Low Rectal Gastrointestinal Stromal Tumor-Multimodality Therapy: Reports and Review

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ABSTRACT

Gastrointestinal stromal tumor (GIST) is one among the most common mesenchymal tumors of the gastrointestinal tract. Common in the stomach, these are also found in other segments, and there has recently been a spate of reports about rectal and colonic GIST. This article highlights two rectal GISTs that were encountered and underwent laparoscopic abdominoperineal resection (APR) and laparoscopic APR plus Total laparoscopic hystrectomy (TLH) (laparoscopic posterior pelvic exenteration) for the involvement of the posterior vaginal wall. The patients both had smooth postoperative periods and are on tyrosine kinase inhibitors, refusing local external radiotherapy. This article highlights the issues surrounding the management of low rectal GIST, a rare but potentially deadly disease.

Keywords: Imatinib, laparoscopic abdominoperineal resection, minimal access rectal surgery, rectal gastrointestinal stromal tumor

INTRODUCTION

Laparoscopic excision of organs of the pelvis for gastrointestinal stromal tumor (GIST) is uncommon. Early tumors are often subjected to local excision. Sometimes, however, they require more aggressive resections and this may amount to even abdominoperineal resections (APRs) of the rectum.

The two patients presented in this article had large low rectal GISTs which could not be resected locally and which were too close to the anorectal junction. Therefore, the preservation of continence was not a possibility. In one of the patients, involvement of the sphincteric complex and anorectal junction precluded preservation of the sphincters, despite neoadjuvant therapy for 3 months with imatinib 400 mg. In the second case, involvement of the vagina and rectum engendered 3 months of neoadjuvant imatinib. Although there was some reduction in the size of both these tumors after 3 months of imatinib, sphincter preservation was not possible because of the position of the malignancy in relation to the anorectal junction and the dentate line. Therefore, a laparoscopic APR was performed in with postoperative imatinib therapy, offered radiation but refused, and remain free of tumor 12 and 18 months after surgery, respectively.

CASE REPORTS

Case 1

A 68 year old male presented with constipation and tenesmus for 3 months.After obtaining an informed consent, rectal examination showed a large globular mass at the anorectal verge, which seemed to extend in the left lateral direction, away from the wall of the rectum. A biopsy showed whorls of spindle cells, and immunohistochemistry confirmed CD117 positivity and CD34 negativity. He was treated with 3 months of

imatinib 400 mg/day. When reassessed 3 months later, there was a marginal reduction in the size of the tumor, but the patient was quite symptomatic and the anal verge obviously involved. After discussion with the patient, laparoscopic APR was performed, with a cylindrical one, and a laparoscopic posterior pelvic exenteration as performed in the other. Both patients were treated

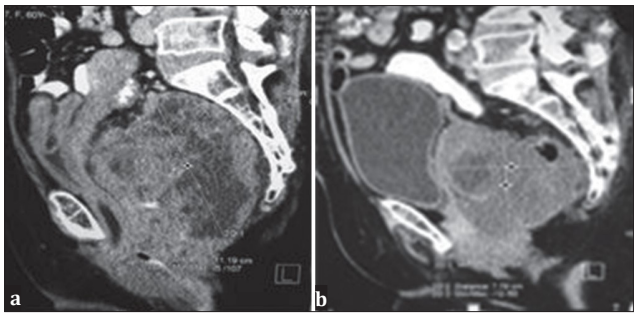

Figure 1: (a) Preimatinib. (b) Postimatinib

specimen including the ischiorectal fossa. Histology showed 2 cm margin clearance circumferentially, and he had no immediate postoperative complication. Postoperatively, he has been treated with 400 mg imatinib once daily, and he remains, 12 months after surgery, free of disease.

Case 2

A 52-year-old female presented with constipation and bleeding from the vagina postmenopause. Examination revealed a hard lobulated mass infiltrating the posterior wall of the vagina. Rectal examination showed a large 8 cm × 7 cm globular mass which was 1 cm above the verge. A biopsy confirmed GIST, and immunohistochemistry showed both CKit and CD34 positivity. Neoadjuvant imatinib was started and the patient followed up for 3 months, but there was only a mild regression in tumor size, although bleeding stopped completely after starting tyrosine kinase inhibitor (TKI). Repeat computed tomographic scan showed extensive infiltration of the posterior wall of the vagina. In view of these findings, she underwent laparoscopic posterior exenteration of the pelvis. This involved laparoscopic rectal and anal resection, as well as the total laparoscopic hysterectomy with an extended vaginal cuff. Postoperatively, she was offered radiotherapy but refused. She continues to be on imatinib and is asymptomatic at 18 months offollow-up.

DISCUSSION

Although GIST is one of the most common GI tumors, rectal GIST is quite uncommon, with an incidence of 5% of GISTs[1] and indeed <0.1% of rectal tumors. Arising from the interstitial cells of Cajal, these tumors originate, in 90% of the cases, from specific gene mutation known as the KIT gene mutation that activates the tyrosine kinase, one of the gatekeepers of cell proliferation. 5%–8% of these tumors arise from a mutation of platelet-derived growth factor alpha. About 10% of these show neither of these mutations,that is, they are wild-type GISTs.[2]

The workup of these patients involves biopsy, immunohistochemistry for specific antigens, computed tomography or magnetic resonance imaging (MRI) of the pelvis, and endosonogram of the rectum to delineate the tumor in terms of layers of the rectum and to identify exact spread. As they arise from the muscularis propria, the tendency is to grow exophytically, and endosonography or endorectal MRI often reveals a circumscribed mural mass.[3] In both the cases published here, the level of rectal involvement was quite low.

Rectal GISTs are not always positive for CD34 and CD117. In the first of our cases (APR), it was CD117 positive but CD34 negative. However, the second case was CD117 and CD34 positivity. This was one of the reasons, i.e., TKI was started on diagnosis and continued for 3 months before surgery in both.

The mitotic figures and the size of the tumor are two commonly used indicators of the virulence of the tumor. Mitotic figures of <5/50 per field are considered representative of a benign process.[4] Further, a diameter of <2 cm is said to be benign. In both these cases, mitotic figures were 30 and above. The size of the tumors was also large, both above 7 cm.

Further discussion on three major issues, viz., sphincter preservation, role of imatinib, and role of radiotherapy,is described below.

Sphincter preservation

In some cases, a 3-month course of imatinib could shrink a rectal tumor significantly, permitting a sphincter saving resection.[5] Several reports are now available in the literature to support this contention. However, both these tumors showed only a mild regression with3 months of TKI [Figure 1] and the patients were both very symptomatic of their tumors. Moreover, the anal verge was significantly involved, leaving no space fora distal line of the section and a colo-anal anastomosis. For all these reasons, the sphincters could not be spared, and APR was performed.

Imatinib Although a number of studies are showing a significant role for the TKI before and after surgery, permitting better oncological outcomes, we found only mild regression of tumor sizes with imatinib.[6-8] The umors were both CD117 positivity, and one tumor was CD34 positivity as well. However, there was nomarked response to imatinib. The bleeding from vaginal infiltration became significantly better. Anyway, the multidisciplinary team decided to continue imatinib post operatively for both the patients, and at this point oftime, they are free of recurrence.

Role of radiotherapy

In large tumors with extensive involvement of the perineum, there is some role of radiotherapy, and it is now being looked at as both neoadjuvant and adjuvant modality in the treatment of this disease.[9] Ideally, especially for Case 2, with extensive vagina involvement, postoperativeperineal radiotherapy might have been helpful. In view of the large size, Multidisciplinary team (MDT) offered radiation for both the patients, but both refused. There has been no local recurrence so far (12 and 18 months).

Conclusion

APR and laparoscopic posterior exenteration were performed for two patients with large low rectal GISTs thathad invaded close to the anal verge. Both patients were given preoperative TKI for 3 months. Surgical section margins were 2 cm clear of the disease. Postoperative imatinib is being continued for both patients. They remain free of local or metastatic disease, 12 and 18 months after the surgical procedure, respectively. This case reportrepresents one of the few published cases of laparoscopic pelvic exenteration for rectal GIST with adjacent posterior vagina wall involvement and highlights issues of an increasing problem.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the legal guardian has given his consent for images and other clinical information to be reported in the journal. The guardian understands that names and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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