Laparoscopic Assisted Resection Of Large Rectal GIST Is Safe And Oncological Feasible: A Case Report And Review Of The Literature

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Laparoscopic Assisted Resection Of Large Rectal GIST Is Safe And Oncological Feasible: A Case Report And Review Of The Literature

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Abstract

Background The incidence of rectal GIST accounts for less than 5% of all rectal malignancies. Complete surgical resection remains the primary end point for all operable rectal GISTs. Neoadjuvant Gleevec therapy has been reported to successfully results in tumour shrinkage and allowing a less extensive surgery. Nevertheless, laparoscopic resection is a minimally invasive treatment option that allows complete resection with negative margin, and a favourable post operative recovery. We present a case of large rectal GIST resected via laparoscopic approach and adjuvant treatment with imatinib. Method A 54-year old male who presented with per rectal bleeding was found to have a submucosal lesion 3cm from anal verge. Colonoscopy and computed tomographic scan revealed a spherical submucosal tumour (5cm x 4.5cm x 5cm) located mostly exophytic at the anterior wall of the rectum. The tumour was abutting the posterior wall of the bladder and seminal vesicle. Patient successfully underwent laparoscopic assisted ultra low resection of the rectal GIST. The procedure was performed using three 5-mm working ports and one camera port. The entire left sided colon and rectum were mobilized laparoscopically up to the level of the tumour. Subsequently, a small pfennenstial incision was made and the tumour was dissected carefully along with the rectum without any spillage. The rectum was transected with a distal margin of 1cm. Finally, primary anastomosis was achieved using circular stapler CDH 29 and a protective ileostomy was fashioned at right iliac fossa.

Results Patient was discharged well on postoperative day 4. Histology showed R0 resected specimen, and size of the tumour was 4cm x 5cm with 19 mitoses per 50 HPF that correspond to a high risk malignant tumour.

Conclusion Laparoscopic-assisted resection for large rectal GIST is both minimally invasive and feasible without compromising oncological clearance. Neoadjuvant therapy with imatinib may be used if R0 resection is not possible.

KEYWORDS: Rectal GIST, Laparoscopic resection
Introduction

Gastrointestinal Stromal Tumour (GIST) represents the most common mesenchymal malignancy of the gastrointestinal tract. Rectal GIST generally demonstrates a more aggressive clinical course with high risk of recurrence. The mainstay of treatment for rectal GIST is complete surgical resection with clear margins. However, surgery for low rectal GIST may lead to extended resection with functional impairment. Lately, there have been reports that showed the use of neoadjuvant therapy with imatinib successfully shrinks the tumour in order to permit less extensive surgery that allows for preservation of function. Due to the rarity of the disease, there is no standardized treatment approach yet for this group of GIST.

Anatomically, rectal GIST is closely surrounded by vital structures of the urogenital and parasympathetic nerve complex. These factors have made it challenging for surgeons to plan for resection. Surgery for rectal GIST may be performed as local extraperitoneal resection or transabdominally. Local excision is recommended in patients with low rectal GIST of less than 5cm in size. For transabdominal approach, laparoscopic anterior resection offers an alternative that allows minimally invasive resection of the tumour, adequate surgical margins and a favourable post operative recovery. This report describes a case of large low rectal GIST that was successfully resected via laparoscopic assisted approach and adjuvant treatment with imatinib.

Case Presentation

A 54-year old gentleman presented to colorectal specialist clinic with the complaints of per rectal bleeding for 3 months duration. He also mentioned that he had experienced nocturia and frequent urination lately. He has no family history of malignancy of any sort. Digital rectal examination showed a smooth, hard mass located just 5cm from the anal verge on the anterior wall of the rectum. Patient underwent colonoscopy which revealed a submucosal lesion with a puckered ulceration on the overlying mucosa at 5cm from anal verge (Figure 1). Tissue biopsy showed that the tumour contained bundles of spindle-like cells. Immunostaining revealed that the tumour was positive for CD117 and CD34, and was negative for desmin and S-100, which are features of GIST. Computed tomographic scan revealed a spherical submucosal tumour measuring 5cm x 4.5cm x 5cm located mostly exophytic at the anterior wall of the rectum. The tumour was abutting the posterior wall of the bladder and seminal vesicle (Figure 2A). Magnetic resonance imaging confirmed that the tumour was not invading into these structures and between them was a thin well circumscribed margin.
On the basis of these findings, trans-abdominal approach of resection of the tumour via laparoscopy was considered.

A mechanical bowel preparation was achieved with 2 litre diluted Polyethylene glycol (PEG) on the day before surgery. The patient was placed in a Lloyd-Davies position. A subumbilical 12-mm trocar was inserted and pneumoperitoneum was maintained at 10 to 14mmHg. In addition, three 5-mm working ports were placed in the right upper quadrant, right iliac fossa and left iliac fossa, respectively (Figure 3). The surgery began by maneuvering the small bowels to the right side of the abdominal cavity. The whole sigmoid colon was mobilized after dividing the left lateral avascular attachment, up to the splenic flexure. The retrorectal space was entered after division of the posterior peritoneal reflection at the sacral promontory. The bilateral pararectal fascia was then separated along the rectum to develop the retrorectal space between the rectal fascia and the presacral fascia. Mobilization of the upper and mid rectum was accomplished after dissecting the anterior wall of the rectum via Denonvillier’s fascia. Laparoscopic dissection was performed until the tumour was exposed. Subsequently, a small Pfannenstiel incision was made. The tumour was further dissected carefully free from the surrounding mesorectal tissue with a clear margin. The rectum was transected with distal margin of 1cm and primary colo-rectal anastomosis achieved with circular stapler CDH 29. A protective ileostomy was fashioned at the right iliac fossa. The operative procedure was completed in 270 minutes and blood loss volume of 100ml. Postoperative recovery was uneventful and patient was discharged on postoperative day 4.

Histopathological examination report revealed rectal gastrointestinal stromal tumour with 5cm in maximum dimension (Figure 4). Mitotic count was 19 per 50HPF. Proximal and distal resected margin were uninvolved by tumour. There was no lymphovascular invasion. A mutation of exon 11 was identified. Based on the size, location and mitotic count per 50 HPF, this tumour has the features correspond to a high risk malignant tumour. Patient was therefore started on adjuvant imatinib mesylate (Gleevec, Novartis Pharmaceuticals Corporation, East Hanover New Jersey). The ileostomy was closed after about 2 months. The patient remains free of recurrence 1 year after surgery.

Discussion

GISTs are mesenchymal tumour that originates from interstitial cells of Cajal. They are characterized by expression of c-kit (CD 117), a transmembrane tyrosine kinase receptor. The annual incidence of GISTs worldwide is approximately 15 per million \(^{6-9}\). The most common site involved is in the stomach, while only 5%
of all GISTs originate in the rectum\textsuperscript{10-11}. A local study by the National Cancer Centre Singapore (NCCS) also confirmed that rectal GIST being uncommon primary site for GIST, representing only 8\% of the patients with resected localized tumour\textsuperscript{12}. GISTs from different sites have shown to express different molecular and clinical characteristics, therefore affecting the overall prognosis.

Rectal GIST is usually seen on endoscopy as a submucosal lesion. Usually there will be a substantial extraluminal growth, so it is of upmost importance to get cross sectional imaging study for rectal GIST. The size of the tumour, invasion to adjacent organs and sphincter involvement are factors to consider when formulating a treatment strategy. Our patient has presented with a relatively large rectal GIST that is located anteriorly and closely abutting the prostate. Although the tumour is low, fortunately there is no involvement of the sphincter complex as seen on MRI. This makes it a resectable tumour, but with potentially high morbidity risk due to its location and size.

Rectal GIST can be resected either by local excision (transanal or transvaginal) or by radical resection including low anterior resection and abdominoperineal resection. There has been no evidence to show that more extensive resection prolongs survival or delays recurrences. While local excision is a less morbid surgery, it also offer the oncological advantage of preserving the integrity of the peritoneal cavity, leading to lower risk of peritoneal metastases. However, its main challenge would be to achieve R0 resection safely, especially in large size tumour. Out of a series of 15 patients reported by Abbas et al, R0 resection following local excision was achieved only in 16\%\textsuperscript{13}. Tumour rupture was frequent during local excisions thus eventually translating into higher risk of recurrence. Changchien et al reported 77\% higher local recurrence rate in patients who underwent local excision as compared to 31\% on those who had radical resection (\textit{P} = 0.006)\textsuperscript{14}. In our case, transanal excision was not suitable because a large portion of the tumour was growing outside the rectum and anteriorly towards the prostate. It would be difficult to locate the tumour transanally, making it at risk of opening the tumour capsule. Our patient is young and curative intent was our top most priority. Another option is via the transsacral approach, which was first described by Kraske, but has lost favour because it is associated with poor perineal wound healing, fistula and anal dysfunction\textsuperscript{15}.

Laparoscopic surgery is an alternative when radical resection is required. Although there have been limited case reports on laparoscopic resection for rectal GIST\textsuperscript{2-3,16}, overall they showed potential benefits with this approach. This procedure provides optimal visualization especially in the pelvic cavity and therefore allows safe dissection around the tumour up to the level of the pelvic floor. Specimen can be brought out transabdominal or transrectal. Fujimoto et al
described the modified laparoscopic intersphincteric resection technique in which
the rectum was first mobilized laparoscopically, followed by transanal
intersphincteric dissection and extraction of specimen through the anus. The
tumours excised were small in size (<2cm). Based on the aforementioned benefits, we
utilized the laparoscopic approach to mobilize the entire left colon up to the level
of the tumour and created a small Pfannenstiel incision to retrieve the specimen
transabdominally as the tumour was deemed too large for transanal extraction.
During the open dissection, we had better tactile feel and handling of the tumour
thus avoid bridging of the capsule and cause spillage. We did not encounter any
intraoperative complication and complete resection was achieved with no tumour
rupture. In our opinion, this is a safe approach for large (>3cm) and low (≤ 5cm
above dentate line) rectal GIST.

The use of imatinib as neoadjuvant therapy is becoming universally more
favourable among the surgeons after several case studies have published
successful surgical treatment for advanced rectal GIST following preoperative
imatinib treatment. Tumours were found to shrink substantially and led to
reduced perioperative morbidity. Blesius et al reported up to 36% of the patients
with locally advanced non-metastatic GIST that were previously deemed
unresectable received neoadjuvant imatinib and subsequently underwent surgical
resection. Fujimoto et al also reported tumour shrinkage between 23 -60% of
initial tumour size after neoadjuvant imatinib therapy rendering all of them
possible for laparoscopic sphincter preserving surgery. Jakob et al found in his
series of 16 patients (total 36 patients) who received preoperative imatinib had
significantly higher rate of R0 resections (P = 0.02).

However, the indication of a neoadjuvant imatinib therapy for locally large rectal
GIST is still not well established due to limited data available and lack of
prospective trials. The prospective study by the Radiation Therapy Oncology
Group, who evaluated the efficacy of neoadjuvant imatinib, has only one rectal
GIST case included even though overall the result was promising. Besides, the
optimal duration and dosage of preoperative imatinib is still unknown. Most
literature reports clinical response after 4 to 12 months. However, imatinib is not
effective in all rectal GISTs. GISTs with exon-11 c-kit mutations have shown to
have high response rate of 84% to imatinib, while GISTs harbouring mutations in
exon-9, 13, or 17 are less responsive. These subgroups may require higher than
usual dose of imatinib to achieve clinical response. It is important therefore to test
for c-kit gene mutation on core biopsy specimen to predict the response of GIST
to imatinib. Patients on neoadjuvant therapy also need to be closely monitored in
order not to lose the opportunity for resection if the GIST is refractory to imatinib
and has become too large. In short, no clinical practice guidelines have
recommended neoadjuvant therapy for resectable rectal GISTs so far and more studies are still needed to address issues like timing for surgery, predictors for responsiveness and cost-effectiveness of preoperative imatinib treatment.

In our case, the rectal GIST was found to be too large for local excision. However, it can be completely resected via laparoscopic surgery. Due to lack of strong evidence to show benefit of neoadjuvant imatinib, its use would only be considered if the tumour is deemed unresectable or if more radical surgery e.g. pelvic exenteration is required.

Conversely, postoperative imatinib therapy has been extensively studied and proven to improve overall survival. Adjuvant therapy for GIST after primary resection has been extensively studied and proven to improve overall survival. One phase III clinical trial showed improvement of recurrence-free survival rate of 98% in high risk GIST treated with imatinib postoperative compared to 83% of patients treated with placebo. Treatment with imatinib after complete resection for primary GIST is currently recommended for at least 12 months for intermediate to high-risk patients. A recently completed study comparing 1-year vs 3-year adjuvant imatinib treatment for high risks GIST (characterized by tumour size more than 5cm diameter, mitoses count more than 5 per 50HPF, intraoperative tumour rupture) showed 3 years adjuvant therapy improved recurrence free survival and overall survival rate (66.5% vs 47.9% P <0.001; and 92% vs 81.7%, P=0.02, respectively). Our patient, being young and having high-risk lesion (rectal GIST, size >5cm and >5/50 mitoses), is recommended for adjuvant imatinib for at least 12 months.

**Conclusion**

As demonstrated in this case, laparoscopic-assisted resection for large rectal GIST is both minimally invasive and feasible without compromising oncological clearance. An updated review of literature offered various treatment approaches and their promising results. However, due to limited well-conducted trials being reported, careful consideration of each potential risks and benefit is necessary to formulate a management plan for each individual with rectal GIST. A multidisciplinary team approach is important to ensure good judgment and optimal providence of best treatment for patients. Neoadjuvant therapy with imatinib may be used if R0 resection is not possible or if more radical surgery is required. Adjuvant therapy is recommended for high risk GIST patient to achieve more optimal oncological outcome.
Reference


Figure 1. Colonoscopy showed a submucosal lesion with irregularity of overlying mucosa at 5cm from anal verge.
Figure 2. Imaging study of rectal GIST. (A) CT abdomen showed a round well-defined mass originating from right rectal wall (5x5.4x4.5cm), abutting right seminal vesicle and extending into pararectal space. (B) MRI showed a thin well-circumscribed margin between rectal mass and adjacent structures. No signs of invasion into adjacent structure or infiltration into perirectal / mesorectal fascia.
Figure 3. Ports placement. A subumbilical 12mm trocar was inserted. Three additional 5mm working ports were placed in the right upper quadrant, right iliac fossa and left iliac fossa respectively under direct vision. A Pfannenstiel incision was created for specimen.
Figure 4. Histopathological examination report revealed rectal gastrointestinal stromal tumour with 5cm in maximum dimension