Case Report

Gastrointestinal Stromal Tumor of the Rectum: A Case Report

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Gastrointestinal stromal tumors (GISTs) are a rare tumor of the gastrointestinal tract and its primary origin from rectum is even rare.[1-3] We presented a case of GIST of rectum arising in a 61-year-old woman, in who the tumor was identified and the diagnosis was confirmed after abdominoperineal resection. Clinical and pathological features of the tumor and types of treatment were then discussed.
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Key Words
Rectum;
Gastrointestinal stromal tumor

Mazur and Clark first introduced the term "stromal tumors" in 1983,[4] but it was not widely adopted until the early 1990s when Miettinen et al discovered that most stromal tumors arising in the GI tract are CD34 positive, the first relatively specific marker for gastrointestinal stromal tumors (GISTs).[5] Kindblom et al. revealed that the actual cells of origin of GISTs are pluripotential mesenchymal stem cells programmed to differentiate into the interstitial cells of Cajal.[6] These are GI pacemaker cells and are largely responsible for the initiation and coordination of GI motility. Perhaps the most critical development that distinguishing GISTs as unique clinical entities is the discovery of c-*kit* proto-oncogene mutations in the tumors.[7]

GISTs are most common in the stomach and small intestine, but less common in colon and rectum.[8] Traditionally, surgery is the cornerstone of treatment for resectable GISTs. In primary diseases, complete surgical resection provides the chance of cure.[9] The standard of care in the management of patients with GISTs rapidly changed after the introduction of tyrosine kinase inhibitors (TKIs), such as imatinib mesylate and sunitinib malate.[10] In the post-imatinib era, surgery shares a role in a multidisciplinary treatment plan.

Case Report

Denying any history of systemic diseases, a 61 year-old female complained of bloody stool with protruding mass after bowel movement for two weeks. She then sought help in a medical center nearby. Colonoscopy with biopsy was thus performed and GIST was suspected. A second opinion was sought at our clinic department. Immunohistochemistry studies of

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the biopsy sample were positive for CD117, CD34, and SMA and negative for both Desmin and S-100, indicating a GIST (Fig. 2). The permanent pathology documented gastrointestinal stromal tumor with high risk of aggressive behavior of the rectum. An abdominoperineal resection was therefore suggested, planned and performed after general survey (Fig. 1). She was then followed up at our OPD regularly.

Discussion

The SEER (Surveillance, Epidemiology, and End Results) study reveals that the age-adjusted yearly incidence rate of GIST is 6.8 per million populations with 54% in men and 46% in women.[2] Some European population-based studies report an annual incidence rate ranging from 6.5 to 14.5 cases per million populations and the median age at diagnosis ranges from 66 to 69 years. These studies might provide conflicting results because they contain GISTs detected both incidentally and at autopsy.[11,12]

Adult GISTs are most common in the stomach (60%) and small intestine (30%), but less common in duodenum (5%) and colorectum (< 5%). Rectal GISTs are uncommon, and GISTs originating from the colon are rare. Only less than 1% of the cases are in the esophagus and appendix. On rare occasions, GISTs develop outside the gastrointestinal tract in the mesentery, omentum, or retroperitoneum.[8] A recent population-based study demonstrates that the median tumor size of GISTs differs when the tumors are identified in different time points, for example, the median size are 8.9, 2.7, and 3.4 cm, respectively when GISTs are detected on symptoms, incidental findings, or during an autopsy.[12]

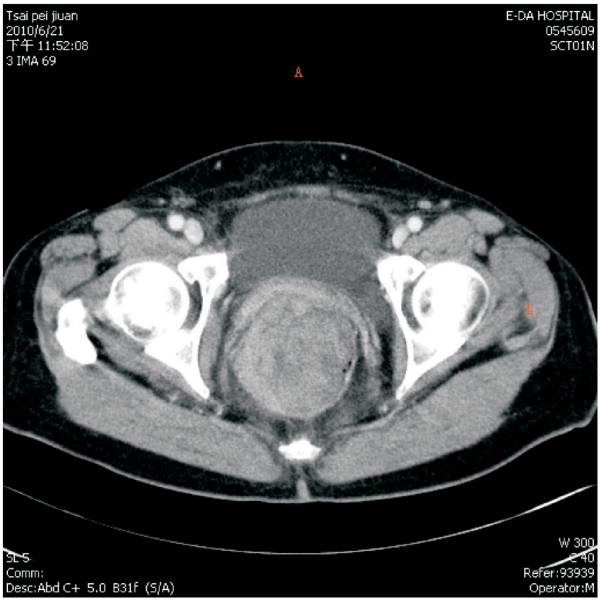

Fig. 1. A 7.0 × 6.9 cm mass noted at rectum. No definite retroperitoneal lymphadenopathy.

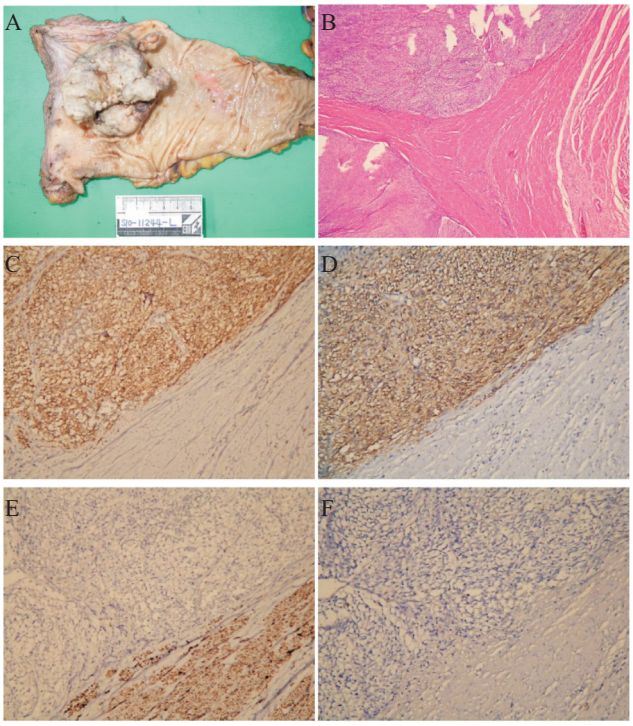

Fig. 2. A: Gross picture: There is one 8.0 cm fungating tumor with surface necrosis at low rectum, 3.5 cm away from distal end and 0.4 cm away from radial margin. B: Lobules of tumor tissue are seen between smooth muscle bundles of colon. (Hematoxylin and eosin stain, magnification, × 40) C: Immunohistochemical staining for CD117. The tumor cells (left upper) are positive for this marker, but the smooth muscle cells (right lower) of colon are not. (magnification, × 200) D: Immunohistochemical staining for CD34. The tumor cells (left upper) are positive for this marker, but the smooth muscle cells (right lower) of colon are not. (magnification, × 200) E: Immunohistochemical staining for desmin. The tumor cells (left upper) are negative for this marker, but the smooth muscle cells (right lower) of colon are positive. (magnification, × 200) F: Immunohistochemical staining for S-100. Both tumor cells (left upper) and smooth muscle cells (right lower) of colon are negative for this marker. (magnification, × 200)

An immunohistochemical profile is characteristic and useful to confirm the diagnosis of GISTs. Approximately 95% of the cases are positive for KIT (CD117), and 5% are truly negative for detectable KIT expression, indicating "KIT-negative GISTs."[13] Staining intensity does not predict the treatment response to imatinib,[14] and although KIT-positivity is a major defining feature for GIST, KIT-positivity alone may not be sufficient for diagnosis. Other commonly expressed markers include CD34 antigen (70%), smooth muscle actin (SMA; 30%-40%), desmin (< 5%), and S100 protein (~5%).[15]

The first small-molecule inhibitor targeting for solid tumors, imatinib mesylate competitively inhibits a few tyrosine kinases, including KIT, BCR-ABL, and the platelet-derived growth factor receptors (PDGFR). Fifty to seventy percent of the patients with GISTs have a partial response to imatinib and 15% to 30% of the patients treated with imatinib are maintained with stable disease.[16] Tumor volume reduces within a median of 3 to 4 months.[17]

Surgery remains the principle therapy for patients with primary GISTs with no evidence of metastasis and should be the initial therapy if the tumor is technically resectable. En-bloc resection without tumor rupture is then the treatment modality. Typically, enucleation only is the treatment option for smaller tumors (≦ 2 cm), local excision for the tumors sized between 2 to 5 cm, and abdominoperineal resection for tumors larger than 5 cm in size.[3] The recurrence rate of rectal GISTs is approximately 68% to 86% after local excision, but is less than 20% with abdominoperineal resection.[18]

The most important and widely used prognostic factors of a primary tumor are the size and mitotic index (Table 1).[1] Our patient is highly risky (Size > 5 cm, and Mitotic count > 5/50 HPFs) and complete resection of the primary rectal GIST is performed. Based on the results of the American College of Surgeons Oncology Group (ACOSOG) Z9000[19] & Z9001,[20] the USFDA approved imatinib for postoperative treatment for adult patients after resection of KIT-positive GIST in December 2008. Optimum duration of postoperative treatment has not yet been determined. Postoperative imatinib after complete resection for primary GIST is recommended for at least 12 months in intermediate- to high-risk patients. Higher-risk patients may require longer treatment.

Table 1. Proposed approach for defining risk of aggressive behavior in GISTs

Risk level	Size	Mitotic count
Very low risk	< 2 cm	< 5/50 HPF
Low risk	2-5 cm	< 5/50 HPF
Intermediate risk	< 5 cm	6-10/50 HPF
	5-10 cm	< 5/50 HPF
High risk	> 5 cm	> 5/50 HPF
	> 10 cm	Any mitotic rate
	Any size	> 10/50 HPF

Adapted from Fletcher CD, Berman JJ, Corless C, et al. Diagnosis of gastrointestinal stromal tumors: A consensus approach. *Hum Pathol* 2002;33:464.

Conclusion

GISTs are the most common mesenchymal tumors found in the gastrointestinal tract. The use of imatinib and a much advanced second-generation tyrosine kinase inhibitors for targeted therapy is a novel paradigm for treating solid tumors. Radiographic and pathologic evaluations are vital for diagnosis and prognosis of GIST. Surgical resection in combination with tyrosine kinase inhibition is the standard of care for treating patients with GIST.

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病例報告

直腸的胃腸間質腫瘤：病例報告

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胃腸間質腫瘤是消化道中罕見的腫瘤，而原發自直腸的更是少見[1-4]。本篇文章提出一位直腸原發性胃腸間質腫瘤的病例，進一步討論其臨床、病理表現及治療方式。

關鍵詞 直腸、胃腸間質腫瘤。