[Case Report]

Uterine Tumor Resembling Ovarian Sex Cord Tumor: A Case Report

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Abstract **:** Uterine tumors resembling ovarian sex cord tumors (UTROSCTs) are extremely rare, occurring in less than 1% of uterine stromal tumors, and they are considered to have a low malignant potential. Due to the small number of cases, no standard treatment has been defined. A 77-year-old woman with postmenopausal bleeding was admitted to our department. Imaging studies revealed a substantial mass around 30 mm in size on the anterior uterine wall. A total hysterectomy and bilateral salpingo-oophorectomy were performed for further diagnosis and treatment. The tumor revealed histopathological findings of a sex cord-like growth pattern in the form of fascicles, cords, or small nests. Immunohistochemical findings revealed that the tumor cells were positively reactive to alpha-SMA, calretinin, CD99, estrogen receptor, and progesterone receptor, collectively diagnosed as UTROSCT. No recurrence was observed over 12 months after treatment. We experienced the treatment of UTROSCT, an extremely rare tumor that occurs in elderly women. Although most cases of UTROSCT have a benign clinical course, several cases of recurrence and metastasis have been reported. It should be followed up for a long term after treatment.

Keywords **:** uterine tumor resembling ovarian sex cord tumor, UTROSCT, endometrial cytology.

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Introduction

Uterine tumor resembling ovarian sex cord tumor (UTROSCT) is an extremely rare uterine neoplasm. It has been reported in fewer than 100 papers in English. UTROSCTs have polyphenotypic immunohistochemical expressions that include sex cords, epithelial, and smooth muscle lineage markers [1]. A small number of recent studies have shown the molecular biological features of UTROSCT, but their origins and characteristics remain unclear. Most cases of UTROSCT have a benign course, although several cases with recurrence or metastasis have been reported. UTROSCT has been treated by hysterectomy with or without bilateral salpingo-oophorectomy (BSO), and there is no standard treatment that considers the risk of recurrence due to

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the small number of reports.

Here we report a case of UTROSCT in a 77-year-old woman with postmenopausal bleeding and discuss the symptoms, pathological findings, including cytological diagnosis of endometrial smear, treatment, and outcome, in comparison with the profiles of previous cases.

Case report

The patient was a 77-year-old Japanese woman (gravida 4, para 2) with a history of hypertension and surgery for thyroid follicular adenoma and no specific family history. She was referred to our department for postmenopausal bleeding. On vaginal examination, there was a small amount of genital bleeding and an enlarged uterus, while the uterine cervix was grossly normal.

Transvaginal ultrasonography revealed a multicystic lesion in the uterine corpus, measuring 3cm in size, including a substantial area. Pelvic magnetic resonance imaging (MRI), showed a well-defined 25×27×22 mm tumor on the anterior uterine wall, with a heterogeneous high-signal area inside, on T2-weighted images (Figure 1). No lymph node or distant metastasis was detected on computed tomography (CT) scan. The tumor markers were as follow: cancer antigen 125 was 12.0 U/m*l* (normal range: <35.0 U/m*l*); carbohydrate antigen 19-9 was 24.1 U/m*l* (normal range: <37.0 U/m*l*); and carcinoembryonic antigen was 2.3 ng/m*l* (normal range: <3.5 ng/m*l*). All of these were within the reference values. Endometrial cytology revealed some oval or spindle-shaped atypical cells with mild nuclear enlargement, resembling endometrial stromal cells (Figure 2). An endometrial biopsy revealed no malignant findings. Cervical cytology was negative for intraepithelial lesion or malignancy (NILM).

Based on the preoperative diagnosis of uterine sarcoma, the patient underwent a total abdominal hysterectomy (TAH) and bilateral salpingo-oophorectomy (BSO). On gross findings, a 3cm well-demarcated tumor was found on the anterior uterine wall, with internal cystic structures containing bloody internal exudate (Figure 3). Intraoperative rapid diagnosis revealed no malignant tissue in the uterine corpus.

Histopathologically, the nodular lesion was composed of oval or spindle-shaped epithelial cells with eosinophilic cytoplasm in a pseudo-infiltrative appearance, arranged in sex cord-like growth patterns such as fascicles, cords, or small nests, with scattered mitoses (3 mitoses/10 high-power fields) (Figure 4A, B). The tumor had a pseudo-invasive appearance with hemorrhaging, whereas most of the tumor was well demarcated from the normal myometrium (Figure 4C: ×4, D: ×20). Except for the hemorrhage areas in the stroma, almost 80% of the tumor was composed of sex cord-

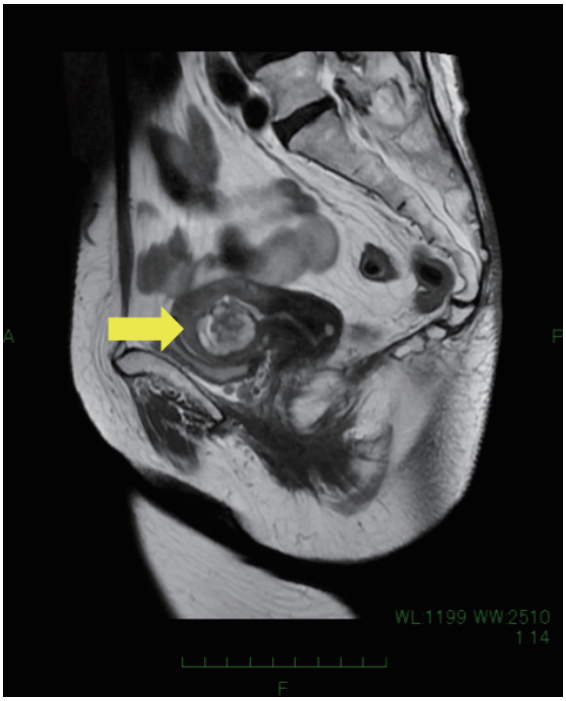

Figure 1. Magnetic resonance imaging (MRI) findings. T2-weighted image revealed a mass measuring 25×27×22 mm in the anterior uterine wall, which showed high and uneven signal intensity (yellow arrow).

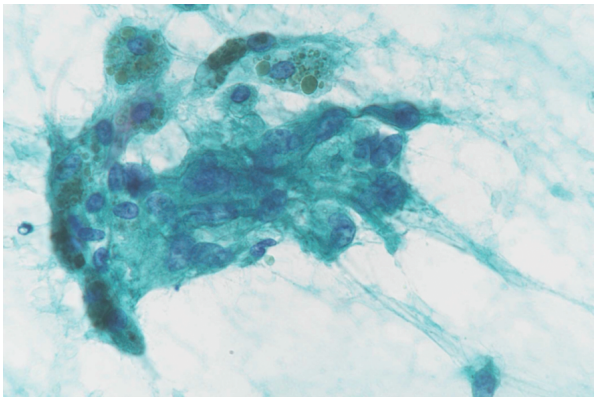

Figure 2. Endometrial cytology (Papanicolaou, ×20). Atypical cells that showed oval or spindle-shaped cells resembling stromal cells with mild nuclear enlargement.

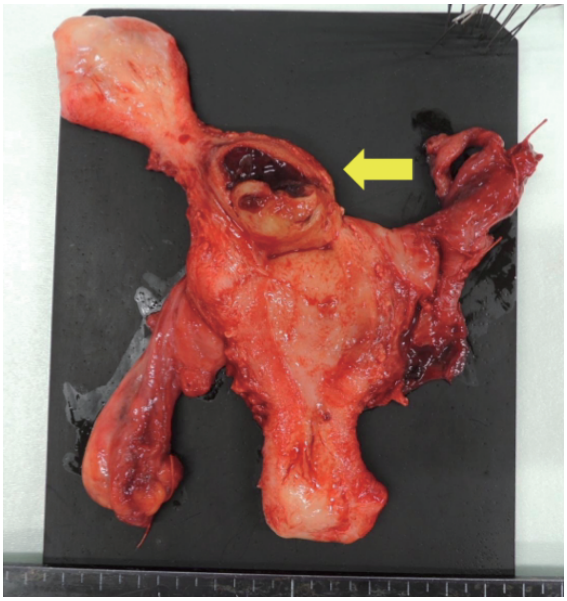

Figure 3. Macroscopic findings. A cystic tumor measuring 3cm was located in the uterine anterior wall (yellow arrow).

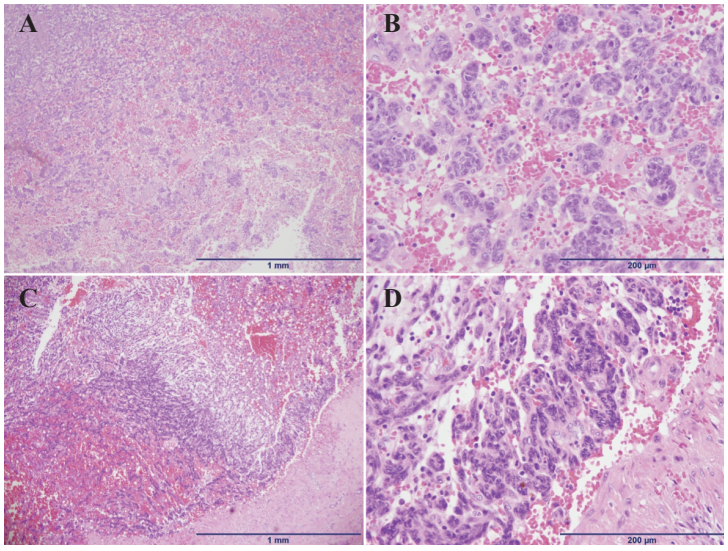

Figure 4. Microscopical findings (hematoxylin-eosin). The nodular lesion was composed of oval or spindle-shaped epithelial cells with eosinophilic cytoplasm, arranged in sex cord-like growth patterns such as fascicles, cords, or small nests (A: ×4, B: ×20). The tumor had a pseudo-invasive appearance with hemorrhage, whereas most of the tumor was well demarcated from the normal myometrium (C: ×4, D: ×20).

like components. There were no neoplastic changes in the uterine cervix and bilateral adnexae.

Immunohistochemically, the tumor cells were positively reactive to alpha-SMA, calretinin (Figure 5A), CD99 (Figure 5B), WT-1, estrogen receptor (ER), and progesterone receptor (PR). Some were also positive for desmin, h-caldesmon, CAM5.2 and inhibin, whereas AE1/AE3, EMA, HMB45, Melan A, CD10, and cyclin D1 were negative. The immunohistochemical results are summarized in Table 1. The histopathological findings were consistent with UTROSCT.

The patient was followed up regularly, and there was no recurrence in 12 months after the initial treatment.

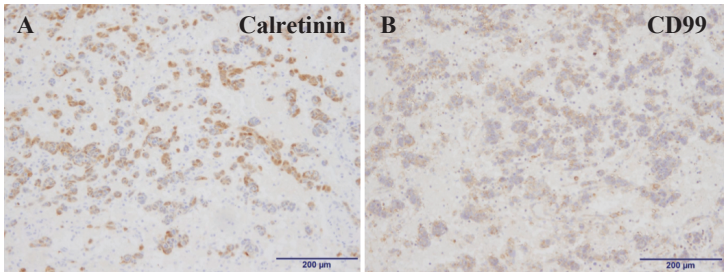

Figure 5. Immunohistochemical positive stain for Calretinin (A: × 10), CD99 (B: ×10).

Table 1. Summary of immunohistochemical results

Antibody		Result
alpha-SMA	myogenic marker	++
desmin	myogenic marker	+
h-caldesmon	myogenic marker	+
calretinin	sex cord marker	++
CD99	sex cord marker	++
inhibin	sex cord marker	+
ER	hormone receptor	++
PR	hormone receptor	++
CAM5.2	epithelial marker	+
AE1/AE3	epithelial marker	−
EMA	epithelial marker	−
WT-1	other	++
CD10	other	−
cyclin D1	other	−
HMB45	other	−
Melan A	other	−

alpha-SMA: alpha-smooth muscle actin, ER: estrogen receptor, PR: progesterone receptor, ++: positive, +: forcal positive, −: negative

Discussion

Uterine tumor resembling ovarian sex cord tumor (UTROSCT) was first reported in 1976. UTROSCTs were classified into two groups based on the composition of the sex cord-like elements [2]. Group I is endometrial stromal tumors containing less than 50% sex cord-like elements, and it is defined as endometrial stromal tumors with sex cord-like elements (ESTSCLE). Group II is defined when the sex-cord-like component accounts for 50% to 100% in a uterine-derived substantial tumor, which corresponds to UTROSCT. In the 2020 World Health Organization Classification, UTROSCT is defined as a uterine neoplasm with morphological patterns that resemble those seen in ovarian sex cord tumors, without a component of recognizable endometrial stroma.

UTROSCT usually occurs in perimenopausal women (mean age was 52.2) [3]. Common symptoms of UTROSCT were reported as postmenopausal bleeding (33.9%), abnormal menstruation (33.9%), and pelvic pain (18.6%)[4]. The present patient was a 77-year-old woman with postmenopausal bleeding. She was older than the mean age, although her symptom was consistent with those reported in the previous literature.

It is difficult to diagnose UTROSCT on imaging modalities such as ultrasonography, computed tomography, and MRI. Specific radiological findings are extremely limited. In our case, low-grade endometrial stromal sarcoma (ESS), leiomyosarcoma, or carcinosarcoma were suspected on preoperative MRI images.

UTROSCT is diagnosed by pathological findings using hematoxylin & eosin (H&E) and immunohistochemical staining. Histologically, it shows sex cord-like growth patterns, such as sheets, nests, trabeculae, cords, or tubules, with/without Sertoli-like or Leydig-like components. Immunohistochemically, UTROSCT is based on various sex cord markers and exhibits epithelial, myogenic, and sex hormone markers [1]. It is recommended to include two sex cord differentiation markers (calretinin and one of either melan A, CD99, or inhibin)[5] for a diagnosis of sex cord differentiation. In our case, the H&E staining revealed several sex cord-like growth patterns, and those tumor cells were positively reactive to calretinin, CD99, and inhibin as sex cord markers, and they were also positive for epithelial (CAM5.2), myogenic (alpha-SMA, desmin, h-caldesmon), and hormone receptors (ER and PR), leading to the diagnosis of UTROSCT.

In previous reports, UTROSCT was not suspected based on endometrial cytology. Preoperative endometrial cytology of uterine stromal tumors is considered to have a poor diagnostic value as well as a low positive rate due to the tumor being covered by normal endometrial tissue. In the present case, however, atypical cells were found, leading us to suspect that the tumor was not a typical benign tumor such as uterine myoma.

The recent literature focuses on the diagnosis of UTROSCT and lacks information on the characteristic symptoms, treatment, and prognosis. The preferred treatment method is surgery, which is hysterectomy with or without BSO, hysteroscopic mass resection, or myomectomy. Cömert *et al* reported that in 77 UTROSCT patients who underwent surgery, 61 underwent hysterectomy with or without BSO, 7 underwent hysterectomy with BSO and lymphadenectomy, and 9 underwent mass resection [6]. There was no disease-free and survival advantage for UTROSCT despite the addition of BSO or lymphadenectomy [3,6]. Due to the lack of data, no recommendations can be made regarding adjuvant radiotherapy, chemotherapy, or hormonal therapy. Hysterectomy is recommended as the standard treatment for UTROSCT.

Most cases of UTROSCT have a benign clinical course. Cömert *et al* reported that the recurrence rate was 6.3%, and the median follow-up time was 30 months (range; 3-296 months) [6]. A large case series reported that 8 of 34 patients (23.5%) diagnosed with UTROSCT developed metastasis outside the uterus and 3 patients (8.8%) died [7]. Malignant behavior has also been related to older age, tumor size, necrosis, lymphovascular invasion, cervical involvement, significant nuclear atypia, and significant mitotic activity [7]. The risk of recurrence and metastasis should be considered when deciding on a surgical approach. Fertility-sparing surgery, such as myomectomy or hysteroscopic tumor resection, has been performed in some patients, some of whom became pregnant and gave birth [8]. Fertility preservation should be considered in young women with UTROSCT. Our patient was a postmenopausal woman and therefore underwent TAH with BSO.

Conclusion

We report a case of UTROSCT with postmenopausal bleeding. Through this case presentation we have discussed the diagnostic procedures, radiological and pathological findings. Hysterectomy is a useful treatment for UTROSCT patients without desire to bear children, but, because of the small number of cases, no standard treatment has been established. Treatment should be considered according to individual UTROSCT cases.

Conflict of Interest

The authors declare that there is no conflict of interest.

References

1. Hurrell DP & McCluggage WG (2007): Uterine tumour resembling ovarian sex cord tumour is an immunohistochemically polyphenotypic neoplasm which exhibits coexpression of epithelial, myoid and sex cord markers. J Clin Pathol 60(10): 1148−1154
2. Clement PB & Scully RE (1976): Uterine tumors resembling ovarian sex-cord tumors. A clinicopathologic analysis of fourteen cases. Am J Clin Pathol 66(3): 512−525
3. Blake EA, Sheridan TB, Wang KL *et al* (2014): Clinical characteristics and outcomes of uterine tumors resembling ovarian sex-cord tumors (UTROSCT): a systematic review of literature. Eur J Obstet Gynecol Reprod Biol 181: 163−170
4. Zhou FF, He YT, Li Y, Zhang M & Chen FH (2021): Uterine tumor resembling an ovarian sex cord tumor: A case report and review of literature. World J Clin Cases 9(23): 6907−6915
5. Irving JA, Carinelli S & Prat J (2006): Uterine tumors resembling ovarian sex cord tumors are polyphenotypic neoplasms with true sex cord differentiation. Mod Pathol 19(1): 17−24
6. Cömert GK, Kiliç Ç, Çavuşoğlu D *et al* (2018): Recurrence in Uterine Tumors with Ovarian Sex-Cord Tumor Resemblance: A Case Report and Systematic Review. Turk Patoloji Derg 34(3): 225−233
7. Moore M & McCluggage WG (2017): Uterine tumour

resembling ovarian sex cord tumour: first report of a large series with follow-up. Histopathology 71(5): 751–759

8. Carbone MV, Cavaliere AF, Fedele C *et al* (2021): Uterine tumor resembling ovarian sex-cord tumor: Conservative surgery with successful delivery and case series. Eur J Obstet Gynecol Reprod Biol 256: 326–332