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Giant leiomyosarcoma of the rectum with lymph node metastasis: A case report and review of the literature

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ABSTRACT

INTRODUCTION: Leiomyosarcoma of the gastrointestinal tract is very rare, with a reported frequency of less than 0.1% of all malignancies of the colorectum. It is important to diagnose leiomyosarcoma definitively by immunohistochemical profiling of smooth muscle actin, desmin, and CD34. True leiomyosarcoma of the colorectum diagnosed by immunohistochemical profiling is extremely rare that only 13 reports have been published in reviews of resected gastrointestinal mesenchymal tumors after 1998. In addition, lymph node involvement is rare in patients with leiomyosarcoma. Herein we report an aggressive case of LMS in a rectosigmoid lesion with lymph node metastasis.

CASE PRESENTATION: A 76-year-old woman visited our hospital complaining of intermittent anal bleeding that had lasted 5 months. Image studies aiming at examining the cause of her anal bleeding revealed a tumor located between the right ovary, uterus, and the rectosigmoid. Histopathology of biopsied materials from the colonoscopy suggested a malignant tumor of mesenchymal origin. Surgical resection was performed with curative intent. The tumor was diagnosed as leiomyosarcoma by pathological examination. Moreover, one of the 31 regional lymph nodes retrieved was metastasized by leiomyosarcoma. Eight months later, follow-up CT scans revealed multiple recurrent lesions in the liver and peritoneum. Despite systematic chemotherapy, she deceased 12 months after the surgery.

CONCLUSION: It is crucial to diagnose leiomyosarcoma precisely based on immunohistochemistry, and thereby distinguish it from GIST. Although lymph node metastasis is rare, lymphadenectomy appears to be important for high-risk LMSs to perform R0 resection. Further investigation on leiomyosarcoma cases so far is required to establish standard treatment strategies.

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1. Introduction

Leiomyosarcoma (LMS) of the rectum was first described by Scott in 1923 [1]. In the former classification of smooth muscle tumor in the gastrointestinal tract, LMS was not distinguished from gastrointestinal stromal tumor (GIST). Since the discovery of the oncogenic role of KIT in 1998 [2], GISTs have been differentiated from other mesenchymal tumors such as leiomyomas, leiomyoblastomas, and LMSs [3]. Although 5% of tumors with

the clinicopathologic features of GIST lack KIT expression, it is important to diagnose LMS definitively by immunohistochemical profiling of smooth muscle actin (SMA), desmin, and CD34 [4].

True LMS of the colorectum diagnosed by immunohistochemical profiling is extremely rare, with a reported frequency of less than 0.1% of all malignancies of the colorectum [5]; only 13 reports with immunohistochemical definition which was performed properly have been published in reviews of resected gastrointestinal mesenchymal tumors after 1998 [6–10]. Furthermore, unlike adenocarcinomas, nodal involvement in LMS is unusual [11]. Herein we report an aggressive case of LMS in a rectosigmoid lesion with lymph node metastasis.

Abbreviation: LMS, Leiomyosarcoma; GIST, gastrointestinal stromal tumor; SMA, smooth muscle actin; HPF, high-power field.

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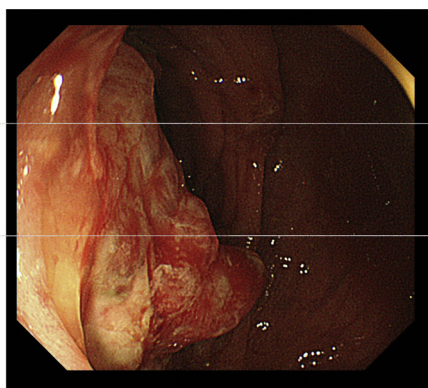


Fig. 1. The colonoscopy showed an elevated tumor with central ulceration in the rectosigmoid.



Fig. 2. An axial view of the abdominal CT scan. A giant tumor was found in the space surrounded by the rectosigmoid segment, uterus, and right ovary.

2. Case presentation

A 76-year-old woman visited our hospital complaining of intermittent anal bleeding that had lasted 5 months. An elevated tumor with central ulceration was found 10 cm from the anal verge by colonoscopy (Fig. 1), and biopsy specimens revealed a spindle cell tumor. The MIB-1 labeling index was high (80%), suggesting a high-grade sarcoma. Abdominal CT scan revealed a 10 cm mass in the rectosigmoid that invaded the uterus (Fig. 2). No distant metastases were observed. Laboratory tests revealed low-grade anemia (serum hemoglobin 12.8 g/dl), but no other abnormalities were noted; serum carcinoembryonic antigen and carbohydrate antigen 19-9 levels were also normal (Table 1).

Surgical resection with curative intent required rectal anterior resection with appendectomy, total hysterectomy, and bilateral salpingo-oophorectomy due to extensive inflammation involving the appendix, uterus, right ovary, and right fallopian tube. The excised mass was 110 × 80 × 60 mm in size. Routine hematoxylin and eosin staining showed proliferation of spindle-shaped tumor cells with enlarged nuclei and eosinophilic cytoplasm (Fig. 3). Immunohistochemically, the tumor was positive for desmin and SMA, whereas c-kit, DOG1, CD34, and S-100 protein were not expressed (Fig. 4). The tumor was of high cellularity, with up to 10 mitoses per high-power field (HPF) and variable areas of necrosis. Direct invasion was histologically proven only in the right ovary, but not in the uterus and right fallopian tube. All surgical margins were negative, and one of the 31 lymph nodes retrieved was metastasized by LMS.

Her postoperative course was uneventful. However, 8 months after the surgery, follow-up CT scanning revealed peritoneal

Table 1
Result of Laboratory Tests.

Variable	Unit		Range
WBC	×1000/μl	10.1	3.5–9.80
Hb	g/dl	12.7	11.0–15.0
Hct		40.4%	38–42%
Plt	×10,000/μl	47.8	15.0–45.0
TP	g/dL	6.1	6.5–8.0
Alb	g/dL	3.3	3.7–5.2
ChE	U/L	279	180–420
AST(GOT)	U/L	20	10–40
ALT(GPT)	U/L	17	5–40
γ-GTP	U/L	58	5–24
T-Bil	mg/dL	0.6	0.2–1.0
D-Bil	mg/dL	0.1	0.1–0.4
Ca	mg/dL	8.7	4.5–5.1
IP	mg/dL	3.0	2.3–4.0
BUN	mg/dL	12.9	8–20
Cre	mg/dL	0.59	0.5–0.9
Na	mEq/L	139	135–146
K	mEq/L	4.3	3.4–4.8
Cl	mEq/L	106	98–108
Amy	U/L	47	50–160
CK	U/L	116	42–138
CRP	mg/dL	0.83	<0.30
CEA	ng/ml	2.5	<5.0
CA19-9	U/ml	19	<7.0
PT		100%	81.0–131.6%
PT-INR		0.93	1.0
APTT	sec	27.6	30–40

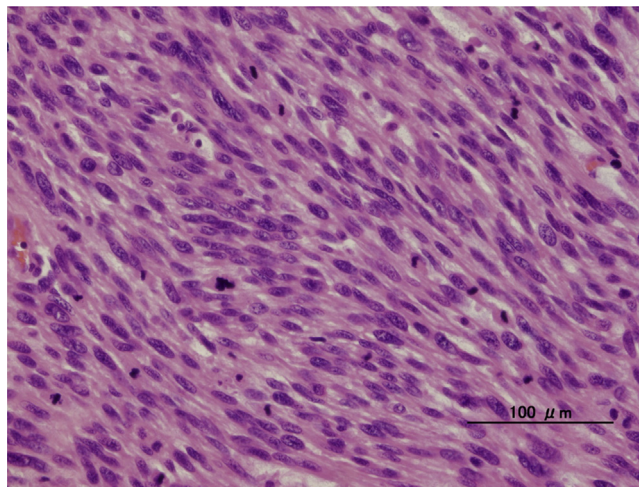


Fig. 3. Hematoxylin-eosin staining of the tumor revealed spindle-shaped cells (original magnification: 40×).

and liver metastases. Palliative chemotherapy using gemcitabine (800 mg/m²) could not control disease progression, and she died 12 months after the surgery.

3. Discussion

Since radiological differentiation between LMS and other mesenchymal tumors is difficult, the final diagnosis needs to be confirmed by postoperative pathological examination. The most definitive feature of LMS is immunohistochemical positivity for desmin and SMA, and negativity for DOG 1, CD34, S-100 protein, and c-kit. True LMS resected completely and with tumor free margins is extremely rare, with only 13 reported cases [6–10]. The clinicopathological profiles of these cases and our patient are reviewed in Table 2. The tumors ranged 20–106 mm in size, with 5–100 mitoses per 50 HPFs in the previous cases. To the best of

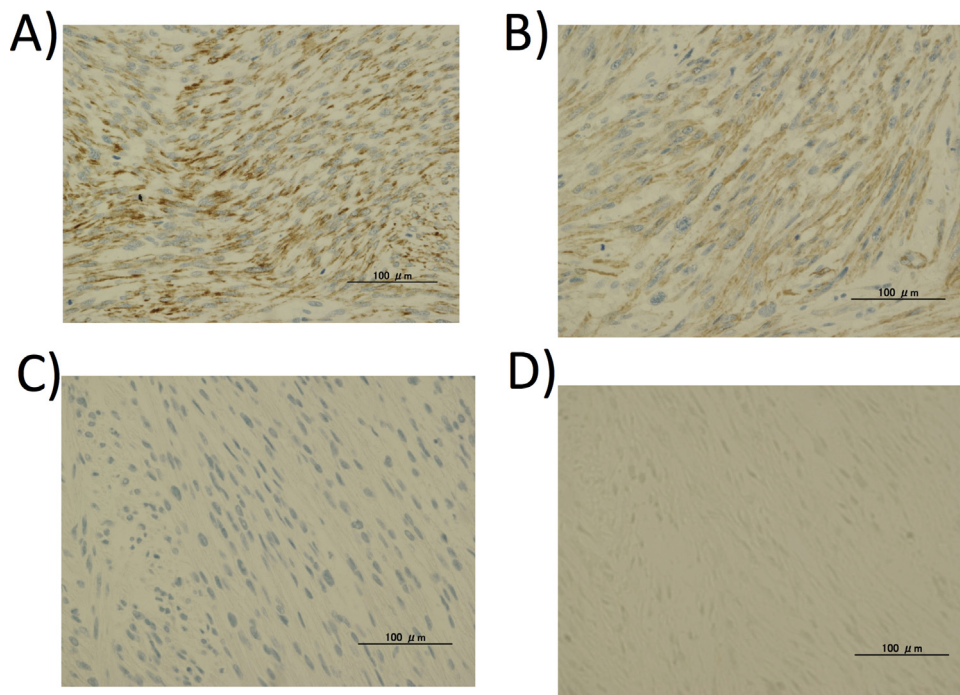


Fig. 4. Immunohistochemical staining of the tumor. (A) Desmin, (B) IA-4, (C) c-kit, and (D) DOG1 (original magnification: 40×).

our knowledge, LMS in the current study is the largest found the rectum, with the highest mitotic index.

The standard treatment of LMS is complete removal of the tumor [12]. Since regional lymph node involvement has not been reported in colorectal LMS [13], the role of extended lymphadenectomy in LMS is controversial [11]. Some authors have suggested that residual lymph node dissection should be considered in patients with enlarged nodes discovered during the surgical procedure [14,15]. Given that lymph nodes can be metastasized as in our case, lymphadenectomy may be recommended for complete removal of giant LMSs and/or LMSs with prominent mitosis.

The accurate identification and pathologic differentiation between GIST and LMS in the gastrointestinal tract are important because of the excellent response rate of GIST to molecular targeted therapy using tyrosine kinase inhibitors [16,17]. Since the five-year relapse-free survival rate has been reported to be 65%, which is longer than those who did not undergo adjuvant chemotherapy, patients with high-risk GIST are recommended to receive adjuvant imatinib after the complete resection of the tumor [18]. Additionally, interruption of treatment with imatinib should not be recommended unless patients experience toxic side effects [19]. Studies have revealed that the use of imatinib for palliative chemotherapy is also effective because the two-year progression free survival (PFS) was 75% with the use of standard imatinib dose in patients with unresectable or metastatic GIST [20,21]. In contrast, it is difficult to assess the efficacy of palliative treatments of LMS due to the paucity of published reports [22]. Doxorubicin, ifosfamide, dacarbazine, and gemcitabine are commonly used in first-line chemotherapeutic regimens, although standardized chemotherapy with currently available agents has not yet been established for LMS. Additionally, gemcitabine and docetaxel are used as second-line therapy in patients with LMS [23]; however, response rates of LMS are usually 10%–25% in palliative chemotherapy [24]. For these reasons, the two-year PFS rate is still reported to be approximately 45%, which is poorer than the prognosis of patients with GIST [25]. Furthermore, the overall survival of LMS is poor and is reportedly 20%–40% at 5 years [16,26]. Several reports

have demonstrated that large tumor size (>5 cm) and high levels of mitotic activity (>10/50 HPFs) are unfavorable prognostic factors in LMS [11,12,14]. In the present case, a large tumor comprising hyperproliferative cells suggested an unpromising outcome at the time of diagnosis; she experienced early relapse, and only survived an additional 3 months despite chemotherapy with gemcitabine.

4. Conclusion

In conclusion, we reported a giant LMS of the rectum. It is crucial to diagnose LMS precisely based on immunohistochemistry, and thereby distinguish it from GIST. Although lymph node metastasis is rare, lymphadenectomy appears to be important for high-risk LMSs to perform R0 resection. Further investigation on LMS cases so far is required to establish standard treatment strategies.

Competing interests

The authors declare that they have no competing interests.

Sources of funding

None.

Ethical approval

Approval has been given from the university of Tokyo.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Table 2
Clinicopathological Profile of reported cases of resected leiomyosarcoma of the rectum.

Case	Author	Year of publication	Age/Gender	Tumor size (mm)	Macroscopic classification	Lymph node metastasis	Immunohistochemistry			S-100	c-kit	Mitoses /50HPFs	Prognosis
							SMA	Desmin	CD34				
1	Miettinen	2001	40/Male	35	Polypoid	Absent	+	+	-	-	45	325 M, Alive	
2	Miettinen	2001	63/Female	20	Polypoid	NS	+	+	-	-	70	191 M, Alive	
3	Miettinen	2001	52/Male	30	Intramural	NS	+	+	-	-	45	70 M, Dead	
4	Miettinen	2001	67/Female	30	Plaque-like	NS	+	+	-	-	100	61 M, Dead	
5	Miettinen	2001	79/Female	25	Polypoid	Absent	+	+	-	-	25	55 M, Dead	
6	Miettinen	2001	32/Female	23	Polypoid	Absent	+	+	-	-	100	39 M, Alive	
7	Miettinen	2001	73/Female	NS	NS	NS	+	+	-	-	100	24 M, Dead	
8	Miettinen	2001	24/Female	55	Polypoid	NS	+	+	-	-	30	NS	
9	Zbar	2004	65/Female	30	Polypoid	Absent	+	+	NS	-	5	NS	
10	Zbar	2004	61/Female	70	Polypoid	Absent	+	+	-	-	5	10 M, Dead	
11	Basu	2011	79/Female	30	Polypoid	NS	+	+	-	-	NS	NS	
12	Yamamoto	2013	88/Female	65	Ulcerated	Absent	+	+	-	-	38	24 M, Dead	
13	Ouh	2013	52/Male	106	Stenosis	Absent	+	+	-	NS	100	NS	
14	Present case	-	76/Female	110	Ulcerated	Present	+	+	-	-	250	12 M, Dead	

SMA = smooth muscle actin; HPF = high power field; NS = not stated; M = months

Author contributions

HA, HN and SI prepared the manuscript and performed the literature search.
KH, TN and KK reviewed and edited the manuscript.
MF and TW corrected and revised the manuscript.
TTanaka, JT, TK and KY treated and observed the patient.
KO, TTakano and MF provided clinical images.
TU an MF provided pathological images.
TW reviewed and edited the manuscript.
All authors read and approved the final manuscript.

Registration of research studies

This research does not involve human participants.

Guarantor

Hiroyuki Anzai.

Disclosures

Our case report is compliant with the SCARE Guidelines [27]. The paper has been reported in line with the SCARE criteria.

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