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Laparoscopic resection of locally advanced gastrointestinal stromal tumour (GIST) of the stomach following neoadjuvant imatinib chemoreduction



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ABSTRACT

INTRODUCTION: Laparoscopic resection of locally advanced gastrointestinal stromal tumours (GISTs) is rarely offered to patients as a first line of treatment.

PRESENTATION OF CASES: We present two cases of locally advanced gastric GISTs successfully treated with neoadjuvant imatinib and followed up by complete laparoscopic excision of the residual tumour mass. There was no evidence of local recurrence or distant metastases after a mean follow up of more than 40 months.

DISCUSSION: Over the last decade, the development of imatinib has totally revolutionized management of metastatic GISTs and it is now possible to achieve primary tumour downstaging of more than 80%. Unfortunately, current literature on laparoscopic excision of locally advanced gastric GISTs following neoadjuvant treatment of imatinib remains scarce. The present cases strongly suggest that this new therapeutic approach might become the preferred medical option in such clinical situation.

CONCLUSION: Patients with locally advanced non-metastatic gastric GISTs should be offered first-line neoadjuvant. Imatinib-based cytoreductive chemotherapy as an alternative to radical debulking surgery, as a substantial proportion of them will experience significant tumour shrinkage and therefore benefit from a much less invasive laparoscopic approach.

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1. Introduction

Gastrointestinal stromal tumours (GISTs) arise from the interstitial cells of Cajal, specialized cells of the autonomic nervous system located within the wall of the gastrointestinal tract and responsible for paced contractions of the intestinal musculature ‘pacemakers’ as well as modulation of enteric neurotransmission [1]. The most common location of GISTs is in the stomach and accounts for around two-thirds of them, followed up by the small intestine, colon and rectum, and rarely oesophagus or appendix [2]. Diagnosis is histological and characterized by a high expression of a c-KIT proto-oncogene (CD117, tyrosine kinase receptor), and CD34 on immunohistochemistry. The prediction of malignancy remains difficult and relies on a combination of several criteria that include mitotic activity count, tumour size, presence of necrosis and invasive growth [3].

Surgery is the treatment of choice of non-metastatic GISTs when a complete R0 resection (clear margins) can be achieved with low morbidity, and routine lymphadenectomy is not required as those

lesions rarely metastasize to the nearby lymph nodes [4]. With the development of stapling devices, laparoscopic wedge resection of small gastric lesions has become the preferred surgical technique as it significantly reduces post-operative pain and morbidity, shortens hospital length of stay, while maintaining adequate overall long-term clinical outcome [5].

Recently published series have demonstrated similar results with gastric GISTs larger than 5 cm in diameter, when performed by experienced surgeons [6–8]. Having said that, caution should be taken when considering laparoscopic excision of locally advanced lesions, where the need for major gastrectomy with or without ‘en bloc’ resection of neighbouring organ might be necessary. In those circumstances it would be more reasonable to favour a conventional open approach that could increase the probability of complete R0 resection.

2. Cases presentation

We present the two cases of locally advanced gastric GISTs who did benefit from a 2-stages approach and where delayed laparoscopic R0 resection could be successfully achieved, without complication. Case one, at the time an 80 years old female patient classified ASA class III with significant cardiopulmonary disease

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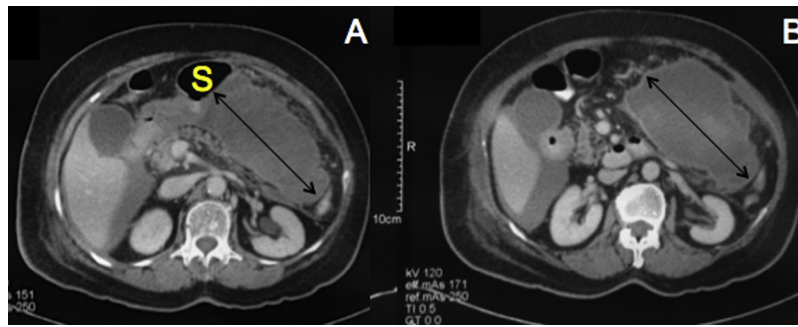


Fig. 1. Pre-treatment CT imaging showing (arrows) a large heterogeneous mass arising from the greater curvature of the stomach (S).

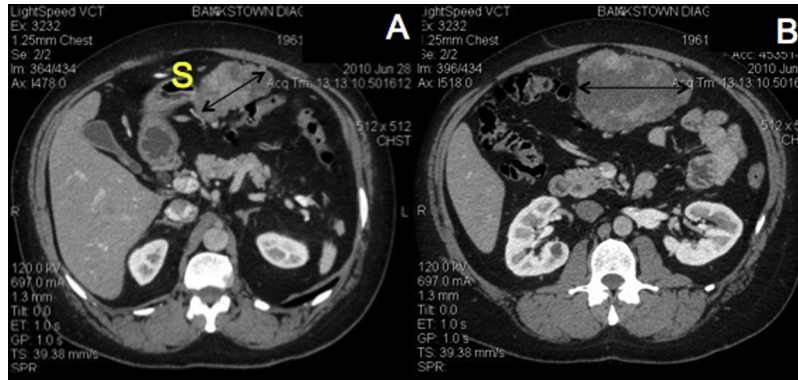


Fig. 2. Repeat CT-scan demonstrating a significant reduction of the gastric GIST following 6-month neoadjuvant treatment of Imatinib (S: stomach).

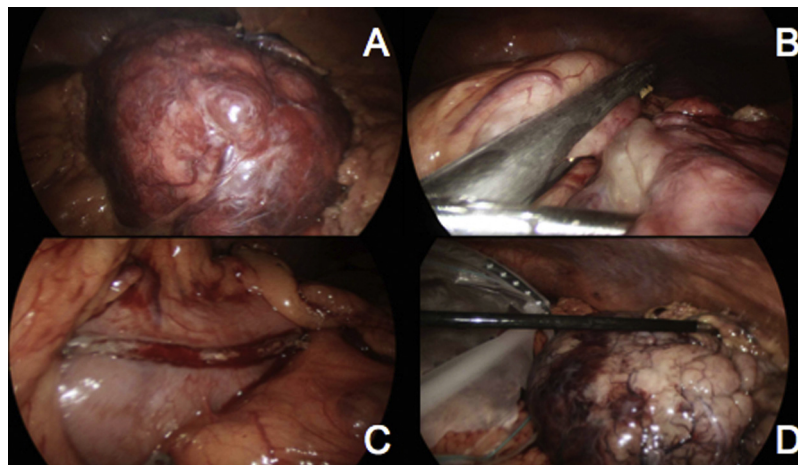


Fig. 3. (A) Laparoscopic view of ‘downgraded’ gastric GIST; (B) Laparoscopic stapling of gastric wall with adequate tumour margin; (C) Control of stapled line for haemostasis; (D) Fully mobilised specimen placed in Endocatch extraction bag.

was investigated for anaemia. Abdominal CT-scan revealed a large heterogeneous gastric mass measuring 13 × 13.5 cm, arising from the greater curvature (Fig. 1) and with classical features of GIST on endoscopic ultrasound (EUS). There was no evidence of distant metastases on positron emission tomography (PET) scan and fine needle aspiration (FNA) biopsy of the lesion confirmed the diagnosis. She received neoadjuvant imatinib 400 mg per day, as a single daily dosing for a total of 6 months and a significant 70% reduction of the mass was achieved as confirmed on repeat CT-scan imaging confirmed (Fig. 2). The patient eventually underwent laparoscopic wedge excision of the gastric wall encompassing the residual GIST (Fig. 3). Although she had an uncomplicated post-operative recovery the patient was discharged home 4 weeks later as she required significant physio mobilisation before being safely

discharged home. Histopathology results demonstrated an excellent response to imatinib with almost complete tumour necrosis and excision was complete (R0). Imatinib was reintroduced at one month following her surgery, but was interrupted 6 months later due to undesired side effects, mainly fluid retention, nausea and loss of appetite. She is today over 5 years post surgery with still no evidence of local recurrence or distant metastases on repeat imaging.

Case two, a 50 years old male patient when he was diagnosed with a locally advanced non-metastatic 14.5 × 11.4 cm gastric GIST abutting (loss of fat plane) the transverse colon. Unrelated, he also had a large cervical lump occupying most of his right thyroid lobe and corresponding to a benign follicular lesion on FNA. Other relevant problem included presence of central obesity and

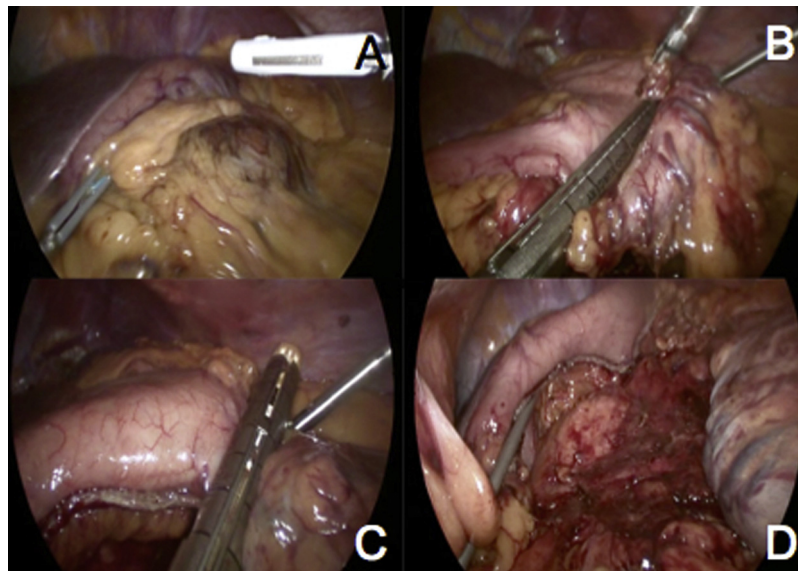


Fig. 4. (A) Laparoscopic view of residual gastric GIST partially wrapped in greater omentum; (B + C) Laparoscopic stapling of the gastric greater curvature; (D) Final control of haemostasis before tumour retrieval.

a 30 pack-years smoking history. The patient received a 6-month neoadjuvant treatment of imatinib 400 mg single daily dose leading to partial tumour response (around 50%) as demonstrated on progressive CT-scan imaging, but showing clear evidence of central necrosis of the GIST. Incidentally, towards the end of his medical treatment he was found to have a left testicular mass that was replacing most of his testis on US. Tumour markers were all negative and there was no evidence of loco-regional or distant metastases on CT-scan. The patient underwent elective laparoscopic excision of the gastric GIST including partial wedge excision of the greater curvature (Fig. 4), as well as radical left orchidectomy. 'En-bloc' colonic resection was unnecessary as the transverse colon and its mesentery were free of tumour, with clear margins (R0) on histopathology. The testicular lesion corresponded to a 4 cm seminoma confined to the testis and the surgical margins were also free of tumour (pT1N0M0). The patient went home on the fourth post-operative day and subsequently received a single dose of adjuvant carboplatin for his seminoma. Imatinib was also recommenced following his surgery for a total of 20 months. Of interest, he underwent right thyroid lobectomy four months following his initial laparoscopic procedure and was diagnosed three months later with a metastatic seminoma, for which he received three supplementary cycles of second-line chemotherapy. The patient is currently still on complete remission from his gastric GIST and metastatic seminoma 3 1/2 years later.

3. Discussion

Surgery is the only potentially curative option for gastric GISTs. Unfortunately, a small proportion of them are locally advanced measuring >10 cm in size or borderline resectable at initial diagnosis, meaning that 'en bloc' removal of neighbouring organ might be necessary to obtain R0 tumour resection. In those situations, minimally invasive laparoscopic approach is generally unsuitable and conventional open surgery is preferred, which is unfortunate especially in high-risk patients where complication rates are expected to be higher. Those two cases are good illustrations of large gastric GISTs successfully treated laparoscopically following neoadjuvant chemotherapy, while initially unfavourable for such minimally invasive approach.

Indeed, while still controversial the currently available KIT-selective tyrosine kinase inhibitor, imatinib (Glivec, formerly known as STI571, Novartis Pharma AG, Basel, Switzerland) may be considered as a first line of treatment in order to achieve substantial tumour chemoreduction and improve success rate of delayed curative-intent surgery, as well as overall survival [9]. One can extrapolate that tumour down-staging of potentially excisable locally advanced GIST lesions, using neoadjuvant imatinib-based chemotherapy may ultimately allow reconsideration to a minimally invasive approach [7,10]. An appealing concept that unfortunately will necessitate a large randomized multicentre study with long-term follow up to prove its validity over conventional open surgery. In the mean time, only anecdotal observational case series may offer a partial answer.

4. Conclusion

In summary, patients with locally advanced non-metastatic gastric GISTs should be offered first-line neoadjuvant imatinib-based cytoreductive chemotherapy as an alternative to radical debulking surgery, as a substantial proportion of them will experience significant tumour shrinkage and therefore eventually benefit from a much less invasive laparoscopic approach.

Conflict of interest

None.

Funding

None.

Consent

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

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