

# Endometrial stromal sarcoma in combination with mixed type endometrial carcinomas

## A case report and literature review

Xiao-Xin Xiu, MD<sup>a,\*</sup>, Hua-Li Wang, MD<sup>b</sup>, Yun-Yi Lv, MS<sup>a</sup>, Fan-Dou Kong, MS<sup>a</sup>, Jin-Ping Hou, BS<sup>b</sup>

### Abstract

**Rationale:** Endometrial stromal sarcoma (ESS) is rare, representing only approximately 0.2% of all uterine malignancies. Mixed type endometrial carcinomas (MT-ECs) are rare tumors with both type I and II features, and are difficult to diagnose. Cases of ESS and MT-ECs coexisting in the same patient are extremely rare. This study aimed to describe a case of ESS in combination with MT-ECs in a 47-year-old premenopausal woman.

**Patient concerns:** A woman presented to the hospital complaining of occasional abdominal pain and had high tumor markers: cancer antigen (CA) 19–9 (263.6U/mL) and CA 125 (428.0U/mL). Transvaginal ultrasound examination revealed a complex mass (12.3 × 9.1 × 6.3 cm) with solid and cystic components on the right rear wall of the uterus. Abdominopelvic computed tomography images showed a pelvic cystic-solid mixed mass. The patient underwent an exploratory midline laparotomy. The mass was hypothesized to be malignant on the uterine posterior wall. Tumor deposits were found on bilateral parametrium. On peritoneal implantation, multiple metastases were seen on the serosal surface of the bowel and greater omentum. A frozen section revealed a spindle cell sarcoma.

**Diagnoses:** Pathological reports following surgery revealed concurrent ESS and MT-ECs.

**Interventions:** The patient underwent a total abdominal hysterectomy, bilateral salpingo-oophorectomy, total omentectomy, and macroscopic clearance of the tumor. Adjuvant chemotherapy was given.

**Outcomes:** The patient was still alive when this report was written.

**Lessons:** Considering the rarity of ESS in combination with MT-ECs, this study presented an overview of the literature and discussed a number of histological and clinical issues. Nevertheless, etiology and pathogenesis of these tumors need further investigation.

**Abbreviations:** ECs = endometrial cancers, ESS = endometrial stromal sarcoma, MT-ECs = mixed type endometrial carcinomas, SC = serous carcinoma, SCCA = squamous cell carcinoma antigen.

**Keywords:** diagnosis, endometrial carcinomas, endometrial stromal sarcoma, histogenesis, serous carcinoma, synchronous tumors, treatment

## 1. Introduction

Endometrial stromal tumors are rare, representing only approximately 0.2% of all uterine malignancies, with an annual incidence of 1 to 2 per million women.<sup>[1]</sup> Endometrial stromal tumors, especially low-grade endometrial stromal sarcoma

(LG-ESS), represent the second most common category of mesenchymal uterine tumors (second to uterine leiomyosarcoma).<sup>[2]</sup> Endometrial cancers (ECs) are common gynecologic malignancies, accounting for 3.2% of all cancers in the United States. The occurrence rates are steadily increasing by ~1% each year.<sup>[3]</sup> ECs are classified as type I or type II. Mixed type endometrial carcinomas (MT-ECs) are tumors with both types I and II components, and represent ~10% of ECs.<sup>[4]</sup> When the second of these components is present in at least 5% of the tumor, the designation of MT-EC is used, the most frequent combination being mixed endometrioid and serous carcinoma (mixed EEC-SC). MT-ECs are rare tumors that are difficult to diagnose. Recent reports suggest that patients with early-stage mixed tumors with a type II component of <10% had worse prognoses compared with patients with pure endometrioid adenocarcinoma (EAC) and should therefore be treated as high-grade tumors.<sup>[5]</sup> This novel study reported a rare case of endometrial stromal tumors in combination with MT-EC in a premenopausal woman and highlighted the association between malignant tumors.

## 2. Case presentation

### 2.1. Patient and diagnosis

This article does not need ethical approval. Written informed consent was obtained from the patient relative for publishing this study.

Editor: Eric Bush.

Written informed consent was obtained from the patient relative for publishing this study.

The authors declare that they have no conflict of interest.

<sup>a</sup> Department of Gynecology and Obstetrics, <sup>b</sup> Department of Pathology, First Affiliated Hospital of Dalian Medical University, Dalian, Liaoning, China.

\* Correspondence: Xiao-Xin Xiu, Department of Gynecology and Obstetrics, First Affiliated Hospital of Dalian Medical University, Dalian, Liaoning, 116011, China (e-mail: lt70@sina.com).

Copyright © 2017 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

Medicine (2017) 96:49(e8928)

Received: 3 May 2017 / Received in final form: 1 November 2017 / Accepted: 7 November 2017

<http://dx.doi.org/10.1097/MD.0000000000008928>

On May 16, 2016, a 47-year-old premenopausal woman presented to the First Affiliated Hospital of Dalian Medical University with the chief complaint of occasional lower abdominal pain. She found out a phyma in the lower abdomen with her fingers over half a month ago. Her gynecologic history included one full-term pregnancy, one normal delivery, and one abortion. Menarche had occurred at the age of 15 years, and menstruation had been irregular for almost a year. Her medical history included hypertension for the past 8 years, not controlled by medication. Blood pressure on admission was 150/100 mm Hg. She had no family history of cancer. She had no history of fever, dysuria, tuberculosis, diabetes, or weight loss. Liver, spleen, and peripheral lymph nodes were nonpalpable. The pelvic examination revealed a normal vagina, unremarkable cervix, and a uterus that was similar in size to that of a 3-month pregnant woman.

The patient was checked immediately after admission to the hospital. Liver function test, urinalysis, coagulation test, kidney function test, electrocardiogram, and chest x-ray showed no specific findings. The serum tumor markers determined were cancer antigen (CA) 19-9, 263.6 U/mL (normal range 0–27), and CA 125, 428.0 U/mL (normal range 0–35). The levels of these 2 markers were increased, but the levels of other markers were within normal range: carcinoembryonic antigen, 1.92 ng/mL (normal range 0–5); alpha-fetoprotein, 2.36 IU/mL (normal range 0–5.8); human epididymis protein 4, 55.10  $\mu$ mol/L (normal range 0–76.2); and squamous cell carcinoma antigen (SCCA), 0.98 ng/mL (normal range 0.1–1.5).

Transvaginal ultrasound examination showed that her uterus measured  $4.9 \times 5.2 \times 4.6$  cm. One uterine fibroid was detected on cervix uteri, measuring  $4.0 \times 3.0 \times 3.9$  cm. The endometrial thickness was 8 mm, and the echogenicity was homogeneous. A complex mass ( $12.3 \times 9.1 \times 6.3$  cm) with solid and cystic components on the right rear wall of the uterus was seen. Abdominopelvic computed tomography images (Fig. 1A and B) showed a pelvic cystic-solid mixed mass, which was thought to have originated from the right ovary and multiple uterine myomas.

The patient underwent an exploratory midline laparotomy on May 23, 2016, after intensive blood pressure control. The pelvic and abdominal organs were closely inspected during surgery. The gross appearance of the tumor was predominantly solid and lobulated, with varying degrees of necrosis on the uterine posterior wall. The tumor was fragile and pale inside, with deposits on bilateral parametrium. On peritoneal implantation,

multiple metastases were seen on the serosal surface of the bowel and greater omentum. The frozen section revealed a spindle cell sarcoma. The patient underwent a total abdominal hysterectomy, bilateral salpingo-oophorectomy, total omentectomy, and macroscopic clearance of the tumor. Postoperative recovery was uneventful.

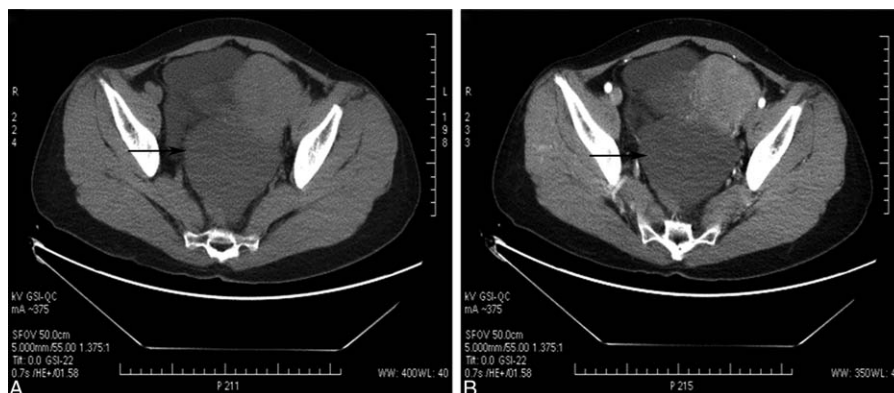
Subsequently, 3 cycles of adjuvant chemotherapy were given. The cycle was paclitaxel plus ifosfamide (270 mg paclitaxel on day 1 and 1.8 g ifosfamide on days 1–5; 21 d/cycle). The patient had to stop chemotherapy due to toxicities. Due to financial reasons, the patient could not afford radiation therapy and she declined any additional treatment. After half a year from diagnosis, surgery, and chemotherapy, the patient did not go back to the hospital for review. The patient was still alive when this report was written.

## 2.2. Pathology

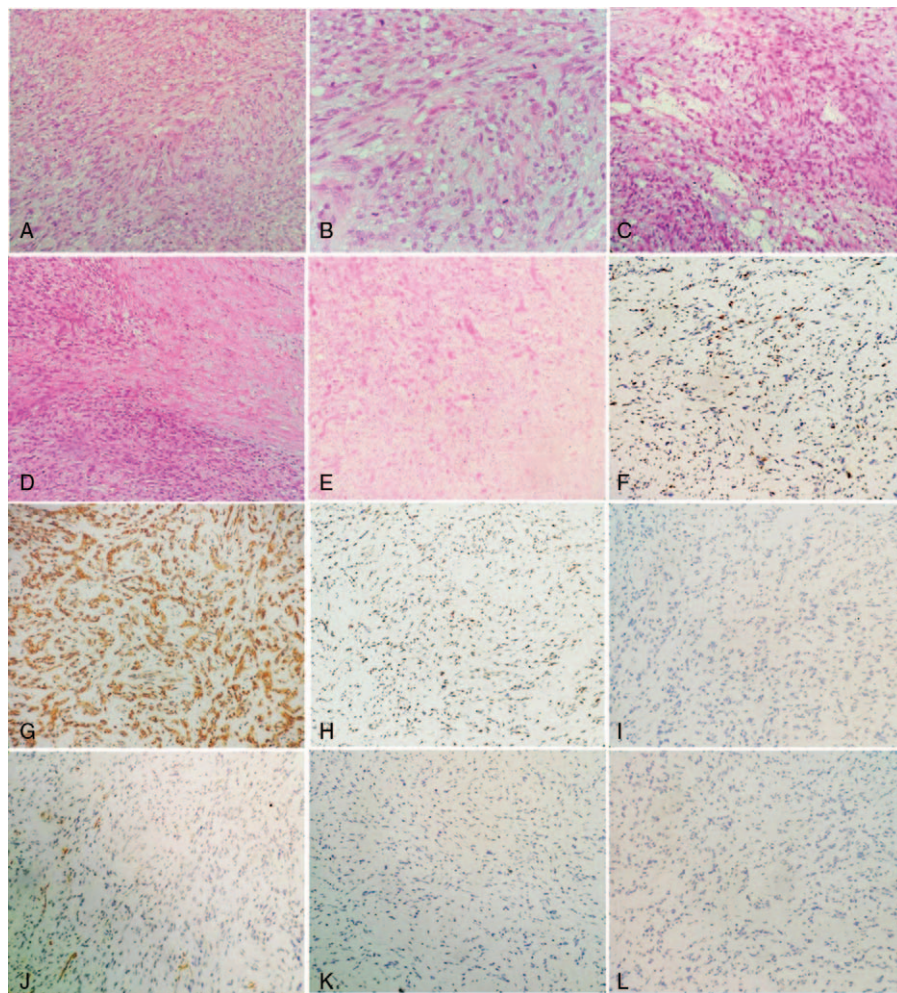
The naked eye examination showed that the uterus measured  $9 \times 7.5 \times 5$  cm, and the thickness of the endometrium was about 0.1 to 0.3 cm with a coarse appearance. A solid gray mass measuring  $17 \times 11 \times 6$  cm was found on the posterior wall of the uterus. Irregular solid masses were found on bilateral parametrium and great omentum. These masses had the same color and texture as those on the posterior wall of the uterus. Besides, a submucosal leiomyoma measuring  $2.8 \times 1.6 \times 1.5$  cm was detected in the cervix. Bilateral adnexa was normal.

For light microscopy examination, the tissues were fixed in 4% neutral buffered formaldehyde solution (pH 7.0) and routinely processed for paraffin embedding. Sections of 4- $\mu$ m thickness were stained with hematoxylin and eosin.

Paraffin-embedded sections also demonstrated the same morphological features as the masses on the posterior wall of the uterus, bilateral parametrium, and great omentum. The tumors were composed predominantly of spindle cells arranged in solid areas with interstitial fibrosis and mucinous degeneration (Fig. 2A, C, and D). Typical spiral arteries could not be found. The cells had bland nuclear features with monotonous oval- to spindle-shaped nuclei, but with relatively higher mitotic activity (about 4/high-power field) (Fig. 2B). Necrosis was found (Fig. 2E). Immunohistochemically, the tumor cells were positive for CD10 (Fig. 2G) and progesterone receptor (PR) (Fig. 2H), but negative for desmin (Fig. 2I), smooth muscle actin (SMA) (Fig. 2J), actin (Fig. 2K), calretinin, S-100 (Fig. 2L), pan-cytokeratin, cytokeratin5/6 (CK5/6), epithelial membrane antigen, CD34, discovered on



**Figure 1.** Abdominopelvic computed tomography images. (A) CT plain scanning. (B) CT enhanced scanning. A pelvic cystic-solid mixed mass (arrowheads), which was thought to have originated from the right ovary and multiple uterine myomas before operation.



**Figure 2.** Light microscopy examination and immunohistochemical expression of different indexes of the endometrial stromal sarcoma (ESS). (A) The tumor was composed predominantly of spindle cells arranged in solid areas. (B) The relatively higher mitotic activity (about 4/high-power field). (C) The mucinous degeneration of the tumor. (D) The interstitial fibrosis of the tumor. (E) Necrosis was found. The immunohistochemical expression of Ki-67 (F), CD10 (G), PR (H), desmin (I), SMA (J), actin (K), and S-100 (L) in the tumor.

gastrointestinal stromal tumors-1 (DOG-1), and cell differentiation (CD117). Besides, the cell proliferation marker Ki-67 was positive in about 15% of the tumor cells (Fig. 2F). A diagnosis of low-grade ESS was considered on the basis of the aforementioned staining results.

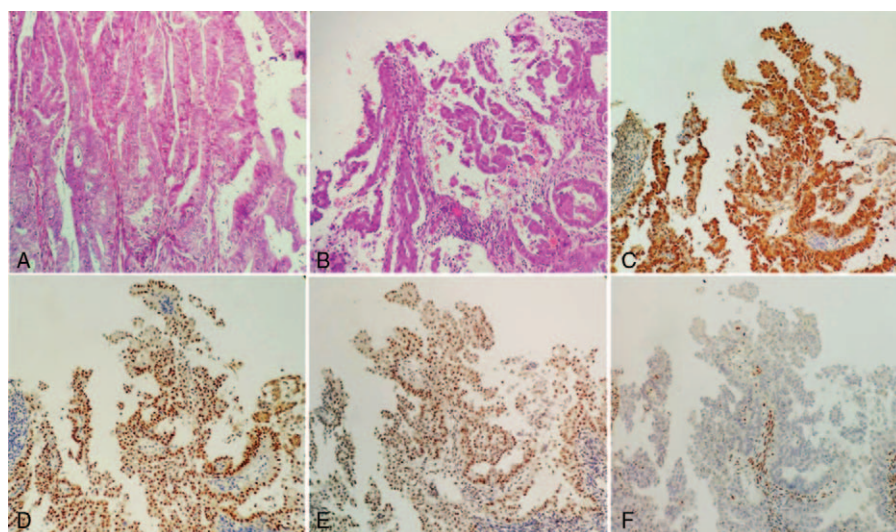
The histological examination revealed a nonencapsulated tumor in the endometrium that had infiltrated into the superficial muscular layer. No tumor cells were found in the cervix of the uterus. Part of this tumor (about 70%) was composed of atypical epithelioid cells arranged in glandular, villoglandular, and cribriform architectures. These cells had irregular round or oval nuclei with prominent nucleoli, and most of the nuclei were located on the basal side of the cells (Fig. 3A). In other areas (about 30%), papillary or micropapillary architectures composed of pleomorphic cells were found, and most of the nuclei were located in the free margin of the cells (Fig. 3B). The immunohistochemical analysis revealed that the pleomorphic cells were diffusely positive for p16 (Fig. 3C), p53 (Fig. 3D), and paired box gene 8 (Pax-8) (Fig. 3E); partially positive for ER; but negative for Wilm tumor gene (WT-1) (Fig. 3F). A diagnosis of mixed EEC-SC (about 70% of EAC and about 30% of serous adenocarcinoma) of the endometrium was made on the basis of morphology and immunohistochemistry, as previously

published.<sup>[6,7]</sup> According to the staging criteria of FIGO 2009 for endometrial carcinoma and FIGO 2010 for endometrial stromal tumor, the patient was diagnosed with Federation International of Gynecology and Obstetrics (FIGO) stage IIIB endometrial stromal tumor and FIGO stage IA MT-EC.

### 3. Discussion

Endometrial stromal tumors account for <1% of all uterine tumors.<sup>[8]</sup> They can be divided into 4 main categories currently recognized by the World Health Organization: endometrial stromal nodule, LG-ESS, high-grade ESS (HG-ESS), and uterine undifferentiated sarcoma.<sup>[6]</sup> Table 1 presents the published cases of similar cases. Tanveer et al<sup>[9]</sup> reported 1 case of a collision tumor of uterus made of high-grade ESS and squamous cell carcinoma. Lam et al<sup>[10]</sup> reported 2 cases of endometrioid carcinoma and stromal carcinoma of the uterus. Liu et al<sup>[11]</sup> reported 1 case of ESS with endometrioid adenocarcinoma of the uterus. Finally, Kim et al<sup>[12]</sup> reported 3 cases of endometrioid adenocarcinoma with ESS.

LG-ESS affects women primarily in the perimenopausal age group, and more than half of patients are diagnosed premenopausally.<sup>[6,8]</sup> The most common symptoms or signs are abnormal



**Figure 3.** Light microscopy examination of mixed endometrioid-serous carcinoma and immunohistochemical expressions of different indexes of the serous component. (A) The endometrioid component was composed of atypical epithelioid cells arranged in glandular, villoglandular, and cribriform architectures. (B) The serous component was composed of pleomorphic cells arranged in papillary or micropapillary architectures. The immunohistochemical expression of p16 (C), p53 (D), Pax-8 (E), and WT-1 (F) in the serous component.

uterine bleeding, pelvic pain, and dysmenorrhea.<sup>[6,8]</sup> Nearly one-third of patients present with symptoms or signs related to extrauterine spread, and one-fourth of patients are asymptomatic.<sup>[6,8]</sup> The most frequent site of extrauterine pelvic extension is the ovary.<sup>[8]</sup> Extrauterine pelvic extension of LG-ESS is also frequently associated with endometriosis.<sup>[13]</sup> LG-ESS might manifest as an endometrial polyp, such that endometrial biopsy is more likely to be diagnostic.<sup>[14]</sup> Obesity, diabetes, younger age at menarche, and tamoxifen are associated with increased risk of LG-ESS.<sup>[14]</sup>

Surgery is the most important procedure in managing patients with LG-ESS. Hysterectomy with bilateral salpingo-oophorectomy (BSO) is a preferred procedure. LG-ESS is often sensitive to hormones. BSO may play an important role to cease the hormonal production. Therefore, hormone replacement therapy for menopausal syndrome is contraindicated, and progestins

(megestrol and medroxyprogesterone acetate) or aromatase inhibitors are the therapeutic choice in managing women with LG-ESS, acting as postoperative adjuvant therapy for residual or recurrent diseases.<sup>[15]</sup> A Phase II study showed that single-agent mifepristone (RU-486) in managing LG-ESS could result in a stable disease rate of 50%.<sup>[16]</sup>

Secondary to the indolent nature of LG-ESS and the effectiveness of hormonal treatment, complete cytoreduction, even radical cytoreduction, is recommended for LG-ESS.<sup>[17-19]</sup> Several studies have investigated the usefulness of lymph node dissection in patients with LG-ESS. The reported lymphatic involvement of ESS ranges from 7% to 9%.<sup>[20-22]</sup> Although removing enlarged lymph nodes may be one of a completely cytoreductive procedure, a survival benefit has not been proven in the literature.<sup>[23]</sup>

**Table 1**

**Published cases similar to that of the present study.**

Date	Author	Age	Pathology components	Treatment	Prognosis
2017	Tanveer et al <sup>[9]</sup>	60	Endometrial stromal sarcoma and squamous cell carcinoma	Radical hysterectomy (Type III) + chemotherapy	Disease-free after 6 months
2015	Liu et al <sup>[11]</sup>	73	Endometrioid adenocarcinoma and endometrial stromal sarcoma	Complete hysterectomy and bilateral adnexectomy + PT chemotherapy: oxaliplatin (70 mg/m <sup>2</sup> , 133 mg) + duoxitasai (75 g/m <sup>2</sup> , 142 mg) × 2 cycles	No evidence of recurrence after 6 months
2015	Kim et al <sup>[12]</sup>	36	Endometrioid adenocarcinoma and endometrial stromal sarcoma	Total abdominal hysterectomy + Megace	Disease-free after 41 months
		55	Endometrioid adenocarcinoma and endometrial stromal sarcoma	Total abdominal hysterectomy + BSO; Carbo/taxol × 6 cycles s/p WPXRT with vaginal brachytherapy	Disease-free after 58 months
		59	Endometrioid adenocarcinoma + endometrial stromal sarcoma	Total abdominal hysterectomy + BSO, debulking planned for chemo but lost to F/U	Lost to follow-up after 2 months
1999	Lam et al <sup>[10]</sup>	85	Endometrioid adenocarcinoma and stromal sarcoma	NA	NA
		47	Endometrioid adenocarcinoma and stromal sarcoma	NA	NA
2017	Present case	47	Mixed endometrioid, serous carcinoma, and endometrial stromal sarcoma	Total abdominal hysterectomy, bilateral salpingo-oophorectomy, total omentectomy, and macroscopic clearance of the tumor; uncompleted chemotherapy	Alive

LG-ESS is an indolent tumor with a favorable prognosis, but characterized by late recurrences even in patients with Stage I disease, suggesting the requirement of a long-term follow-up.<sup>[18,20,24]</sup> Moreover, a literature review has shown that recurrent LG-ESS can occur 10 to 20 years after the initial diagnosis.<sup>[16]</sup> Stage is the most significant prognostic factor, and the 5-year overall survival rate for Stage I patients is >90%, but decreased to 50% for Stages III and IV.<sup>[18,20]</sup> The most common sites for recurrence are the pelvis and abdomen.<sup>[8]</sup> Because of relatively limited and focused areas of recurrence, it is possible to consider aggressive and intensive en bloc metastasectomy, similar to the treatment for other gynecological malignancies.<sup>[25,26]</sup> Nevertheless, due to the rarity of the disease, no prospective, randomized trials have been completed yet.

ECs are classified as type I or type II. Type I tumors are mostly of endometrioid histology and present as low-grade, early-stage tumors (FIGO I and II) with favorable outcomes. Meanwhile, type II carcinomas, which represent <10% of total EC cases, typically have serous or clear cell histologies and are usually high-grade tumors with myometrial and lymphovascular invasion and an aggressive clinical course. MT-ECs are tumors with both types I and II. SC is the prototype of type II EC and accounts for more than 10% of all ECs. SC usually occurs in a pure form, but occasionally, it may coexist with endometrioid EC (EEC).<sup>[5,27,28]</sup> It has been suggested that the serous component may arise as a result of the progression of endometrioid elements. When the second of these components is present in at least 5% of the tumor, the designation of MT-EC is used, the most frequent combination being mixed EEC-SC. The correct diagnosis of the second component is crucial to determine treatment options and outcome for these patients,<sup>[5,27,29]</sup> as it has been suggested that the presence of as little as 10% of a type II component can adversely affect patient's outcome. Some interobserver variation in histological typing exists in EC. This is partly due to the fact that some EEC may exhibit papillary arrangements and may be erroneously mistaken as SC. On the contrary, some pure SC may show a glandular growth that may be misinterpreted as EEC. Inappropriate interpretation of these unusual patterns may lead to incorrect diagnosis of mixed EEC-SC. Rigorous criteria should be used to avoid an incorrect diagnosis of either pure EEC or SC as mixed EEC-SC, and diagnosis should be confirmed with the help of immunohistochemistry or molecular tools. Mixed EEC-SCs are ambiguous tumors. The microdissected EEC component has molecular features of EEC, but also some features of SC. In contrast, the microdissected SC component has molecular characteristics of SC (p53 mutations) but retains EEC features (Kirsten rat sarcoma [K-RAS] and phosphatase and tensin homolog deleted from chromosome 10 [PTEN] mutations). Furthermore, a small group of high-grade EC tumors is molecularly and morphologically ambiguous. Classifying this small subset of tumors into SC or EEC is difficult and probably artificial.<sup>[28]</sup>

No consensus exists among gynecologic oncologists about the best approach to the management and treatment of patients with mixed tumors. Table 1 shows that the published cases were treated using a variety of approaches. Historically, early-stage ECs with a type II component of >25% of tumor volume are thought to behave as high-grade tumors and should be managed as such by treating with chemo/radiation therapy.<sup>[30]</sup> More recent reports suggest that patients with early-stage mixed tumors with a type II component of even >10% had worse prognoses compared with patients with pure EAC and should therefore also be treated as high-grade tumors.<sup>[5]</sup> A retrospective study by Fader

et al found all patients with a uterine SC component within their tumor specimens to be at a significant risk of recurrence and poor survival.<sup>[31]</sup> MT-ECs are rare tumors that are difficult to diagnose and, as a consequence, current occurrence estimates are probably inaccurate.

The patient in the present case was a 47-year-old premenopausal woman. The chief complaint of this patient was an occasional lower abdominal pain. She found out a phyma in the lower abdomen with her fingers. The symptoms or signs did not present abnormal uterine bleeding and dysmenorrhea. The patient's bilateral ovaries had no pathological changes. Pathological reports following surgery revealed concurrent endometrioid stromal tumors and MT-ECs. Cases of mixed EEC-SC and ESS coexisting in the same patient are extremely rare. The etiology and pathogenesis of this combination remain to be elucidated. Whether the development involves common carcinogenic agents or is just a coincidental event remains unclear. Perhaps their development may involve common carcinogenic agents. Further studies are needed to elucidate this phenomenon. No clear causal association has been established between ESS and MT-ECs. Hence, future studies should investigate synchronous malignant tumors. This extremely rare combination of tumors lacks standard management and therefore presents a challenge for treatment. Surgery is the mainstay approach, with adjuvant therapy consisting of chemotherapy and radiotherapy.

This study aimed to present a 47-year-old woman diagnosed with mixed EEC-SC and ESS. It represented an underreported area of gynecological medicine. The combination is extremely rare, and its etiology and pathogenesis need further exploration. This case study added to the knowledge of the biological behavior of rare mixed EEC-SC and ESS. More studies are needed to elucidate this combination.

## References

- [1] Hendrickson MR, Tavassoli FA, Kempson RL, Tavassoli FA, Devilee P. Mesenchymal tumors and related lesions. World Health Organization Classification of Tumors Pathology and Genetics of Tumors of the Breast and Female Genital Organs IARC Press, Lyon: 2003;233–44.
- [2] Wen KC, Horng HC, Wang PH, et al. Uterine sarcoma Part I-Uterine leiomyosarcoma: The Topic Advisory Group systematic review. *Taiwan J Obstet Gynecol* 2016;55:463–71.
- [3] Lawrenson K, Pakzamid E, Liu B, et al. Molecular Analysis of Mixed Endometrioid and Serous Adenocarcinoma of the Endometrium. *PLoS One* 2015;10: e0130909.
- [4] Ronnett BM, Zaino RJ, Ellenson LH, Kurman RJ. Endometrial Carcinoma. *Blaustein's Pathology of the Female Genital Tract* Springer, New York, NY:2002;538.
- [5] Quddus MR, Sung CJ, Zhang C, et al. Minor serous and clear cell components adversely affect prognosis in "mixed-type" endometrial carcinomas: a clinicopathologic study of 36 stage-I cases. *Reprod Sci* 2010;17:673–8.
- [6] Nucci MR. Practical issues related to uterine pathology: endometrial stromal tumors. *Mod Pathol* 2016;29(suppl 1):S92–103.
- [7] Gattius S, Matias-Guiu X. Practical issues in the diagnosis of serous carcinoma of the endometrium. *Mod Pathol* 2016;29(suppl 1): S45–58.
- [8] Prat J, Mbatani . Uterine sarcomas. *Int J Gynaecol Obstet* 2015;131 (suppl 2):S105–10.
- [9] Tanveer N, Gupta B, Pathre A, et al. A rare collision tumour of uterus—squamous cell carcinoma and endometrial stromal sarcoma. *J Clin Diagn Res* 2017;11:ED20–2.
- [10] Lam KY, Khoo US, Cheung A. Collision of endometrioid carcinoma and stromal sarcoma of the uterus: a report of two cases. *Int J Gynecol Pathol* 1999;18:77–81.
- [11] Liu G, Zhang C, Ma Z, et al. Endometrial stromal sarcoma with endometrioid adenocarcinoma of the uterus: a case report. *Int J Clin Exp Pathol* 2015;8:5242–6.

- [12] Kim G, Pham HQ, Ramzan A, et al. Endometrioid adenocarcinoma associated with endometrial stromal sarcoma: a rare, often unrecognized collision tumor. *Gynecol Oncol Rep* 2015;13:8–12.
- [13] Ali RH, Rouzbahman M. Endometrial stromal tumours revisited: an update based on the 2014 WHO classification. *J Clin Pathol* 2015; 68:325–32.
- [14] Amant F, Floquet A, Friedlander M, et al. Gynecologic Cancer InterGroup (GCIg) consensus review for endometrial stromal sarcoma. *Int J Gynecol Cancer* 2014;24(suppl 3):S67–72.
- [15] Ryu H, Choi YS, Song IC, et al. Long-term treatment of residual or recurrent low-grade endometrial stromal sarcoma with aromatase inhibitors: a report of two cases and a review of the literature. *Oncol Lett* 2015;10:3310–4.
- [16] Ramondetta LM, Johnson AJ, Sun CC, et al. Phase 2 trial of mifepristone (RU-486) in advanced or recurrent endometrioid adenocarcinoma or low-grade endometrial stromal sarcoma. *Cancer* 2009;115:1867–74.
- [17] Bai H, Yang J, Cao D, et al. Ovary and uterus-sparing procedures for low-grade endometrial stromal sarcoma: a retrospective study of 153 cases. *Gynecol Oncol* 2014;132:654–60.
- [18] Amant F, Moerman P, Cadron I, et al. The diagnostic problem of endometrial stromal sarcoma: report on six cases. *Gynecol Oncol* 2003; 90:37–43.
- [19] Thomas MB, Keeney GL, Podratz KC, et al. Endometrial stromal sarcoma: treatment and patterns of recurrence. *Int J Gynecol Cancer* 2009;19:253–6.
- [20] Chan JK, Kawar NM, Shin JY, et al. Endometrial stromal sarcoma: a population-based analysis. *Br J Cancer* 2008;99:1210–5.
- [21] Shah JP, Bryant CS, Kumar S, et al. Lymphadenectomy and ovarian preservation in low-grade endometrial stromal sarcoma. *Obstet Gynecol* 2008;112:1102–8.
- [22] Lange SS, Novetsky AP, Powell MA. Recent advances in the treatment of sarcomas in gynecology. *Discov Med* 2014;18:133–40.
- [23] Hensley ML. Role of chemotherapy and biomolecular therapy in the treatment of uterine sarcomas. *Best Pract Res Clin Obstet Gynaecol* 2011;25:773–82.
- [24] Donertas A, Nayki U, Nayki C, et al. Prognostic factors, treatment and outcome in a Turkish population with endometrial stromal sarcoma. *Asian Pac J Cancer Prev* 2015;16:881–7.
- [25] Wang PH, Wen KC, Yen MS. Challenges in the management of recurrent endometrial cancer. *J Chin Med Assoc* 2016;79:171–3.
- [26] Chen JR, Chang TC, Fu HC, et al. Outcomes of patients with surgically and pathologically staged IIIA-IVB pure endometrioid-type endometrial cancer: a Taiwanese Gynecology Oncology Group (TGOG-2005) retrospective cohort study (a STROBE-compliant article). *Medicine (Baltimore)* 2016;95:e3330.
- [27] Roelofsen T, van Ham MA, Wiersma van Tilburg JM, et al. Pure compared with mixed serous endometrial carcinoma: two different entities? *Obstet Gynecol* 2012;120:1371–81.
- [28] Soslow RA. Endometrial carcinomas with ambiguous features. *Semin Diagn Pathol* 2010;27:261–73.
- [29] Williams KE, Waters ED, Woolas RP, et al. Mixed serous-endometrioid carcinoma of the uterus: pathologic and cytopathologic analysis of a high-risk endometrial carcinoma. *Int J Gynecol Cancer* 1994;4: 7–18.
- [30] Roelofsen T, van Ham MA, de Hullu JA, et al. Clinical management of uterine papillary serous carcinoma. *Expert Rev Anticancer Ther* 2011; 11:71–81.
- [31] Fader AN, Starks D, Gehrig PA, et al. An updated clinicopathologic study of early-stage uterine papillary serous carcinoma (UPSC). *Gynecol Oncol* 2009;115:244–8.