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CASE REPORT

Primary leiomyosarcoma of the colon

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Abstract Primary leiomyosarcomas of the gastrointestinal (GI) tract are extremely rare and highly aggressive neoplasms, and only a small number of true cases have been reported since the concept of GI stromal tumors was established. Here, we report a case of a primary leiomyosarcoma of the transverse colon. A 46-year-old Japanese male with a large mass in the right upper abdomen was admitted to our hospital. Computed tomography and magnetic resonance imaging revealed long segments of wall thickening of the transverse colon with large consecutive tumors measuring 12 cm in diameter. A projecting irregular mass with marked mucosal necrosis was found on colonoscopy. Pathological examination revealed a spindle cell tumor growing circumferentially and transmurally to replace the muscularis propria in the transverse colon. The spindle cells were positive for smooth muscle actin, and negative for KIT, CD34, DOG-1, and S-100 protein. The patient has shown repeat recurrence in spite of sufficient surgical excision being promptly performed.

Keywords Leiomyosarcoma · Colonic mesenchymal tumor · GIST

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Introduction

Primary leiomyosarcomas of the gastrointestinal (GI) tract are extremely rare neoplasms. Many mesenchymal tumors previously reported as leiomyosarcomas in the era of pre-gastrointestinal stromal tumors (GISTs) were reviewed and proved to be GISTs [1]. At present, most GI mesenchymal tumors are differentiated into GISTs, smooth muscle tumors, and schwannomas. Immunohistochemically, smooth muscle tumors are positive for smooth muscle actin (SMA) and desmin, negative for GIST markers—KIT, CD34, and DOG1, and negative for the schwannoma marker S100-protein [2, 3]. Most mesenchymal tumors of the colon are leiomyomas; GISTs are extremely rare in the colon, and leiomyosarcomas of the colon are even rarer [4]. Only a small number of colonic leiomyosarcomas have been reported and all of them were highly aggressive and associated with a poor prognosis [5, 6]. Here, we describe a rare case of a primary leiomyosarcoma of the transverse colon.

Case report

A 46-year-old Japanese male had experienced intermittent abdominal pain, appetite loss, and body weight loss since November 2012. He was admitted to our hospital in March 2013 because his abdominal pain was gradually worsening,

and watery diarrhea appeared. On physical examination, a huge mass with tenderness was palpable in the right upper abdomen. Laboratory tests revealed iron-deficiency anemia, leukocytosis (14,000/mL) and raised C-reactive protein (11 mg/dL). He was negative for sIL2R, carcinoembryonic antigen, and carbohydrate antigen 19-9, while the neuron specific enolase level was slightly increased to 27.6 ng/mL. Computed tomography (CT) demonstrated bulky, long-segmental circumferential wall thickening of the transverse colon and a continuous bulging, solid enhancing mass measuring 12 cm in diameter outside the colonic wall. There was a low-density area, suspected of being necrosis in the mass (Fig. 1).

On magnetic resonance imaging (MRI), most of the tumor showed low intensity on T1-weighted imaging and more than half of the tumor showed high intensity on T2-weighted imaging. Colonoscopy revealed an irregular, protruding tumor with ulceration in the right transverse colon (Fig. 2). The lumen of the oral side was extended and the mucosa was diffusely ulcerated and friable. The biopsy specimens of hematoxylin and eosin (H&E) staining showed an interlacing fascicular pattern of spindled tumor cells with eosinophilic cytoplasm. Inmunohistochemically, the tumor cells were positive for α-SMA, vimentin, calponin, desmin, and negative for c-KIT, CD34, DOG-1, and S-100 protein. The tumor was diagnosed as a leiomyosarcoma based on histological and immunohistochemical findings. Right hemicolectomy with partial ileotomy was performed, because the ileum at 70 cm toward the oral side of the ileocecal valve was attached to the tumor. On gross examination, a solid, multinodular whitish tumor grew circumferentially and transmurally in the transverse colon with a subserosal exophytic mass measuring 118 mm in maximum diameter and a large polypoid mass with ulceration in the tract (Figs. 3, 4). Microscopically, the tumor was composed of spindle cells with eosinophilic cytoplasm and slightly atypical nuclei (Fig. 5). The mitotic count was

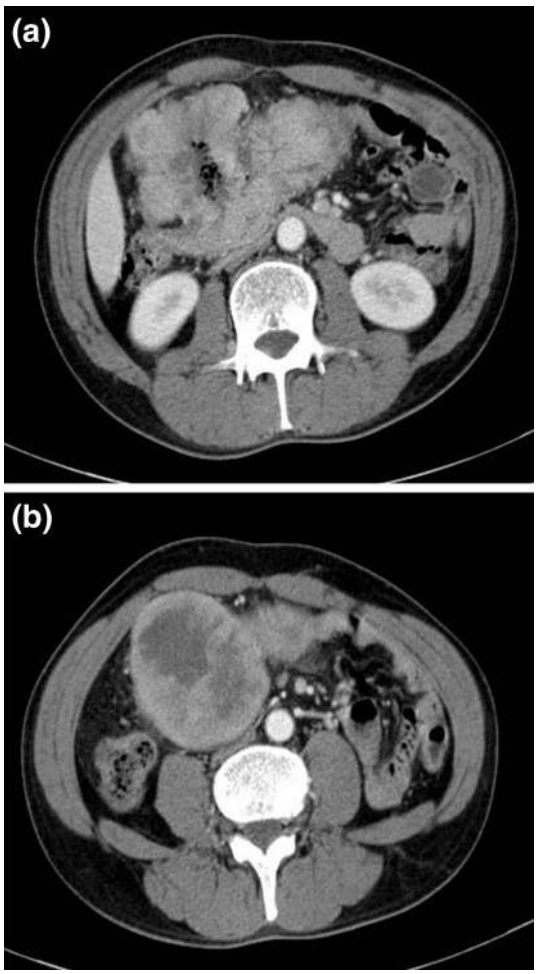

Fig. 1 **a** Contrast-enhanced CT showed diffuse, homogeneous, and lobulated wall thickening of the right transverse colon. **b** Contrast-enhanced CT caudad to **a** showed a solid mass with a central low-density area suggesting necrosis

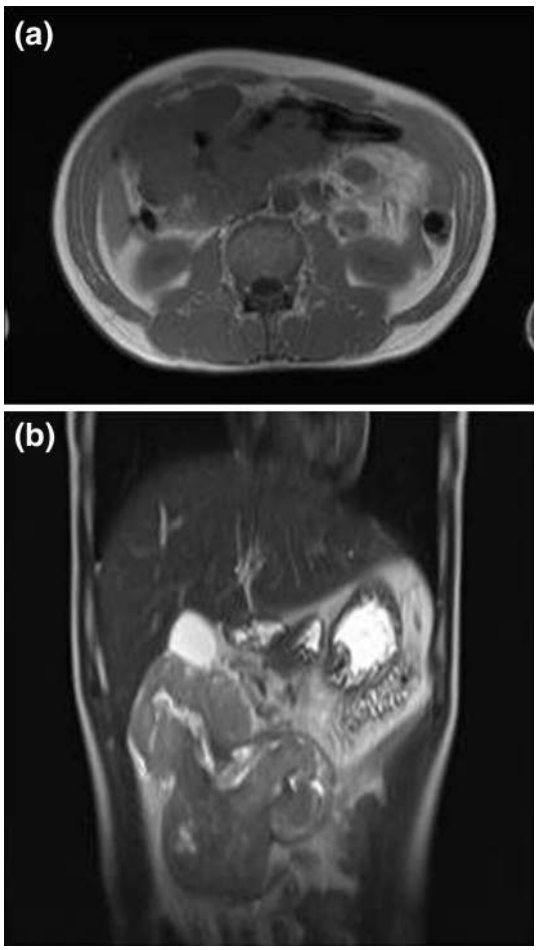

Fig. 2 **a** On magnetic resonance imaging, axial T1-weighted imaging showed a homogeneous lesion isointense to muscle. **b** Sagittal T2-weighted imaging showed a heterogeneous signal

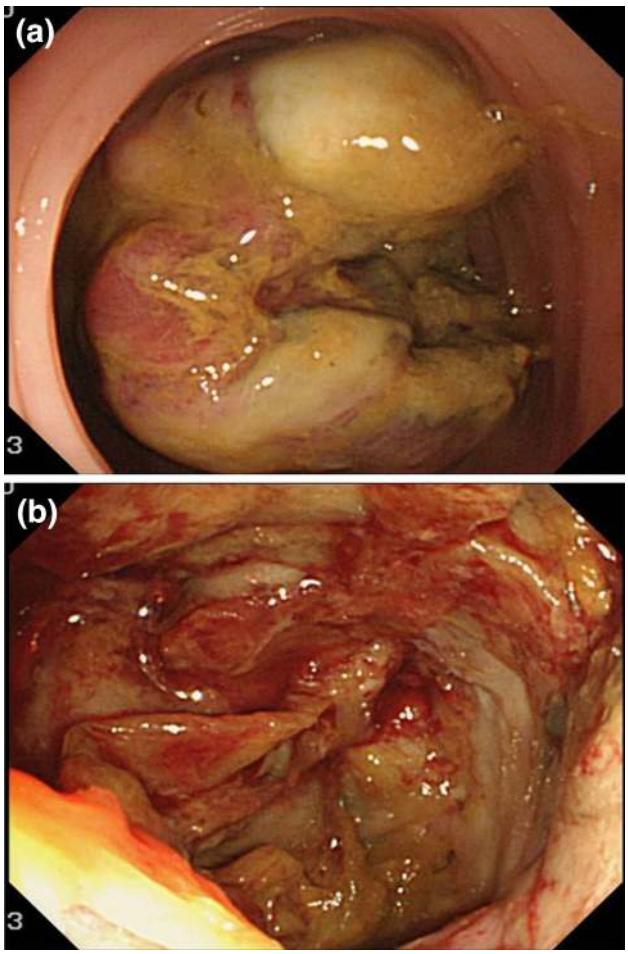

Fig. 3 **a** Colonoscopy showed a large polypoid mass with ulceration in the right transverse colon. **b** The oral side of **a** showed dilatation of the lumen with diffuse ulceration of the mucosa

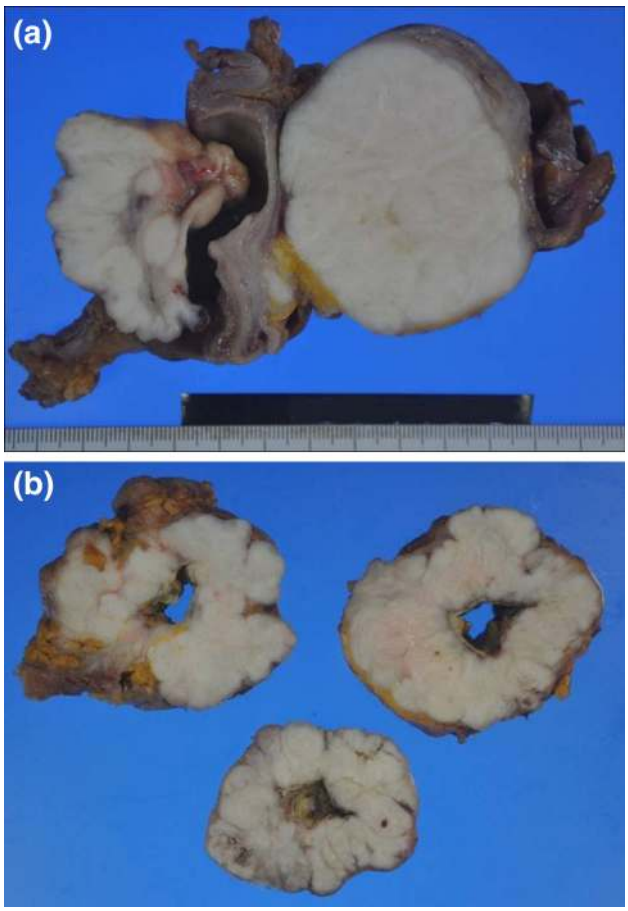

Fig. 4 **a** Gross specimen showed a whitish, multinodular, extraluminal, large tumor and intraluminal polypoid mass. **b** The tumor also grew circumferentially and transmurally in the transverse colon

61 per 10 high-power fields. On immunohistochemistry, the tumor cells were strongly positive for α-SMA and muscle actin (HHF35), positive for calponin, and negative for c-KIT, CD34, DOG1, pan-keratin, and S-100 protein. The circumferential tumor showed continuity with the muscularis propria of the transverse colon, suggesting that the leiomyosarcoma was of muscularis propria origin. There was no regional lymph node metastasis.

In spite of complete resection, peritoneal recurrence in the pelvis occurred 9 months later, and the recurrent tumor was surgically removed. After 4 months, another recurrent tumor appeared on the surface of the liver, and was also removed. The patient is now being followed up carefully.

Discussion

Primary leiomyosarcomas of the GI tract became extremely rare neoplasms after Hirota et al. reported the oncogenic role of KIT in GISTs in 1998 [1]. Most mesenchymal tumors of the GI tract which were previously diagnosed as leiomyomas, leiomyoblastomas, or leiomyosarcomas are now classified as GISTs. GISTs are diagnosed based on immunohistochemical positivity for KIT, CD34, and DOG1, and sometimes with molecular evaluations of activating mutations in the *KIT* or *PDGFRA* gene [7]. Immunohistochemical features of smooth muscle tumors are positivity for SMA and desmin, and negativity for GIST markers—KIT, CD34, and DOG1 [8]. The proposed cellular origin of GISTs is the interstitial cells of Cajal in the muscularis propria, while the proposed cellular origin of smooth muscle tumors is the fibers of the muscularis mucosae and muscularis propria. GISTs span the clinical spectrum from benign to malignant, and the prognosis is highly dependent on tumor size and mitotic activity [9]. Smooth muscle tumors of the GI tract are divided into leiomyomas and leiomyosarcomas. Leiomyomas are classified into polypoids and intramural leiomyomas [10]; the former originates from the muscularis mucosae and the latter originates from the muscularis propria. In a large series of GISTs and smooth muscle tumors reported by the

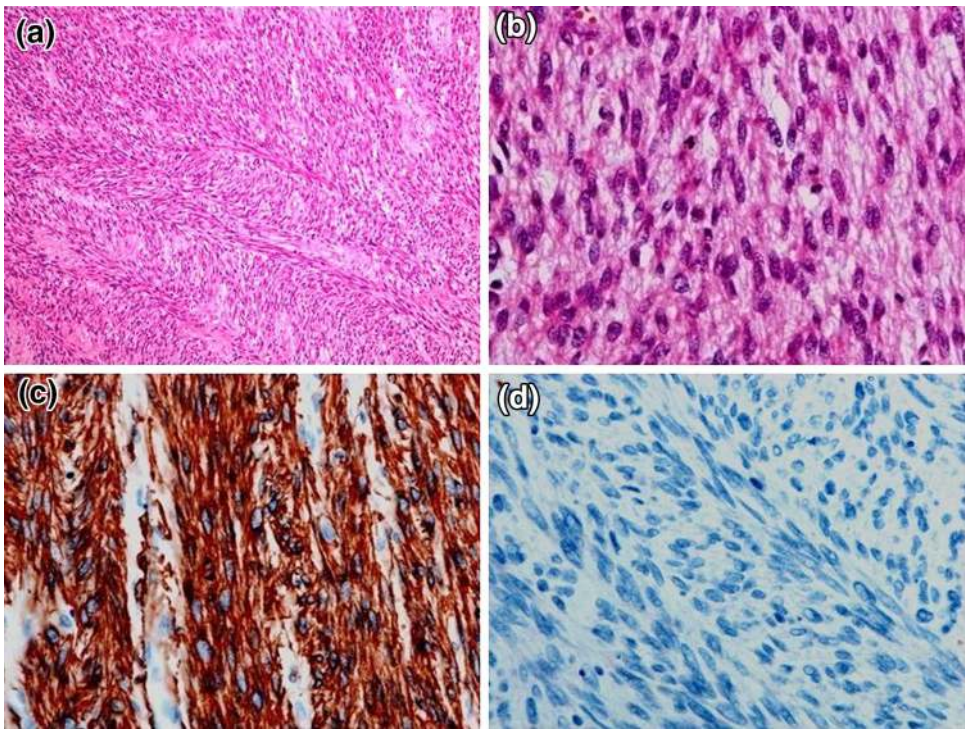

Fig. 5 **a** Microscopic photograph of the tumor showed a fascicular esoinophilic spindle cell tumor. **b** There was marked mitosis on high-power view (H&E staining), and (**c**) strong expression of SMA, (**d**) while it was negative for KIT (immunostaining)

Armed Forces Institute of Pathology, >90 % of mesenchymal tumors were GISTs, and true smooth muscle tumors were rare [8, 11–13]. However, in a series of 262 GI mesenchymal lesions in a single institute reported by Agaimy and Wünsch, GISTs comprised 54 %, while smooth muscle tumors comprised 32 %, representing the second most common mesenchymal tumor of the GI tract [10]. As most of the series was investigated using surgical resected materials or sometimes endoscopically resected materials, the true incidence of smooth muscle tumors of the GI tract is uncertain, but leiomyosarcomas are extremely rare neoplasms, with only approximately 60 cases reported in the English literature in the post-GIST era [5, 6]. Many leiomyosarcomas reported before 1998 appeared to be GISTs. Leiomyosarcomas closely resemble GISTs both macroscopically and histologically, which is why immunohistochemistry and sometimes genetic searches may be necessary for differentiation; however, there are various differences. GISTs occur most commonly in the stomach (60–70 %), followed by the small intestine (20–25 %), the rectum and anus (4 %), and are rare in the esophagus (1 %) and colon (1 %). In contrast, leiomyosarcomas occur preferentially in the small intestine (45 %) and colon (38 %), and are extremely rare in the stomach and esophagus [5, 6]. Leiomyomas, which are benign counterparts, occur chiefly in the esophagus and colon. According to Miettinen et al., the border between leiomyomas and leiomyosarcomas is sharp, and they raised doubts about the malignant transformation of benign leiomyomas into leiomyosarcomas, which was reported in the pre-GIST era [12]. Yamamoto et al. proposed the classification of GI smooth muscle tumors into leiomyomas, smooth muscle tumors of undetermined malignant potential, and leiomyosarcomas [6]. They reviewed and analyzed the prognosis of patients with leiomyosarcoma of the GI tract. They reported an estimated 5-year overall survival rate of 51.6 %, a tumor size of >5 cm as the only significant poor prognosis factor, and mitosis and the primary site were not risk factors. The most common mesenchymal tumors of the colon are leiomyomas, and they appear as small, polypoid, intraluminal masses originating from the muscularis mucosae and most of them are endoscopically removed [4]. Only 12 adult cases of primary colonic leiomyosarcomas have been reported. They included 8 males and 4 females with an average age of 66 years (range 36–94 years). Their locations were the cecum in 1 case, ascending colon in 3 cases, transverse colon in 1 case, descending colon in 2 cases, sigmoid colon in 4 cases, and left colon not otherwise specified in 1 case. Tumor sizes ranged from 3.2−25 cm. Their gross appearance was reported as polypoid, plaque-like, Borrmann type-2-like, and intramural-infiltrating type [6]. Our case showed an intramural-infiltrating pattern with long-segmental circumferential wall thickening. Circumferential intramural-infiltrating growth replacing the muscularis propria appears to be an extremely rare and unique pattern, and we suspect this pattern is one of the characteristic growth patterns of GI smooth muscle tumors. A few cases of GISTs showing

an infiltrating pattern replacing the muscularis propria have also been reported [14]; these types of GIST were called long segmental hyperplasia of interstitial cells of Cajal, and seemed to be a special type of GIST which did not form macroscopic masses and were diagnosed by microscopic examinations.

Surgery is the standard treatment for all patients with an adult-type, localized soft tissue sarcoma [15], and surgical resection appears to be standard therapy for leiomyosarcomas of the GI tract, as most of the reported cases were diagnosed using surgically resected materials. Even after adequate resection, many of them recur. There is no standard therapy for recurrent or metastatic tumors. Conventional chemotherapy for soft tissue sarcomas is based on anthracyclines as the first-line treatment. Doxorubicin plus dacarbazine is an option for multi-agent first-line chemotherapy of leiomyosarcomas [15]; however, leiomyosarcomas are relatively insensitive to chemotherapy [5]. Surgery for responding metastases may be offered as an option as in our case. Imatinib, a multi-targeted tyrosine kinase inhibitor, is highly effective for GISTs [16], and sunitinib, another multi-targeted tyrosine kinase inhibitor is also active against imatinib-refractory GISTs [17]. Unfortunately, as imatinib is not effective for leiomyosarcomas such as other adult-type soft tissue sarcomas [18], and the efficacy of sunitinib is also limited [19, 20], a differential diagnosis of these two tumors is essential.

There is no systematic review of the radiological imaging features of GI leiomyosarcomas, as the majority of the lesions previously reported as leiomyosarcomas of the GI tract have now been classified as GISTs. CT and MRI features of retroperitoneal and peripheral soft tissue leiomyosarcomas are non-specific. In large tumors, there is a central area of low density which demonstrates hemorrhage, necrosis, or cystic change on CT. Moderate contrast enhancement is seen at the periphery of large primary and metastatic lesions. On MRI, it is isointense to muscle on T1-weighted imaging and intermediate to hypointense to fat on T2-weighted imaging [21]. In our case, the exophytic tumor outside the colon revealed CT and MRI imaging patterns similar to retroperitoneal or peripheral leiomyosarcomas; however, our case also showed circumferential wall thickening as if imitating the muscularis propria. Radiological differential diagnoses for leiomyosarcomas include GISTs, large necrotic lymphomas, and neuroectodermal tumors; tissue-based diagnosis is necessary as these tumors are chemosensitive whereas leiomyosarcomas are not.

In conclusion, we described a case of a primary leiomyosarcoma of the transverse colon. The tumor showed long-segmental wall thickening of the transverse colon with a large extraluminal mass. Intramural-infiltrating circumferential growth replacing the muscularis propria seemed a significant feature of our case. In spite of complete resection, the patient has shown repeat recurrence.

Compliance with ethical standards

Conflict of Interest Masatoshi Kudo received honoraria for giving lectures for Banyu Yakuhin and Eisai.

Human/Animal Rights All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008(5).

Informed Consent Informed consent was obtained from the patient to be included in this report.

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