



## Case report

# Complete laparoscopic wedge resection of a giant locally advanced gastric GIST with near pathological complete response after preoperative treatment with imatinib mesylate: A case report

Honghai Guo, Yong Li, Dong Wang, Bibo Tan, Peigang Yang, Qun Zhao<sup>\*</sup>

Department of Gastrointestinal Surgery, Fourth Hospital of Hebei Medical University, Hebei, China

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## ABSTRACT

**Introduction and importance:** Surgical resection is the only curative treatment for gastrointestinal stromal tumor (GIST). Laparoscopic approach for large (>5 cm) and giant (>10 cm) gastric GIST remains under controversy. What's more, whether laparoscopic surgery could be performed after preoperative imatinib treatment of giant gastric GIST is still unknown.

**Case presentation:** We report a 68-year-old man with a giant (almost 30 cm) locally advanced gastric GIST which required resection of contiguous organs initially. After received 12 months imatinib therapy, the tumor became resectable and he finally achieved a complete laparoscopic wedge resection. Pathological evaluation of the resected specimen revealed a near pathological complete response was obtained. The imatinib treatment was ongoing after surgical resection and there was no radiological or clinical evidence of disease recurrence until to October 2021.

**Clinical discussion:** Laparoscopic approach is safe and effective for gastric GIST. Even for lesions greater for 5 cm. However, there are few reports for the application of laparoscopic wedge resection for gastric GIST larger than 10 cm. Preoperative use of imatinib can decrease the tumor size, so that may increase the chance of laparoscopic approach.

**Conclusion:** Preoperative imatinib therapy was effective for reducing the gastric GIST, which may increase the chance of minimally invasive approach and organ preservation. Patients with locally advanced GIST could benefit from the multidisciplinary approach.

## 1. Introduction

Gastrointestinal stromal tumor (GIST) is the most common mesenchymal tumor in the gastrointestinal tract with the mutation in either C-KIT or platelet-derived growth factor receptor alpha (PDGFRA) [1]. And the majority of them originate from the stomach [2]. Although Surgical resection is the only curative treatment for GIST, the introduction of imatinib therapy has revolutionized the management of GIST. And the preoperative use of imatinib for patients with locally advanced or marginally resectable primary GIST is recommended by the current National Comprehensive Cancer Network (NCCN) guideline [3]. Laparoscopic resection of gastric GIST, especially for tumors smaller than 5 cm is recommended as standard treatment by many guidelines [3,4]. However, laparoscopic approach for large (>5 cm) and giant (>10 cm)

gastric GIST remains under controversy due to the high risk of intra-operative tumor rupture and bleeding. What's more, whether laparoscopic surgery could be performed after preoperative imatinib treatment of giant gastric GIST is still unknown.

We report a case of a giant (almost 30 cm) locally advanced gastric GIST received 12 months imatinib therapy, which became resectable and finally achieved a complete laparoscopic wedge resection with a near pathological complete response. This case report was drafted and submitted according to the CARE guidelines [5].

## 2. Case presentation

A 68-year-old man presented with epigastric distention for 2 months was preferred to local hospital. Enhanced computed tomography (CT)

<sup>\*</sup> Corresponding author at: Department of Gastrointestinal Surgery, Forth Hospital of Hebei Medical University, No. 12 Jiankang Road, Shijiazhuang 050011, China.

E-mail address: [zhaqun@hebmh.edu.cn](mailto:zhaqun@hebmh.edu.cn) (Q. Zhao).

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showed 30\*20 cm solid mass with blurred margins in left upper abdomen and no distant metastases (Fig. 1). Gastric endoscopy reported an ulcerative lesion in the cardia and fundus of stomach. Biopsy was suggestive of spindle cell tumor. And the immunohistochemistry in our hospital showed positive of CD34, CD117 and DOG-1. Genetic testing is impossible because of the insufficient specimen tissue. The CT and immunohistochemical findings led to the diagnosis of a giant locally advanced GIST.

The patient was administrated for preoperative imatinib therapy (400 mg/day). During the preoperative therapy CT was carried out every 2–3 months. An important morphologic and clinical response was rapidly obtained. CT after 2 months of treatment showed marked shrinkage of the tumor. The lesion presented central aerial cavitation as with necrotic tissue. Restaging after 6 months initiation of imatinib mesylate revealed a reduction in tumor diameter of approximately 50%. He continued the treatment with imatinib mesylate for 12 months (Fig. 2). The patient had tolerated preoperative therapy well, with minor side effects including the periorbital edema, hydrothorax, and arm rash, with no serious adverse events. The CT showed a significant 60% reduction of the mass. We thought that the tumor achieved maximal response to preoperative imatinib treatment. Hence a surgical operation was performed on the residual disease. Imatinib mesylate was stopped for 1 week preoperatively.

A laparoscopic approach was attempted (Fig. 3). The lesion was located at the gastric fundus, closely adhered to the upper abdomen wall, the diaphragm, the lower spleen and the pancreas. After dissection and mobilization of the stomach and adhesion with careful intraoperative manipulation, it became apparent that the mass could be resected by wedge gastrectomy without need for reconstruction. The laparoscopic wedge resection was performed with the gastric wall encompassing the residual GIST without intraoperative tumor rupture and bleeding. Specimen was placed in a sterile plastic bag that could avoid dissemination when removed through the small umbilical incision. The operative time was 150 min. Estimated blood loss was less than 50 ml. The postoperative course was uneventful. An upper gastrointestinal series obtained on postoperative day 5 showed no leak from the gastric resection line. He was discharged home on the sixth postoperative day and subsequently received adjuvant imatinib therapy (400 mg/day).

Pathological evaluation of the resected specimen revealed a 12 \* 10 \* 4.5 cm tumor mass with diffuse fibrotic regression and a few fusiform cells hyperplasia (Fig. 4). All surgical margins were negative. The immunohistochemistry staining of CD34, CD117 or DOG-1 were all negative. A near pathological complete response was obtained.

Until to October 2021, twenty-eight months following the surgical resection, the imatinib mesylate treatment was ongoing, the patient was asymptomatic and there was no radiological or clinical evidence of

disease recurrence.

### 3. Discussion

In unresectable or metastatic tumors, imatinib therapy is the first-line therapy that resulted in a significant clinical benefit and increased survival [6]. Complete resection and adjuvant imatinib therapy has been the standard treatment for patients with intermediate-risk and high-risk GIST. However, GIST usually shows expansive growth and maybe initially found with quite large size. For radical surgery, it may be necessary to sacrifice organ function or to require resection of contiguous organs. And preoperative use of imatinib may facilitate R0 resection and organ-preserving surgery by decreasing the tumor size [7].

In our case, the patient was diagnosed gastric GIST by pathology. The CT revealed the tumor was very large, the anatomical location and the association between the giant primary tumor and the contiguous organs was not clear, with some doubt regarding the invasion to the diaphragm, the pancreas and splenic hilum. Although we could not obtain the mitotic index of this patient, he was classified as high risk, based on tumor size. Thus, he was administrated with imatinib mesylate. The optimum duration of preoperative treatment is controversial. During the past years, reported durations of imatinib prior to surgery tended to be inconsistent, varying from several weeks to several months [8–11]. A retrospective multicenter study including 161 patients with locally advanced nonmetastatic GIST with a median of 40 weeks preoperative imatinib therapy from 10 European Organization for Research and Treatment of Cancer-Soft Tissue and Bone Sarcoma Group (EORTC-STBSG) sarcoma centers showed a high R0 resection of 83.2% [11]. The prospective RTOG 0132 trial of 8–12 weeks preoperative imatinib therapy for advanced primary GIST showed R0 resection rate of 77% [8]. As these studies included heterogeneous tumor characteristics (size, risk classification, tumor location), it was difficult to evaluate the efficacy of preoperative imatinib for gastric GIST. A multinational prospective phase II study showed patients with large(>10 cm) gastric GIST of 6 to 9 months preoperative imatinib administrated achieved a high R0 resection rate of 91% [12]. A more recent prospective study showed the maximal shrinkage time was 4.3 months for the stomach, 8.6 months for the small bowel and 6.9 months for the rectum with locally advanced GIST [9]. And we think the duration of preoperative imatinib should be case-based depending upon the response to treatment. In the present case, although dramatic tumor shrinkage was obtained after 6 months of treatment, only a little tumor shrinkage was observed after 12 months. This represented almost maximum tumor response. Therefore, we decided to operate at this point.

Open surgery is still a commonly used method of surgery in GIST. In recent years, the indications for laparoscopic surgery have been expanding, more and more studies have demonstrated that laparoscopic

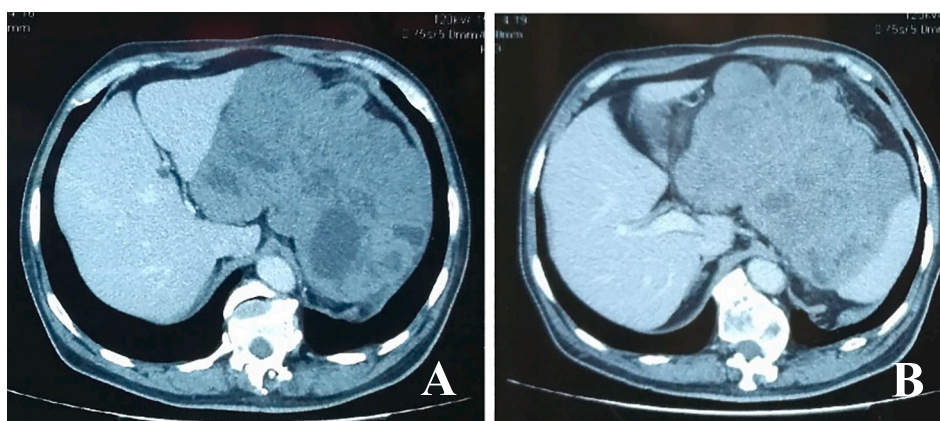
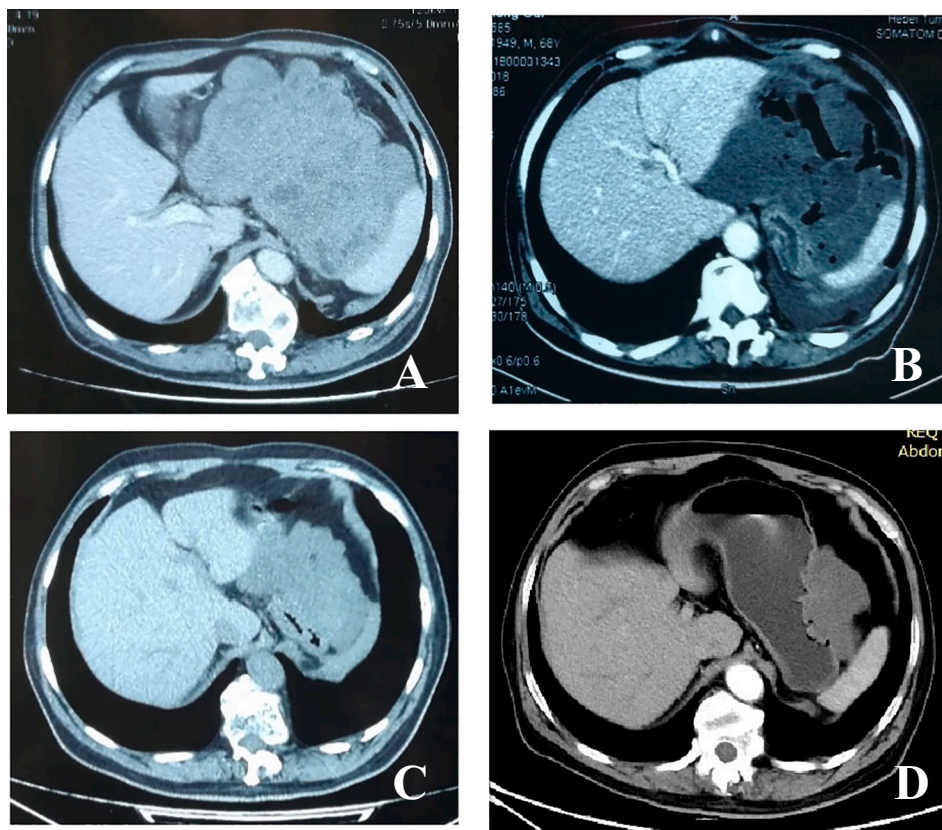
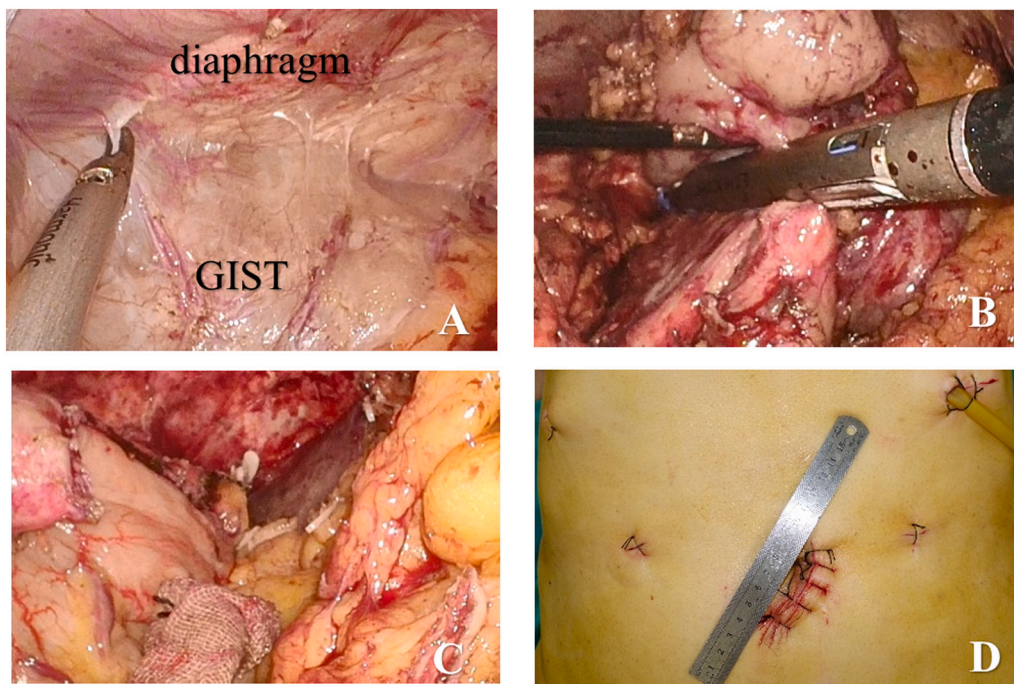


Fig. 1. Enhanced CT scan showed a giant solid mass with blurred margins in left upper abdomen with some doubt regarding the invasion to the diaphragm (A), splenic hilum (B). CT, computed tomography.



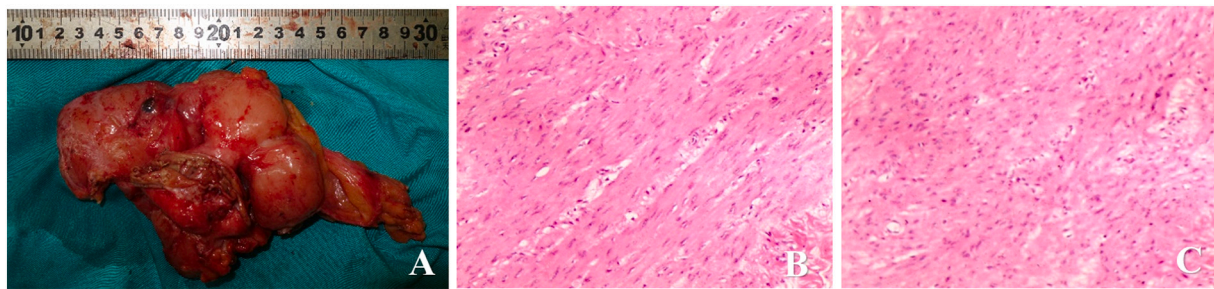
**Fig. 2.** Enhanced CT scan of GIST (A) before imatinib treatment, and (B) 2, (C) 6, (D) 12 months after therapy revealed dramatic decrease in the tumor size. CT, computed tomography; GIST, gastrointestinal stromal tumor.



**Fig. 3.** (A) Laparoscopic view of the giant gastric GIST invaded to the diaphragm; (B) laparoscopic stapling of gastric wall with adequate tumor margin; (C) control of stapled line for hemostasis; (D) small incision in abdomen; GIST, gastrointestinal stromal tumor.

surgery is safe and effective in the treatment of gastric GIST [13,14]. However, the feasibility of laparoscopic resection for large gastric GIST remains largely unknown. The European Society for Medical Oncology

(ESMO) guidelines discouraged the use of a laparoscopic procedure with large tumors due to the risk of tumor rupture [15]. The NCCN guidelines and consensus of Chinese experts recommend laparoscopic surgery only



**Fig. 4.** (A) The resection specimen demonstrated a 12 cm lobulated mass involving the wall of the stomach. (B, C) Histologic examination showed diffuse fibrotic regression and a few fusiform cells hyperplasia (hematoxylin-eosin, original magnification  $\times 20$ ).

when the GIST less than 5 cm in diameter and located in favorable anatomic sites, such as the greater curvature or anterior wall of gastric body and fundus, can be considered [3,4]. The mainly concern may be the high risk of intraoperative tumor rupture or tumor capsule rupture, resulting in peritoneal seeding and a worse prognosis. In recent years, many studies have demonstrated the safety and feasibility of laparoscopic surgery for GISTs larger than 5 cm [16,17]. What's more, many studies have also demonstrated the feasibility of laparoscopy for GIST even in emergency situations [18,19]. However, there are few reports for the application of laparoscopic wedge resection for gastric GIST larger than 10 cm. In this case, he successfully underwent a laparoscopic wedge resection without tumor rupture that might experience an extended surgery with unnecessary multiple organ resection initially. We could not deny the surgeon's excellent skilled and gentle intraoperative manipulation, the success of this surgery was probably owing to the magic function of preoperative imatinib administrated. Preoperative imatinib therapy may decrease the risk of bleeding, consolidate the tumor capsule so that might make the laparoscopic approach easier.

Since the first report of a dramatic response to imatinib of a GIST patient [20], this agent has been the standard treatment in the management of advanced or metastatic GIST patients. Despite this, pCR after neoadjuvant imatinib remains rare [21]. The majority of the prospective and retrospective studies investigated the preoperative imatinib therapy always focused on the R0 resection rate, RFS and OS, few described its pCR rate. Many of the reported pCR occurred in patients with colorectal or pelvic GIST [22,23]. A pCR is a rare occurrence for a giant gastric GIST. This case achieved near pCR after the preoperative imatinib therapy. Unfortunately, because of the lack of genetic mutation testing, we do not know whether this is associated with specific genetic mutation. What more, although the pCR after preoperative imatinib therapy in patients with locally advanced GIST correlated with a better prognosis is unknown, preoperative imatinib administration has the potential to promote curative minimally invasive surgery for some patients with giant gastric GIST.

Preoperative imatinib therapy for locally advanced gastric GIST remains investigational. We present a successful case of a patient with a giant gastric GIST who underwent laparoscopic wedge resection procedure after preoperative imatinib therapy and achieved near pCR.

#### 4. Conclusion

This case report adds to the growing consensus that preoperative imatinib therapy may facilitate R0 resection, organ preservation and increase the chance of minimally invasive approach by decreasing the tumor size. Patients with locally advanced GIST could benefit from the multidisciplinary approach including preoperative imatinib therapy, surgery and adjuvant imatinib therapy. Our report might encourage us to conduct future study of preoperative imatinib therapy for giant locally advanced gastric GIST that are initially considered to be unresectable.

#### Abbreviations

GIST	gastrointestinal stromal tumor
NCCN	National Comprehensive Cancer Network
CT	computed tomography
ESMO	European Society for Medical Oncology
RFS	relapse free survival
OS	overall survival
pCR	pathological complete response

#### Informed consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

#### Sources of funding

None.

#### Ethical approval

This case report was exempted from ethical approval from the institution.

#### Consent

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

#### Authors' contribution

HG, DW, and QZ performed the operation. HG and PY were involved in the management of the patient and interpreted the data. HG wrote the manuscript. QZ and YL reviewed and revised the manuscript. The authors read and approved the final manuscript.

#### Research registration

N/A.

#### Guarantor

Qun Zhao is the Guarantor for this work.

#### Provenance and peer review

Not commissioned, externally peer-reviewed.

## Declaration of competing interest

The authors declare that they have no competing interest.

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