Uterine tumor resembling ovarian sex-cord tumor (UTROSCT) with sarcomatous features without recurrence after extended radical surgery

A case report

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Abstract

Objective: The malignant potential and the appropriate treatment of uterine tumor resembling ovarian sex-cord tumor (UTROSCT) is controversial. Although these tumors generally have benign outcomes, several reports have described recurrences, metastases, and deaths associated with this disease.

Patient concerns: A 57-year-old Japanese woman (gravida 2, para 2) was referred to our hospital for the evaluation and treatment of uterine fibroids. Magnetic resonance imaging revealed a right ovarian mass and multiple fibroids in the uterine myometrium.

Diagnoses: The patient was diagnosed with UTROSCT with sarcomatous features.

Interventions: She initially underwent a total abdominal hysterectomy and bilateral salpingo-oophorectomy, followed by second-stage surgery comprising pelvic and para-aortic lymphadenectomy and subtotal omentectomy.

Outcomes: No postoperative recurrence was observed in the patient in 36 months.

Lessons: In this case, extended radical surgery prevented the development of recurrent disease in a patient with UTROSCT with sarcomatous features. These clinicopathological findings suggest that UTROSCT is associated with several risk factors, including older age, presence of necrosis, lymphovascular invasion, significant nuclear atypia, and significant mitotic activity. This lesion type should be considered malignant and treated with curative intent.

Abbreviations: ESTSCLE = endometrial stromal tumors with sex cord-like elements, MRI = magnetic resonance imaging, UTROSCT = uterine tumor resembling ovarian sex-cord tumor.

Keywords: case report, extended radical surgery, immunohistochemistry, malignant behavior, uterine tumor resembling ovarian sex-cord tumor (UTROSCT)

1. Introduction

Uterine tumors infrequently exhibit ovarian sex cord-like features. In 1976, Clement and Scully further classified the tumors into two subgroups. The first subgroup, endometrioid stromal tumors with sex-cord-like elements (ESTSCLE), was characterized as containing focal (10%–40%) sex cord differentiation and was associated with an increased risk of recurrence and metastasis. These tumors are considered endometrioid stromal tumors. Tumors in the other subgroup contain more than 50% sex cord-like cells, with no recognizable endometrial stromal component. Unlike ESTSCLEs, these uterine tumors resembling ovarian sex-cord tumor (UTROSCT) are clearly separated from the surrounding tissues, exhibit distinct clinicopathological features, and are generally benign. Nevertheless, several cases of UTROSCT with recurrence and metastasis have been reported. Therefore, the malignant potential of UTROSCT, as well as the appropriate treatments, remains controversial.

The immunohistochemical expression profile of UTROSCT is polyphenotypic, and a diagnostic panel of four stains (calretinin, inhibin, CD99, and melan-A) has been proposed. Specifically, positivity for calretinin plus one of the other three stains is considered diagnostic. Researchers have attempted to identify the risk factors associated with recurrence and metastasis of UTROSCT. Moore et al reported several features associated with
a UTROSCT with malignant behavior, including older age, larger mass, presence of necrosis, lymphovascular invasion, cervical involvement, significant nuclear atypia, and significant mitotic activity. Nevertheless, only the presence of necrosis and significant mitotic activity were statistically significant. Lee et al reported that older age, larger mass, and significant mitotic activity were risk factors for malignant behavior. Here, we report a case of UTROSCT in an older patient who exhibited the presence of necrosis, lymphovascular invasion, significant nuclear atypia, and significant mitotic activity. However, no recurrence of this tumor occurred following the extended radical surgery.

2. Case presentation
A 57-year-old Japanese woman (gravida 2, para 2) had previously visited another clinic because of lower abdominal pain. A right ovarian mass and multiple uterine masses were detected using transvaginal ultrasonography, and she was referred to our hospital for evaluation and treatment. She had a history of hypertension and a family history of stomach cancer (father) and uterine leiomyomas and auditory tumor (mother). Magnetic resonance imaging (MRI) revealed a 50-mm mass in the right ovary and multiple fibroids in the uterine myometrium that were suspected to be an ovarian serous adenoma and uterine leiomyomas, respectively (Fig. 1A, B). No metastasis was detected on a systemic computed tomography scan. The serum levels of the tumor markers cancer antigen 125, carbohydrate antigen 19-9, and cancer antigen 72-4 were 11.5, 11.5, and 9.4 U/mL, respectively. Cervical and endometrial cytology were negative for neoplastic lesions.

The patient underwent a total abdominal hysterectomy and bilateral salpingo-oophorectomy. The uterine body contained a tumor measuring 25 mm × 20 mm located in the posterior wall that was not continuous with the endometrium. It had a mixed white, yellow, and black cut surface (Fig. 1C, D). Histologically, the tumor exhibited proliferating spindle- to oval-shaped cells with non-uniform nuclei, distinct nucleoli, and eosinophilic or scant cytoplasm arranged in sheets, follicles, fascicles, cords, and a tubular pattern (Fig. 2A, B). The majority of the tumor cells appeared mesenchymal in origin but did not appear to be endometrial stroma. Frequent mitotic figures were observed in the sarcomatous fascicular components (15–20/10 high-power fields; Fig. 2C). Myometrial invasion, lymphovascular invasion, necrosis, and hemorrhage were detected (Fig. 2D–F). No associated endometrial lesions were seen. The other uterine fibroids and the right ovarian tumor were diagnosed as leiomyomas and serous adenoma, respectively. No other neoplasias were present in the uterus or adnexa.

An immunohistochemical analysis of the surgical sample revealed that the tumor cells were positive for calretinin (diffuse), α-inhibin (focal), CD99 (focal), AE1/AE3 (diffuse), CD10 (focal),
estrogen receptor (diffuse), progesterone receptor (diffuse), S-100 protein (diffuse), vimentin (diffuse), CD56 (focal), chromogranin A (focal), and synaptophysin (very focal; Fig. 3A–D). The cells were negative for FOXL2, melan-A, epithelial membrane antigen, α-smooth muscle actin, desmin, human melanoma black-45, CD34, c-kit, and h-caldesmon (Fig. 3E). The MIB-1 labeling index was approximately 70% in the hot spot (Fig. 3F). Based on these findings, the patient was diagnosed with a UTROSCT with sarcomatous features. She underwent two-stage surgery (pelvic and para-aortic lymphadenectomy and subtotal omentectomy). Pathologically, the tumor had not extended into the cervix, adnexa, resected lymph nodes, or omentum. No recurrence was observed in the patient since the first surgery (39 months). We obtained written informed consent from the patient for publication.

3. Discussion

UTROSCT is a controversial disease entity, as several reports have described recurrences, metastases, and deaths associated with these usually benign tumors. Moore et al reported that 8 of 34 patients (23.5%) with UTROSCT developed extrauterine metastases to a variety of sites, including the pelvic and abdominal peritoneum, ovary, lymph nodes, bone, liver, and

Figure 2. Histology of the uterine tumor resembling ovarian sex-cord tumor (UTROSCT). The tumor exhibited a variety of histologic patterns including (A) sheets and follicle-like, (B) cord-like, and tubular structures. (C) The tumor contained significant nuclear atypia and mitotic activity. (D) Myometrial invasion, (E) lymphovascular invasion, and (F) necrosis were detected. Magnification: 20× for all but (C), 100×.
We reviewed these reported cases of UTROSCTs with malignant behavior (Table 1) and found that patients who underwent extended radical surgery did not develop recurrences. In contrast, hysterectomy alone was associated with a higher rate of recurrence. Therefore, extended radical surgery, including bilateral salpingo-oophorectomy, lymphadenectomy, and omentectomy, may reduce the rate of recurrence among cases of aggressive UTROSCTs.

In previous studies of UTROSCTs, malignant behavior was associated with older age, larger tumors, the presence of necrosis, lymphovascular invasion, cervical involvement, significant nuclear atypia, and significant mitotic activity. In particular, the presence of necrosis and significant mitotic activity was statistically significant. The present case exhibited mitotic activity, a high MIB-1 labeling index, necrosis, and lymphovascular invasion and hence, was considered high-risk for recurrence. Nevertheless, the patient underwent a second extended radical surgery, including lymphadenectomy, and progressed without recurrence. These results suggest that, for a high-risk UTROSCT, both hysterectomy and extended radical surgery, including salpingo-oophorectomy, parametrium resection, and pelvic and para-aortic lymphadenectomy, should be considered. Although no effective chemotherapy regimen has been identified, high-dose progesterone therapy may be effective for UTROSCTs which often exhibit diffuse positivity for hormone receptor expression.

UTROSCT is challenging because it is often detected incidentally after surgery for other benign lesions. For this reason, the initial treatment often does not involve sufficiently extensive surgery. Because UTROSCTs are often located within the uterine myometrium and do not involve the endometrium, they are not detected by endometrial biopsy. Takeuchi et al reported that UTROSCTs exhibited high signal intensity on MRI diffusion-weighted images in contrast to the generally low signal associated with leiomyoma. Therefore, this modality is useful for
a differential diagnosis.\(^{14}\) A combination of diffusion-weighted imaging and apparent diffusion coefficient maps are useful for distinguishing benign leiomyomas from leiomyosarcomas and smooth muscle tumors of uncertain malignant potential.\(^{15}\) Because the tumor in the present case exhibited high signal intensity on MRI diffusion-weighted images, we should have considered the possibility of malignancy. The initial surgery led to a diagnosis of UTROSCT, and a second-stage extended surgery was performed. We believe that second-stage surgery should not be avoided when a UTROSCT associated with several risk factors is encountered.

This study was limited by a lack of molecular analysis. UTROSCTs lack the \(JAZF1-SUZ12\) fusion that is characteristic of endometrial stromal tumors, indicating that these lesions are unlikely to be of endometrial stromal origin.\(^{16}\) Instead, we confirmed the presence of the characteristic immunohistochemical features of UTROSCT, the absence of morphological features of the endometrial stroma, and the absence of continuity with the endometrium.

In conclusion, we encountered a patient with UTROSCT with sarcomatous features who was successfully treated by extended surgery and did not develop recurrent disease. These clinicopathological findings suggest that a UTROSCT associated with several risk factors (e.g., older age, the presence of necrosis, lymphovascular invasion, significant nuclear atypia, and significant mitotic activity) should be considered a malignant tumor and treated with curative intent.

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**Author contributions**

MS: conception and writing of the manuscript. SS, YA, SA, HM: collection of clinical data. IY: pathologic diagnosis and immunohistochemical analysis. KN: collection of clinical data and revision of the manuscript. MY: conception, pathologic diagnosis, immunohistochemical analysis, and revision of the manuscript. All authors read and approved the final manuscript prior to submission.

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