Is high-grade endometrial stromal sarcoma the key to disease prognosis in cases of coexisting leiomyosarcoma? A case report

Feng Ling
The Affiliated Hospital of Southwest Medical University
Sibei Ruan
The Affiliated Hospital of Southwest Medical University
XiaoMing Xiong
The Affiliated Hospital of Southwest Medical University
Na Li
School of clinical medicine, Southwest Medical University
DongMei Zhao
The Affiliated Hospital of Southwest Medical University
Cuiwei Zhang (zcw.37@163.com)
The Affiliated Hospital of Southwest Medical University https://orcid.org/0000-0002-1248-6875

Case report

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Is high-grade endometrial stromal sarcoma the key to disease prognosis in cases of coexisting leiomyosarcoma? A case report

Feng LING[1], SiBei RUAN[1], XiaoMing XIONG[1], Na LI[2], DongMei ZHAO[3], and CuiWei ZHANG[1]

1. Department of Pathology, The Affiliated Hospital of Southwest Medical University, Luzhou, Sichuan 646000, P.R. China

2. School of clinical medicine, Southwest Medical University, Luzhou, Sichuan 646000, P.R. China

3. Department of Radiology, The Affiliated Hospital of Southwest Medical University, Luzhou, Sichuan 646000, P.R. China

***Correspondence to*:** Dr Cuiwei Zhang, Department of Pathology, The Affiliated Hospital of Southwest Medical University, 25 Taiping Street, Luzhou, Sichuan 646000, P.R. China

E-mail address: zcw.37@163.com

Abstract

Background: The uterine leiomyosarcoma combined high-grade endometrial stromal sarcoma (ESS) is quite rare.

Case presentation: We reported such a case in which high-grade ESS with BCOR gene alterations and leiomyosarcoma coexist in a patient. And, most impressively, high-grade ESS with BCOR gene alterations caused ovarian and pelvic metastases, although its volume was less than 1% of leiomyosarcoma.

Conclusions: We suggested that when both high-grade ESS BCOR gene alterations and leiomyosarcoma are present in a patient, the high-grade ESS needs to be noted in the pathological report even if it accounts for less than 1% of the tumour mass.

Key Words: uterine leiomyosarcoma, endometrial stromal sarcoma

Background

Uterine leiomyosarcoma and endometrial stromal sarcoma (ESS) are both malignant mesenchymal tumours originating from the primitive paramedian duct. Among them, uterine leiomyosarcoma is the most universal malignant

mesenchymal tumor, accounting for 1% of uterine malignant tumor[1]. ESS accounts for 0.2% of malignant uterine tumors[2]. The coexistence of these two kinds of malignant tumours in one patient is extremely rare.

Case presentation

Clinical history and findings

A 46-year-old female patient who had a history of abdominal pain for more than 4 months, with aggravated pain for half a month, went to the hospital. Admission examination: A palpable mass of approximately 20 cm in diameter was found on palpation of the abdomen. The mass was hard, with poor movement, a poor boundary and no tenderness. Total abdominal enhanced computed tomography (CT) showed multiple solid intrapelvic masses with accessory blood supply (FIGURE 1). The patient underwent bilateral resection of pelvic metastases, pelvic adhesions and intestinal adhesions under general anaesthesia.

Pathological findings

A 17 cm×13 cm×19 cm solid mass was under the serous membrane of the anterior uterine wall. There was no polyp or mass in the uterine cavity. The thickness of the endometrium was approximately 0.1 cm. The left ovary was enlarged, sized approximately 6 cm×5 cm×3 cm. There was a solid mass of approximately 2.8 cm×2.4 cm×2.2 cm in the left pelvic cavity. The cut surfaces

of the masses were grey-white and grey-yellow, with necrosis and cystic changes (FIGURE 1).

The pathological sections were stained with haematoxylin and eosin (H&E) and observed under a microscope. The normal structure of the entire endometrial structure was absent. The endometrial glands could not be observed. Most tumour cells were fusiform and fascicular with abundant eosinophilic cytoplasm, moderate to severe nuclear atypia, coarse chromatin, and prominent nucleoli. Haemorrhage and necrosis (indicative of coagulative necrosis), as well as multinucleated giant cells and vascular infiltration, were obvious (FIGURE 2). There were approximately 11 mitotic figures per 10 high power field (HPF). Sections were diffusely positive for α-smooth muscle actin (α-SMA), Vimentin, Desmin and Wilm's tumor gene-1 (WT-1) and partly positive for H-Caldesmon, estrogen receptor (ER) and progesterone receptor (PR). The Ki-67 proliferation index was approximately 10% (FIGURE 3). In summary, the diagnosis of leiomyosarcoma was supported by morphology and immunohistochemistry. This tumor accounted for more than 99% of the volume of the mass in the uterine.

The otherwise normal endometrium was replaced by a small portion of round or oval tumor cells that differed from the tumor cells in leiomyosarcoma. Their total volume was less than 1% of leiomyosarcoma. Compared with leiomyosarcoma cells, these tumour cells were larger and more heteromorphic, hyperchromatic and pleomorphic than leiomyosarcoma cells, similar to tumour

giant cells, and they had higher mitotic activity (50 MF/10 HPF). Tumour cell necrosis and vascular invasion were visible. Tumour cells had grown diffusely around the thin-walled vasculature (FIGURE 2). The sections were diffusely positive for CD10 and Vimentin, and partly positive for cyclinD1. The Ki-67 proliferation index was approximately 40%. The α-SMA, H-caldesmon, Desmin, WT-1, ER and PR were not expressed (FIGURE 3). The morphology and immunohistochemical results tended to indicate highly malignant ESS. Currently, based on different molecular characteristics, two subtypes of high-grade ESS have been identified: YWHAE-FAM22 gene fusion and BCOR gene alteration[3]. Furthermore, alterations in the YWHAE and BCOR genes (GSP YWHAE and GSP BCOR, Guangzhou LBP Medicine Science and Technology Co., LTD., China) were detected by fluorescence in situ hybridization, which identified BCOR gene alterations but not YWHAE gene alterations. However, the genetic alterations of BCOR or YWHAE were not detected in leiomyosarcoma (FIGURE 4). Therefore, less than 1% of the tumour cells were diagnosed as high-grade ESS with BCOR gene alterations, a newly described subtype of high-grade ESS[4]. More interestingly, the metastases on the left ovary and pelvis showed the same histological morphology and immunophenotype as the high-grade ESS.

Discussion

The presence of both leiomyosarcoma and ESS with ovarian and pelvic

metastases in a patient is extremely rare. Immunohistochemistry is a very useful adjunct method to identify ESS and leiomyosarcoma, which has helped in the present case as well. As far as this case was concerned, although only one mass was seen, we were more inclined to be two primary tumors, which involves several reasons. Firstly, the two tumors were completely separated, and there was no intersections and transition between them, which could be proved by the results of immunohistochemistry. Of course, ESS can be accompanied by smooth muscle differentiation. It have been are diagnosed as mixed endometrial stromal-smooth muscle tumors (MSST) when a minimum of 30% of the minor component is present in an otherwise typical stromal neoplasm or leiomyoma[5]. In other words, the mixed tumors are those tumors in which each of the two components comprises at least 30% of the area of the whole tumor[4]. Obviously, this case was not. In addition, it was reported that the MSST was benign or low-graded[6,7]. But it is inconsistent, depending on the both of two cells in this case are were malignant and poorly differentiated. In addition, fluorescence in situ hybridization revealed that the genetic changes of the two tumors were different: BCOR gene alterations were only detected in high-grade endometrial stromal sarcoma, and neither the BCOR gene alterations nor the YWHAE gene alterations were detected in leiomyosarcoma. Based on, we considered that high-grade ESS and leiomyosarcoma were coexisting in this patient. The size of leiomyosarcoma was so large that the uterine structure was deformed and the mass formed by

ESS was compressed. As a result, only one mass was observed.

Furthermore, high-grade ESS in the current World Health Organization classification is limited to tumors characterized by high-grade round cell morphology and harboring t(10;17)(q22;p13) resulting in YWHAE-NUTM2 fusion[8], A recent study have described another genetic alteration of ESS, harboring t(X;22)(p11.4;q13.2) resulting in ZC3H7B-BCOR fusion. It has been proposed as another morphologic variant of high-grade ESS[9]. The present case had been confirmed the existence of BOCR gene alterations. It has been reported that the clinical biological behavior of ESS with BOCR gene alterations is more aggressive[9].

However, some questions about this case remain: According to the principle of superiority, high-grade ESS, which accounts for less than 1% of tumour volume, may be easily neglected in a pathological diagnosis. in this case, the high-grade ESS metastasized to the left ovary and pelvis, naturally, seems to be the key factor determining the patient's clinical prognosis. Does this finding indicate that high-grade ESS with BCOR gene alterations metastasizes earlier than leiomyosarcoma[10]? Should the high-grade ESS drive the disease prognosis when both two tumours are present? At present, limited case reports cannot answer these questions. More similar case reports are needed to enrich the existing sparse knowledge of these rare tumors.

Conclusions

we suggest that when both high-grade ESS with BOCR gene alterations and leiomyosarcoma are coexistent in a patient, the high-grade ESS with BOCR gene alterations needs to be noted in the pathological report even if it accounts for less than 1% of the tumour mass.

List of abbreviations

ESS, endometrial stromal sarcoma

CT, computed tomography

MSST, mixed endometrial stromal-smooth muscle tumors

H&E, hematoxylin and eosin

HPF, high power field

α-SMA, α-smooth muscle actin

WT-1, wilm's tumor gene-1

ER, estrogen receptor

PR, progesterone receptor

Declarations

Ethics approval and conset to participate

The clinical sample used in the present study was obtained from a patient at the Affiliated Hospital of Southwest Medical University (Luzhou, Sichuan, China). The present study was approved by the Medical Ethics Committee of the Institutional Review Board of the Affiliated Hospital of Southwest Medical

University.

Consent for publication

Written informed consent for publication was obtained from patient in the present study.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Feng Ling and SiBei Ruan performed immunohistochemical staining and molecular experiments. XiaoMing Xiong contributed to morphological

observation. Na Li was responsible for clinical data collection. DongMei Zhao performed radiographic observation. CuiWei Zhang participated in and supervised the whole progression, wrote the manuscript and provided funding support. All authors read and approved the final manuscript.

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FIGURE 1. Radiographic findings. A1, Horizontal CT image showing the solid mass in the enlarged uterus; A2, Coronal and sagittal CT images of the uterus mass (yellow arrow); B1, The enlarged cystic solid mass in the ovary shown by horizontal CT; B2, Coronal and sagittal CT images of the ovary mass (orange arrow); C1, CT image of a horizontal plane through the mass in the left region of the uterus; C2, Coronal and sagittal CT images of the mass (red arrow).

FIGURE 2. H&E staining. A. The two types of cells were separated by hyalinized collagen and showed a clear dividing line: ESS with round-like tumour cells (black star) and the leiomyosarcoma with spindled tumour cells (red star); B. ESS; C. Leiomyosarcoma; D. Coagulative necrosis in leiomyosarcoma; E. Ovarian metastasis; F. Pelvic metastasis;

FIGURE 3. Immunohistochemical analysis of the uterine mass. A. Vimentin was diffusely positive in both tumor cells; B-H. Partial immunophenotyping (CD10, CyclinD1, α-SMA, H-caldesmon, Desmin, ER, PR) of the two kinds of cells showed almost opposite results; I. Ki-67 proliferation index was about 10% of leiomyosarcoma and 40% of ESS.

FIGURE 4. Fluorescence in situ hybridization (red probe centromeric, green probe telomeric). High-grade ESS cells were confirmed to have BCOR rearrangements (A) but not YWHAE rearrangements (B). Cells with no

rearrangements in either BCOR (C) or YWHAE (D).

Figures

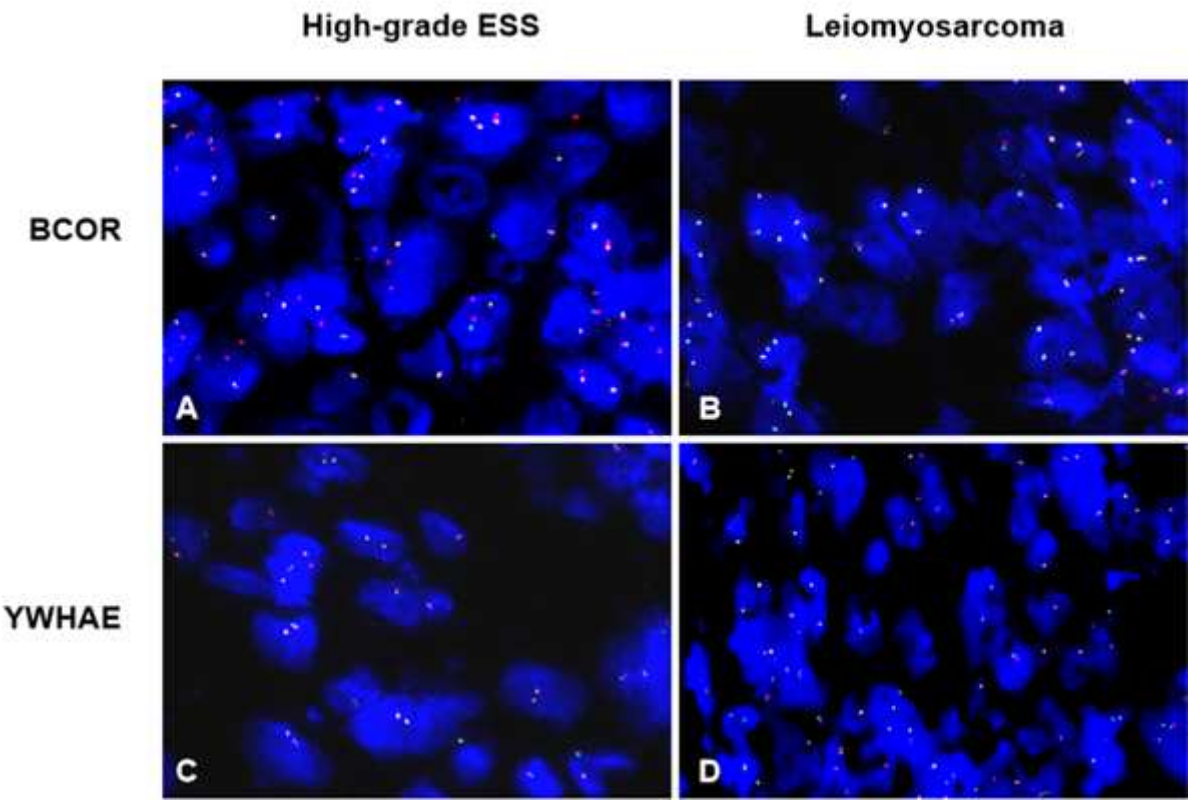


Figure 1

Fluorescence in situ hybridization (red probe centromeric, green probe telomeric). High-grade ESS cells were confirmed to have BCOR rearrangements (A) but not YWHAE rearrangements (B). Cells with no rearrangements in either BCOR (C) or YWHAE (D).

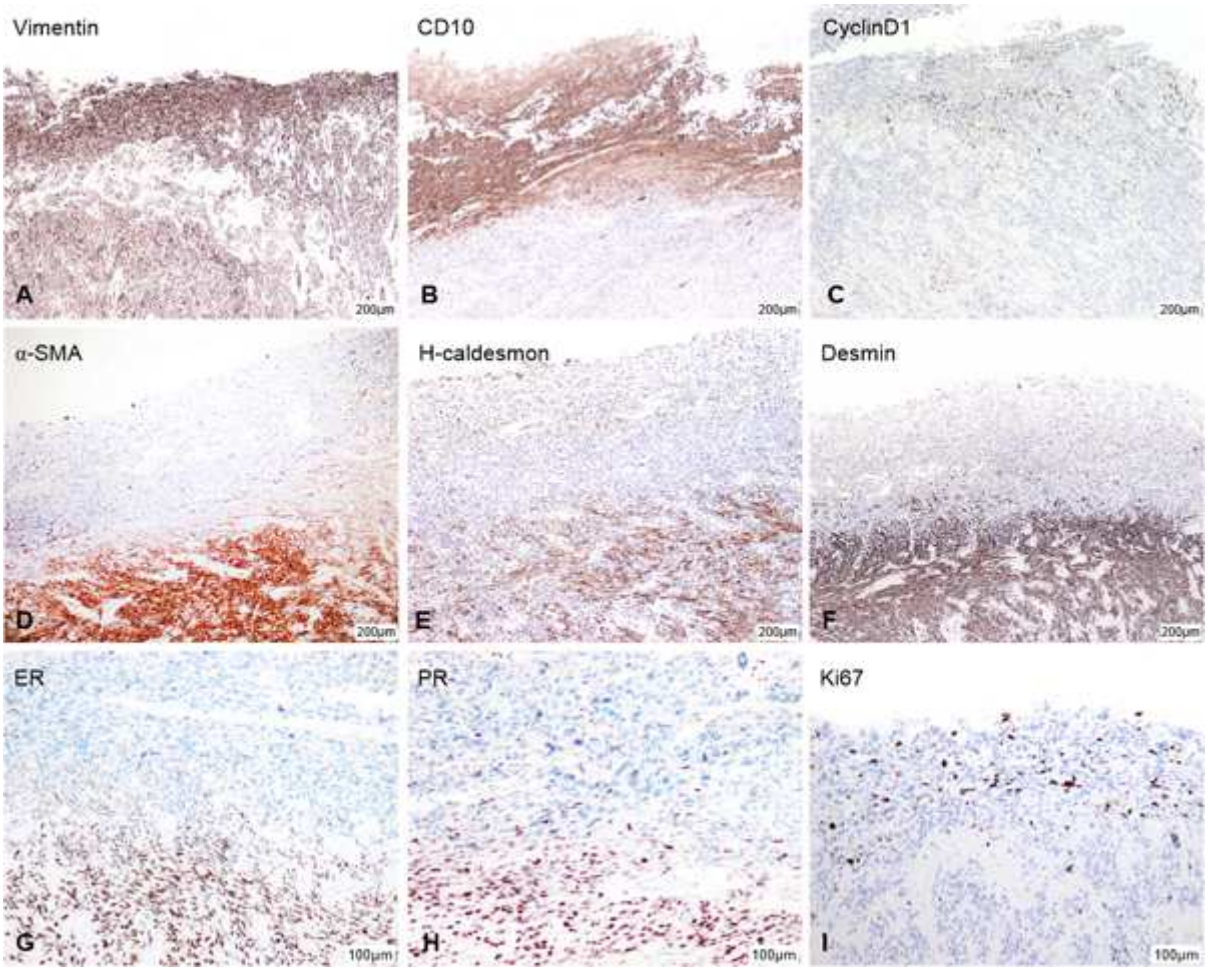
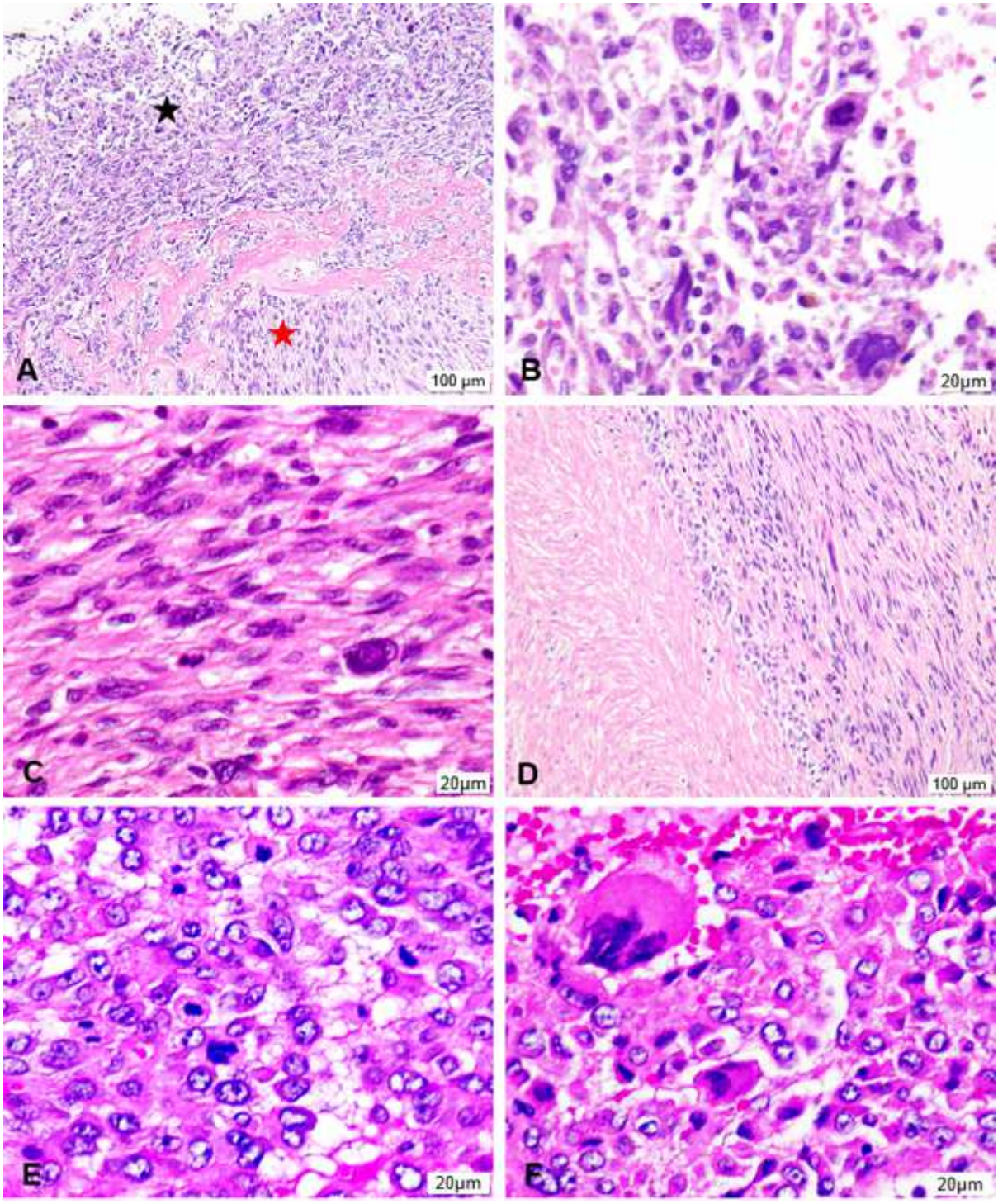


Figure 2

Immunohistochemical analysis of the uterine mass. A. Vimentin was diffusely positive in both tumor cells; B-H. Partial immunophenotyping (CD10, CyclinD1, α-SMA, H-caldesmon, Desmin, ER, PR) of the two kinds of cells showed almost opposite results; I. Ki-67 proliferation index was about 10% of leiomyosarcoma and 40% of ESS.



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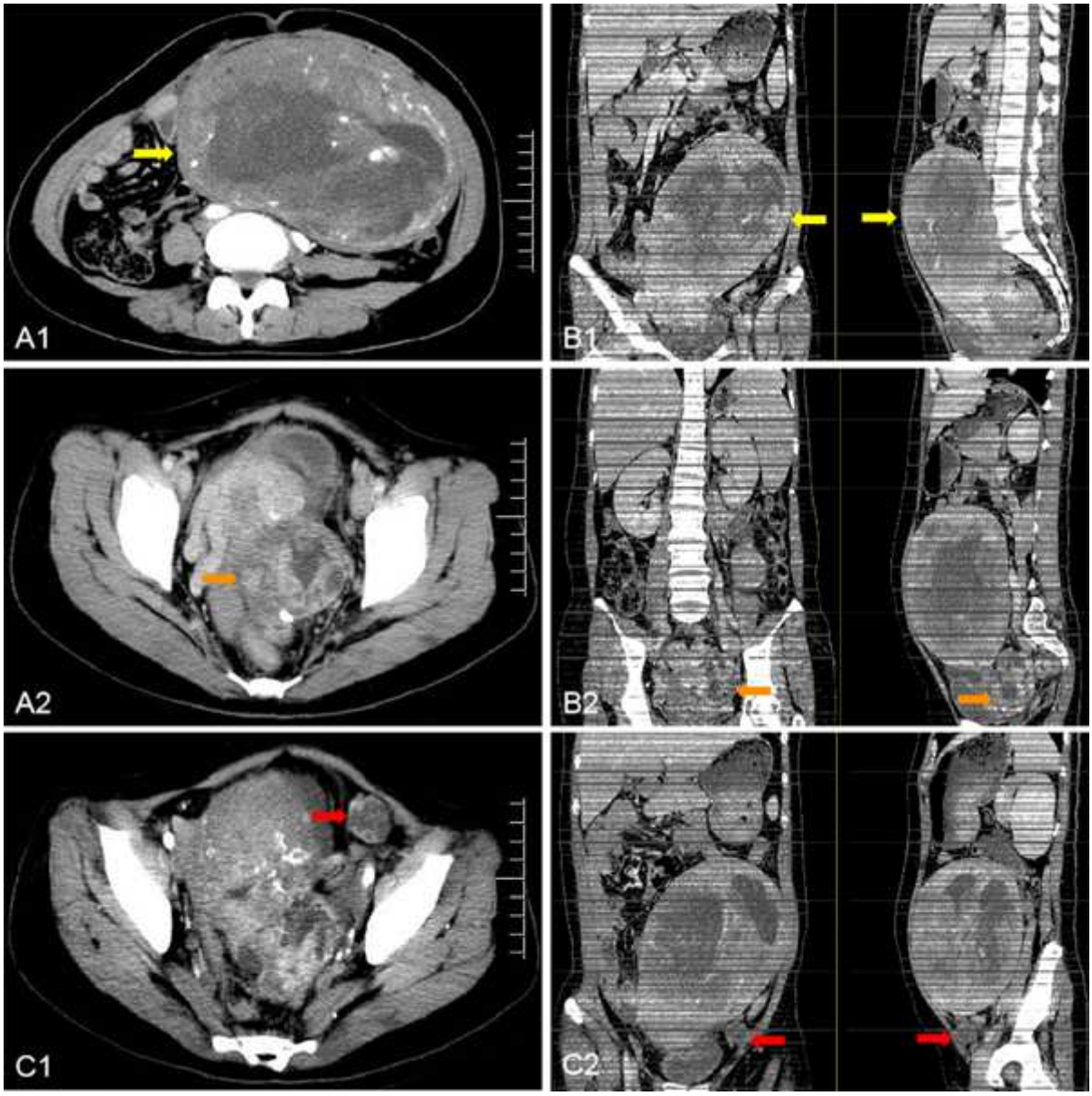

Figure 4

Radiographic findings. A1, Horizontal CT image showing the solid mass in the enlarged uterus; A2, Coronal and sagittal CT images of the uterus mass (yellow arrow); B1, The enlarged cystic solid mass in the ovary shown by horizontal CT; B2, Coronal and sagittal CT images of the ovary mass (orange arrow); C1, CT image of a horizontal plane through the mass in the left region of the uterus; C2, Coronal and sagittal CT images of the mass (red arrow).