have not been associated with improved oncologic outcomes and routine lymphadenectomies are unnecessary as these tumors rarely spread to regional lymph nodes [7]. Larger tumors are at a higher risk of rupture during surgery and so the oncologic principles of minimal tissue handling and avoidance of tumor spillage should be maintained. The safety and oncologic outcome of laparoscopic GIST resection is well established especially for lesions <5 cm in diameter [8]. The use of intraoperative endoscopy during laparoscopic resections is well-described in the literature and facilitates smaller wedge resections under direct endoscopic visualization [9]. This is particularly important for lesions near the gastro-esophageal junction and the gastric outlet where endoscopy helps avoid luminal narrowing. Gastric GISTs larger than 10 cm are more difficult to manage. These tumors are generally not suitable for a laparoscopic approach and require an open partial or total gastrectomy. They can invade into adjacent organs such as the colon and liver requiring extensive en-bloc resections with higher *peri*-operative morbidity.

The KIT tyrosine kinase inhibitor Imatinib Mesylate (IM) has been the standard first-line pharmacologic therapy for unresectable or metastatic GISTs since its approval in 2001 [10]. Several studies have examined the role of IM in the neoadjuvant setting to help shrink locally advanced tumors and facilitate attainment of R0 surgical margins with good results [11,12]. As such, therapy with neoadjuvant IM is now recommended for consideration in the management of locally advanced tumors [13].

Despite neoadjuvant treatment and tumor shrinkage, the majority of giant GISTs will require extensive gastric resections. The use of intraoperative endoscopy may minimize the extent of gastric resection in such cases but has not been described in the literature.

2. Methods

We present a case of a giant GIST on the lesser curvature on the stomach. The patient was treated with neoadjuvant IM with

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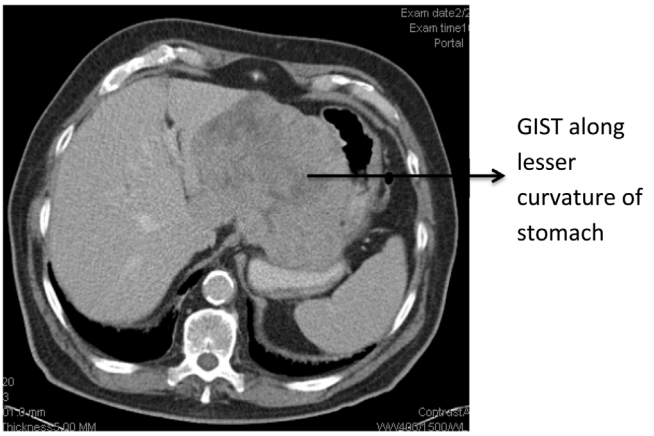

Fig. 1. GIST pre-Imatinib (14.5 cm × 12 cm × 11 cm).

response and underwent surgery. We sought to reduce the extent of gastric resection using intraoperative endoscopy.

3. Case report

The patient is a 78 year old male who presented to clinic with an abdominal mass. He was undergoing an echocardiogram to evaluate mitral valve regurgitation when an abdominal mass was incidentally discovered. A computed tomography scan (CT scan) of the abdomen and pelvis demonstrated a large mass (14.5 × 12 × 11 cm) closely related to the lesser curvature of the stomach and the left hepatic lobe (Fig. 1). He underwent an upper endoscopy with a biopsy demonstrating a gastrointestinal stromal tumor. The patient was referred to medical oncology and was able to tolerate IM for only 3 months. Fig. 2 illustrates tumor response to neoadjuvant IM.

A diagnostic laparoscopy did not show any signs of occult metastasis. A limited upper midline incision was then performed. The left lateral segment of the liver was mobilized off the tumor by dividing the left triangular and coronary ligaments and taking down the falciform ligament to expose the hepatic veins. The omentum was taken off the transverse mesocolon to enter the lesser sac, and gastric adhesions to the pancreatic capsule were divided. The left gastric artery was dissected, ligated, and divided.

Intraoperative endoscopy demonstrated a small fistulous opening to the tumor on the lesser curvature of the stomach (Fig. 3). A 75-mm GIA stapler (Ethicon US, LLC) was used to divide the stomach to include the fistulous tract under endoscopic guidance. The

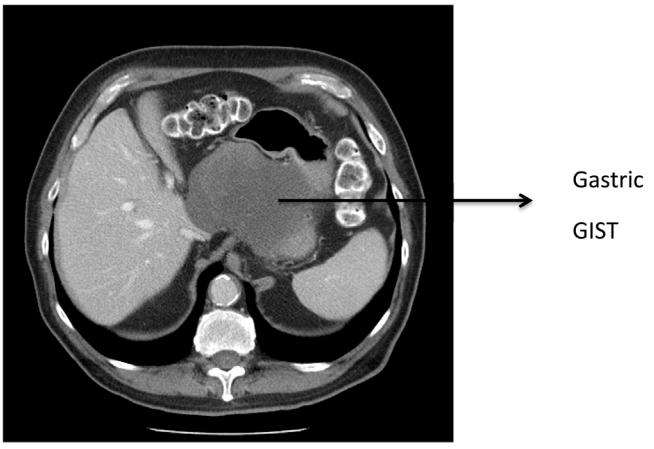

Fig. 2. GIST post-Imatinib (9.5 × 9.2 × 8.7 cm).

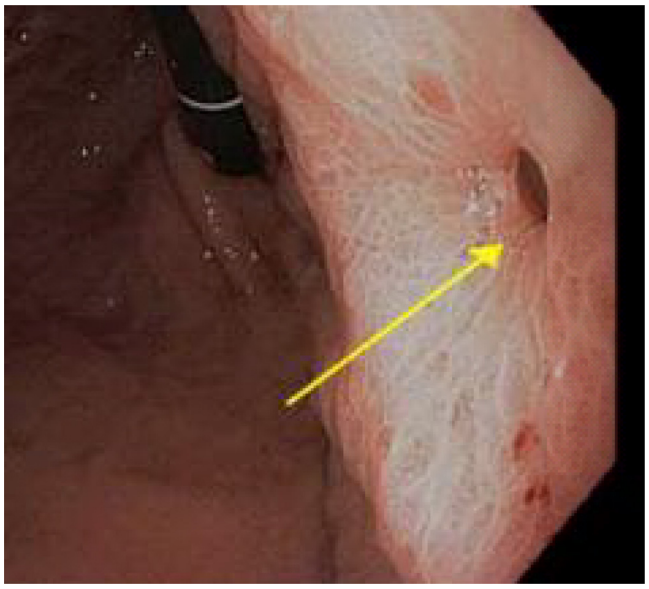

Fig. 3. Fistulous opening to the tumor on the lesser curvature.

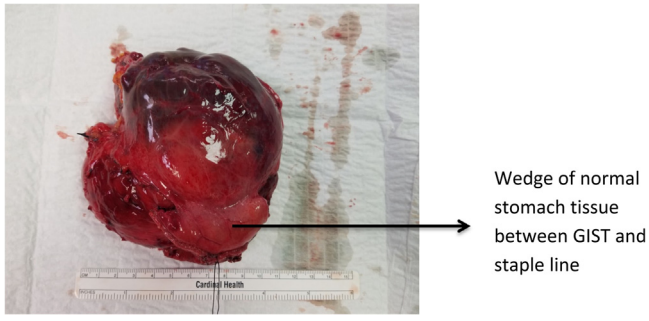

Fig. 4. Removed GIST.

specimen was removed using 2 fires (Fig. 4). A frozen section confirmed negative margins, and an air-leak test was performed prior to closure. There was minimal blood loss and the surgery was completed in 3 h. The patient was discharged on postoperative day 4 without complications.

Pathology demonstrated a gastrointestinal stromal tumor of bland cytology, a low Ki-67 index (5%), and no mitotic figures. The tumor measured 9.5 × 9.2 × 8.7 cm and was composed of spindled cells. Immunohistochemically stains were performed and the tumor tested positive for Vimentin, DOG-1, and CD 117.

The patient was continued on adjuvant IM. A CT scan performed 6 months later showed no recurrence (Fig. 5).

4. Discussion

The management of giant gastric GISTs is challenging and should be approached in a multidisciplinary fashion. Initial treatment with neoadjuvant IM should be considered when the tumor is locally advanced and the required resection is too extensive carrying a higher risk of morbidity or resulting in poor functional outcomes [6]. Tumor shrinkage can also decrease the risk of intraoperative complications such as tumor rupture or hemorrhage. Following a 6–12 months period of neoadjuvant therapy, studies have shown a decrease in tumor volume allowing for complete resection [14,15]. Longer periods of treatment have been associated with Imatinib resistance caused by secondary KIT mutations [15].

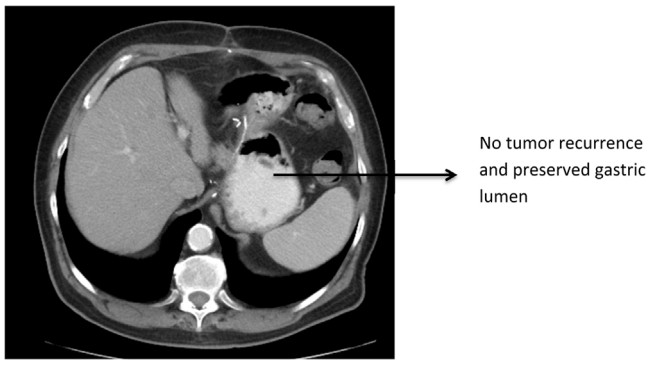

Fig. 5. CT 6 months post resection and neoadjuvant therapy.
Authors contribution

Following initial therapy, axial imaging studies should be obtained to help plan the surgical procedure. The goal of surgery should be the complete resection of the tumor with negative margins while observing the oncologic principle of minimal tumor manipulation to avoid spilling. More extensive resections should be avoided when possible due to the long-term dysfunction associated with organ loss [16].

Intraoperative endoscopy has been introduced in laparoscopic surgery to minimize the extent of resection, avoid luminal narrowing and directly visualize the staple line. We demonstrate how intraoperative endoscopy can also be used during open surgery with similar benefits. Endoscopy allows the surgeon to better localize the tumor or fistula. It allows for the direct visualization of the staple-line to make sure it encompasses the well-circumscribed GIST, while preserving luminal diameter. Endoscopy can also be used to rule out multifocal disease and chest the staple line for any leaks. All this can be established with minimal tumor manipulation and without the need for a partial or total gastrectomy.

The patient in this case report underwent a wedge resection of a 14.5 cm submucosal lesser curvature mass. This could not have been possible without the multidisciplinary approach described. We therefore recommend neoadjuvant tyrosine kinase inhibitor therapy for locally advanced or initially unresectable disease. Following therapy, giant gastric GISTs should be resected with the use of intra-operative endoscopy to limit the extent and duration of surgery, avoid anastomoses and reduce postoperative morbidity. Intraoperative endoscopy is most useful when the lesion is close to the gastroesophageal junction or at the pylorus. Resections performed at these locations can narrow the gastric inlet or outlet and result in significant dysfunction. The GIST described in this case report was on the lesser curvature extending to the gastroesophageal junction. Blind application of the stapler in these anatomically challenging locations is discouraged.

The presence of a gastric fistula facilitated the intraluminal localization of the tumor in this case. Intraluminal localization may not always be possible as gastric GISTs commonly present as an exophytic mass or as a subtle submucousal mass without any overlying mucosal ulceration [17]. Intraluminal localization, however, is not a pre-requisite for a wedge resection as GISTs are well circumscribed and can easily be displaced using a stapling device. In these cases, the endoscope serves to visualize the planned transection line prior to firing the stapler, preserving as much tissue as possible without narrowing the gastric lumen.

Postoperatively, patients with completely resected intermediate or high-risk GISTs should receive adjuvant IM for at least 1 year. The patient presented had a tumor size >10 cm with no mitotic figures which places him in the moderate risk group (10–12%) [18]. Adjuvant IM was therefore recommended.

5. Conclusions

Giant gastric GISTs should be treated in a multidisciplinary setting and consideration should be given to neoadjuvant IM. Intraoperative endoscopy can reduce the extent of gastric resection for large gastric GISTs while maintaining the oncologic principles of negative margins and minimal tissue handling.

Ethical standards

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and later versions. Informed consent or substitute for it was obtained from all patients for being included in the study.

No animals were used in this study.

Conflict of interest

None of the authors have any conflicts of interest to disclose.

Source of funding

No funding.

Ethical approval

Ethical approval has been given by the University of Texas at Tyler Ethics Committee and written consent has been obtained.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Authors contribution

Hishaam Ismael: study concept and design, writing the paper.
Yury Ragoza: Data collection.
Steven Cox: Editing and proofing the article.

Registration of research studies

Not applicable.

Guarantor

Hishaam Ismael.

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