Clinical Case Report

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An estrogen receptor-positive locally aggressive smooth muscle neoplasm of the transverse colon

A case report

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Abstract

Rationale: Extrauterine leiomyomas (LMs) in women are often positive for the estrogen receptor (ER); however, almost all extrauterine leiomyosarcomas (LMSs) are negative for ER. Invasive smooth muscle neoplasms (SMNs) of the gastrointestinal tract walls are very rare and those ER statuses have not been well studied.

Patient concerns: A 48-year-old woman presented to our hospital with a 10 years history of recurrent severe abdominal pain and diarrhea lasting about an hour, with frequency of about twice per year. She was clinically diagnosed with a submucosal tumor (SMT) of the transverse colon and underwent a partial transverse colectomy.

Diagnosis: A colonoscopy revealed a 30-mm SMT in the transverse colon. A contrast abdominal computed tomography detected a 21-mm mass with significant late phase enhancement in the transverse colon and the lesion was clinically diagnosed as an SMT. Post-operative pathology confirmed a diagnosis of ER-positive locally aggressive SMN.

Interventions: The patient underwent laparoscopic partial transverse colectomy.

Outcomes: The patient received no adjuvant therapy postoperatively. The patient has remained disease-free without recurrence 13 months after the surgery.

Lessons: This is the first case of an ER-positive invasive SMN in the gastrointestinal tract. It highlights the difficulty in classifying some gastrointestinal SMNs as either LMs or LMSs and the importance of ER status in SMNs.

Abbreviations: α-SMA = α-smooth muscle actin, CT = computed tomography, ER = estrogen receptor, FNCLCC = French Federation Nationale des Centres de Lutte Contre le Cancer, GIST = gastrointestinal stromal tumor, HPF = high-power field, IMT = inflammatory myofibroblastic tumor, LM = leiomyoma, LMS = leiomyosarcoma, PEComa = perivascular epithelioid cell tumor, SMN = smooth muscle neoplasm, SMT = submucosal tumor, STUMP = smooth muscle tumor of uncertain malignant potential.

Keywords: colon, estrogen receptor, leiomyoma, leiomyosarcoma, smooth muscle tumor of uncertain malignant potential

1. Introduction

Smooth muscle neoplasms (SMNs) are mesenchymal tumors that differentiate into smooth muscle cells and comprise benign leiomyomas (LMs) and malignant leiomyosarcomas (LMSs).[1–3] SMNs are common in the uterus and are much rarer in soft tissues and the gastrointestinal tract.[1–3] It is sometimes difficult to classify a uterine SMN as either a LM or a LMS, and in this case, the neoplasm is classified as a smooth muscle tumor of uncertain malignant potential (STUMP).[1,4] Extrauterine LMs in women are often positive for the estrogen receptor (ER);[5–8] however, extrauterine LMSs are usually negative for ER.[8] Invasive SMNs of the gastrointestinal tract walls are very rare and those ER status have not been well studied. Here, we present a case of ER-positive locally aggressive SMN arising from the muscularis propria of the transverse colon.

2. Case report

A 48-year-old woman (gravida 2, para 1) presented to our hospital with a 10 years history of recurrent severe abdominal pain and diarrhea lasting about an hour, with frequency of about twice per year. Her past medical history was unremarkable with a negative history of irregular menstruation or gynecological diseases such as uterine LM and uterine LMS, and there was no family history of malignancies. Her subsequent colonoscopy revealed a 30-mm submucosal tumor (SMT) in the transverse colon (Fig. 1A). The complete blood count and examination of

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The patient has provided informed consent for publication of the case.

The authors have no conflicts of interest to disclose.

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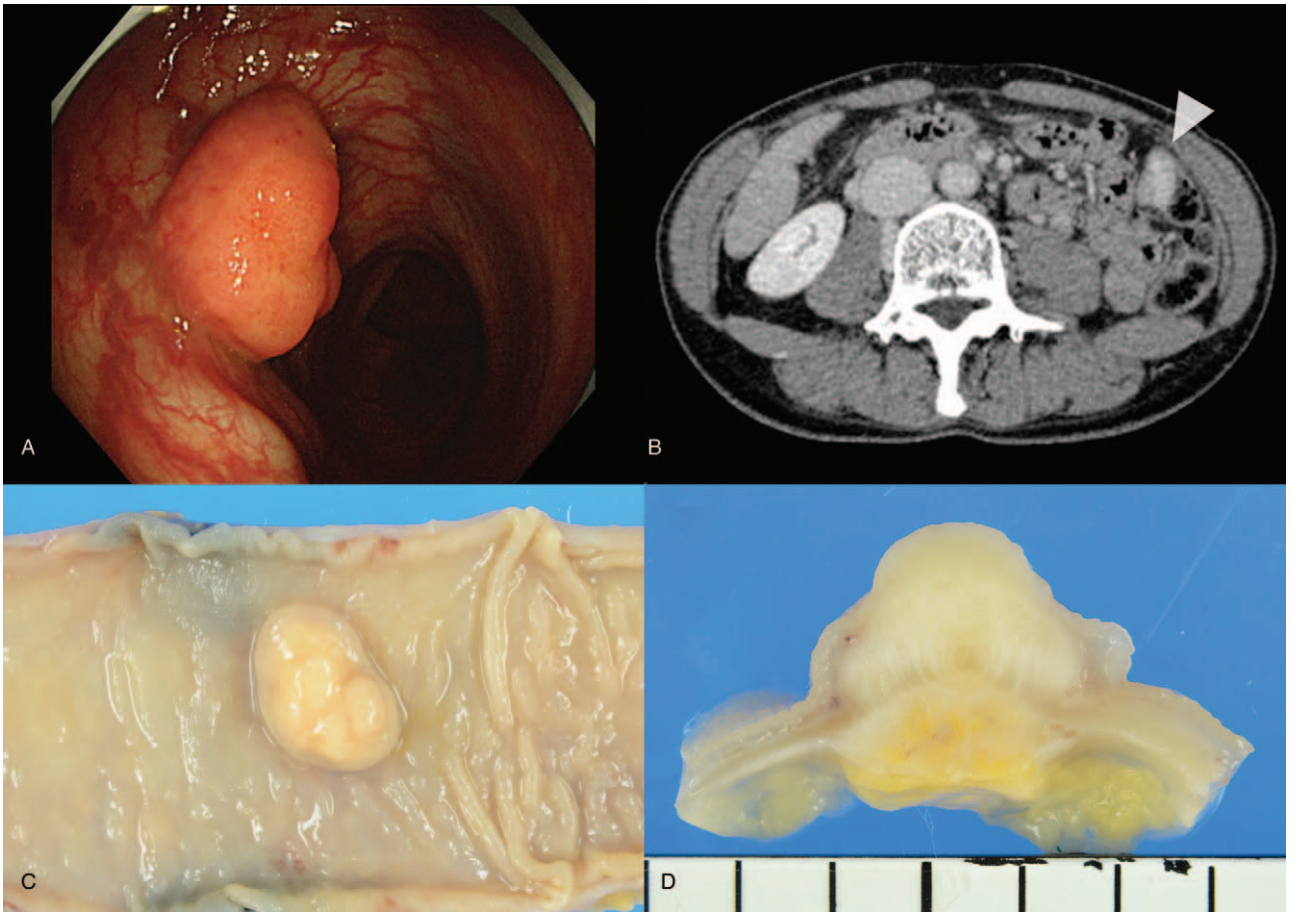

Figure 1. Tumor in the gastrointestinal tract. (A) Colonoscopy detected a 30-mm SMT in the transverse colon. (B) Contrast-enhanced abdominal computed tomography detected a 21-mm mass in the transverse colon that demonstrated strong late-phase enhancement (arrowhead). (C) Macroscopically, the tumor resembled an SMT. (D) The cut surface of the mass was grayish white with milky-white areas near the mucosa. Invasion into the adipose tissue of the subserosa was suspected. SMT = submucosal tumor.

the peripheral serum were within normal limits, as were tumor marker levels: the serum carcinoembryonic antigen level was 0.7 ng/mL (normal: < 5.0 ng/mL) and the serum carbohydrate antigen 19-9 level was 3 U/mL (normal: < 37 U/mL). Human immunodeficiency virus-serology was negative. The contrast abdominal computed tomography (CT) detected a 21-mm mass with significant late phase enhancement in the transverse colon (Fig. 1B). There was no invasion beyond the gastrointestinal tract, and no evidence of swollen lymph nodes, distant metastasis or any other masses including uterine tumors. The mass was clinically diagnosed as an SMT, and laparoscopic partial transverse colectomy was conducted 2 months after the patient's first visit to our hospital.

The resected specimen was pathologically examined. Macroscopically, a 21 × 18 × 15-mm SMT-like protuberant mass with a smooth mucosal surface was observed in the transverse colon (Fig. 1C). The resected surface of the mass revealed greyish white areas with milky-white areas near the mucosa, and the local invasion into the adipose tissue of the subserosa was suspected (Fig. 1D). Microscopically, the tumor seemed to arise from the muscularis propria and was composed of diffuse proliferation of spindle cells, with eosinophilic cytoplasm, forming intersecting fascicles (Fig. 2A). In the superficial area of the colonic wall, these cells extended to the lamina propria mucosa between the crypts (Fig. 2B). In the deep area of the colonic wall, the cells invaded the adipose tissue of the subserosa (Fig. 2C). The spindle cells showed mild atypia and pleomorphism, with a mitotic count of 8/50 high-power fields (HPFs) (Fig. 2D). There was no evidence of necrosis detected.

Immunohistochemical analyses revealed that most of the tumor cells were positive for α-smooth muscle actin (α-SMA), h-caldesmon and calponin, while some were positive for desmin, indicating that this tumor consists of smooth muscle cells (Fig. 3A). The spindle cells were negative for CD34, c-kit, DOG1, CD10, ALK, melan A and HMB45, and showed no β-catenin accumulation in the nuclei. The cells were diffusely positive for both ER and progesterone receptor (PgR) (Fig. 3B and 3C), and the MIB-1 index was 4.9% (Fig. 3D).

The SMN in our case could be diagnosed as an ER-positive LM according to the diagnostic criteria for uterine SMNs,[1,8] although the mitotic count and the MIB-1 index were slightly higher than those of typical LMs. On the other hand, some pathologists might consider this tumor to be an ER-positive LMS because of the local invasion. However, the atypia and pleomorphism of the spindle cells were mild, the mitotic count was lower than that of typical LMSs, and there was no necrosis. Because it was not appropriate to diagnose the SMN as either a LM or a LMS, we classified the tumor as an ER-positive STUMP.

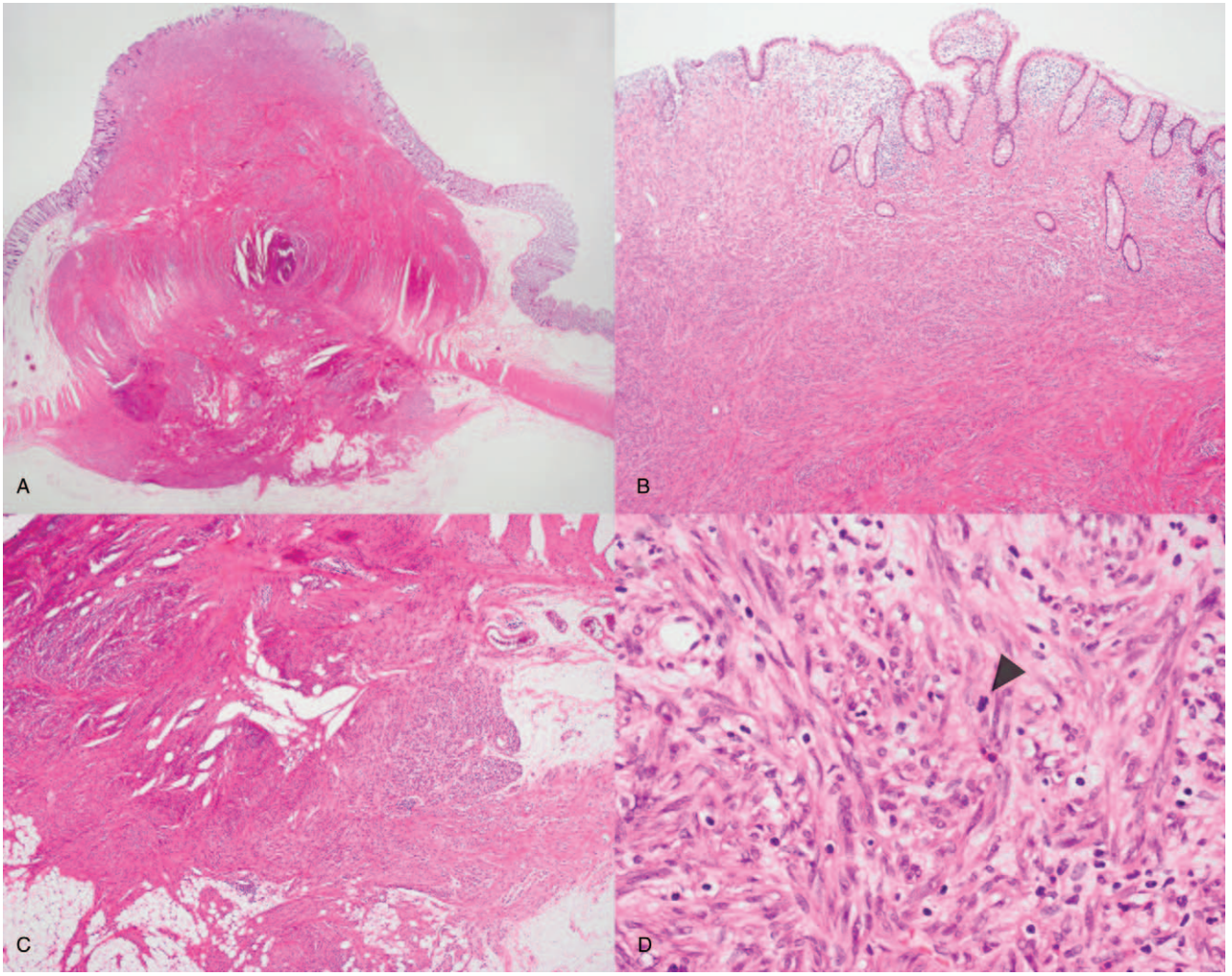

Figure 2. Histology of the tumor. (A) Microscopically, the tumor arose from the muscularis propria and was composed of a diffuse proliferation of spindle cells, with eosinophilic cytoplasm, that formed intersecting fascicles. (B) Spindle cells extended to the lamina propria mucosa between the crypts. (C) Spindle cells invaded the adipose tissue of the subserosa. (D) Although the spindle cells showed mild atypia and pleomorphism, some mitotic figures (8/50 high-power fields) were detected (arrowhead).

The neoplasm did not appear to contact either the resected surface or the serosal surface. There was no evidence of metastasis to regional lymph nodes observed.

There was no adjuvant therapy postoperatively. The patient has been followed up at an outpatient, and she remains healthy without recurrence 13 months after the surgery.

3. Discussion

Mesenchymal tumors arising from the colon are rare, and the differential diagnosis includes the following: SMNs (including LMs and LMSs), gastrointestinal stromal tumors (GISTs), inflammatory myofibroblastic tumors (IMTs) and perivascular epithelioid cell tumors (PEComas) and desmoid tumors.[3] GIST was thought to be highly unlikely due to the immunohistochemical negativity for CD34, DOG1, and c-kit. IMT was also excluded due to the immunohistochemical negativity for ALK. In addition, the immunohistochemical negativity for melan A and HMB45 suggested that PEComa was also unlikely.[9] The lack of accumulation of β-catenin in the nuclei rules out desmoids tumor. We, therefore, classified this tumor as SMN supported by immunohistochemical positivity for α-SMA, h-caldesmon, calponin, and desmin. The direct metastasis from uterine LMS was thought to be highly unlikely, as uterine mass was not detected by our contrast abdominal CT and there was no past history of uterine LMS.

The observation of mild atypia, mild pleomorphism and lack of necrosis suggested this might be LM; however, a grade 1 LMS according to French Federation Nationale des Centres de Lutte Contre le Cancer (FNCLCC) grading system was also possible,[10] due to the local invasion and slightly higher mitotic count (8/50 HPFs) than that of typical LMs of deep soft tissues or gastrointestinal tract.[2,11] A review article by an eminent author stated that SMNs that are difficult to classify as either LMs or LMSs should be diagnosed in accordance with the diagnostic criteria of uterine SMNs.[8] Based on this approach, this case could be considered as a LM; however, it is difficult to conclude that it was a benign tumor given that it was locally invasive as above mentioned. Because it was difficult to classify this SMN as either a LM or a LMS, we diagnosed it as an ER-positive STUMP.

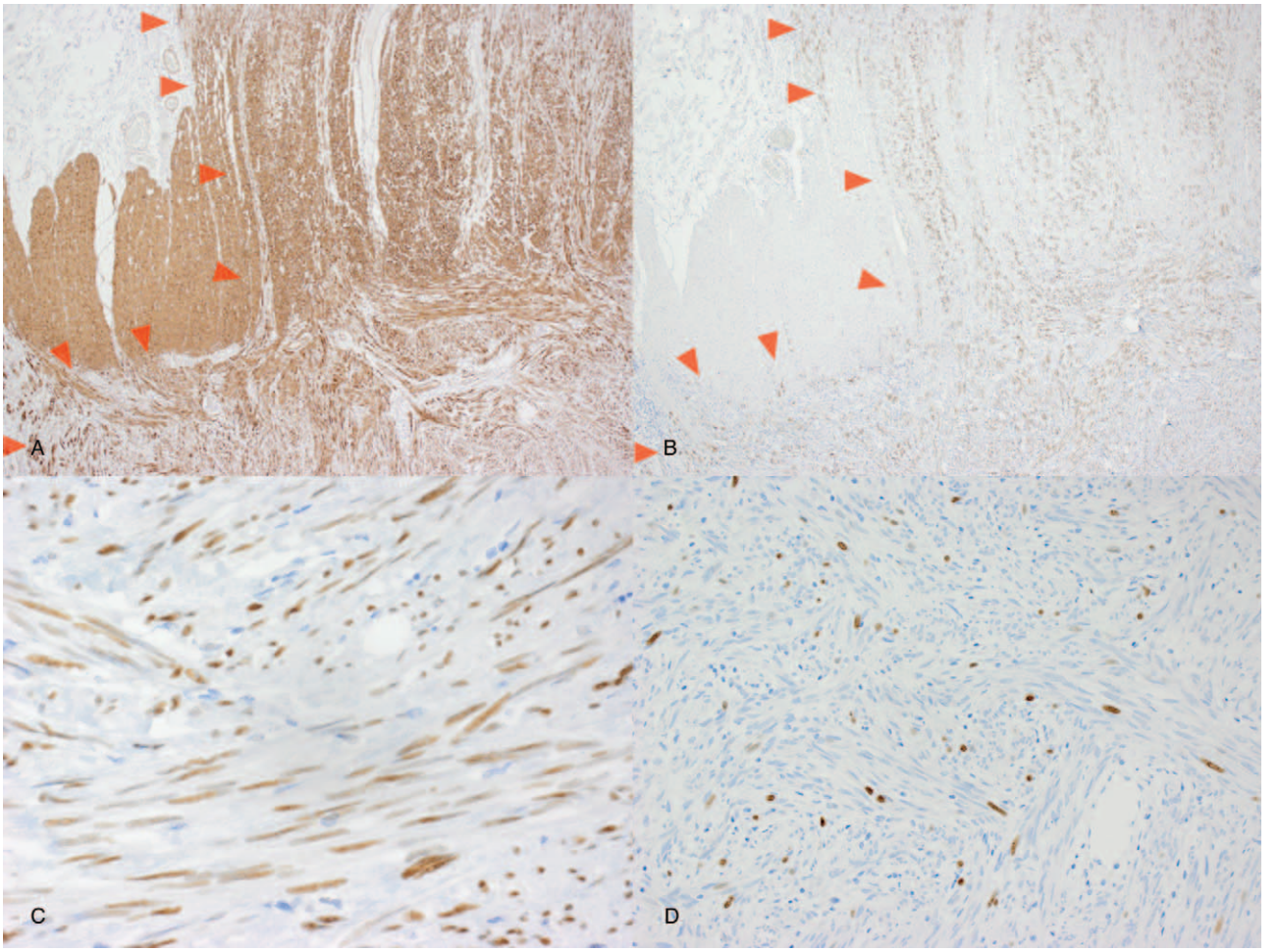

Figure 3. Immunohistochemistry of the tumor. (A) The neoplastic spindle cells (arrowheads) were positive for calponin. This finding indicated differentiation into smooth muscles. (B) Neoplastic spindle cells were positive for ER (arrowheads), although the smooth muscle cells of the muscularis propria were negative for ER. (C) Nuclear staining pattern for ER was confirmed by a high-power field. (D) The MIB-1 index was 4.9%. ER= estrogen receptor.

Some pathologists may diagnose it as a grade 1 LMS based on the FNCLCC grading system because of the presence of local invasion; however, STUMPs include some of low grade LMSs.[1] Our diagnosis of STUMP does not deny the possibility of LMS.

This is the first case of an ER-positive locally aggressive SMN in the gastrointestinal tract. ER status of the LMSs may become clinically important in terms of treatment selection in the future. To date, the effectiveness of adjuvant hormonal treatment for the uterine LMSs has not been established;[12] however, a randomized phase II study that investigates the effectiveness of aromatase inhibitor (letrozole) after a hysterectomy for the ER-positive uterine LMSs was recently studied [NCT00414076].[12] Because ER-positivity strongly seems to correlate with the sensitivity for the adjuvant hormonal treatment, this form of treatment may confer additional benefit to treating ER-positive gastrointestinal LMSs in future. Since gastrointestinal SMNs are rare, further studies should accumulate additional cases and establish a classification system for gastrointestinal SMNs that take the ER status into account.

In summary, we present a case of locally aggressive, ER-positive, SMN arising from the muscularis propria of the transverse colon and we classified this tumor as an ER-positive STUMP. This is the first case of an ER-positive invasive, SMN in the gastrointestinal tract. It highlights the difficulties in classifying some gastrointestinal SMNs as either LMs or LMSs and the importance of ER status in SMNs.

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Author contributions

K.W., E.S. and Y.H. treated this patient. G.U., Hi.Ha., Y.S., M. K., Ha.Ho. and T.M. diagnosed this patient. G.U., Hi.Ha., T.M. and Ha.Ho wrote this manuscript. All authors have read and approved this manuscript.

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Writing – review & editing: Hirotsugu Hashimoto, Yasushi Harihara, Hajime Horiuchi, Teppei Morikawa.

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