Anorectal gastrointestinal stromal tumor (GIST) is a rare disease entity with malignant potential. Medical records of six patients (median age 68 years) with anorectal GIST who underwent surgical treatment at our institution between 1992 and 1999 were retrospectively reviewed. Four patients presented with rectal bleeding. The tumors were located in the mid and lower rectum in 4 patients and in the anal canal in 2 patients. The median tumor diameter was 4.5 cm. One patient who had undergone local excisions in another hospital presented with recurrent GIST. He refused radical excision and underwent wide local excision again. He developed recurrence 2 years later and underwent salvage pelvic exenteration, but finally died of disseminated disease. Five patients underwent initial radical excision. Among them, 3 developed recurrences (one each local, distant, and both) at a median duration of 50.3 months. Two patients died of the disease, while one patient who had both local and distant recurrences resected remained alive till the end of the study period (median duration of follow-up of the 5 patients was 84.6 months).

The clinical characteristics and surgical outcome of the patients are shown in the Table. Four patients presented with rectal bleeding while one presented with anal pain. One patient who had undergone low anterior resection for presumed rectal carcinoid tumor was found to have a GIST in the resected specimen. The tumors were located in the mid- to lower rectum in 4 patients and in the anal canal in 2 patients. The median tumor diameter was 4.5 cm (range, 1.2-8).

All the other 5 patients with primary anorectal GIST underwent initial radical excision, including low anterior resection (1), abdomino-perineal resection (3), and pelvic exenteration (1). One patient developed postoperative chest infection and perineal wound infection. Otherwise there was no morbidity or operative mortality in the series.

Pathological examination of the resected specimens revealed transmural involvement by the tumors in all cases. Two of the tumors had invaded into the mesorectum. No patient had regional nodal metastasis. All except one tumor had mitotic counts of more than 5 per 50 high-power fields (HPF) (Table). All the tumors were positive for CD117 (KIT), CD34, vimentin, smooth muscle actin, S-100, desmin on immunohistochemical staining (Fig).

The median duration of follow-up of the 5 patients who underwent initial radical excision was 84.6 months.
Among them, 3 developed recurrences (one each had local recurrence, liver metastasis, and both) at a median duration of 50.3 months (range, 24.7-94.8) after surgery. Two patients finally died of the disease (one had received a short course of imatinib), while one patient who had both local recurrence and liver metastasis resected remained alive without disease till the end of the study period. At 5 years, 3 and 4 patients, respectively, who underwent initial radical excision, had disease-free and overall survival.

**Discussion**

The biological behavior of GIST varies according to tumor size and mitotic activity. Anorectal GIST with tumor size <2 cm and <5 mitoses per 50 HPF were virtually indolent, with rare recurrence (5%) and no metastasis after surgery. On the other hand, those that were >5 cm in size with any number of mitoses or had >5 mitoses per 50 HPF regardless of size were highly malignant, with high rates of recurrence or metastasis after surgery (55% to 85%).

Changchien et al\(^1\) identified age <50 years and tumor size >5 cm but not histological grade or mitotic activity as being independent prognostic factors for the overall survival. In the present study, the median tumor size was 4.5 cm, and all except one had >5 mitoses per 50 HPF. These factors may account for the high recurrence rate (3 of 5) despite radical excision. On the contrary, the patient who was incidentally found to have a small GIST (1.2 cm) with low mitotic activity (<1 per 50 HPF) in the low anterior resection specimen had excellent prognosis after surgery. The mainstay of treatment of anorectal GIST is surgical resection, and neither radiotherapy nor conventional chemotherapy has any proven efficacy as adjuvant therapy.\(^4\) However, the best type of surgical approach (local or radical excision) remains controversial.\(^5,6\) Local excision has the advantages of minimal morbidity and sphincter preservation, while radical excision may offer a better oncological cure. There are few published data with long-term follow-up on the outcome of anorectal GIST treated by local versus radical excision. In a study comparing wide local excision versus radical excision in 42 patients with anorectal GIST, the local recurrence rate was significantly higher in the local excision group than that in the radical excision group (77% vs. 31%), despite the former having small tumors (4.5 cm vs. 7.2 cm).\(^3\) There was, however, no difference in the incidence of distant metastasis. In another study of 9 patients with malignant rectal stromal tumors, all patients treated by local excision encountered local recurrence, versus 66.7% in patients treated by abdomino-perineal resection.\(^7\) Our study has also shown similar recurrence rates. These

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**Table: Clinicopathological data and surgical outcome of 6 patients with anorectal GIST**

<table>
<thead>
<tr>
<th>Sex</th>
<th>Age</th>
<th>Presentation</th>
<th>Location of tumor</th>
<th>Size of tumor (cm)</th>
<th>Mitoses per 50 HPF</th>
<th>Surgical procedure</th>
<th>Nodal disease</th>
<th>Sites of disease recurrence</th>
<th>Disease-free interval (mo)</th>
<th>Follow-up Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>M</td>
<td>42</td>
<td>Rectal bleeding</td>
<td>Rectal low rectum</td>
<td>5</td>
<td>20</td>
<td>Local excision</td>
<td>Negative</td>
<td>Local, liver</td>
<td>36</td>
<td>294</td>
</tr>
<tr>
<td>M</td>
<td>57</td>
<td>Rectal bleeding</td>
<td>Rectal low rectum</td>
<td>4</td>
<td>25</td>
<td>APR</td>
<td>Negative</td>
<td>Local, liver</td>
<td>94.8</td>
<td>110.7</td>
</tr>
<tr>
<td>F</td>
<td>73</td>
<td>Anal pain</td>
<td>Anal canal Mid-rectum</td>
<td>3.5</td>
<td>24</td>
<td>APR</td>
<td>Negative</td>
<td>/</td>
<td>138</td>
<td>138</td>
</tr>
<tr>
<td>M</td>
<td>69</td>
<td>Rectal bleeding</td>
<td>Rectal low rectum</td>
<td>1.2</td>
<td>&lt;1</td>
<td>Low anterior resection</td>
<td>Negative</td>
<td>/</td>
<td>66.9</td>
<td>66.9</td>
</tr>
<tr>
<td>M</td>
<td>67</td>
<td>Rectal bleeding</td>
<td>Rectal low rectum</td>
<td>5</td>
<td>5</td>
<td>Pelvic exenteration</td>
<td>Negative</td>
<td>Liver</td>
<td>24.7</td>
<td>26.4</td>
</tr>
<tr>
<td>F</td>
<td>82</td>
<td>Rectal bleeding</td>
<td>Rectal low rectum</td>
<td>8</td>
<td>&gt;100</td>
<td>APR</td>
<td>Negative</td>
<td>Local, liver</td>
<td>50.3</td>
<td>84.6</td>
</tr>
</tbody>
</table>

HPF, high-power field; APR, abdomino-perineal resection; DOD, died of disease; AWR, alive with recurrence resected; AND, alive with no disease

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*a: 3 previous local excisions in another hospital. b: salvage pelvic exenteration for local recurrence; liver metastasis later. c: resection of pelvic recurrence and liver metastasis*
data support the suggestion that more aggressive and radical excision should be used in order to reduce the incidence of local recurrence, although it may not necessarily translate into overall survival benefit.\(^3,^8\) In selected patients with small ‘benign’ anorectal GIST of size <2 cm and <5 mitoses per 50 HPF (which may be determined by frozen section intraoperatively), local excision can be an acceptable treatment option, especially when sphincter sacrifice would be required for radical excision.\(^2\) However, a salvage radical excision may be necessary if the final histology and mitotic count turn out to be unfavorable.

Recurrence or metastatic patterns of anorectal GIST are similar to other GIST. Local, peritoneal, and liver recurrences or metastases are common.\(^2\) Remarkably, a long course of disease is commonly observed, and recurrence 10 years after resection of the primary tumor is not rare.\(^2,^3\) In our study, the median time interval between primary radical excision and recurrence was 50.3 months (range, 24.7-94.8). Moreover, the patient who was referred to us with recurrent anorectal GIST had a survival of 24 years despite repeated recurrences and multiple excisions. As shown in our study, a reasonable survival rate could still be achieved in patients with anorectal GIST despite a high recurrence rate.

Therefore, all patients with anorectal GIST should be regularly followed up for an infinite period. If recurrent disease is detected, further excision can be attempted (for cure or palliation) if the lesion is resectable. For unresectable primary or recurrent GIST, the use of imatinib, a tyrosine-kinase-receptor inhibitor specific for KIT, has been shown to be effective in reducing tumor volume and controlling disease progression.\(^9\) About 50% of patients with metastatic GIST have a measurable response after administration of imatinib, while about 75% will have at least stable disease.\(^10\) Treatment with imatinib appears to improve 2-year survival of metastatic GIST by approximately 20% when compared to surgery alone.\(^10\) There are ongoing studies to investigate the efficacy of imatinib as adjuvant or neoadjuvant therapy for GIST.\(^11\) Patients with high risk of recurrence after ‘curative’ surgery (e.g., large tumor size, high mitotic activity, tumor rupture on presentation, or limited metastatic disease completely removed at surgery) are good candidates for adjuvant imatinib therapy.\(^12\)

In conclusion, recurrence of anorectal GIST is common despite radical excision. Nevertheless, a reasonable survival rate can still be achieved. Long-term follow-up is necessary for these patients as recurrences may develop many years after the initial surgery.

References


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