Large Gastrointestinal Stromal Tumor Mimicking a Gynecologic Tumor

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SUMMARY

Objective: Gastrointestinal stromal tumors (GISTs) are a group of uncommon bowel tumors. We report two cases of GISTs arising from the ileum and jejunum, both of which appeared to mimic a gynecologic tumor. **Case Reports:** In the first case, an 83-year-old, postmenopausal, woman presented with poor appetite, abdominal fullness and constipation for the preceding 3–4 days. Physical examination and imaging studies revealed a huge pelvic mass, suggestive of a huge cystic degenerated myoma. An exploratory laparotomy revealed a large tumor originating from the ileum, and immunohistochemical stains confirmed the presence of CD-117. In the second case, a 48-year-old woman presented with intermittent right lower abdominal pain and urinary frequency over the preceding 4 months. Physical examination and imaging studies revealed a pelvic mass of 21-week-gestational size. An exploratory laparotomy showed a huge fragile pelvic tumor, measuring 20 × 20 cm, arising from the jejunum. Immunohistochemical staining confirmed the presence of CD-117. **Conclusion:** GISTs express c-kit proteins (CD-117) on immunohistochemistry. They may mimic gynecologic tumors since they share the same pelvic cavity. One should always consider GISTs as part of the differential diagnosis in pelvic tumors. [*Taiwanese J Obstet Gynecol* 2005;44(2):187–191]

Key Words: c-kit protein, CD-117, gastrointestinal stromal tumor

Introduction

Gastrointestinal stromal tumors (GISTs) are rare cancers, accounting for 0.1–3.0% of all gastrointestinal neoplasms [1]. These tumors are now defined as mesenchymal tumors of the gastrointestinal tract, featuring expression of the c-kit protein (CD-117) on immunohistochemistry staining [2–6]. Most GISTs detected were asymptomatic and discovered incidentally, typically only at laparotomy performed for cancer survey [7] or on radiologic investigation [5]. It is difficult to diagnose GISTs preoperatively. Detailed history taking, comprehensive physical examination, and extensive imaging studies using ultrasound and computed tomography may still provide results that, on most occasions, prove to be deceptive with regards to tumor identification. Here, we report two cases of GISTs arising from the ileum and jejunum, both of which appeared to mimic gynecologic tumors. We also performed immunohistochemical analysis for the expression of the c-kit protein.

Case Reports

Case 1

Our gastrointestinal outpatient department referred an 83-year-old postmenopausal Taiwanese woman, gravida 7, para 7, to us after having detected a large low abdominal mass. The patient had presented symptomatically with poor appetite, abdominal fullness and

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constipation for the preceding 3–4 days. There was no apparent loss in body weight, change in urination habits, or abnormal vaginal bleeding.

A physical examination revealed a low abdominal pelvic mass of approximately 20 weeks' gestational size, arising from the suprapubic region and extending to the umbilicus. A pelvic mass was found upon pelvic examination. An abdominal ultrasound revealed an atrophied uterus measuring 3.3 cm in length, and a large mid-lower abdominal mass with heterogeneous echogenicity and an irregular anechoic area within the mass, somewhat suggestive of a huge cystic degenerated myoma. We were not able to identify any connection between the patient's uterus and the mass since the tumor was too large and the uterus too small to obtain a clear view. A computed tomography (CT) scan revealed that the lesion was a huge heterogeneous enhanced mass with no real clear interface with the uterus, suggesting a tumor of uterine origin, there being no evidence of lymphadenopathy, hepatic, liver or pancreatic disease. This patient had undergone prior surgery for an inguinal hernia some 20 years previously and had denied any history of medical disease. All routine blood and biochemical markers were normal. The levels of tumor markers assessed, including CA-125 and carcinoembryonic antigen (CEA), prior to the patient's intended surgical procedure were within the normal ranges.

An exploratory laparotomy under general anesthesia was performed under the suspicion of a malignant leiomyoma of the uterus. A huge intratumoral necrotic thin-walled pelvic tumor measuring approximately 20 × 15 cm in diameter was encountered; the tumor adhered densely to the ileum and the bladder dome. The uterus and both adnexae appeared normal. There were multiple nodules (between 0.5 and 1.5 cm in diameter) seeded over the entire bowel. The parasurgical report by frozen section noted the presence of a "myogenic tumor". In order to completely extirpate the tumor, the small intestine was segmentally resected and repaired with an end-to-end anastomosis. Partial cystectomy of the bladder was conducted as well. Microscopic examination revealed interlacing fascicles of bland-appearing spindle cells with slightly increased cellularity, but rarely any mitotic figures (two mitoses per 50 high-powered fields, hpf). The tumor appeared to develop from the intestinal wall and invade directly into the urinary bladder dome. Immunohistochemical stains confirmed the tumor's reactivity against an antibody to c-kit. A diagnosis of a low-grade GIST of the ileum was made following the operation. The patient was discharged a week later in a satisfactory condition, but was lost to follow-up 2 months later.

Case 2

A 48-year-old Taiwanese woman, gravida 1, para 1, was admitted to our hospital in September 2003 complaining of intermittent right lower abdominal pain and urinary frequency over the preceding 4 months. This patient had a history of abdominal total hysterectomy and colpopexy due to uterine prolapse approximately 8 years previously. In addition, the patient had suffered from hyperthyroidism and chronic hypertension over the past almost 30 years, although her condition had been stabilized with regular medication during the intervening period. The patient revealed no history of nausea, change in gastrointestinal habits, or abnormal vaginal bleeding preceding her presentation at our hospital.

A physical examination revealed a tense, firm, pelvic mass of approximately 21-weeks' gestational size. Upon pelvic examination, a huge pelvic mass was identified; an abdominal ultrasound revealed a large irregularly shaped tumor featuring a well-circumscribed border that extended beyond the umbilicus. The tumor was multicystic in appearance with papillary growth apparent in the solid parts of the tumor. Color Doppler study disclosed hypovascularity within the tumor. A CT scan revealed a huge complex tumor of varying density lying between the lower abdomen and the pelvic cavity. The tumor contained inhomogeneous cystic components mixed with solid elements and was accompanied by papillary growth soft-tissue foci. Lymph nodes were detected at the left common iliac chain and ascites appeared to be minimal. A small, ill-defined, low-density nodule was apparent at hepatic segment 7, indicating the possibility of tumor-associated liver metastasis. All routine blood and biochemical markers were normal. Levels of tumor markers were assessed prior to surgery, including CA-125 (46.13 U/mL; normal range, 0–35 U/mL), CA-199 (11.81 U/mL; normal range, 0–37 U/mL) and CEA (1.18 ng/mL; normal range, 0–5 ng/mL).

An exploratory laparotomy under general anesthesia was performed under the suspicion of a malignant ovarian tumor. A huge fragile pelvic tumor measuring about 20 × 20 cm in diameter, with 1,600 mL of bloody content emerging from the antimesenteric side of the jejunum at 40 cm below the Treiz ligament, was encountered (Figure 1). The tumor densely adhered to the jejunum but only loosely to the bladder dome. Both ovaries appeared normal. Multiple nodules measuring 0.5–1.5 cm in diameter were noted, seeded over the peritoneum, small bowel and pelvis. Parasurgical frozen-section biopsy demonstrated the presence of spindle-cell type tumors, favoring the diagnosis of a sarcoma, although GIST could not be completely ruled out. The jejunum was segmentally resected and repaired with an

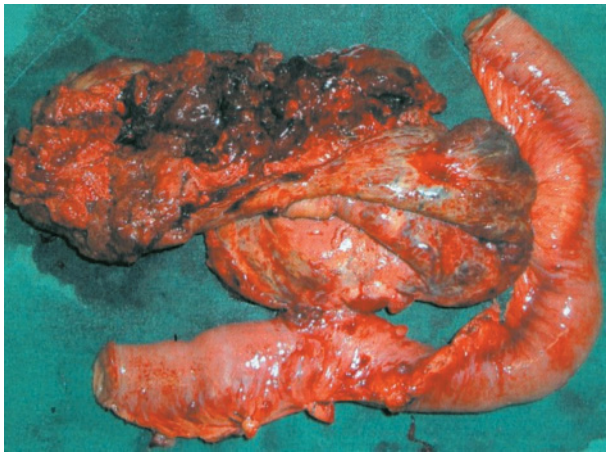

Figure 1. A huge fragile pelvic tumor measuring approximately 20 × 20 cm in diameter, featuring 1,600 mL of bloody content, and emerging from the antimesenteric side of the jejunum at a position 40 cm below the Treiz ligament.

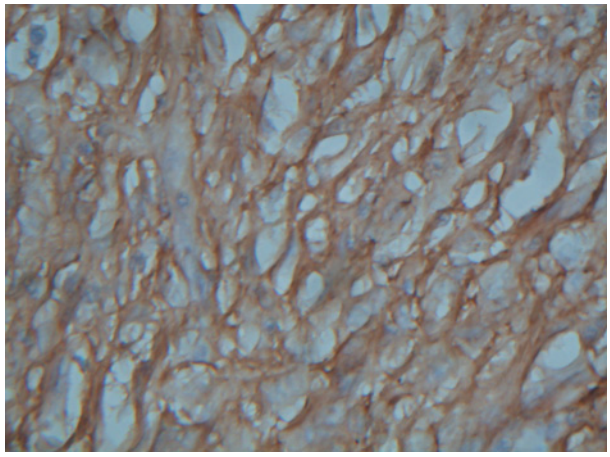

Figure 2. Immunohistochemical staining of CD-117 shows diffuse cytoplasmic staining of almost all tumor cells.

end-to-end anastomosis. Microscopic examination revealed a proliferation of spindle cells that were arranged in a short whirl-like pattern or as focal interlacing bundles within the muscular propria of the jejunum. Prominent nuclear palisading, mild nuclear pleomorphism and rare mitoses (up to three mitoses per 50 hpf) were noted. The tumor revealed evidence of focal hemorrhage and necrosis. Immunohistochemical staining confirmed the tumor's reactivity to c-kit antibody (Figure 2). A diagnosis of jejunal GIST with a high risk of aggressive behavior was made. The patient was discharged 1 week later in a satisfactory condition and commenced taking imatinib (Glivec®, Novartis Pharma AG, Basel, Switzerland) 1 month later. She is continuing to receive follow-up investigation and treatment at our general surgery department.

Discussion

GISTs are a group of tumors with malignant potential that are currently believed to derive from mesenchymal stem cells, the interstitial cells of Cajal (intestinal pacemaker cells), or from more primitive stem cells from which both Cajal cells and smooth muscle cells arise [2, 3,5,8]. Such tumors exhibit a broad spectrum of clinical behavior from benign to malignant, and somewhere between 10% and 30% of cases are malignant [1,7]. In general, it would appear that a GIST may arise from any location in the gastrointestinal tract. It affects mostly the stomach (60–70%), followed by the small bowel (25–35%), colorectal areas (5%) and, extremely rarely, the esophagus (< 2%) [2,4]. Some GISTs may also appear to present in the omentum, mesenteries, and retroperitoneum as primary tumors, but most of these are metastases from the stomach or intestine [1, 3,4]. The majority of affected patients are middle-aged or older, and there does not appear to be any sexual preponderance [1,5]. Recent studies have revealed that up to 94% of GISTs express a growth factor receptor with tyrosine kinase activity, named c-kit [5]. Immunochemical staining for CD-117 (the *c-kit* proto-oncogene product) and CD-34 (a sialylated transmembrane glycoprotein found in mesenchymal cells and that appears to be reactive for 70–80% of GISTs) are suggested to be sensitive markers for GISTs [2,3, 5,6]. CD-117 is currently believed to be the only diagnostic immunochemical staining technique required for the unambiguous detection of GIST [1,8], and its application in our patients confirmed that both had GISTs.

The modes of presentation of GISTs can depend on tumor size and location, but, in the majority of cases, GIST remains silent in presentation [1]. Most small GIST tumors are typically asymptomatic and are discovered only incidentally at laparotomy performed for other reasons or on radiologic examination [7]. For larger GIST tumors, the patient may present with vague abdominal discomfort, fullness, pain, the presence of a palpable mass, and gastrointestinal hemorrhage if the tumor has caused mucosal ulceration or signs of obstruction [2,7]. Many patients, however, may need more time to recognize the relative significance of such symptoms. Melena or an acute abdominal condition associated with mucosal ulceration, intestinal obstruction, invagination, or tumor rupture with hemoperitoneum, are present in a large proportion of GIST patients (30–50%). Surgical emergency is always inevitable, and it appears to be the only means by which the true nature of the tumor may be determined, particularly in combination with histologic confirmation [1–3,5,7].

Case 1 presented with non-specific gastrointestinal discomfort, which can easily be explained as a consequence of the mass compression effect of a huge uterine myoma. Her tumor markers were normal, and the results of imaging studies had convinced us to make a presumption of huge leiomyoma uterine, which is the most commonly seen intra-abdominal large tumor in females. Case 2 showed a similar picture: an apparent mass compression effect, tolerable abdominal pain, slight elevation of the tumor marker CA-125, and a failure to identify the involved ovary (both from a pelvic examination and by imaging studies); all ultimately led us to a misdiagnosis at the time of patient examination.

There are only a few large intraperitoneal tumors that typically arise amongst women. The differential diagnoses for such lesions commonly include myomas of a uterine origin, an ovarian origin, or originating in the bowel, and also lymphomas and sarcomas. However, in both our patients, presentation was associated with only vague signs and symptoms of GIST, thus raising the difficulty as regards to initial accurate disease differentiation. Typically, GISTs involve the outer muscular layer of the gastrointestinal tract and, mostly, reflect exophytic growth [5]. When affected individuals maintain an intact intestinal mucosa, as was the case for our two patients, there is typically no ulceration, bleeding or obstruction that would encourage the clinician to include an intestinal tumor within the differential diagnosis repertoire. Generally speaking, most clinicians facing such a dilemma would seek diagnostic assistance from imaging studies such as sonography, CT and magnetic resonance imaging in order to attempt to determine the origin of the tumor, to depict the full extent of the (often large) tumor, as well as to identify any possible distant metastases. There still appears to be a general paucity of characteristic radiologic criteria that may be used to effectively distinguish GISTs from other large tumors preoperatively [9].

It has been previously reported that a large proportion of GIST patients (11–47%) have metastases upon first diagnosis of their condition [1]. The liver and peritoneal surfaces are the most commonly noted metastatic sites, whilst the involvement of lymph nodes and extra-abdominal sites is rare [1]. Complete surgical resection of the tumor is the current standard treatment for GIST, and STI571 (imatinib mesylate, Gleevec), a kit-selective tyrosine kinase inhibitor, is the most effective adjuvant therapy both pre- and post-surgery, even for an unresectable tumor [1,2,10,11].

There is no general agreement on the prognosis for GIST [1], although the two most important histologic criteria that differentiate malignant GIST tumors from their benign counterparts are tumors featuring mitotic figures more than 5/50 hpf and a size greater than 5 cm in diameter [2]. Such GISTs are commonly associated with a fairly high incidence of intra-abdominal recurrence, spread and liver metastasis [2]. In contrast to this, tumors that are smaller than 2 cm and those with mitotic figures less than 5/50 hpf have been shown to be associated with a good prognosis [2,12].

In conclusion, GIST is an extremely rare tumor that may present as a pelvic mass in women. At the time of patient presentation, and then at diagnosis, every effort should be made to successfully diagnose the condition. These efforts should include a complete history, a review of the patient's general condition, a scrupulously detailed physical examination, and a meticulous review of the imaging results, so that the chances of accurately determining the condition and differentiating between possible origins of the tumor can be increased [13]. Some studies have reported on the relative practicability and utility of fine-needle biopsy for the early diagnosis of GIST [1], although the possibility of tumor rupture, bleeding and seeding must always constitute a great concern. Therefore, unless we have already ruled out the possibility of a malignancy of gynecologic origin or can conclusively exclude the above-mentioned biopsy risks, we would not perform such a biopsy prior to surgery [11]. It remains challenging for most gynecologists to undertake and complete a preoperative summation of GIST. Therefore, it is a surgeon's responsibility to be aware of and to be receptive to the possibility of a diagnosis of GIST, and to recognize the tumor for what it is, either prior to or during initial surgery, in order to deliver the best treatment possible [1].

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