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Surgical management of rectal GIST. A case report and a review of literature

AIM: *Rectal GIST is a rare tumor of the gastrointestinal tract. The few literature cases didn't show significant evidence about diagnostic and therapeutic management. We present a rare case of rectal GIST treated with laparoscopic anterior rectal resection (RARLs) preceded by neoadjuvant therapy with Imatinib Mesylate (IM).*
CASE REPORT: *A 68-year-old woman with abdominal pain, rectal bleeding and palpable mass on rectal exam has been subjected to computerized tomography (CT) of the abdomen and pelvis and magnetic resonance imaging (MRI) that revealed a rectal GIST of 5x4x2 cm at 3 cm from anal verge. The diagnosis was confirmed with colonoscopy. After 3-mounts neoadjuvant therapy with IM, which allowed to down-stage the neoformation, the patient underwent RARLs without intraoperative or postoperative complications. Immunohistochemistry revealed cluster of differentiation CD 117 positive, HPF 5/50, Ki 67overexpressed. PDGF mutation was detected. The patient was therefore taken in charge by the oncologist.*
DISCUSSION AND CONCLUSION: *Resection appear curative for rectal GIST. Extensive resections aren't necessary because of downstaging after IM therapy. However, the appropriate surgical technique is still debated. Further studies are necessary for a correct surgical standardization.*

KEY WORDS: Rectal GIST, Cajal cell, Laparoscopic rectal resection, Imatinib

Introduction

GISTs (Gastrointestinal Stoma Tumors) are rare tumors that represent 0.1-3% of all malignant gastrointestinal tumors [1]. They appear as epithelioid or spindle-cell histology and they are characterized of positive CD 117 [1-3]. Rectal GIST is extraordinarily rare [1,2]. The clinical symptomatology is non-specific: characterized by abdominal pain [1,2] often associated with intestinal occlusion [4,5] and rarely by rectal bleeding or diarrhea due to the alteration of intestinal permeability [6]. Comparing to the other localization the rectal GIST is characterized by an highest biological aggressiveness [7]. Radical resection "en bloc" of the mass is the main treatment although there is not in literature significant evidence about a standardization of the best surgical option [5,8]. We present a case of rectal GIST who was treated with neoadjuvant therapy with Imatinib Mesylate (Glivec @) followed by a laparoscopic anterior rectal resection.

Case Report

A 68-year-old woman arrived to the hospital with abdominal distension associated to pain and rectal bleeding. With clinical history of hypertension and chronic constipation, the patient had performed a colonoscopy two years before without any anomaly. In the rectal examination a submucosal mass was found at antero-superior region without signs of macroscopic rectal bleeding. Blood tests were normal and bioumoral findings

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(CEA, GICA, AFP, NSE) were negative. Abdominal and pelvic CT and RMN (Figs. 1, 2) revealed a rectal GIST with centre-nodular hematoma, measuring about 5x4x3 cm involving the anterior and superior side of the rectum located 4 cm from anal verge without metastatic disease. The following colonoscopy found an ulcerated swelling in correspondence of the lesion shown at the radiological finding. Biopsy did no show significant alterations. After a multidisciplinary meeting the patient underwent neoadjuvant therapy with Imatinib Mesylate (IM) 400 mg once/day for 3 months. The following revaluation showed a volume reduction of 2x3x3 cm without centre-nodular hematoma.

Surgical Technique

Three 10 mm-trocars have been positioned in periumbilical region, right Mc Burney and left hypochondrium. A 5 mm-trocar has been positioned in left Mc Burney. After dissection of the mesosigma and ligation of distal sigmoid vessels, the rectum was mobilized in anterior region following the Denonvillier's fascia up to the seminal vesicles and nearly to the Walsh vessels; in posterior region following the Toldt's fascia up to the plane of the elevator with complete dissection of the mesorectum; laterally the dissection was performed close to rectum. The distal section of the bowels was performed with mechanical linear stapler (Echelon 60@ - Ethicon Cincinnati). A Pfeinnesteil incision was performed to pull out the surgical specimen and to perform the Knight-Griffen anastomosis by a 29 mm circular stapler. The methylene blue test was negative therefore a ghost ileostomy was performed. The surgical procedure lasted about 3 hours and the blood loss was insignificant.

No post-operative complication was shown during the hospitalization. The feeding was introduced in the second post-operative day; drainage tubes were removed on the third post-operative day; the patient was discharged on the fifth post-operative day. Histological examination

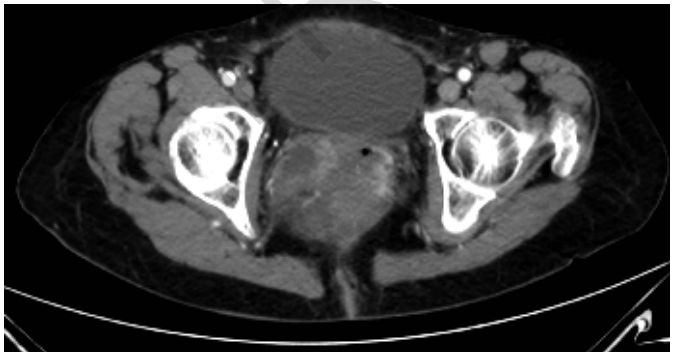

Fig. 1: Computer tomography with intravenous contrast of the abdomen showing a thickening of the lower rectum.

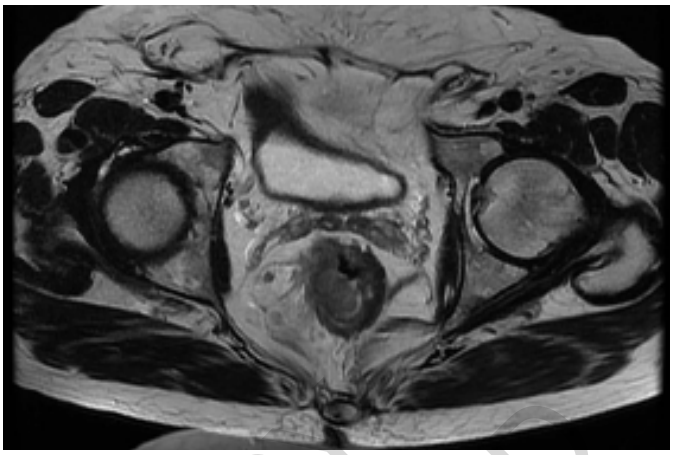

Fig. 2: Abdominal and pelvic Magnetic Resonance Imaging showing the rectal GIST.

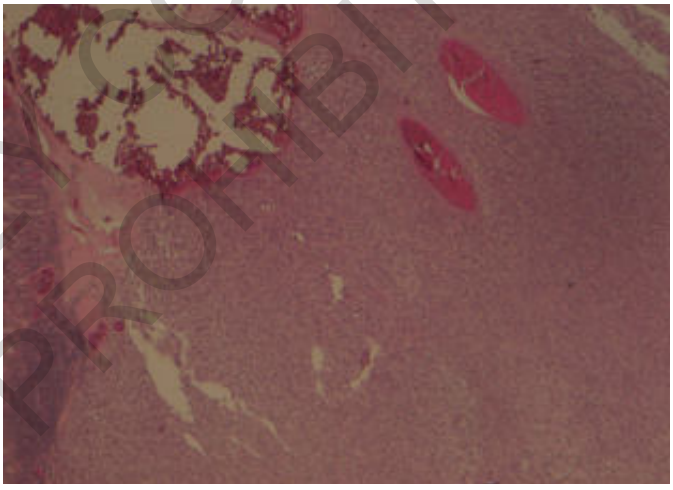

Fig. 3: Histological examination: Fusiform low-grade GIST cells composed of spindle cells arranged in short fascicles (nuclear palisading); hight cellularity with mitotic index of 5/50 HPF (High Power field); areas of necrosis and calcification – 10X.

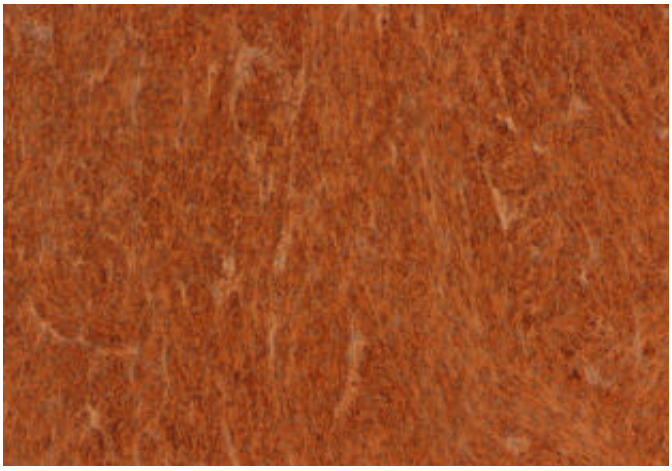

Fig. 4: Immuno-histochemical features of GIST: c-KIT/ CD117 (tyrosine kinase growth factor receptor) positivity – 20X.

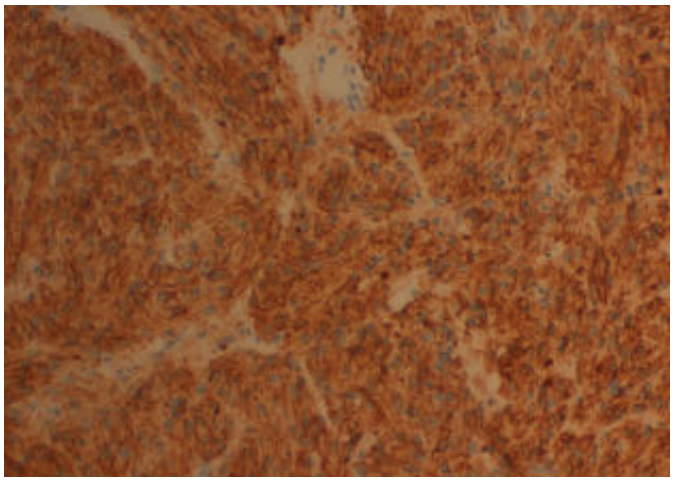

Fig. 5: Immuno-histochemical features of GIST: CD34 positivity – 20X.

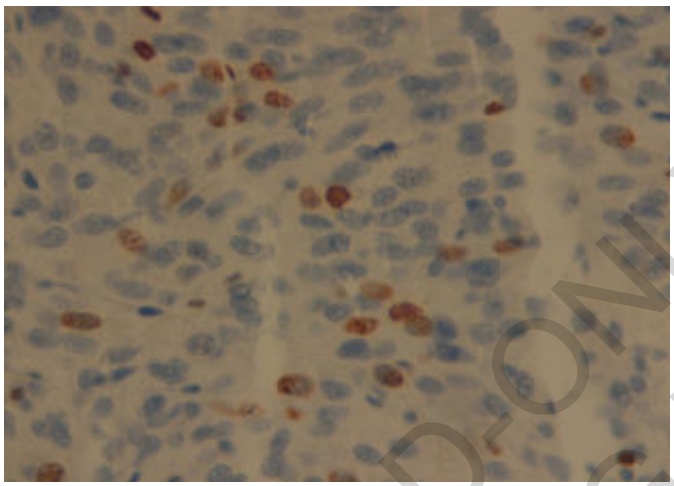

Fig. 6: Overexpression of Ki67 - 20X.

(Fig. 3) showed a GIST composed by proliferating spindle-shaped cells with nuclear palisading. Its cellularity was hight, its mitotic index (number of mitoses per 50 high-power fields) was 5/50 HPF (High Power field) with areas of necrosis and calcification, positivity for KIT/CD117 (Fig. 4), CD34 (Fig. 5) and negativity for SMA (smooth muscle actin) and Vimentine. Ki67 expressed at 40% (Fig. 6). The molecular analysis of this tumor showed a PDGFR gene mutation. The patient was therefore taken in charge by the oncologist for subsequent adjuvant therapies.

Discussion and review of literature

GISTs are rare tumors arising from Cajal cells [1-3]. The rectal localization represents about the 5% of the total GIST [9]. They present a worse outocome and prognosis than those in another location [1-3]. Inappropriately, in the past, have been classified as Leiomyomas, Schwannomas and Leiomyoblastoma. Afterwards, when immunohistochemistry in the late 90's has identified the gene KIT (CD117), they were classified as a separately neoplastic entity [3,10,11]. It is a tumor characterized by loco regional growth that often causes intestinal obstructions, haemorrhages, hematomas, and in a very few of cases, prolapse of the tumor or an incarcerated haemorrhagic mass protruding from the rectum [9]. Indeed, although the presence of an intramural hematoma in the rectum is a rare event [12,13] the cancerous reason is the most frequent. While the hematoma in the Gastric GIST is an evidence described in the literature [14] there is no scientific evidence on the intramural hematoma in the rectal GIST, so our case is the first report in the literature. The number of mitosis/HPF, the presence of areas of necrosis and the tumor size determine the degree of malignancy of GIST according with the Bucher Grading System [15]. GISTs recurrence risk after an R0 resection is determined by three factors: tuomr size, site and mitotic rate. There are several prognostic systems to determine this risk (MSKCC Nomogram, NIH, AFIP) but in literature seems to be no agreement as to which is the most reliable to predict the GISTs recurrence rate [16]. Genetic analysis of the PDGFRA gene is needed to assess the need for neoadjuvant therapy with Imatinib Mesylate even if the overexpression is not associated with its mutation: indeed, up to 7% of cases this gene is changed in case of over-expression [1,5]. In our case it was a high-grade GIST. Lymphonodal infiltration in this stadium is 0-3,4 % [15]. The most accurate method to evaluate the lymphonodal invasion is the MRI, while endoscopic ultrasound (EUS) has an hight accuracy in the evaluation of the T parameter [17]. Given the low tendency to lymphatic invasion, a laparoscopic approach is facilitated compared to that performed for the most common rectal tumors, to whom a more radical surgery is required [19]. In fact, in our case a small resection of left colon with a sigmoid vessels ligation was adequate for rectal GIST. However, laparoscopic resection can be difficult when the tumor is large, adherent to near structures or if it is too close to the sphincters. Although CT with contrast is the standard method for evaluating and staging GIST, a careful study with MRI allows to identify these characteristics to plan a better therapeutic strategy: for this reason it represents the best technique for the study of pelvic locations. If various types of surgical techniques have been proposed for borderline gastric GISTs with classical or atypical resections [1,7], some of this deriving from bariatric and other upper Gastrointestinal surgery [20-22], for low rectal localizations there are no clear guidelines [7,23-26]. Unlike other localizations, for rectal GIST surgery is often performed on the second line after neoadjuvant therapy with Imatinib Mesylate, due to anatomical difficulties related to proximity to the sphincters. Indeed, many scientific evidences [26-29] have shown an excellent down staging response, allowing more radical resections with a low local recurrence rate. A recent study [28] shows an anus preserving

rate of 33% in the resection after therapy with Imatinib Mesylate, compared to first-line surgery. Furthermore, this treatment, unlike the RT performed for adenocarcinoma, allows a downstaging without tissue sclerosis which makes anterior rectal resection difficult.
Some Authors [23,24] have described intrasfinter resections after treatment with Imatinib, others [29] have described local excisions but only for tumors less than 5 cm in diameter without neoadjuvant therapy. For local excisions in addition to the trans-anal one, a trans-sacral [24] approach was proposed, later abandoned in favour of a trans-perineal approach [25]. The latter one has been proposed to preserve sphincter functionality in patients with GIST involving both anterior and posterior rectal wall. The need for negative margins is also controversial: while many authors [1,3,5,29] show the need for a resection margin greater than 2 cm, recently McCarter [26] did not show any difference between R0 and R1in terms of disease free survival. The variety of evidences, often consisting of small and contradictory series, did not allow defining standardized guidelines. In our opinion, the laparoscopic approach, thanks to the magnification of the images, allows better dissections at the level of the pelvic floor without sphincter compromises. Furthermore, in the presence of an associated intramural hematoma, as in our case, the minor compressions can reduce the probability of mass rupture and the risk of spreading malignant cells.

Conclusion

Rectal resection is curative in the treatment of GISTs. Large dissections are not necessary and neoadjuvant therapy with IM can provide a valuable aid in the down staging of tumor. The multidisciplinary approach is mandatory to plan a therapeutic strategy. The best type of surgery to be performed is still under discussion. Further studies with larger series are therefore necessary to provide scientific evidence in this regard.

Riassunto

I tumori stromali gastrointestinali (GISTs) sono tumori rari che rappresentano lo 0,1-3% di tutti i tumori maligni gastrointestinali. I GISTs rettali rappresentano circa il 5% di tutti i tumori stromali gastrointestinali e sono caratterizzati da un'alta aggressività biologica. Nonostante in letteratura manchino evidenze significative, il trattamento chirurgico e l'asportazione "en bloc" della lesione neoplastica sembra essere il trattamento che assicura una migliora sopravvivenza. Nel case report da noi presentato viene esposto il caso di un paziente di 68 a cui, in seguito ad esami clinici e strumentali, veniva diagnosticato un GIST rettale a circa 4 cm dal margine anale, in assenza di malattia metastatica. Il paziente è stato trattato con chemioterapia neo-adiuvante con Imatinib Mesilato per tre mesi, al termine dei quali si evidenziava una risposta terapeutica parziale del 50% circa. Dopo attenta rivalutazione chirurgica il paziente veniva sottoposto a resezione anteriore del retto laparoscopica. In assenza di complicanza post-operatorie, il paziente è stato dimesso in quinta giornata postoperatoria ed è stato inviato presso il nostro centro oncologico per la prosecuzione dell'iter terapeutico. I GISTs rettali, rispetto ad altre localizzazioni più tipiche, vengono trattati chirurgicamente solo dopo down-staging con chemioterapia neoadiuvante. Questo è dovuta principalmente alla frequente vicinanza della neoformazione con lo sfintere anale. Molti studi evidenziano come la percentuale di preservazione dello sfintere anale dopo chirurgia aumenti sensibilmente se il paziente viene sottoposto a chemioterapia neo-adiuvante con Imatinib Mesilato. Per quanto riguarda invece il miglior approccio chirurgico per questo tipo di patologia non c'è concordanza tra i vari studi clinici. In base alla nostra esperienza possiamo affermare che l'approccio laparoscopico permette una sicura dissezione a livello del retto distale evitando una compromissione dello sfintere. Inoltre, è ancora controversa la necessità di una resezione margini negativi (R0) rispetto ad una con margini positivi (R1). Le discordanze dei dati riportati in letteratura non permetto di definire ad oggi delle linee guida standardizzate.

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