

Original Article

Low-grade endometrial stromal sarcoma in the abdominal wall: a metastatic or protopathic one?

Zehong Chen^{1*}, Jialin Wu^{1*}, Xubin Liu², Jinning Ye¹, Zhihui Chen¹, Jianjun Peng¹, Yin Li¹, Yihua Huang¹, Wu Song¹

Departments of ¹Gastrointestinal Surgery, ²Pathology, The First Affiliated Hospital, Sun Yat-sen University, Guangzhou 510080, China. *Equal contributors.

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Abstract: Being a family of scarce endometrial stromal tumor, low-grade endometrial stromal sarcoma (LGESS) is an uncommon malign neoplasm, whose occurrence outside the uterus, like peritoneum, is extremely rare in the absence of metastasis or invasion of a primary uterine neoplasm. Herein we present the patient of a 44-year-old woman with no specific discomfort and abdomen-related symptoms who underwent her laparotomy after a diagnosis of recurrent LGESS. She had a history of hysterectomy for leiomyoma of uterus long before the surgical excision of her first LGESS. Exploration of the abdominal cavity revealed a colossal peritoneal mass with accompanying invasion of rectus abdominis and mesentery. Left ovarian cyst was validated by pathological examination. There was no pathologic evidence showing the exact origin of her primary low-grade ESS on the peritoneum. The possible origin, which is believed to be either a metastasis or protopathic one, is discussed in our study.

Keywords: Low-grade endometrial stromal sarcoma, peritoneum, metastasis

Introduction

Endometrial stromal sarcoma (ESS) is a kind of uncommon malignant mesenchymal neoplasm, which mostly develops in the uterus, and sporadically in the ovary and peritoneum. This rare tumor comprises only approximately 0.2-0.5% of all uterine malignancies and about 10% of all uterine sarcoma, with the median age being 52 years [1, 2]. In 2014, the World Health Organization (WHO) recognizes 4 categories of endometrial stromal tumor: endometrial stromal nodule (ESN), low-grade endometrial stromal sarcoma (LG-ESS), high-grade endometrial stromal sarcoma (HG-ESS), and undifferentiated uterine sarcoma (UUS) [3]. Among them, the low-grade endometrial stromal sarcoma (LG-ESS) is relatively more common class.

In general, LG-ESS is a slow-growing hormone-sensitive malignancy and is notorious for its propensity towards late recurrence [4]. Morphologically, the tumor cells are small, round or oval to spindle, with low cellular atypia and rela-

tively low mitotic activity (usually <5/10HPFs) [5]. Furthermore, this tumor shows a proliferation of cells resembling normal proliferative endometrial stroma [6]. A useful initial IHC panel is CD10, desmin, ER, and PR. The majority of the LG-ESS cases are intrauterine. However, rarely, this sort of tumor may initially present at distant sites such as the ovary and lymph node [7, 8], not to mention the peritoneum. Nevertheless, it is characterized by late recurrence, which generates in approximately 30% of patients, most frequently in the pelvis and abdomen [9].

So, in this case, we describe this patient who presented no distinct clinical manifestation, and was found tumor recrudesced on the abdominal wall after 3 years free of disease after the resection of the primary peritoneal LGESS. It is worth noting that whether the first sarcoma that this one recurred from initially developed at peritoneum or metastasized from the undetected ESS cells of the uterine that have been removed long before, remains unclear and it is of value to discuss over.

Low-grade endometrial stromal sarcoma in abdominal wall

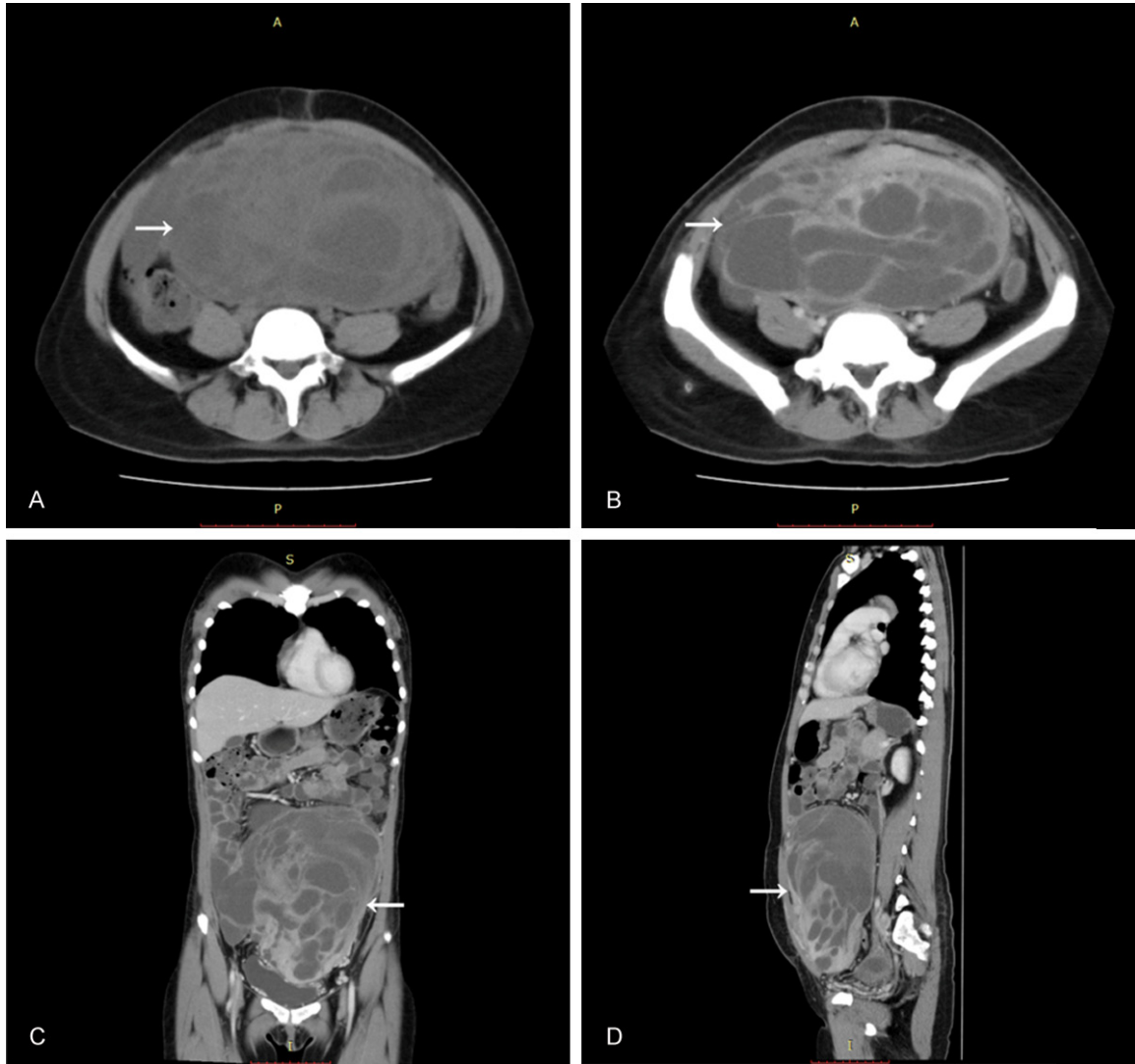


Figure 1. CT imaging of the tumor. The plain CT showed a huge oval mass involving abdominal wall, with indistinct substances and border (white arrow) (A). Enhanced CT scan detected this giant cystic-solid mass with differential density signal (white arrow) (B). Coronal and sagittal section showed clear demarcation with intraperitoneal tissues, as well as obvious compression and displacement of the organs nearby (white arrow) (C, D).

Clinical presentation

Without any discomfort, the 44-year-old housewife was admitted to the department of thoracic surgery, after the discovery of bilateral pulmonary multiple nodules during the routine physical examination. This patient had a history of hysterectomy for leiomyoma of uterus and oophorectomy of right adnexa 15 years previously. Moreover, a pelvic mass was detected, which was later confirmed to be a low-grade endometrial stromal sarcoma, by the histopathological examination. And afterwards the resection of this lower abdominal neoplasm was performed in local hospital 3 years back. This

time, along with the lesion in the lungs, the positron emission tomography-computed tomography (PET-CT) demonstrated that an enormous cystic-solid tumor was newly generated in the abdominal cavity, as well as a cystic mass located on the left adnexa.

Throughout the procession of her disease, she remained well and with no aches and pains until her grumble about abdominal distention short after her arrival. Soon she was transferred to our department for further examination and treatment. The initial diagnosis was peritoneal and ovarian recurrence of low-grade endometrial stromal sarcoma on the basis of

Low-grade endometrial stromal sarcoma in abdominal wall

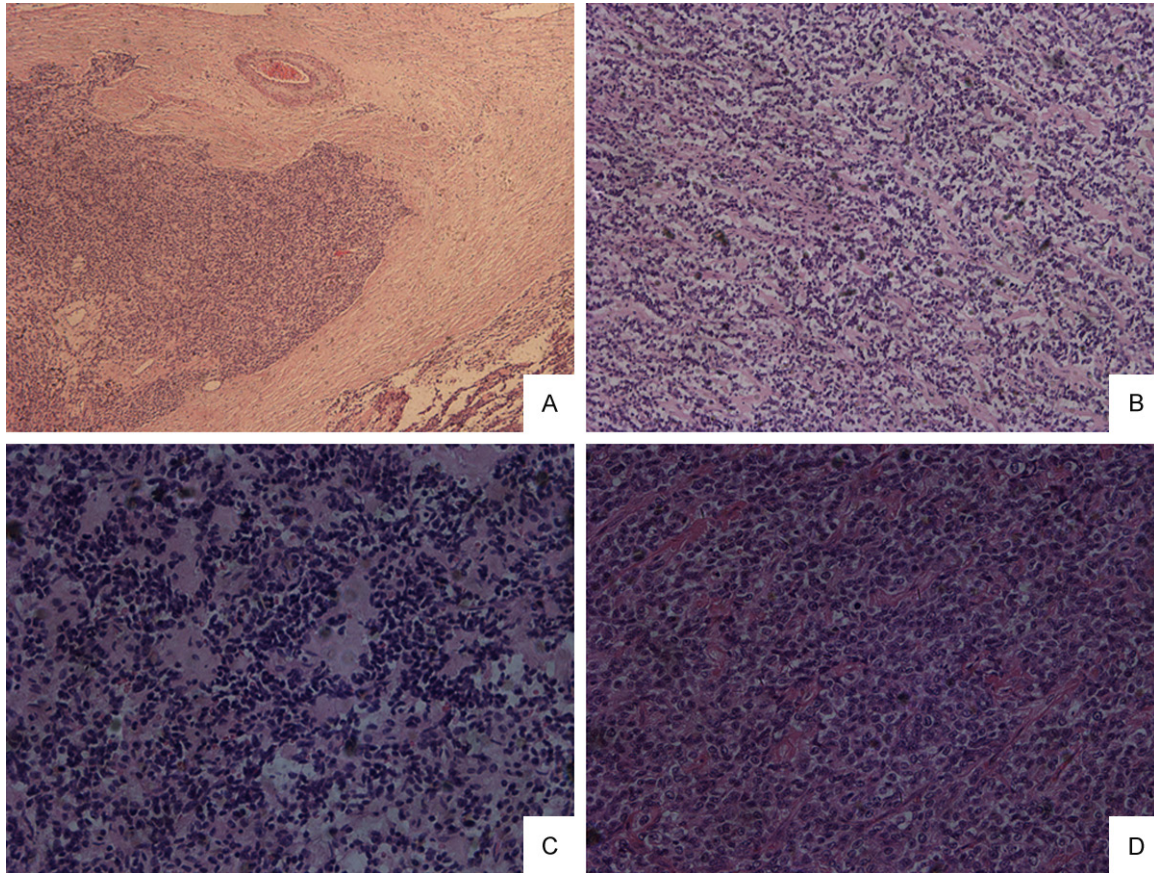


Figure 2. Photomicrograph from postoperative specimen (H&E staining). Ligulate invasion to serosal layer of peritoneum and other tissues were found (A). Cord-like architectures were formed in some areas (B). Nubby and disorganized architectures were detected (C). The nuclei were round or oval, with frequent mitotic figure (D).

PET-CT inference, in company with bilateral pulmonary multiple nodules. Laboratory investigations showed rise of the NSE level which reached 40.38 ng/mL, as well as the increased leukocyte reading of $20.31 \times 10^9/L$, despite other figures within the normal ranges.

Materials and methods

The tissue blocks of the resected gross specimen were conserved in the formalin-fixed and paraffin-embedded (FFPE) way. The slides of tumor specimens we made were about 4- μ m thick and were then dewaxed and rehydrated and washed stepwise. The blockages of endogenous peroxidase activity were performed with 3% H_2O_2 , afterwards the antigen retrieval was completed with citrate buffer (10 mM, pH 6.0). The following commercially available primary antibodies were used: CD10, ER, PR, Vimentin, CD-99, cytokeratin (CK), EMA, Inhibin-a, NSE, Desmin, Myogenin, S-100, ctin, and CgA.

We used standard avidin-biotin-complex immunoperoxidase technique to operate the immunohistochemical detection, concurrently with appropriate positive and negative controls of the markers. Hematoxylin was applied to counter-staining step. Again the sections were washed, dehydrated, and then steeped in xylene before mounting. Also the hematoxylin and eosin (H&E)-stained slides were restored by us and available for review.

Results

Imaging and gross features

For confirmation of the progression of the tumor, once again the CT scanning was carried out. The plain and enhanced CT scan revealed that there was a 106×201×218 mm giant cystic-solid mass in the abdomen, with distinct demarcation and partly intensity in the solid and low-density signal in the cystic, causing the

Low-grade endometrial stromal sarcoma in abdominal wall

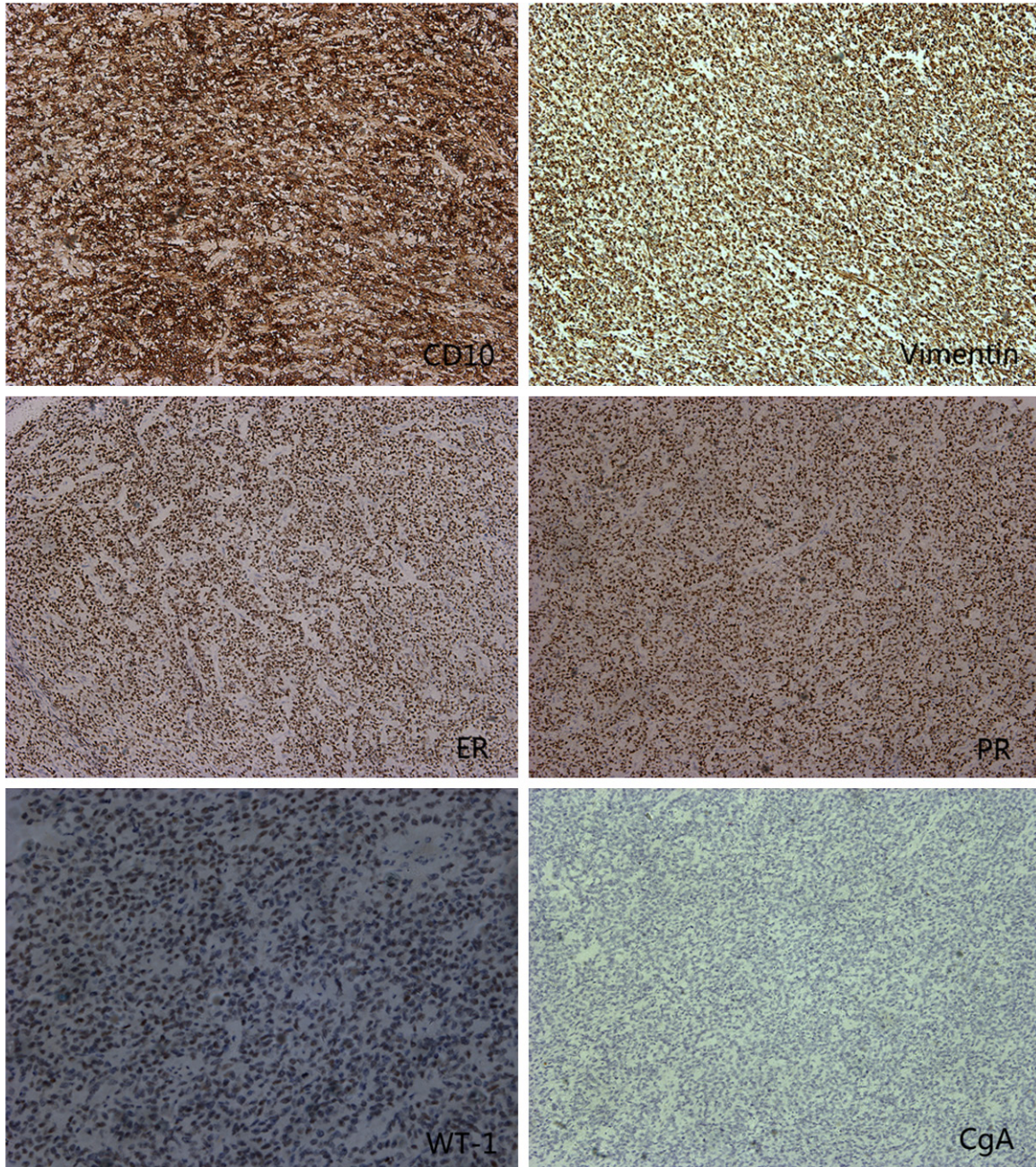


Figure 3. Immunohistochemical staining of postoperative specimen. CD10, Vimentin, ER and PR were strongly and diffusely positive in tumor cells. WT-1 was about 50% positive focally. CgA was negative.

obvious compression and displacement of intestine, mesentery as well as bladder. The rest of the neighborhood of the colossal lesion remained normal, apart from a similar cystic-solid mass, which had the size of 73×59×55 mm and partially enhanced margin, accompanied by several suspected swelling lymph nodes (**Figure 1**). Grossly, being took down from the abdominal wall, this oval mass measured about 21×19×6 cm, with the attachment of rectus

abdominis. The cross-section was grey-yellow and bloody, partly cystic, and multifocal necrosis and congestion was found. No suspected lymph node metastasis was detected.

Microscopic features

Histopathological examination was applied with stained tissue slice of the tumor. Microscopically, the tumor cells' development

Low-grade endometrial stromal sarcoma in abdominal wall

seemed nodular and lived with a infiltrative growth pattern (**Figure 2**). In some areas, ligulate invasion to local and adjacent tissue could be frequently found. It consisted of diffuse small round cells and short spindle cells resembling proliferative phase endometrial stromal cells, forming locally cord-like structures. Nubbly and disorganized architectures were also detected. The nuclei of tumor cells were uniformly round or oval and had accordant size with inconspicuous nucleoli, surrounded by moderate and clear cytoplasm with ill-defined cell borders. Mitotic figure was frequently found.

Immunophenotype

Immunohistochemical studies indicated that the tumor cells were labeled strongly and diffusely with CD10, ER, PR, Vimentin, CD99, focally with WT-1, but had negative staining for CgA, desmin, EMA, inhibin-a, NSE, CK, S100 or Actin (**Figure 3**). Attached with clinical representation, the findings were powerful evidence of recurrence of low-grade endometrial stromal sarcoma.

Discussion

Low-grade endometrial stromal sarcoma (LG-ESS) is known as a kind of extremely rare malignant neoplasm with an indolent clinical course. Its favorite occurring anatomic site is intrauterine, which makes it very scarce to initially present on other district like peritoneum. This very type of tumor most commonly metastasizes to the abdomen and pelvis. It is microscopically characterized by the tumor cells resembling normal proliferative endometrial stroma, and also the representation of immunohistochemical examination.

In this case, the neoplasm that had been removed was clarified to be relapsed tumor of the first LGEES. However, as it is mentioned in the preamble, the origin of this first LGEES, either a metastasis or protopathic one, is of value to discuss over.

The metastasis of LGEES is relatively common. It is revealed that ESS tends to spread throughout the lymph nodes and veins, and rarely involves the large vessels. Lymph node metastases occur in up to 30% of cases [10]. Moreover, metastasis to bones, heart, brain,

lungs, kidney, and bladder etc has been reported [4, 11, 12]. Few cases reporting peritoneal metastasis are reviewed. One of them showed low-grade ESS of the uterus with direct spread to retroperitoneum without serosal metastases [6]. Michael et al found it was possible that morcellation of uterine mesenchymal neoplasms could be resulted in peritoneal dissemination [13], which implied the procedure of surgical excision may lead to greater likelihood of peritoneal implantation of the LGEES, like this case.

A primary uterine tumor needs to be excluded before the diagnosis of primary extrauterine ESS can be established. In this case, since the patient underwent abdominal hysterectomy due to leiomyoma of uterus, meaning that the endometrial tissue or cells could be totally removed, the long 12-year duration between uterine resection and her first diagnosis of LGEES indicates little possibility of metastasis from the primary ESS tumor in the uterus. Besides, it would probably be notified on the final histopathological report, if any evidence instructing the occurrence of ESS in the specimen of uterine lesion was found in the first place. So it is reasonable to believe that the first low-grade endometrial stromal sarcoma, which occurred in the abdominal cavity and was removed 3 years ago, could be arisen from initial nidus of itself at the very spot of peritoneum, rather than considering it to be the metastasis of intrauterine tumor.

The occurrence of ESS outside the uterus is extremely rare in the absence of metastasis of a primary uterine neoplasm [6]. In case it occurs, it is probably arises from the foci of endometriosis [14] or associated with tumor in the adnexa [15]. This patient in our case, with one of her ovaries remaining functional, complicating endometriosis is conceivable. A probable assumption could be that although her uteri was excided, the endometriosis had taken in place at somewhere of her peritoneum. After the 12-year period of time, gradually, the LGEES raised from the foci of endometriosis. Still, due to the fragmentary information and lack of details of the patient's first and second surgery, the exact origin of her malignant neoplasm remains indeterminate.

The major therapeutic procedure of patients with LGEES is primarily surgical resection, but

Low-grade endometrial stromal sarcoma in abdominal wall

the standard treatment for its recurrent disease including radiotherapy and chemotherapy has not been established [16, 17]. Recurrences are common, occurring in 1/4 to 1/2 of patients, and the risk is greater in those with more advanced-stage disease. Stage is the most important prognostic factor. FIGO stage I and II tumors have a 5-year survival rate exceeding 90%, comparing with advanced-stage tumors having a 5-year survival rate of 40% to 50% [18]. And its prognosis is related to extrauterine development [19].

The patient was also discovered bilateral pulmonary multiple nodules by enhanced CT scan, which was reasonably suspected to be metastatic tumor, meaning that further medical intervention is needed. Considering highly recurrent nature of low-grade ESS, it probably would not be her last relapse this time. In this regard, a life-long follow-up is necessary for this woman.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Wu Song, Department of Gastrointestinal Surgery, The First Affiliated Hospital, Sun Yat-sen University, 58 Zhongshan 2nd Road, Guangzhou 510080, China. Tel: 86-20-28823388; Fax: 86-20-28823388, E-mail: songwu@mail.sysu.edu.cn

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Low-grade endometrial stromal sarcoma in abdominal wall

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