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Multilocular cystic leiomyoma of the anterolateral abdominal wall

A case report and literature review

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Abstract

Rationale: Leiomyomas arising from the anterolateral abdominal wall are uncommon, and their pathogenesis remains unknown. We present the 15th case of such a tumor, having this unique tumor morphology, followed by a detailed discussion on disease pathogenesis.

Patient concerns: A 48-year-old, asymptomatic perimenopausal, multiparous Japanese woman presented with a left-sided pelvic mass. She had no history of previous surgeries or uterine leiomyomas. Although a transabdominal ultrasonogram raised suspicions of an ovarian tumor, a transvaginal ultrasonogram confirmed normal ovaries. Radiological images showed a multilocular cystic mass with enhanced solid lesions connected to the uterus. Retrospective radiological evaluation showed that the mass was largely connected to the peritoneum of the anterolateral abdominal wall.

Interventions: Intraoperatively, the mass appeared as a dome-like protrusion from the left lower quadrant of the abdominal wall, without connection to the uterus, ovaries, or the left round ligament. No other peritoneal masses were seen. The mass was easily enucleated from the abdominal wall. Pathology confirmed that the mass was a leiomyoma with hydropic and myxoid degeneration. No striated muscle tissues were noted between the tumor and resection margin, but a thin smooth muscle layer, positive for hormone receptors, was present at the periphery, suggesting the origin of the tumor.

Lessons: Benign leiomyomas of the anterolateral abdominal wall likely originate from Müllerian-like smooth muscle remnants in this region. They should be considered in the differential diagnosis of solid and cystic masses and be distinguished from uterine and ovarian masses on imaging to avoid unnecessary organ resection.

Abbreviations: AR = androgen receptor, CT = computed tomography, ER = estrogen receptor, MRI = magnetic resonance imaging, PgR = progesterone receptor, US = ultrasonography.

Keywords: abdominal wall, leiomyoma, pathogenesis

1. Introduction

Leiomyomas of the anterolateral abdominal wall are rare, with only 14 cases reported, to date.[1–13] Herein, we present a case of an anterolateral abdominal wall leiomyoma, as well as a literature review describing the clinicopathological characteristics of these lesions. This is the first case showing an ovarian tumor-like multilocular cystic morphology in conjunction with a discussion of differential diagnoses and tumorigenesis.

2. Case presentation

2.1. Patient information

A 48-year-old, asymptomatic, Japanese woman was referred to our hospital for further investigation of a left pelvic cavity tumor identified on transabdominal ultrasonography (US) and initially thought to represent an ovarian tumor. She had a history of atopic dermatitis, but no history of surgery or treatment of uterine leiomyomas. She had given birth to 2 healthy children by vaginal delivery. Her menstrual cycle was regular, with no history of dysmenorrhea.

2.2. Clinical findings

The patient's vital signs were unremarkable. On clinical examination, the mass was smooth, firm, well demarcated, and nontender. A transvaginal US confirmed a $93 \times 90 \times 62$-mm multilocular mass, which appeared connected to the posterior wall of the uterus. Her bilateral ovaries were normal, and there was no associated ascites. Based on these features, a uterine

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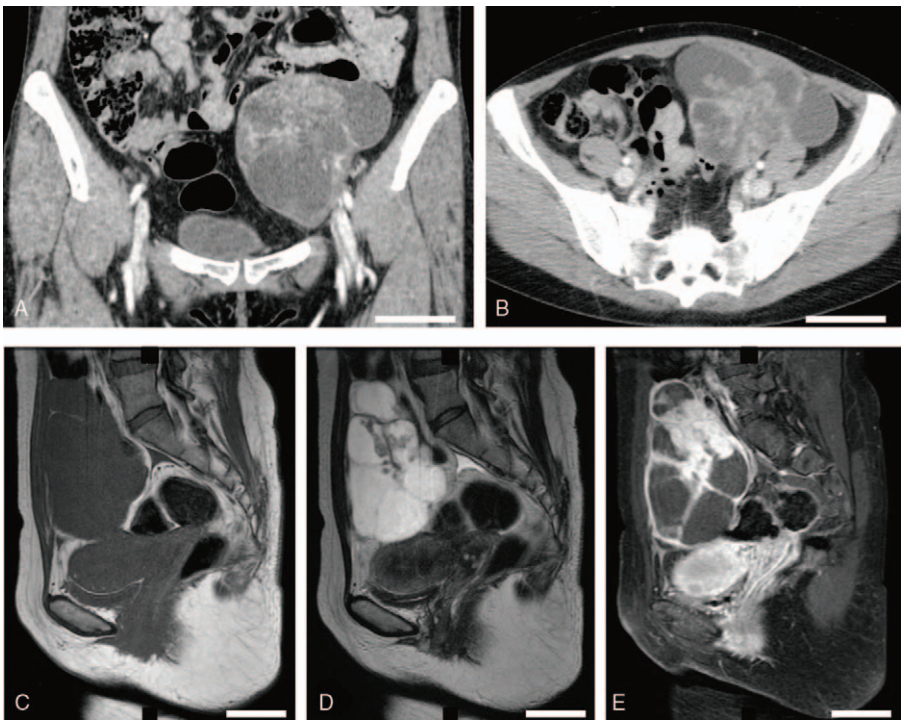

Figure 1. Radiographic images of the tumor. (A and B) Enhanced computed tomography images. A heterogeneously enhanced nodular lesion is present mainly in the left pelvic cavity (A). The tumor appears broadly connected to the anterolateral abdominal wall (B). (C–E) Magnetic resonance images of the sagittal planes. The tumor appears to connect to the posterior wall of the uterus and to the anterior abdominal wall. The tumor had low signal intensity on a T1-weighted image (C). High-signal-intensity areas with low-intensity lesions are seen on a T2-weighted image (D). A multilocular enhancement pattern with enhanced solid lesions is seen on a contrast-enhanced, fat-suppressed T1-weighted image (E). The white bars represent 5 cm.

tumor was suspected. Endoscopy did not reveal any abnormality of the upper and lower intestinal tracts. Various tumor markers, including carcinoembryonic antigen, cancer antigen 72–4, carbohydrate antigen 19–9, and cancer antigen 125 were within normal ranges. Computed tomography (CT) showed a low-density mass located mainly in the left pelvic cavity, and contrast enhanced CT revealed heterogeneous enhancement of the tumor (Fig. 1A and B). Nonenhanced and enhanced magnetic resonance imaging (MRI) (Fig. 1C–E) revealed that the mass was a multilocular cystic lesion containing solid portions and fluid-filled cavities. A subserosal uterine tumor was suspected, but the presence of a left ovarian tumor could not be excluded because the left ovary was not visible on CT and MRI images. Due to suspicion of malignancy, surgical resection was planned. During surgery, the mass was found adherent to the left lower quadrant of the anterolateral abdominal wall and showed dome-like protrusions towards the peritoneal cavity (Fig. 2A and B). The intestinal tract, uterus, bilateral uterine adnexa (Fig. 2A), and left round ligament were not adherent to the tumor, and they appeared normal. No other peritoneal masses or signs of disseminated leiomyomatosis peritonealis were present. The cystic lesion was easily exfoliated from the abdominal wall, without damage to the abdominal wall muscle layers. The feeding vessel was an inferior epigastric artery. The patient was discharged 6 days, postoperatively, without sequelae; she remained disease-free at the 4-month follow-up. Retrospective

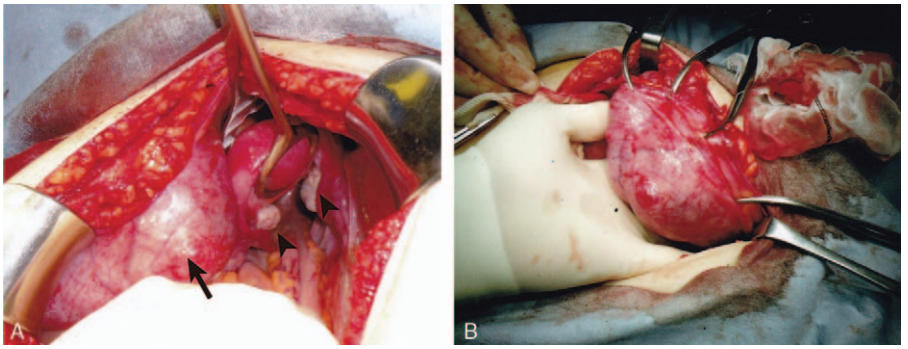

Figure 2. Macroscopic images during the surgery. (A) The tumor (arrow) attaches to the left lower quadrant of the anterolateral abdominal wall and does not connect to the bilateral ovaries (arrowheads) or to the uterus that is grasped with forceps. (B) The tumor shows dome-like protrusions towards the peritoneal cavity and does not attach other peritoneal organs.

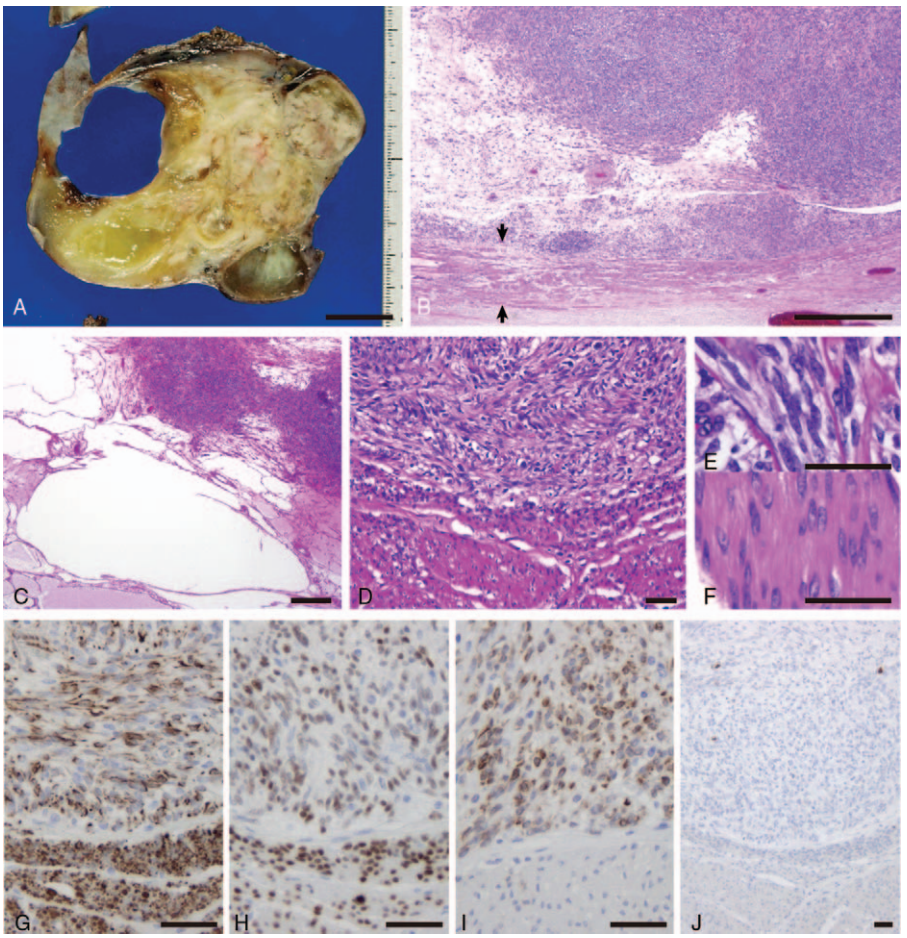

Figure 3. Macroscopic and microscopic findings. (A) The cut surface of the formalin-fixed tumor demonstrates a solid and cystic appearance. (B–F) Microscopic findings of hematoxylin-and-eosin-stained sections. Low magnification photos of the tumor (B and C) show hydropic (cystic) and solid components, consisting of thick to thin bundles or an interlacing arrangement of bland spindle cells (upper portion of D and E). Adjacent to the tumor and/or near the resection margin, a thin layer is evident (arrows, B) that consists of normal spindle cells (lower portion of D and F). (G–J) Immunohistochemical findings of the tumor cells (upper two-third) and the surrounding layer of nonatypical spindle cells (lower third). Both cell types are positive for desmin (G) and estrogen receptor (H). The tumor cells are diffusely positive for Bcl-2 protein (I) and show a Ki-67 ratio of <1% (J), whereas the nonatypical spindle cells are almost negative for Bcl-2 protein and Ki-67. The black bars in A, B, C, and D–J represent 2 cm, 1 cm, 0.5 mm, and 50 μm, respectively.

evaluation of the radiological images confirmed that the mass was largely connected to the anterolateral abdominal wall, confirming the intra-operative findings (Fig. 1B–E).

2.3. Pathological findings

Macroscopically, a well-demarcated mass measuring 110 × 85 × 65 mm and weighing 300 g was seen. The cut surface was solid, with several cavities containing gelatinous materials (Fig. 3A). Microscopically, the solid and cystic portions of the mass were composed of fascicular and interlacing bland spindle cells (Fig. 3B–E). The various-sized cavities were likely due to edematous changes (Fig. 3C); mucinous degenerations, highlighted by periodic acid-Schiff and Alcian Blue, were identified. There was no evidence of mitoses or coagulation necrosis, and no features of endometriosis. A leiomyoma was suspected, with possible differential diagnoses including a solitary fibrous tumor, endometrial stromal tumor, extragastrointestinal stromal tumor, perivascular epithelioid cell tumor, and schwannoma. Immunohistochemically, the spindle cells were diffusely positive for α-smooth muscle actin (1A4, DAKO, Glostrup, Denmark), desmin (D33, DAKO, Fig. 3G), estrogen receptor (ER; 1D5, DAKO, Fig. 3H), and partly positive for h-caldesmon (h-CD, DAKO), progesterone receptor (PgR; PgR636, DAKO), androgen receptor (AR; AR27, Novocastra Laboratories, Newcastle, UK), WT-1 (6F-H2, DAKO), CD10 (56C6, Novocastra Laboratories), CD34 (My10, Becton Dickinson, San Diego, CA), and Bcl-2 protein (124, DAKO, Fig. 3I). They were negative for S-100 protein (polyclonal, DAKO), melanosome (HMB45, DAKO), melan-A (A103, Novocastra Laboratories), CD117 (polyclonal, DAKO), DOG-1 (SP31, Nichirei, Tokyo, Japan), and STAT6 (S-20, Santa Cruz Biotechnology, Santa Cruz, CA). The Ki-67 (MIB-1, DAKO) labeling index was <1% (Fig. 3J). These findings were consistent with a final diagnosis of a leiomyoma with mucinous and hydropic degeneration. Between the tumor and the resection margin, a layer of nonatypical spindle cells (Fig. 3B, D, F–J) was seen extending throughout the whole mount preparation of the resected tissue. The spindle cell layer was diffusely positive for smooth muscle markers (Fig. 3G), ER (Fig. 3H), and PgR; largely negative for Bcl-2 protein (Fig. 3I), AR, and WT-1; and almost negative for Ki-67 (Fig. 3J). Striated

Table 1

Literature review of anterolateral abdominal wall leiomyomas.

	First author, published year	Age/ Sex	Clinical diagnosis	Maximum size, cm	Localization on the abdominal wall	Histological diagnosis	IHC
1	Schindl, 2000	60/F	Dermoid cyst	6	The surgical scar of the left lower abdomen	Lipoleiomyoma	aSMA+/desmin+/ ER+/PgR+
2	Lalor, 2005	67/F	NA	18	Preperitoneal mass from the umbilicus to pubic symphysis occurred from the incisional scar	Lipoleiomyoma	aSMA+/HMB45/ ER+/PgR-
3	Schwarz, 2009	44/F	Metastatic ovarian tumor	NA	Left lower abdominal wall between the rectus sheath and peritoneum	Leiomyoma	desmin+/ER+/ PgR+/Ki-67<1%
4	Igberase, 2009	31/F	Abdominal wall cyst or fibroid	10	Periumbilical area between the subcutaneous tissue and rectus sheath	Leiomyoma	NA
5	Ono, 2010	37/F	Abdominal wall leiomyoma	3.3	Between the peritoneum and the muscular layer	Leiomyoma	ER+/PgR+
6	Goyal, 2010	45/F	Desmoid tumor	8	Parietal wall of left iliac fossa and inguinal region	Leiomyoma	aSMA+
7	Goyal, 2010	42/F	Desmoid tumor	3.5	Infra-umbilical region right to midline extending into rectus	Leiomyoma	aSMA+
8	Narayanaswamy, 2011	42/F	Uterine leiomyoma or ovarian mass	26	Right iliac, suprapubic area extending up to the umbilicus	Myxoid leiomyoma	NA
9	Yesilkaya, 2011	32/F	NA	18	Right inferior quadrant, in the subcutaneous tissue	Leiomyoma	aSMA+/S100-/ CD34-/Ki-67<1%
10	Dsouza, 2012	34/F	NA (exploratory laparotomy)	17.5	Periumbilical lump between the subcutaneous tissue and rectus sheath	Leiomyoma	NA
11	Al-Wadaani, 2012	45/F	NA	18	Preperitoneal mass within the anterolateral abdominal wall muscles	Leiomyoma	aSMA+/desmin+/CD34-
12	Midya, 2014	32/F	NA	8	Right and lower of the umbilicus, between the rectus muscle and posterior rectus sheath	Leiomyoma	NA
13	Ernest, 2016	72/M	NA	4.7	Parietal wall of the left iliac fossa, deep to the anterior abdominal wall	Leiomyoma	aSMA+/CD117-/CD34-
14	Cho, 2016	33/F	NA	10.4	Left lower quadrant, in the left rectus abdominis muscle	Leiomyoma	aSMA+/desmin+/S100-
15	The present case	48/F	Ovarian tumor, uterine tumor	11	Left lower quadrant, under the abdominal wall muscles	Leiomyoma	aSMA+/desmin+/ER+/ PgR+/AR+/WT-1+

+ = positive, − = negative, AR = androgen receptor, aSMA = alpha-smooth muscle actin, ER = estrogen receptor, F = female, HMB45 = human melanoma black 45, IHC = immunohistochemistry, M = male, NA = not available, PgR = progesterone receptor, WT-1 = Wilms tumor 1.

muscle tissue, suggestive of abdominal wall muscle, was not seen in the resected tissue.

3. Discussion

The present case can be classified as a leiomyoma of the deep soft tissue, according to the latest World Health Organization guidelines.[14] The vast majority of these types of leiomyomas occur in the retroperitoneum, mesentery, omentum, or abdominal wall. These leiomyomas are seen almost exclusively in women, are most common in young adulthood or middle age, and are almost uniformly positive for ER and PgR.[14] Thus, the tumor is considered an analog of uterine leiomyomas.[14] In Table 1, we summarized 15 cases, including the present case, of leiomyomas possibly arising from the anterolateral abdominal wall. The 15 cases had a predilection for women (mean age, 44 years; range, 31–72 years) and a mean maximal size of 11 cm (range, 3–26 cm). Although some tumors were asymptomatic, others presented with pain or with a palpable mass. Progressive enlargement of the tumor, which can be seen in cases of malignant tumors, can occur within 1 year of symptom onset.[4,11,13] Anterolateral abdominal wall leiomyomas tend to be located either above, within, or under the rectus abdominis muscle. Those that are located beneath the rectus abdominis muscle may result in a delayed diagnosis, possibly because they are grossly invisible or poorly palpable.

Our literature review revealed that clinical differential diagnoses of anterolateral abdominal wall leiomyomas include ovarian tumors,[1,8] uterine leiomyomas,[4,8] and desmoid tumors.[6] The preoperative diagnosis of a degenerated abdominal wall leiomyoma is difficult when the tumor is located close to the uterus or uterine adnexa. Clinicians should pay attention to the positional relationship between a pelvic cavity tumor, uterus, uterine adnexa, and the abdominal wall. If the pelvic cavity tumor broadly attaches to the abdominal wall, as in the present case, clinicians should be mindful of the possible differential diagnosis of an abdominal wall tumor. Parasitic leiomyomas can grow in abdominal wall incisions after laparoscopic myomectomy;[15] therefore, obtaining a patient's past medical history and carefully examining the abdomen are important. Pathological exploration is required to rule out a desmoid tumor because more than two-third of abdominal wall desmoid tumors show well-defined borders.[16]

The multilocular, partially cystic morphology of the present tumor was likely due to marked hydropic and myxoid

degeneration. Degenerative or regressive changes, such as fibrosis, calcification, and cystic and myxoid changes, are frequently seen in leiomyomas of the deep soft tissue;[14] however, a multilocular cystic tumor has not been previously reported in published cases of leiomyomas of the deep soft tissue or abdominal wall. One case of an anterior abdominal wall lipoleiomyoma was clinically diagnosed as a dermoid tumor due to the fatty tumor component, rather than due to cystic degeneration.[1] Degenerative or regressive changes are also frequently found in uterine leiomyomas, and multilocular uterine leiomyomas mimicking ovarian tumors have been reported.[17] Hydropic and mucinous degeneration can contribute to the cystic morphology of uterine leiomyomas.[17] Leiomyomas of the deep soft tissue are considered analogs of uterine leiomyomas. The cause of degeneration is unknown. Kamat et al[18] suggested that cystic degeneration of uterine leiomyomas represents a late stage of hyaline degeneration; however, no hyaline degeneration was observed in our case.

The histological diagnosis of our case was uncomplicated due to the presence of smooth muscle differentiation features, confirmed by diffuse immunoreactivity for multiple smooth muscle markers. An adenomyoma[19] or uterus-like mass[20] occurring in the peritoneal wall was excluded due to the absence of endometrial tissue. Interestingly (worrisome), the tumor cells were positive for CD34, Bcl-2, and CD10. Spindle cell tumor immunoreactivity for these 3 markers leads to possible differential diagnoses that include extragastrointestinal stromal tumor, solitary fibrous tumor, and endometrial stromal tumor; all of which may occur in the abdominal wall.[21–23] Similarly, abdominal wall recurrence of gastrointestinal stromal tumors is possible after laparoscopic surgery.[24] We excluded extragastrointestinal stromal and parasitic gastrointestinal stromal tumors because our case was negative for CD117 and DOG1. A solitary fibrous tumor was also excluded because our case did not have a staghorn-like vascular structure and was negative for STAT6. Other potential differentials included an endometrial stromal nodule and a low-grade endometrial stromal sarcoma because the tumor cells of the present case were positive for CD10, ER, and PgR; however, these diagnoses were excluded due to the lack of endometrial spiral arteriole-like vessels, diffuse immunoreactivity for CD10, and endometriosis. Endometrial stromal nodules/sarcomas can show smooth muscle differentiation that is not usually diffuse.[23]

In this case, the lack of mitosis and coagulation necrosis is more in keeping with a benign tumor. Furthermore, the proportion of Ki-67-positive cells was very low. The presence of a leiomyoma with myxoid changes raised the suspicion of a myxoid leiomyosarcoma, but this was ruled out due to the focal myxoid degeneration and absence of mitoses and atypia. However, peritoneal and retroperitoneal leiomyomas can have mitoses up to 5 per 50 high power fields and show frequent degeneration, including myxoid changes,[14] making diagnostic exclusion of myxoid leiomyosarcomas difficult, according to the uterine smooth muscle tumor criteria. Using the PubMed database, 3 cases of abdominal wall leiomyosarcomas have been reported.[25–27] Two cases[25,26] showed frank sarcomatous features, including nuclear pleomorphism, frequent mitoses, and tumor necrosis, whereas 1 case[27] described tumor cells with nuclear pleomorphism, but a low mitotic index (4 per 50 high-power fields) and an unknown necrosis status. Given the lack of specific data on abdominal wall leiomyosarcomas, suspected cases should be approached with caution until further cases are available for review. The most important issues regarding this and similar cases is the recognition of their Müllerian (uterine-like) nature and distinguishing them from nonuterine-type smooth muscle tumors. Hence, the same malignancy histological criteria are applied as for their uterine counterparts. This approach should help to prevent the overdiagnosis of leiomyosarcomas at this unexpected location.

The pathogenesis of abdominal wall leiomyomas is poorly understood, but 6 hypotheses have been suggested. The secondary/parasitic theory, which presumes that uterine leiomyomas detach from their subserosal location and attach to other peritoneal sites, is plausible. Uterine leiomyomas can grow in the abdominal wall incisional site after gynecological surgeries, including laparoscopic procedures,[28,29] implying the seeding and growth of uterine leiomyoma cells in the incisional scar. The parasitic theory might explain the pathogenesis of our case; however, the present patient did not demonstrate a concurrent uterine leiomyoma nor have a history of uterine leiomyomas or abdominal surgeries. Second, these tumors may arise from vascular smooth muscle cells, but there is limited published immunohistochemical evidence to confirm whether vascular leiomyomas/angioleiomyomas frequently express ER and PgR, which are seen in leiomyomas of the deep soft tissue.[30–32] Third, de novo leiomyomas arising from abdominal wall surgical scars have been reported,[1,2] but an incisional scar was absent in our case. Fourth, the rectus sheath may be the origin of anterolateral wall leiomyomas,[6,10] but the present tumor was removed easily from the rectus sheath, making this unlikely. Fifth, leiomyomas can primarily occur in the inguinal region, and the round ligament is postulated to be the origin of leiomyomas in these locations.[33] In particular, round ligament smooth muscle cells that are immunohistochemically positive for ER and PgR[34] can be the origin of leiomyomas. The present tumor was radiologically close to the left round ligament (Fig. 1A) and was identified close to the inguinal canal at the point where it is transected by the round ligament. However, a gross evaluation during surgery indicated that the tumor was not connected to the left round ligament. Further, the localization of the present tumor differed from that of previously published cases of round ligament leiomyoma.[35] Finally, a thin layer of nonatypical smooth muscle cells adjacent to the leiomyoma could be the origin of the present tumor because the smooth muscle layer was intimately associated with the tumor and the layer was ER- and PgR-positive. Interestingly, Bcl-2 protein expression differed between the tumor and the adjacent smooth muscle layer. As in the present case, uterine leiomyoma cells are prominently immunoreactive for Bcl-2, but very few of the background uterine smooth muscle cells are positive for Bcl-2 protein.[36] Thus, the tumorigenesis of our case might be similar to that of uterine leiomyomas. AR expression in the present tumor has not been reported in previously reported for abdominal wall leiomyomas, but AR expression in uterine leiomyomas has been.[37] We firstly described that the ER- and PgR-positive smooth muscle layer was present in the left lower quadrant of the abdominal wall, and the localization was postulated to be between the abdominal wall skeletal muscle and the peritoneal membrane. The smooth muscle layer has not been previously reported as a component of the abdominal wall or in cases of abdominal wall leiomyoma, suggesting that the structure might be acquired later in life, possibly in the sense of a Müllerian metaplasia or representing embryological remnants.

In conclusion, we presented a case of an anterolateral abdominal wall leiomyoma with cystic and myxoid degeneration. Although clinical modalities, including transvaginal US, CT, and MRI, failed to identify the abdominal wall origin of the tumor,

the broad attachment of the tumor to the abdominal wall was the key feature that raised suspicion of an abdominal wall tumor. Hydropic and mucinous degeneration of the tumor induced its ovarian tumor-like multilocular cystic morphology. Clinicians should be aware of this presentation to adopt an organ-sparing surgical approach.

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