

Rectal GIST resection following neoadjuvant therapy. Reporting two cases from a single institute

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Summary

Gastrointestinal stromal tumours (GIST) are the most common neoplasms arising from the mesenchymal cells of the gastrointestinal tract. Although GIST can arise in any gastrointestinal site, the most common are stomach and small bowel. Less than 5% of all GIST are located in rectum. Surgery is the main treatment option for resectable GIST. Currently, local excision has been increasingly employed thanks to neoadjuvant therapy. This paper reports two cases of rectal GIST treated with Imatinib neoadjuvant therapy followed by trans anal local resection.

Key words. Gastrointestinal stromal tumours, rectal neoplasms, case reports, neoadjuvant therapy.

Resección del GIST rectal tras la terapia neoadyuvante. Relato de dos casos de un único instituto

Resumen

Los tumores del estroma gastrointestinal (GIST) son las neoplasias más comunes que se originan en las células mesenquimales del tracto gastrointestinal. Aunque los GIST pueden surgir en cualquier sitio gastrointestinal, los más frecuentes son el estómago y el intestino delgado. En el recto se localizan menos del 5% de todos los GIST. La cirugía es la principal opción de tratamiento para los GIST resecables. Actualmente, la escisión local se emplea cada vez más gracias a la terapia neoadyuvante. Este artículo describe dos casos de GIST rectal tratados con terapia neoadyuvante Imatinib seguida de resección local transanal.

Palabras claves. Tumores del estroma gastrointestinal, neoplasias del recto, informes de casos, terapia neoadyuvante.

Introduction

Gastrointestinal stromal tumours (GIST) are the most common neoplasms arising from the mesenchymal cells (mesoderm) of the gastrointestinal tract.¹ The development of this neoplasm is attributed to c-kit gene mutation or, less often, PDGFRA gene mutation.² Although GIST

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can arise in any gastrointestinal site, the most common are stomach and small bowel.³ Rectal GIST accounts for less than 5% of all GIST.⁴

Surgery is the main treatment option for resectable GIST. However, even after a curative resection, recurrence and progression rates are around 40-60% after 2 years.⁵

Concerning rectal GIST, previous treatment were broad resections, such as pelvic exenteration and abdominoperineal rectal amputation.^{6,7} Currently, thanks to neoadjuvant therapy, local excision has been increasingly employed.⁸

GIST usually responds to tyrosine kinase inhibitors, such as Imatinib and Sunitinib. These medications can be used as neoadjuvant therapy, reducing tumour size and increasing resect ability. Also, tyrosine kinase inhibitors potentially could increase the probability of sphincter preservation and reduce the need for rectal amputation.⁹

This study address two cases of rectal GIST treated by Imatinib neoadjuvant therapy followed by trans-anal local resection. These were two consecutive cases managed in a single institute. This study is in accordance with the declaration of Helsinki.

Presentation of cases

Case 1

A 56-years-old male patient was complaining of tenesmus and perianal pain for over a year. Rectal digital exam revealed a 7 cm mass in the left rectal wall, right above the dentate line.

Colonoscopy evinced a round and regular mass, covered by normal mucosa. A trans-rectal biopsy was performed. Histological analysis showed epithelioid neoplasm with moderate atypia, certain necrotic areas, and up to 3 mitosis per 10 high-power field (HPF). Immunohistochemically positivity for CD117 (c-kit) and negative for smooth muscle actin or S-100 protein confirmed the diagnosis of a submucosal rectal GIST (Figure 1). Magnetic resonance evidenced a lesion invading external anal sphincter and reaching the mesorectal fat (Figure 2).

Patient received neoadjuvant therapy with Imatinib (400 mg per day) during 6 months.

After that, patient was submitted to trans-anal resection. The postoperative period was uneventful. The length of hospital stay was 4 days.

Histological analysis showed residual GIST measuring 4.3 cm, with viable cells comprising 5% of tumoral mass (Figure 3). Margins were negative.

Patient was submitted to adjuvant Imatinib. Following 2 years follow-up, the patient did not show any sign of recurrence and had no intestinal complaints.

Figure 1.

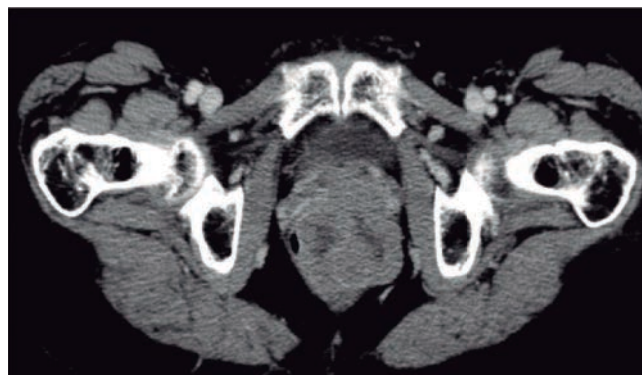


Figure 2.

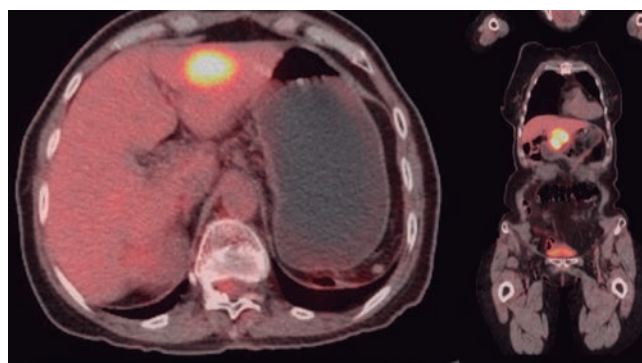
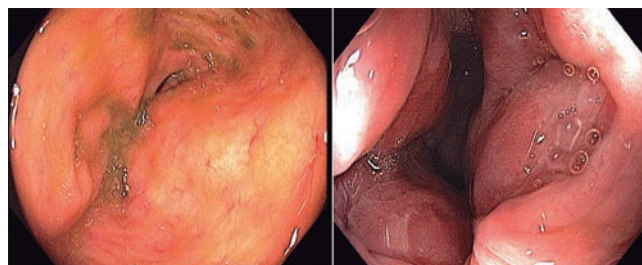


Figure 3.

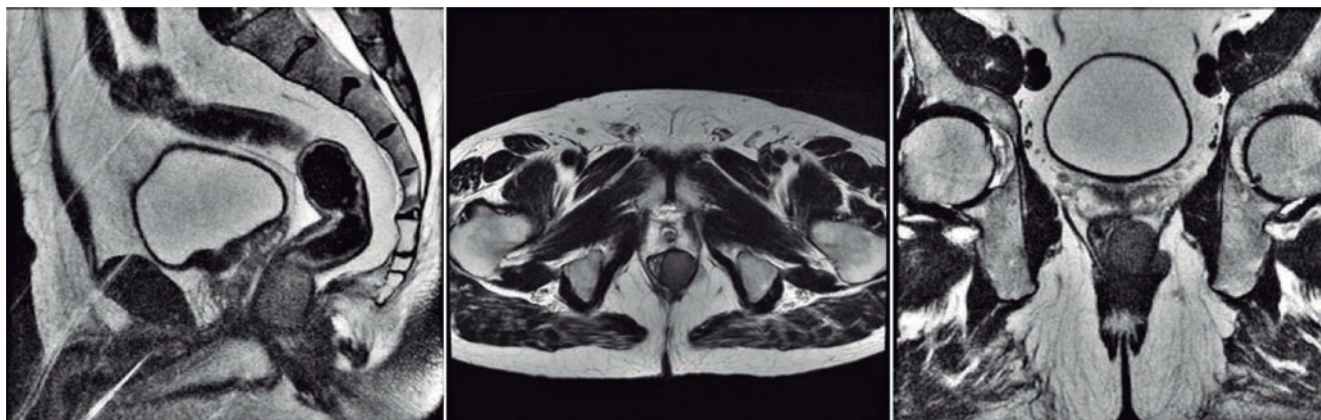


Case 2

A 63-year-old female patient was complaining of constipation. Rectal digital exam revealed a 5 cm mass in the left anterior rectal wall, located 2 cm above the dentate line. Colonoscopy showed a round mass with normal mucosa. A biopsy was performed and immunohistochemically positivity for CD117 and CD34 antigens confirmed the diagnosis of a submucosal rectal GIST. The mitotic activity was 2x10 HPF, and no necrosis was identified.

Computed tomography showed the presence of a tumour in contact with the vaginal wall and invasion of the levator ani muscle (Figure 4).

Neoadjuvant therapy with Imatinib (400 mg per day) was started for a period 6 months long, and was interrupted due to myalgia.

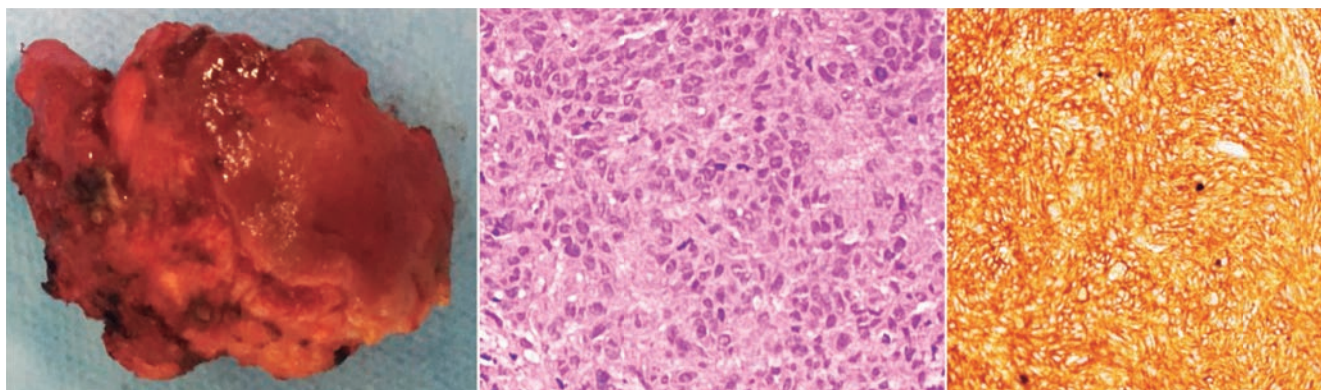
Figure 4.

The patient was then treated by local excision using the trans-anal endoscopic microsurgery technique. The tumour mass was completely excised with part of the posterior wall of the vagina and a minimal portion of tissue from the *levator ani* muscle.

The rectal and vaginal walls defect was closed primarily. A laparoscopic loop ileostomy was established. The postoperative period was uneventful and patient was dis-

charged on 4th postoperative day. The specimen margins were negative. The lesion expressed CD34 or CD117 and showed no mitotic activity (zero mitoses in 50 HPF). Patient received adjuvant therapy with Imatinib for 3 years.

Four years after the surgery, patient underwent a new cycle of Imatinib and subsequent liver surgery, due to a liver nodule (segment III) detected with a PET-Scan exam. (Figure 5).

Figure 5.

Intraoperative ultrasound identified two other nodules (liver segments V and VI). Patient underwent liver segmentectomy (segment III); nodulectomy (nodule in segment VI); radiofrequency ablation (nodule in segment). The postoperative period was uneventful, and patient was discharged on the 6th postoperative day. Immunohistochemistry was positive for c-kit and CD34 for both resected nodules.

Once recurrence developed after Imatinib was stopped, chronic Imatinib therapy was indicated. After

6 years after liver surgery, the patient is now disease-free and has no complaints, still under Imatinib therapy, and no signs of toxicity.

Discussion

The surgical approach is the main step for curative intent GIST management. The surgical procedure aims primarily to remove the tumour with R0 resection, as well as its surrounding pseudo capsule, without rupturing it, and avoiding tumoral bleeding.¹⁴

Neoadjuvant therapy prior to resection may be considered in cases where poor prognostic factors, such as big tumour size or high mitotic index are identified. Also, neoadjuvant therapy should be considered in cases of neoplasms next to important structures, such as great vessels or anal sphincter.¹⁵

Liu et al.⁹ reported 21 cases of rectal GIST resection, of which 13 underwent local excision (10 trans-anal, 2 Tran sacral, 1 transvaginal), and 8 patients underwent transabdominal approach. Trans anal approach was used for most small tumours of distal rectum. Tran-sacral approach was used for medium rectum. Neoadjuvant Imatinib was used in 5 patients, and those who received preoperative Imatinib therapy had a higher rate of negative resection margins than those without preoperative Imatinib therapy.

Adjuvant therapy should be considered in patients with significant risk of recurrence after GIST resection. Patient risk of recurrence is based upon tumour location, size and mitotic count.^{16,17} The SSG XVIII trial,¹⁸ a large, Scandinavian, prospective, randomized phase 3 trial, demonstrated superior relapse-free survival with 3 years of adjuvant IM compared with 1 year. Both of the current cases underwent Imatinib adjuvant therapy. The second patient developed recurrence after Imatinib stopped, and thus, a chronic therapy (> 5 years) was indicated after metastases resection.

Although genetic testing was not performed in the present study, mutation status of the primary tumour or metastasis could also be considered in assessing patient prognosis. It is well known that certain mutations may predict Imatinib response.¹⁸ As tumour sequencing becomes faster and more widespread, neoadjuvant, adjuvant and palliative therapies will become more tailored.

Conclusion

The current study report two cases of rectal GIST treated with neoadjuvant therapy, which allowed local excision, preserving sphincter and with a fast and satisfactory postoperative recovery.

Up to the current manuscript publication, both cases are disease-free.

Conflict of interest. *Authors have no conflict of interest. The Institutional Ethics Committee approved this study protocol.*

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