

# High-grade Endometrial Stromal Sarcoma With BCOR Gene Alterations is Recommended as an Independent Subtype of Endometrial Carcinoma: A Case Report

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#### **Case Report**

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# Abstract

**Background:**The uterine leiomyosarcoma combined high-grade endometrial stromal sarcoma (HGESS) with BCOR gene alterations is exceedingly rare. The subtype of YWHAE-FAM22 HGESS is shown in the current World Health Organization classification, but not HGESS with BCOR alterations.

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

**Conclusions:** Given the more aggressive of HGESS with BCOR gene alterations, we suggest that it is classified as an independent subtype of HGESS, and when it coexists with other types of tumors, the HGESS with BCOR gene alterations needs to be noted in the pathological report even if it accounts for less than 1% of the tumour mass.

# **Case Presentation**

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, especially when the volume of ESS accounts for less than 1% of the tumour mass but causes ovarian and pelvic metastases. We reported such a case and confirmed that the existence of BOCR gene alterations in HGESS.

# Patient Information

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. She has no previous medical history, unusual psychosocial history and relevant family history.

## **Clinical findings**

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 (MF) per 10 high power field (HPF). Sections were diffusely positive for  $\alpha$ -smooth muscle actin ( $\alpha$ -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 2). 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 2). The morphology and immunohistochemical results tended to indicate highly malignant ESS. Currently, based on different molecular characteristics, two subtypes of HGESS 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 3). Therefore, less than 1% of the tumour cells were diagnosed as HGESS with BCOR gene alterations, a newly described subtype of HGESS (4). More interestingly, the metastases on the left ovary and pelvis showed the same histological morphology and immunophenotype as the HGESS.

## Therapeutic intervention and follow-up

The patient was treated with combination chemotherapy with docetaxel and gemcitabine followed by doxorubicin. No regeneration or metastasis was observed within 6 months after surgery. The long-term effect is still under review.

# 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, there were significant differences in the morphology and mitotic activity of the two kinds of tumor cells, and there was no intersections between them, which have been proved by the results of H&E staining and mmunohistochemistry. In addition, fluorescence in situ hybridization revealed that the genetic changes of them were different: BCOR gene alterations were only detected in HGESS, and neither the BCOR gene alterations nor the YWHAE gene alterations were detected in leiomyosarcoma. Of course, ESS can be accompanied by smooth muscle differentiation. It should been 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 lowgraded (6). But it is inconsistent, the both of two kinds of tumor cells were malignant and poorly differentiated in this case. Based on, we considered that HGESS and leiomyosarcoma were coexisting in this patient. The volume 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.

The HGESS 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 (7), A recent study have described a rare subtype of ESS with high grade features and BCOR alterations, caused by either a gene fusion between BCOR and ZC3H7B or a mutually exclusive somatic internal tandem duplication of exon 15 of BCOR (8). In the only few cases reported in the literature to date, it has been proposed that it is more aggressive as another morphological variant of HGESS (4). The present case had been confirmed the existence of BOCR gene alterations.

However, some questions about this case remain: According to the principle of superiority, HGESS, which accounts for less than 1% of mass volume, may be easily neglected in a pathological diagnosis. In this case, the HGESS 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 HGESS with BCOR gene alterations metastasizes earlier than leiomyosarcoma (7)? Should the HGESS 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

Given the high aggressive of HGESS with BCOR gene alterations, we suggest that it be classified as an independent subtype of HGESS. Further, we recommend that when both HGESS with BOCR gene

alterations and other malignant tumors such as leiomyosarcoma are coexistent in a patient, the HGESS with BOCR gene alterations needs to be noted in the pathological report even if it accounts for less than 1% of the tumour mass.

# Abbreviations

HGESS, high-grade endometrial stromal sarcoma

- CT, computed tomography
- H&E, haematoxylin and eosin
- MF, mitotic figures
- HPF, high power field
- α-SMA,α-smooth muscle actin
- WT-1, Wilm's tumor gene-1
- ER, estrogen receptor
- PR, progesterone receptor
- MSST, mixed endometrial stromal-smooth muscle tumors

# Declarations

### Ethics approval and consent 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 (No.:KY2019254). Written informed consent for publication was obtained from patient in the present study.

### Patient cinsent for publication

It is attached to the submission.

### Availability of data and materials

The datasets used 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. Na Li analyzed and interpreted the patient data. XiaoMing Xiong contributed to morphological observation. 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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# Figures



## Figure 1

Radiographic findings. A. 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 and Immunohistochemical analysis. 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; G. Vimentin was diffusely positive in both tumor cells; H-N. Partial immunophenotyping (CD10, CyclinD1, α-SMA, H-caldesmon,

Desmin, ER, PR) of the two kinds of cells showed almost opposite results; O. Ki-67 proliferation index was about 10% of leiomyosarcoma and 40% of ESS.



# High-grade ESS

## Leiomyosarcoma

# Figure 3

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