Gastrointestinal stromal tumors of the rectum : report of five cases

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Abstract

We report on five patients (three males and two females), with a median age of 66.2 years (range, 58-73 years) who were admitted in our department from April 1998 until January 2004 with the diagnosis of rectal gastrointestinal stromal tumor (GIST). Their main symptoms were rectal bleeding, constipation and abdominal discomfort. Two patients were treated by an abdominoperineal resection of the rectum. One patient received palliative surgical treatment and adjuvant therapy with imatinib for metastatic disease. Another patient presented with complete rectal prolapse, and was treated with Delorme's procedure. The subsequent pathological examination of the resected specimen showed positive resection margins and was given adjuvant therapy with imatinib. Finally, one case was considered inoperable. However, after nine months of treatment with imatinib, the magnetic resonance imaging (MRI) scan revealed a significant reduction in the tumor size, and the patient was treated with abdominoperineal excision of the rectum. All cases have been proved to be immunohistochemically positive for the CD117 and the CD34 stain. During the follow-up period (mean duration 3.7 years), one patient died of progressive disease while the other four had no sign of recurrence. (Acta gastroenterol. belg., **2009**, 72, **257-261**).

Key words : rectum, gastrointestinal stromal tumor, rectal prolapse, imatinib.

Introduction

GISTs are the most common non epithelial tumors of the gastrointestinal tract (1). Their annual incidence (cases per million) ranges from 6.8 in the USA to 14.5 in Sweden, with an estimated 5-year survival rate of 45-64% (2). Approximately 60% of GISTs appear in the stomach, 35% in the small intestine, and less than 5% in the rectum, esophagus, omentum, and mesentery (3). Their diagnoses is based upon the immunohistochemical staining of the CD117 (1-3). Surgical resection with negative margins whenever possible is the suggested treatment, while locally advanced or metastatic GISTs can be treated with imatinib (4).

Rectal GISTs are rare and account for a small percent of the tumors in this area. We report our experience on five patients with rectal GISTs treated in our department and we present two rare cases of advanced rectal GISTs one presented with complete rectal prolapse and the other exhibiting significant response, allowing surgery, after therapy with imatinib.

Case reports

Case 1

A 68-year-old female patient with a history of long-standing constipation was admitted to the emergency department due to acute rectal bleeding. Examination of the anorectal area revealed a large protruding mass from the anorectal orifice consisting of a polypoid-like lesion adherent to the rectal wall. The patient was immediately led to the operating room with the diagnosis of non reducable full-thickness rectal prolapse, which was treated with mucosal sleeve resection (Delorme's procedure). The excised specimen contained an elastic tumor with a reddish-white cut surface with areas of central necrosis and hemorrhage (Fig. 1). Histopathologic examination showed that the tumor was mainly composed of spindle-shaped cells and focally of epithelioid type cells with a high mitotic rate [> 5/50 High-power field (HPF)]. Immunohistochemical analysis showed that the tumor was positive for CD117, CD34, vimentin, SMA and S100. Based on these features, the tumor was diagnosed as GIST of the rectum and due to the positive resection margins, the patient received adjuvant treatment with imatinib. The patient had an uneventful postoperative period and during her two year follow-up, there has been no sign of recurrence.

Case 2

A 60-year-old male with a history of chronic constipation and long-term use of purgative medicines was referred to our department due to the manifest of decrease of the calibre of the stools over the last two weeks. Rectal examination revealed a firm and nontender

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Fig. 1. — Case 1. Resected specimen of the tumor adherent to the prolapsed rectum.

mass which was palpable to the anterior wall of the rectum. Abdominal and pelvic computed tomography (CT) and MRI scanning demonstrated a large low-density lesion emerging from the lower rectum (Fig. 2A) without evidence of distant metastasis. The patient was led to the operating theatre where the laparotomy revealed extensive adhesions and infiltration of the adjacent to the tumor tissues. The tumor was not excised and an incisional biopsy was taken. Pathological examination of the incisional biopsy specimen yielded results consistent with GIST thus leading to the initiation of imatinib treatment. After nine months of treatment, the MRI scan revealed a significant reduction in the tumor size with signs of necrosis (Fig. 2B). In view of these findings, the patient was re-evaluated and finally underwent an abdominoperineal resection. No evidence of recurrence was found during his four year follow-up.

Case 3

A 68-year-old woman with no prior medical history, presented to our department with painful defecation and rectal bleeding. Abdominal and pelvic CT scanning demonstrated a well-defined mass with soft tissue density located in the lower rectum without evidence of distant metastasis. Preoperative diagnosis was that of rectal leiomyosarcoma and the patient was scheduled for abdominoperineal resection of the rectum. Gross examination disclosed a 2×1.5 cm submucosal lesion. The cut surface of the tumor was white and elastic with no signs of necrosis or haemorrhage. Immunohistochemical examination revealed numerous tumor cells being positive for CD117, CD34, NSE and S100 stain with a mitotic rate of 5/50 HPF and with negative margins. Thus, our initial diagnosis was changed to rectal GIST. During her three year follow up, the patient had no sign of recurrence.

Case 4

A 58-year-old male was referred to our department for investigation of his recent complains of vague pelvic pain and discomfort during defecation. Digital examination revealed a firm mass with smooth surface emerging from the anterior wall of the rectum. Endorectal ultrasound showed a well-defined mass confined to the submucosal layer (Fig. 3). Abdominal and pelvic CT scanning was confirmatory of an extra luminal mass, protruding from the anterior wall of the rectum, with no signs of tumor infiltration into any adjucent organs. Preoperatively diagnosed with a mesenchymal tumor the patient was treated by an abdominoperineal resection of the rectum. The excised tumor measuring $8 \times 5 \times 4$ cm, had a white cut surface with no sign of necrosis. Microscopic examination showed that the lesion was a stromal tumor, mainly composed of spindle-shaped cells and focally of epithelioid type cells with a mitotic count of 2-5 mitoses per 50 HPF. Immunohistochemical stain was positive for CD117, CD34, vimentin and SMA, proving the tumor to be a GIST type. The patient has had no recurrence or metastasis after three years.

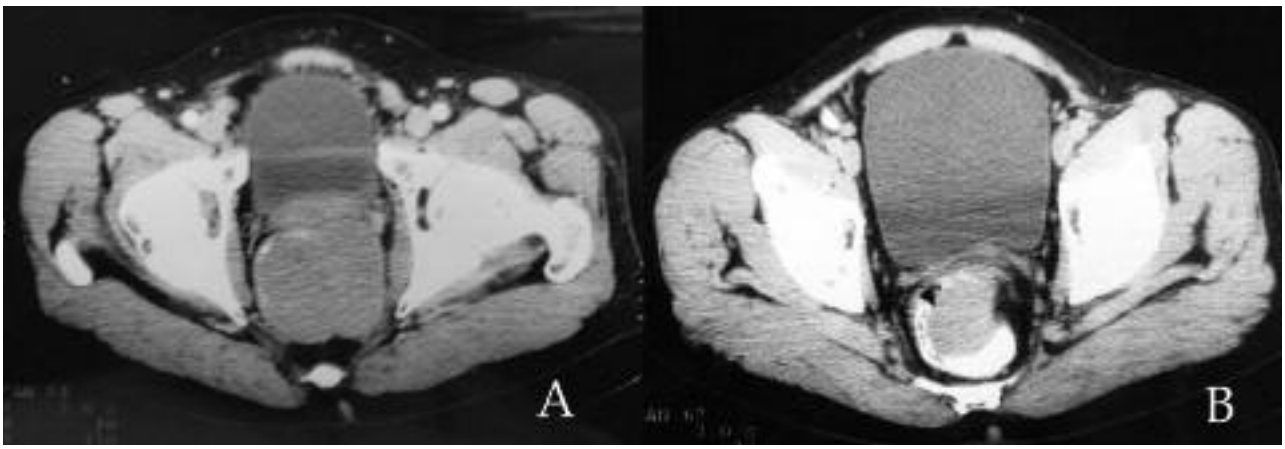

Fig. 2. — Case 2. A : CT scan of the pelvis showing a large mass in the lower rectum ; B : Remarked response on MRI in tumor size after 9 months treatment with imatinib.

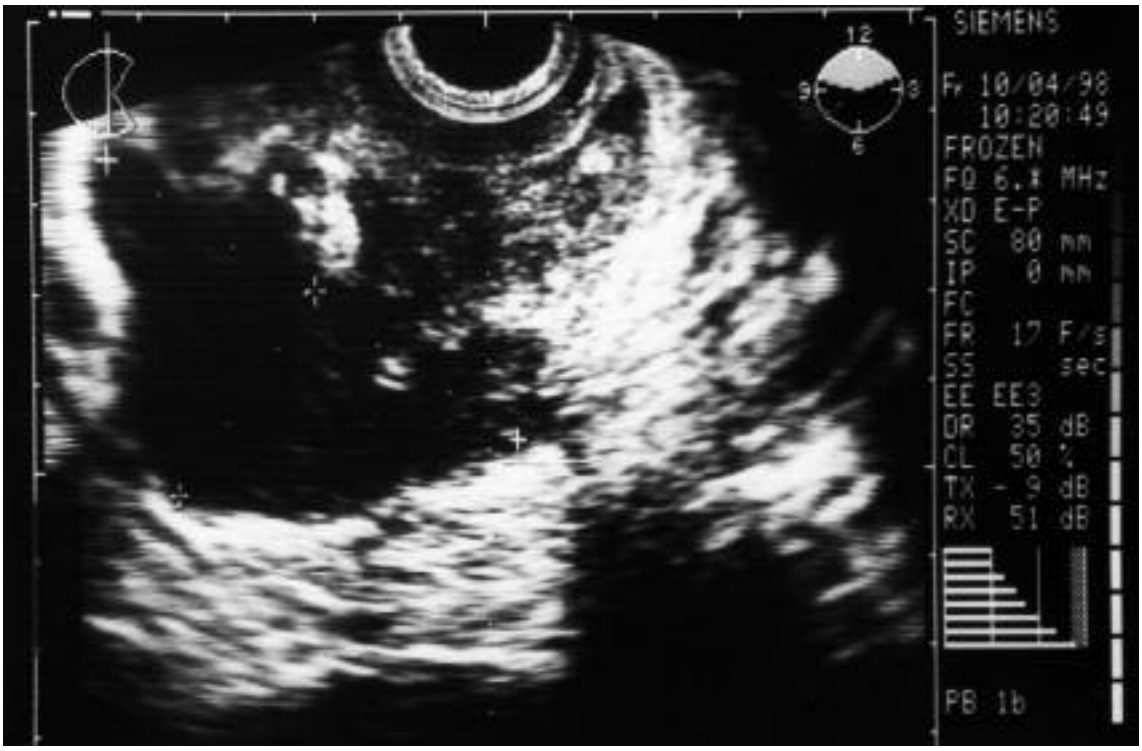

Fig. 3. — Case 4. Endorectal ultrasound showed a $8 \times 5 \times 4$ cm well-defined mass confined to the submucosal layer of the rectal wall

Case 5

A 73-year-old male presented with a history of constipation and weight loss during the last seven months. Physical examination showed a distended abdomen with loud borborygmi. Abdominal and pelvic CT scanning revealed a large lesion emerging from the lower rectum and several mixed density lesions on the peritoneum and in the liver. The patient underwent Hartmann's operation for palliative treatment. Histopathologic examination of the resected specimen showed that the tumor was mainly composed of spindle-shaped cells with a high mitotic rate (> 10/50 HPF). Immunohistochemical stain was positive for CD117, CD34 and vimentin. Based on these findings, the tumor was considered to be GIST and the patient received palliative therapy with imatinib. The patient finally died of progressive disease one year later.

Discussion

Anorectal GISTs account for less than 5% of all GISTs. They occur in older adults with a male predominance. The tumor size ranges from small asymptomatic tumors to large nodules causing rectal bleeding, pain and obstruction (5). Our case series included an unusual case of rectal GIST presented with complete rectal prolapse. To date only a few reports of concomitant rectal prolapse and cancer have been documented (6-8). It appears that the rectal prolapse may be caused by constipation accelerated by the malignancy.

The diagnosis of GIST of the rectum relies on the immunohistochemical staining with CD117. Miettinen *et al.* (5) reported that GISTs of the rectum are more consistently positive for CD34 and only rarely actin positive compared with other GISTs. In our series, all patients were positive for the CD117 and CD34 stain but we also found that 2 of our cases (40%) were positive for the Smooth Muscle Actin (SMA) stain. Prognosis did not appear to be different in the SMA positive tumors. It is possible that the high prevalence of SMA positive tumors is incidental due to the small number of patients in our series.

Imaging techniques such as CT, MRI and endoscopic ultrasound are useful in detecting the extent of the disease (4). In addition, abdominal ultrasound should be among the first line diagnostic procedures in younger patients presenting with lower gastrointestinal haemorrhage (9). Moreover, CT is the imaging modality of choise for the evaluation of the progression of advanced GISTs treated with imatinib (4, 10). Reduction of the tumor size and alterations of the tumor density are significant features indicating tumor response. However, it is not uncommon that the tumor size remains stable or even becomes larger despite clinical improvement. This pattern can be observed in the early post-treatment phase as a result of hemorrhage and edema and not tumor progression (11, 12). Fluorine-18-fluorodeoxyglucose (FDG) positron emission tomography (PET) is a very sensitive method for evaluating early response to imatinib, however it is still of limited use (13, 14).

Complete surgical resection with negative tumor margins remains the treatment of choise (4, 15). According to the consensus conference of 2004 (4), laparoscopy should be avoided due to the high risk of tumor rupture, although small (< 2 cm) intramural tumors may be acceptable candidates for laparoscopic resection. Furthermore, cases of large tumors being treated succesfully via laparoscopy have been documented (16). The type of the surgical resection remains also a subject of controversy. Changchien *et al.* (17) report that radical resection was superior to wide local excision in the prevention of local recurrence but not that of distant metastases. His findings come to agreement with other published series (18). However Miettinen *et al.* (5) and Randleman *et al.* (19) in their series, they postulate that small(< 2 cm) benign (< 5 mitoses per 50 HPF) rectal GISTs may be treated via local excision.

Imatinib,a tyrosine kinase inhibitor, is the only promising agent for the treatment of unresectable or metastatic GISTs (4, 20). An open-label Belgian trial showed that Imatinib is an active agent against unoperable GIST with manageable toxicities with 85% of the patients treated showed stable disease or partial response (21). Tumor response can be monitored with CT scan or FDG PET scan as stated above. Treatment with imatinib must be continued, even in cases of complete remission, until progression, intolerance or patient refusal (22). The role of imatinib as a neoadjuvant or adjuvant therapy remains under evaluation. Until now Verweij *et al.* (23) and Salazar *et al.* (24) have published some rather promising results concerning the use of imatinib as a neoadjuvant therapy. In our study, one patient with an unresectable rectal GIST had a significant decrease in tumor size, after being treated with imatinib, and therefore became suitable for surgical resection. Although this case does fall into the category of neoadjuvant treatment, the positive outcome supports this specific role of imatinib.

Rectal GISTs can be detected during routine digital examination in their early phase, thus leading to better prognosis compared with colon or small intestine GISTs which are often detected as advanced tumors. Moreover, the tumor size and the mitotic activity rather than the location appear to be more informative for the prediction of the tumor behavior.

However, in our case series, 3 patients underwent abdominoperineal resection due to advanced disease in two cases and wrongful preoperative diagnosis of leiomyosarcoma in one case.

Miettinen *et al.* (5) in their series, report that rectal GISTs less than 2 cm in diameter and with less than 5 mitoses per 50 HPF had rare recurrence(5%) and no metastases. In contrast, tumors more than 5 cm with any number of mitoses or with more than 5 mitoses per 50 HPF regardless of size had a rate of recurrence or metastasis ranging from 55% to 85%. Moreover, Changchien *et al.* (16) suggest that younger age(< 50 years) and positive Bcl-2 status are significant factors associated with poorer prognosis. Both series presented cases of disease relapsing many years after the surgical resection, thus suggesting the importance of long-term follow-up.

In conclusion, the prognostic features and the treatment modalities for the anorectal GISTs do not appear to be different from those applicable to the other GISTs. Surgical resection with free margins remains the only curative treatment. Imatinib is recommended for unresectable or metastatic GISTs. Its role as a neoadjuvant treatment, although promising, remains under evaluation.

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