

## Case Report

# Subsequent leiomyoma and intra-abdominal fibromatosis mimicking recurrent gastrointestinal stromal tumor: a case report

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**Abstract:** Gastrointestinal stromal tumor (GIST) is the most common mesenchymal tumors of the gastrointestinal tract. In this report, we present a case of GIST patient who had been treated with imatinib, but developed leiomyoma and intra-abdominal fibromatosis (IAF) at the site of GIST resection beds mimicking recurrent GIST. To our knowledge, no patient with the 3 gastrointestinal tumor types we encountered, GISTs, leiomyomas and IAF has ever been reported. Leiomyoma and IAF might be confused with recurrent GIST for similar imaging findings and the overlap in immunophenotypic profiles such as c-Kit, SMA and desmin. The current case highlights the need for careful consideration of leiomyomas and IAF when a rapidly growing spindle cell tumor is encountered in a post-GIST patient.

**Keywords:** Gastrointestinal stromal tumor (GIST), intra-abdominal fibromatosis (IAF), leiomyoma

### Introduction

Gastrointestinal stromal tumor (GIST) is the most common gastrointestinal mesenchymal tumor of the gastrointestinal (GI) tract, accounting for 1% to 3% of all malignant GI tumors. In the past, without effective drugs, the main course of treatment is surgery. Tyrosine kinase inhibitors such as sunitinib malate and imatinib mesylate are targeted therapies for GIST patients with KIT mutations [1].

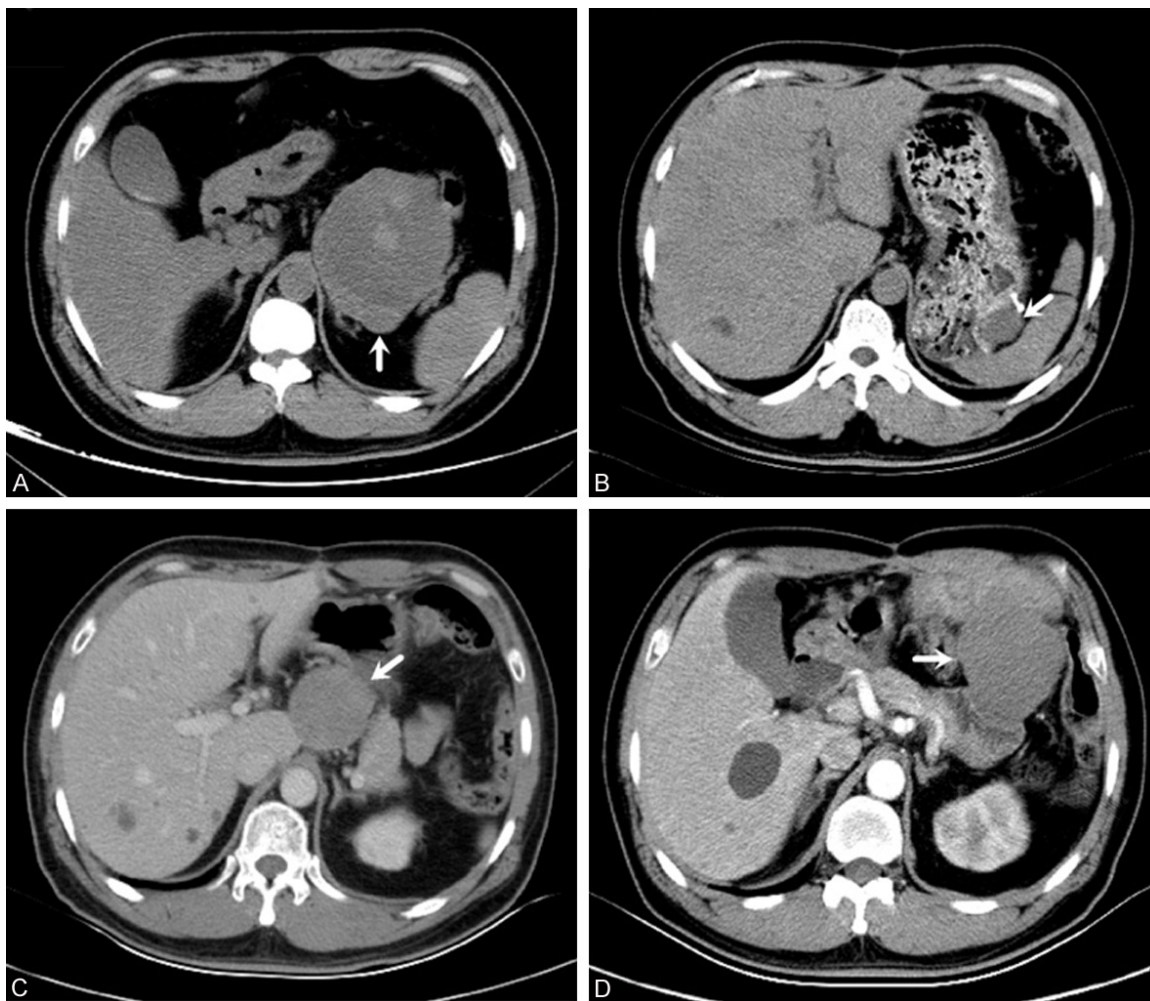
A number of soft tissue neoplasms share many similarities in the morphological and immunophenotypic profiles with GIST. Leiomyomas and intra-abdominal fibromatosis (IAF) might be confused with recurrent GIST from the clinical point of view.

IAF is a group of fibroblastic or myofibroblastic tissues, which generally lacks metastatic potential but tends to exhibit local invasion with a very high rate of recurrence [2]. It is often associated with conditions such as familial adenomatous polyposis and Gardner syndrome. IAF developed spontaneously or after

abdominal surgery and individual with both GIST and IAF were reported recently [3, 4]. Surgery also remains a reasonable first treatment option. The differential diagnosis between IAF and GIST has been further complicated by the reports of positive cytoplasmic immunostaining of MF with CD117, a marker being regarded as one of the key criteria for the diagnosis of GIST [5].

Leiomyoma usually originates from the uterus and alimentary tract, which are totally benign and usually asymptomatic [6]. Leiomyoma mimicking a GIST have been reported recently [7, 8]. Open surgical resection is considered the standard for removing these tumors. However, recent improvements in endoscopic and laparoscopic equipment have made it possible to utilize minimally invasive techniques of tumor removal, in which way, functional deficits and morbidity could be avoided.

The present study describes a case of GIST patient who had been treated with imatinib, but developed more than one type of localized proliferation of soft-tissue neoplasms at the site of



**Figure 1.** Computed tomography showing a mass (90 × 78 mm) involving the gastric greater curvature (A), a mass (24 × 20 mm) involving the gastric greater curvature and posterior wall (B), a low-density, homogeneous tumor (5 cm in diameter) with moderate enhancement in the left upper abdominal cavity (C) and a localized abdominal tumor (5 cm in diameter) with slight enhancement involving the gastric lesser curvature (D). Arrow (white) identifies those mass.

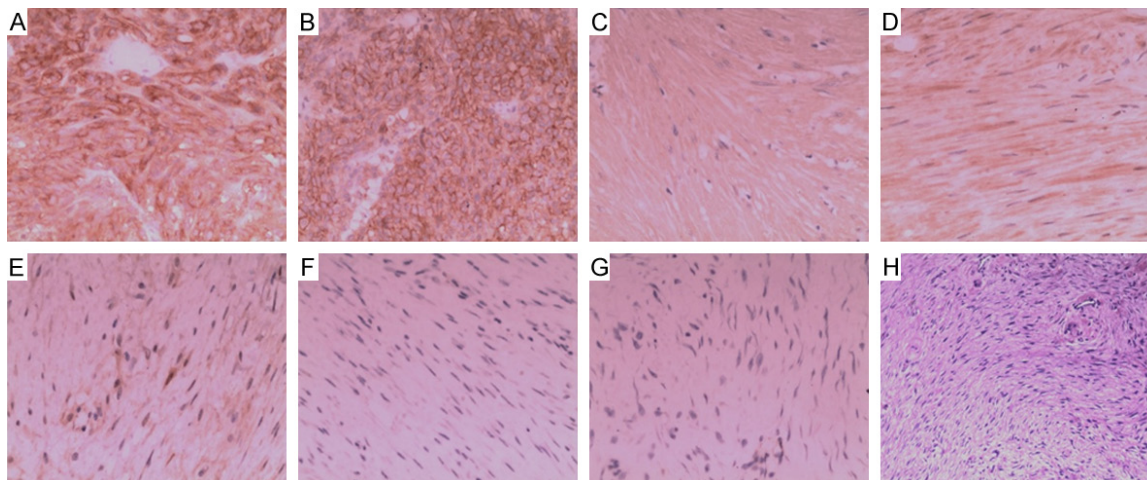
GIST resection beds mimicking recurrent GIST. It would be useful to be aware of the possibility of different tumor types after removal of gastrointestinal stromal tumor. To accumulate further information on these rare diseases, a central database that includes rare diseases will be necessary.

#### Case presentation

At age 54 (February 2012), a previously healthy man admitted to our hospital due to tarry black stools and anemia for one week. Computerized tomography (CT) examination revealed a 90 × 78 mm mass involving the gastric greater curvature (**Figure 1A**). Blood tests showed hemoglobin of 69 g/L. Colonoscopy found no abdominal changes. After the preoperative examina-

tion, the patient underwent partial gastrectomy via laparotomy. The resected tumor (8 × 6 × 6 cm) showed outward growth pattern and contained an ulcer of approximately 1 cm on the mucosa. Extensive blood clot was found in tumor. Microscopical examination found spindle cells with abundant collagen and no more than 5 mitoses per 50 high-power fields (HPFs). Immunohistochemical staining results showed that the tumor cells were positive for CD117 (**Figure 2A**), Dog-1 (**Figure 2B**) and VIM, but negative for CD34, S-100, desmin and smooth muscle actin (SMA). Based on these results, a final diagnosis of GIST with a medial grade malignant potential was made. Post-operatively, this man recovered well from his surgery and was commenced on imatinib 400 mg daily.

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**Figure 2.** Immunohistochemical staining and histopathology of the tumor cells. CD117 (A) and DOG-1 (B) were diffusely and strongly positive in tumor cells ( $\times 200$ ). SMA (C) and S-100 protein (D) were diffusely positive in tumor cells ( $\times 200$ ).  $\beta$ -catenin (E) was weakly positive in tumor cells ( $\times 200$ ). Immunostaining for CD117 (F) and SMA (G) were not detected ( $\times 200$ ). Histopathology of the tumor cells (H) ( $\times 100$  magnification microscope).

At age 55 (March 2013), an asymptomatic mass ( $24 \times 20$  mm) involving the gastric greater curvature and posterior wall was identified on a surveillance CT (**Figure 1B**). The patient was treated with laparotomy without any hesitation since clinical impression was a recurrent tumor. At laparotomy, the greater curvature lesion adjacent to the pylorus was excised via wedge resection. Immunohistochemical staining results showed that the tumor cells were positive for SMA (**Figure 2C**), VIM, CD68 and S-100 (**Figure 2D**), but negative for CD117, CD34, desmin and Dog-1. Based on these results, a final diagnosis of leiomyoma was made.

At age 56 (February 2014), a localized abdominal tumor (5 cm in diameter) with slight enhancement involving the gastric lesser curvature adjacent to the ligamentum hepatogastricum and a nodule in front of gastric lesser curvature (1 cm in diameter) were detected in routine CT scanning (**Figure 1C**). At laparotomy, a firm greater curvature lesion with the same size described in CT-scan was excised via partial gastrectomy. A lesser omentum lesion measuring  $1.5 \times 1.5$  cm was excised. Microscopic examination of the tumor showed that nondysplastic fibroblasts proliferating in the gastric lesser curvature. Immunohistochemical staining results showed that the tumor cells were positive for  $\beta$ -catenin (**Figure 2E**), but negative for CD117 (**Figure 2F**), CD34, desmin, Dog-1, S-100, SMA (**Figure 2G**) and VIM. Based on

these results, a final diagnosis of intra-abdominal fibromatosis was made.

At age 57 (March 2015), the patient was admitted again to our hospital with mild upper abdominal pain. CT examination revealed a low-dense, homogeneous tumor (5 cm in diameter) with moderate enhancement in the left upper abdominal cavity (**Figure 1D**). At laparotomy, three colonic abnormalities were found: (1) a firm mass ( $8 \times 5 \times 6$  cm) involving the transverse colon and descending colon; (2) a firm mesocolon nodule ( $2 \times 2$  cm) which appeared to originate from transverse colon, involving proximal jejunum (25-cm distal to the ligament of Treitz) and partially obstructing the involved parts of jejunum; and (3) a firm nodule ( $2 \times 2$  cm) which closed to mesocecum, involving ascending colon. Histopathology showed a tumor mass composed of spindle shaped fibrocytic/fibroblastic like cells amongst intervening collagen with low mitotic rate (less than 1 per 50 HPFs) (**Figure 2H**). However, a definitive uniform diagnosis could not be made without Immunohistochemical results. The possible differential diagnose of this soft-tissue tumor was colonic fibromatosis.

Imatinib was continued 400 mg daily, with brief cessation during the peri-operative period, as metastatic GIST remained radiologically stable. The postoperative course was uneventful without adjuvant therapy and no local recurrence has been noted as of August 2015.

### Discussion

The patient we describe had four types of gastrointestinal tumors: (1) gastric GIST, (2) gastric leiomyoma, (3) gastric fibromatosis, and (4) colonic fibromatosis. The gastric lesions were first found in 2013 when the patient was 55 years old. Subsequently, she underwent a laparotomy annually for asymptomatic or symptomatic abdominal mass. Imatinib was continued 400 mg daily. The patient is presently asymptomatic with a recent abdominal CT examination showed postoperative changes only. No member of his family was similarly affected.

GIST is the most common mesenchymal tumors of the GI tract, most frequent primary site of which is the stomach (60-70%). GIST may present with massive gastrointestinal hemorrhage or an acute abdomen but may also be asymptomatic. It is usually secondary to trauma or hormonal stimulation or associated with familial polyposis coli or Gardner's syndrome [9] and the majority contains KIT or PDGFRA-activating mutations [10]. GIST typically exhibits immunohistochemical positivity for vimentin (VIM) in almost all cases, for CD117 (c-Kit) in 95% and for CD34 in 60-70% (80% in gastric location) [11]. Dog1, especially for KIT negative GISTs, had a good sensitivity and specificity as a kind of newly discovered marker [12]. Surgical resection is considered the standard treatment for removing these tumors. While recurrence is frequent, approximately 50% in 5 years following curative resection of the primary tumor [13]. A number of soft tissue neoplasms share many similarities in the imageological, morphological and immunophenotypic profiles with GIST. Leiomyoma and IAF might be confused with recurrent GIST for similar imaging findings and the overlap in immunophenotypic profiles such as c-Kit, SMA and desmin [14].

Leiomyomas are the most frequent benign tumors of the GI and asymptomatic in general. When symptoms are present, they most frequently consist of abdominal pain, hemorrhage, and acute intestinal obstruction with or without intussusception. Enucleation or tumor-averting method can be chosen to remove gastric leiomyomas. In contrast, more-aggressive procedures including wedge resection or gastrectomy with a negative margin were performed for the malignant potential of GISTs [15]. Leiomyoma of the gastrointestinal tract mimic

a GIST were reported previously [7, 8]. SMA is stained commonly in leiomyoma. More importantly, leiomyoma did not stain for C-Kit in most cases. For C-Kit-negative GIST cases, gene mutation and cytogenetic analyses were suggested to distinguish the leiomyoma and Kit-negative cases [8]. However, Deshpande et al. encountered esophageal leiomyoma with a high proportion of Kit-positive and DOG1-positive spindle-shaped cells, makes it more difficult to distinguish the Kit-positive leiomyoma and KIT-positive GIST [7]. In addition, Hyun Kyung et al. revealed the possibility of CT features in differentiating leiomyomas from GISTs in the gastric cardia particularly in the manner of combination [16].

Simultaneous or metachronous fibromatoses mimic a recurrence of GIST have been reported recently [3, 4]. IAF arising within or involving the GI wall are potentially misdiagnosed as a recurrence of GISTs. CT is most commonly used to investigate IAF, which may appear as a soft tissue mass that resembles a GIST. However, IAF can be differentiated from GIST on a CT image by ovoid or irregular contours, homogeneous enhancement and an absence of central necrosis [17]. In many cases, a multidisciplinary approach including surgery, chemotherapy and radiation therapy was adopted for IAF. Surgery remains a reasonable first treatment for operable tumors but may lead to high rates of morbidity and recurrence [18]. Therefore, pathological diagnosis is required to optimize the surgical approach and preclude unnecessary radical surgery. In IAFs, many features, such as large size, infiltration of adjacent structures and mitotic activity can cause diagnostic confusion with recurrent GISTs. In addition, IAFs may show analogous degree of mitotic activity with malignant GISTs and their immunophenotypes may vary and overlap. C-Kit staining in IAF is controversial. Previous studies have reported that most IAF's do not express a demonstrable level of C-Kit, while Yantiss et al. reported that up to 75% of cases were C-Kit positive [5]. However, fibromatoses were stain for positive for  $\beta$ -catenin [19] but usually not stain for CD34 and S-100, while CD34 and S-100 protein positivity were seen in GIST but not  $\beta$ -catenin. Differences in those immunophenotypic profiles might be helpful in distinguishing between them [5, 20, 21]. In addition, usefulness of mutational analysis has been corroborated in

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diagnosing  $\beta$ -catenin-negative mesenteric desmoids [22].

To our knowledge, no patient with the 3 gastrointestinal tumor types we encountered, GISTs, leiomyomas and IAF has ever been reported. Pathological diagnosis is required to optimize the surgical approach and preclude unnecessary radical surgery. Moreover, excluding diagnosis of recurrence of GIST is crucial for further management of our patients due to the increasing use of imatinib in the treatment of advanced GIST. In rare instance as illustrated in our case, more than one type of gastrointestinal tumors mimicking recurrent gastrointestinal stromal tumor should be considered. The current case highlights the need for careful consideration of leiomyomas and IAF when a rapidly growing spindle cell tumor is encountered in a post-GIST patient.

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### Disclosure of conflict of interest

None.

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### References

- [1] Nishida T, Shirao K, Sawaki A, Koseki M, Okamura T, Ohtsu A, Sugiyama T, Miyakawa K and Hirota S. Efficacy and safety profile of imatinib mesylate (ST1571) in Japanese patients with advanced gastrointestinal stromal tumors: a phase II study (STI571B1202). *Int J Clin Oncol* 2008; 13: 244-251.
- [2] Burke AP, Sobin LH, Shekitka KM, Federspiel BH and Helwig EB. Intra-abdominal fibromatosis. A pathologic analysis of 130 tumors with comparison of clinical subgroups. *Am J Surg Pathol* 1990; 14: 335-341.
- [3] Jiang D, He D, Hou Y, Lu W, Shi Y, Hu Q, Lu S, Xu C, Liu Y, Liu J, Tan Y and Zhu X. Subsequent intra-abdominal fibromatosis mimicking recurrent gastrointestinal stromal tumor. *Diagn Pathol* 2013; 8: 125.
- [4] Lee CK, Hadley A, Desilva K, Smith G and Goldstein D. When is a GIST not a GIST? A case report of synchronous metastatic gastrointestinal stromal tumor and fibromatosis. *World J Surg Oncol* 2009; 7: 8.
- [5] Yantiss RK, Spiro IJ, Compton CC and Rosenberg AE. Gastrointestinal stromal tumor versus intra-abdominal fibromatosis of the bowel wall: a clinically important differential diagnosis. *Am J Surg Pathol* 2000; 24: 947-957.
- [6] Machonko A. [Benign tumors of the stomach and duodenum]. *Med Dosw* 1968; 38: 107-128.
- [7] Deshpande A, Nelson D, Corless CL, Deshpande V and O'Brien MJ. Leiomyoma of the gastrointestinal tract with interstitial cells of Cajal: a mimic of gastrointestinal stromal tumor. *Am J Surg Pathol* 2014; 38: 72-77.
- [8] Kuhlitz J, Sander B, Golas MM, Gunawan B, Schulze T, Schulten HJ, Wardelmann E and Fuzesi L. Differential diagnosis of gastrointestinal leiomyoma versus gastrointestinal stromal tumor. *Int J Colorectal Dis* 2006; 21: 84-88.
- [9] Al-Nafussi A and Wong NA. Intra-abdominal spindle cell lesions: a review and practical aids to diagnosis. *Histopathology* 2001; 38: 387-402.
- [10] Kara T, Serinsoz E, Arpacı RB, Gubur O, Orekiç G, Ata A, Colak T and Arıcan A. Contribution of DOG1 expression to the diagnosis of gastrointestinal stromal tumors. *Pathol Res Pract* 2013; 209: 413-417.
- [11] Bosoteanu M, Bosoteanu C, Deacu M and Aschie M. Differential diagnosis of a gastric stromal tumor: case report and literature review. *Rom J Morphol Embryol* 2011; 52: 1361-1368.
- [12] Sui XL, Wang H and Sun XW. Expression of DOG1, CD117 and PDGFRA in gastrointestinal stromal tumors and correlations with clinicopathology. *Asian Pac J Cancer Prev* 2012; 13: 1389-1393.
- [13] Fletcher CD, Berman JJ, Corless C, Gorstein F, Lasota J, Longley BJ, Miettinen M, O'Leary TJ, Remotti H, Rubin BP, Shmookler B, Sobin LH and Weiss SW. Diagnosis of gastrointestinal stromal tumors: A consensus approach. *Hum Pathol* 2002; 33: 459-465.
- [14] Mikami T, Nemoto Y, Numata Y, Hana K, Nakada N, Ichinoe M, Murakumo Y and Okayasu I. Small gastrointestinal stromal tumor in the stomach: identification of precursor for clinical gastrointestinal stromal tumor using c-kit and alpha-smooth muscle actin expression. *Hum Pathol* 2013; 44: 2628-2635.
- [15] Emory TS, Sobin LH, Lukes L, Lee DH and O'Leary TJ. Prognosis of gastrointestinal smooth-muscle (stromal) tumors: dependence

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- on anatomic site. *Am J Surg Pathol* 1999; 23: 82-87.
- [16] Yang HK, Kim YH, Lee YJ, Park JH, Kim JY, Lee KH and Lee HS. Leiomyomas in the gastric cardia: CT findings and differentiation from gastrointestinal stromal tumors. *Eur J Radiol* 2015; 84: 1694-1700.
- [17] Zhu H, Chen H, Zhang S and Peng W. Intra-abdominal fibromatosis: differentiation from gastrointestinal stromal tumour based on biphasic contrast-enhanced CT findings. *Clin Radiol* 2013; 68: 1133-1139.
- [18] Kasper B, Strobel P and Hohenberger P. Desmoid tumors: clinical features and treatment options for advanced disease. *Oncologist* 2011; 16: 682-693.
- [19] Montgomery E, Torbenson MS, Kaushal M, Fisher C and Abraham SC. Beta-catenin immunohistochemistry separates mesenteric fibromatosis from gastrointestinal stromal tumor and sclerosing mesenteritis. *Am J Surg Pathol* 2002; 26: 1296-1301.
- [20] Monihan JM, Carr NJ and Sobin LH. CD34 immunorexpression in stromal tumours of the gastrointestinal tract and in mesenteric fibromatoses. *Histopathology* 1994; 25: 469-473.
- [21] Rodriguez JA, Guarda LA and Rosai J. Mesenteric fibromatosis with involvement of the gastrointestinal tract. A GIST simulator: a study of 25 cases. *Am J Clin Pathol* 2004; 121: 93-98.
- [22] Huss S, Nehles J, Binot E, Wardelmann E, Mittler J, Kleine MA, Kunstlinger H, Hartmann W, Hohenberger P, Merkelbach-Bruse S, Buettner R and Schildhaus HU. beta-catenin (CTNNB1) mutations and clinicopathological features of mesenteric desmoid-type fibromatosis. *Histopathology* 2013; 62: 294-304.