

Successful delivery after conservative resectoscopic surgery in a patient with a uterine tumor resembling ovarian sex cord tumor with myometrial invasion

Kyung Hee Jeong¹, Hye Nam Lee¹, Mi Kyoung Kim¹, Mi-La Kim¹, Seok Ju Seong¹, Eunah Shin²

Departments of ¹Obstetrics and Gynecology, ²Pathology, CHA Gangnam Medical Center, CHA University, Seoul, Korea

Uterine tumor resembling ovarian sex cord tumors (UTROSCT) is an extremely rare type of uterine stromal neoplasm that exhibits prominent sex cord-like differentiation. The clinical characteristics of a UTROSCT are not fully understood. Most reported cases of UTROSCT were treated by hysterectomy with or without bilateral salpingo-oophorectomy; however, a few cases have been treated by only tumor resection in patients who had a strong desire to preserve their fertility. We present a case of UTROSCT with myometrial invasion, which resulted in a successful delivery after the patient was treated by resectoscopic surgery and conservation of the uterus, and a brief review of the literature.

Keywords: Fertility preservation; Myometrial invasion; Tumor resection; Uterine tumor resembling ovarian sex cord tumor

Introduction

Uterine tumor resembling ovarian sex cord tumor (UTROSCT) is an extremely rare type of uterine stromal neoplasm, which was initially described by Morehead and Bowman in 1945 [1]. Clement and Scully [2] classified tumors with sex cord-like differentiation into 2 groups: endometrial stromal tumors with <50% sex cord-like elements (ESTSCLE, type I) and uterine tumor resembling ovarian sex cord tumors showing >50% sex cord differentiation (UTROSCT, type II). This morphologic distinction is clinically significant because ESTSCLE is associated with recurrences and metastases of the tumors; however, UTROSCT usually shows more benign clinical behavior. According to recent literature, UTROSCTs have been considered as uncertain malignancies with polyphenotypic immunohistochemical expression characterized by positive sex cord, epithelial, smooth muscle markers, and hormone receptors [3-5]. The treatment choice for UTROSCTs is hysterectomy with or without bilateral salpingo-oophorectomy. However, less than 10 cases of women who had a strong desire to preserve their fertility were treated conservatively, and only 2 subsequent pregnancies were reported [6-11]. We present a case of UTROSCT with myometrial invasion, which was successfully treated by resectoscopic surgery and conservation of the uterus, and a brief review of the literature.

Case report

A 32-year-old nulligravid woman visited our hospital in September 2010 for 3 years of infertility and prolonged menstruation. Previously, she underwent infertility work-up at another hospital. And she was diagnosed with right tubal obstruction on hysterosalpingography. In addition, a 3 cm sized submucosal myoma and multiple small follicles consistent with polycystic ovaries were observed in both ovaries on transvaginal ultrasonography. She failed to conceive despite multiple timed coitus and intrauterine insemination. In the initial transvaginal ultrasonography in our institution, a 3.2x2.6-cm-sized hetero-

Received: 2015.3.5. Revised: 2015.4.18. Accepted: 2015.5.6.

Corresponding author: Mi-La Kim

Department of Obstetrics and Gynecology, CHA Gangnam Medical Center, CHA University, 566 Nonhyeon-ro, Gangnam-gu, Seoul 06135, Korea

Tel: +82-2-3468-3671 Fax: +82-2-558-1112

E-mail: mila76@naver.com

Articles published in *Obstet Gynecol Sci* are open-access, distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/3.0/>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

Copyright © 2015 Korean Society of Obstetrics and Gynecology

geneous echoic mass was protruding into the endometrial cavity. Magnetic resonance imaging was conducted to study the possibility of a hysteroscopic approach, and a 3.6×3-cm-sized intracavitary protruding mass was observed in the anterior uterine wall. The image findings and treatment options were discussed with the patient, and she selected hysteroscopic resection of the mass despite the possible risk of incomplete removal or laparoscopic conversion. She underwent resectoscopic submucosal mass resection with complete removal of the presumed submucosal myoma. A diagnosis of type II UTROSCT with myometrial invasion was reported after pathologic evaluation. On hematoxylin/eosin staining, tumor showed a mixed pattern of cords, tubules, and nests related to sex cord-like differentiation with myometrial invasion (Fig. 1A, B). According to the immunohistochemical results, the neoplastic cells were positive for calretinin, CD99, CD56, and cytokeratin, but negative for CD10, CD34, inhibin, and WT1 (Fig. 1C-F). The diagnostic criteria for UTROSCT in immunohistochemical markers of sex cord differentiation should include calretinin and one of either melan A, CD99, or inhibin, WT1. Additionally, CD10, the endometrial stromal cell marker, should be

negative. Therefore, final diagnosis of this tumor was type II UTROSCT with myometrial invasion. After detailed discussions regarding the clinical behavior of UTROSCT with myometrial invasion, the patient chose to undergo pregnancy trial with *in vitro* fertilization (IVF), despite the possible risk of recurrence or metastasis.

The patient was then additionally evaluated with positron emission tomography-computed tomography, which revealed no evidence of strong focal fluorodeoxyglucose uptake to suggest malignant lesion or metastasis, but only mild heterogeneous fluorodeoxyglucose uptake in the uterus. The possible differential diagnosis for the latter was physiologic uptake or tumorous condition. Three months after the resectoscopic surgery, the patient was transferred to our fertility center for IVF and successfully conceived after the first postoperative IVF cycle.

Her pregnancy continued to progress without significant complications. At 36 weeks and 4 days of gestation, she visited the emergency room due to regular uterine contraction. She underwent an emergency cesarean section and a healthy baby (3.07 kg) was delivered. Her postoperative recovery was uneventful. Five months after delivery, she underwent total

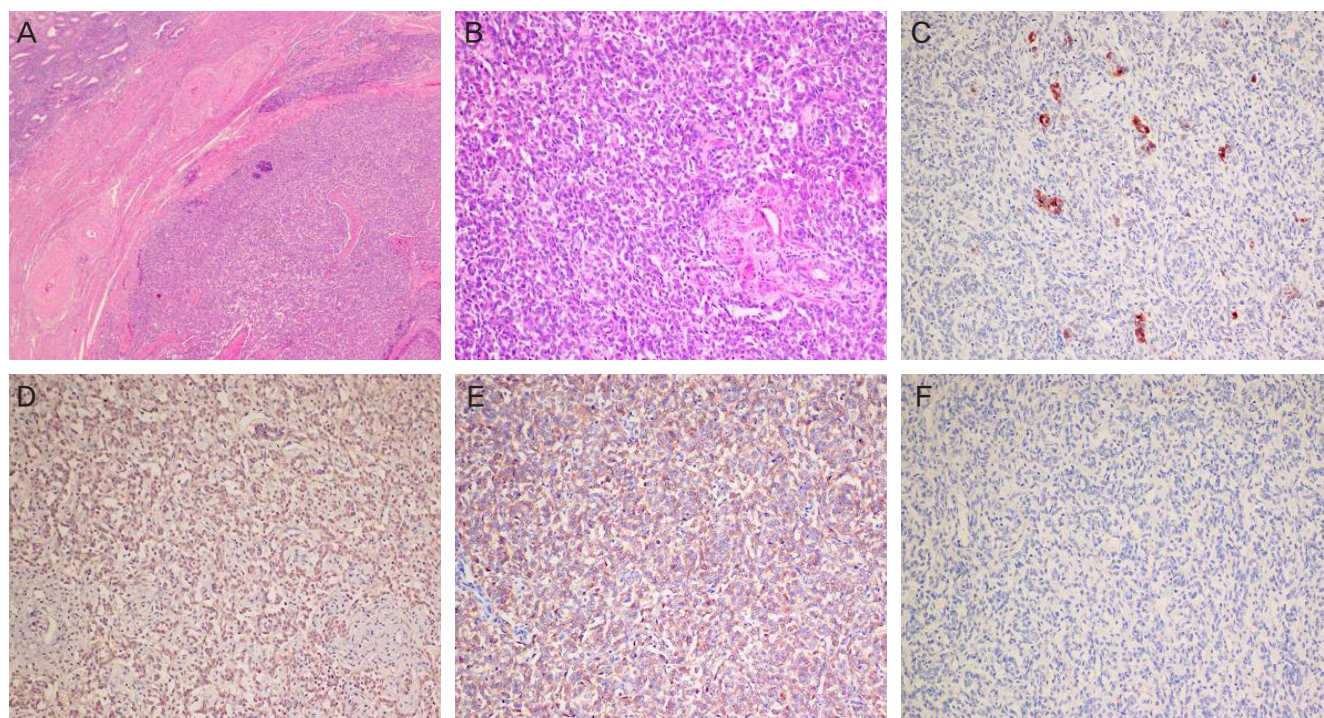


Fig. 1. Microscopic architectural patterns of the mass removed by resectoscopic surgery. (A) A relatively well-demarcated nodular mass within the superficial myometrium (H&E, ×40). (B) The tumor cells have relatively benign appearing, small round vesicular nuclei with nucleoli and eosinophilic cytoplasm (H&E, ×200). Immunohistochemical profile of the uterine tumors resembling ovarian sex cord tumor. (C) Positive for calretinin (calretinin, ×200). (D) Positive for CD99 (CD99, ×200). (E) Positive for CD56 (CD56, ×200). (F) Negative for CD10 (CD10, ×200).

laparoscopic hysterectomy with bilateral salpingectomy. After pathologic evaluations, the remaining type II UTROSCT was confirmed in the myometrium with similar immunohistochemical results. The patient was followed-up for 47 months after the initial resectoscopic surgery without evidence of recurrence.

Discussion

UTROSCT is a rare tumor and is usually regarded as a unique variant of uterine stromal sarcomas. In 1976, Clement and Scully classified 14 cases of UTROSCT as type I (ESTSCL) and type II (UTROSCT) according to composition of sex-cord like element [2]. The current World Health Organization classification defines type II tumors (UTROSCT) as miscellaneous tumors, and type I tumors (ESTSCL) are considered as rare variant of endometrial stromal tumors. World Health Organization classified endometrial stromal tumors as endometrial stromal nodules, low-grade endometrial stromal sarcomas, high-grade endometrial stromal sarcomas, and undifferentiated endometrial sarcomas. In this classification, endometrial stromal nodules and low-grade endometrial stromal sarcomas that include sex cord-like areas are regarded as rare variant-endometrial stromal nodules and sarcomas with sex cord-like pattern, so called ESTSCL (type I). However, UTROSCTs (type II) were defined as neoplasms that resemble ovarian sex cord tumors without a component of recognizable endometrial stroma [12]. These tumors are polyphenotypic neoplasms, and in the literature, they are termed as endometrial stromal tumors with sex cord-like differentiation, endolymphatic stromal myosis with sex cord-like differentiation, or low-grade endometrial stromal tumors with sex cord-like pattern. In a recent systemic review, the mean age at the time of UTROSCT diagnosis was 52.2 ± 18.2 years; approximately, $<1/3$ of the cases were observed in women aged <40 years [13]. Preoperative diagnosis of UTROSCTs is difficult because there are no specific imaging findings. This type of tumor is usually diagnosed based on the histomorphologic features including a predominant pattern of the cords, nests, and trabeculae resembling granulosa or Sertoli cell tumors of the ovary, and confirmed by immunohistochemical staining characterized by the co-expression of epithelial, smooth muscle, and sex cord markers, and steroid receptors [3-5].

In an immunohistochemical study, Irving et al., advocated for a polyphenotypic profile of these tumors by hypothesizing that they may arise from pluripotent mesenchymal cells and

predominantly differentiate into sex cord cells. They recommended that immunohistochemical markers of sex cord differentiation should include calretinin and one of either melan A, CD99, or inhibin [3]. de Leval et al. [14] also found that UTROSCTs exhibit sex cord markers, such as calretinin, inhibin, CD99, WT1, and Melan A. In our case, calretinin and CD99 were positive and CD10, the endometrial stromal cell marker, was negative.

A UTROSCT is generally discovered only after hysterectomy or tumor mass resection, and most patients with UTROSCT have been treated with hysterectomy with or without bilateral salpingo-oophorectomy. The long-term clinical behaviors of UTROSCT are less aggressive than ESTSCL; however, these tumors should be considered as neoplasms with an uncertain, but probably low, malignant potential [3,11,13,15]. UTROSCTs recur in very few cases with regional spread and late abdominal relapses; however, no deaths have been reported [2,11,13]. Therefore, conservative management can be considered with caution in young women who have a strong desire for fertility preservation. The results of subsequent pregnancies and recurrence after only conservative tumor resection in patients diagnosed with UTROSCT are shown in Table 1 [6-11]. There were only 2 reports of subsequent pregnancy after conservative surgery [6,7]. Our case was the third pregnancy report after conservative treatment in a patient with UTROSCT. More importantly, this was the first report of conservative management of a UTROSCT with myometrial invasion. After surgery, the patient successfully delivered, and then underwent definite surgical management. There were no reports of recurrence among patients who were conservatively managed during variable follow-up durations (13 months to 7 years) [6-11].

In a systemic review by Blake et al., the risk factors for disease free survival in UTROSCT were related to pelvic pain at the time of diagnosis, Clement type I tumor (ESTSCL), tumor size >10 cm, presence of cervical/extra-uterine disease, and lymphovascular space invasion [13]. According to a review article by Pradhan and Mohanty [15], infiltrative border, vascular invasion, frequent mitotic figures, serosal rupture, stromal predominance, and cytologic atypia were associated with recurrence of UTROSCT. Although UTROSCT with myometrial invasion was revealed through initial pathologic findings, the patient in our case was able to become successfully pregnant with IVF and subsequently delivered a healthy baby. There was no evidence of disease progression during the 17-month time interval between initial and definite surgery. This patient was followed-up for 47 months after initial surgery without evi-

Table 1. Review of the English-language published reports of conservative tumor resection only in patients with UTROSCT: subsequent pregnancies and recurrence^{a)}

Case no.	Study	Age at operation (yr)	Subsequent pregnancy	Follow-up duration	Recurrence
1	Hillard et al. (2004) [6]	32	Spontaneous conception after 15 months of surgery. No available delivery outcomes	18 mo	No
2	Anastasakis et al. (2008) [7]	28	Spontaneous conception after 6 months of surgery, and uneventful delivery	18 mo	No
3	Garuti et al. (2009) [8]	29	NA	13 mo	No
4	Berretta et al. (2009) [9]	26	NA	NA	NA
5	Giordano et al. (2010) [10]	26	NA	15 mo	No
6	Bakula-Zalewska et al. (2014) [11]	24	NA	5 yr	No
7	Bakula-Zalewska et al. (2014) [11]	25	NA	7 yr	No
8	Present case ^{b)}	32	In vitro fertilization after 3 months of surgery due to known PCO, cesarean delivery at 36+4 weeks due to preterm labor	47 mo	No

UTROSCT, uterine tumor resembling ovarian sex cord tumor; NA, not available; PCO, polycystic ovarian syndrome.

^{a)}In this literature review, cases with no or inadequate clinical information were excluded. ^{b)}After completion of family planning, she underwent hysterectomy with bilateral salpingectomy.

dence of recurrence.

In conclusion, gynecologists should consider conservative management of selected cases of UTROSCT with informed consent from the patients even though the ultimate outcome is unknown. A longer follow-up is needed to evaluate the safety of this conservative treatment.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

References

1. Morehead RP, Bowman MC. Heterologous mesodermal tumors of the uterus: report of a neoplasm resembling a granulosa cell tumor. *Am J Pathol* 1945;21:53-61.
2. Clement PB, Scully RE. Uterine tumors resembling ovarian sex-cord tumors: a clinicopathologic analysis of fourteen cases. *Am J Clin Pathol* 1976;66:512-25.
3. Irving JA, Carinelli S, Prat J. Uterine tumors resembling ovarian sex cord tumors are polyphenotypic neoplasms with true sex cord differentiation. *Mod Pathol* 2006;19:17-24.
4. Hurrell DP, McCluggage WG. 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* 2007;60:1148-54.
5. Czernobilsky B. Uterine tumors resembling ovarian sex cord tumors: an update. *Int J Gynecol Pathol* 2008;27:229-35.
6. Hillard JB, Malpica A, Ramirez PT. Conservative management of a uterine tumor resembling an ovarian sex cord-stromal tumor. *Gynecol Oncol* 2004;92:347-52.
7. Anastasakis E, Magos AL, Mould T, Economides DL. Uterine tumor resembling ovarian sex cord tumors treated by hysteroscopy. *Int J Gynaecol Obstet* 2008;101:194-5.
8. Garuti G, Gonfiantini C, Mirra M, Galli C, Luerti M. Uterine tumor resembling ovarian sex cord tumors treated by resectoscopic surgery. *J Minim Invasive Gynecol* 2009;16:236-40.
9. Berretta R, Patrelli TS, Fadda GM, Merisio C, Gramellini D, Nardelli GB. Uterine tumors resembling ovarian sex cord tumors: a case report of conservative management in young women. *Int J Gynecol Cancer* 2009;19:808-10.
10. Giordano G, Lombardi M, Brigati F, Mancini C, Silini EM. Clinicopathologic features of 2 new cases of uterine tumors resembling ovarian sex cord tumors. *Int J Gynecol Pathol* 2010;29:459-67.
11. Bakula-Zalewska E, Danska-Bidzinska A, Kowalewska M, Piascik A, Nasierowska-Guttmejer A, Bidzinski M. Uterine tumors resembling ovarian sex cord tumors, a clinicopathologic study of six cases. *Ann Diagn Pathol* 2014;18:329-32.

12. Kurman RJ, Carcangiu ML, Herrington CS, Young RH, editors. WHO classification of tumours of female reproductive organs. Lyon: International Agency for Research on Cancer; 2014.
13. Blake EA, Sheridan TB, Wang KL, Takiuchi T, Kodama M, Sawada K, et al. Clinical characteristics and outcomes of uterine tumors resembling ovarian sex-cord tumors (UTROSCT): a systematic review of literature. *Eur J Obstet Gynecol Reprod Biol* 2014;181:163-70.
14. de Leval L, Lim GS, Waltregny D, Oliva E. Diverse phenotypic profile of uterine tumors resembling ovarian sex cord tumors: an immunohistochemical study of 12 cases. *Am J Surg Pathol* 2010;34:1749-61.
15. Pradhan D, Mohanty SK. Uterine tumors resembling ovarian sex cord tumors. *Arch Pathol Lab Med* 2013;137:1832-6.