# Low-grade endometrial stromal sarcoma of the endocervix. Report of a case and review of the literature

**D. Hasiakos**[1], *M.D., Assist. Prof.*; **K. Papakonstantinou**[1], *M.D.*; **A. Kondi-Paphiti**[2], *M.D., Assoc. Prof.*; **S. Fotiou**[1], *M.D., Assoc. Prof.*

[1]*2nd Department of Obstetrics and Gynecology,* [2]*Department of Pathology, University of Athens, School of Medicine, Aretaieion Hospital, Athens (Greece)*

**Summary**

Cervical sarcomas are rare entities comprising 0.5% of all primary cervical malignancies. Endometrial stromal sarcoma (ESS) is the least common (< 10%) type of uterine sarcoma. It has traditionally been divided into two categories: low-grade stromal sarcoma (LGSS), which constitutes 50-60% of all ESS, and high-grade stromal sarcoma (HGSS). Low-grade ESS may arise in extrauterine locations, classically described as arising in foci of endometriosis. In our case, a 44-year-old woman presented with a 4-week history of abnormal vaginal secretions and occasional bleeding. Physical examination revealed a soft, hemorrhagic mass on the posterior cervix, approximately 7 x 4 x 3 cm, looking like a degenerated myoma. The patient underwent a radical hysterectomy with bilateral salpingo-oophorectomy and bilateral pelvic lymphadenectomy. Histopathological findings, including immunohistochemical study, led to the diagnosis of a LGSS of the endocervix, which was in close relation with endometriotic foci. Our case represents an extrauterine low-grade ESS arising in the endocervix, where a problem in the differential diagnosis was encountered and which was finally treated only with surgery. Adjuvant treatment of ESS is controversial. Generally, low-grade ESS is associated with good prognosis and long overall and disease-free survival.

*Key words:* Cervical sarcoma; Low-grade endometrial stromal sarcoma; Endocervix.

## Introduction

Endometrial stromal sarcoma (ESS) is the least common (< 10%) type of uterine sarcoma and constitutes 0.2% of all uterine malignancies. ESS was first described by Norris and Taylor in 1966, and has traditionally been divided into two categories: low-grade stromal sarcoma (LGSS) and high-grade stromal sarcoma (HGSS). Women with low-grade ESS, which constitute 50-60% of all ESSs, are younger than women with other uterine sarcomas, with an average age between 45-55 years [1]. Low-grade ESS may arise in extrauterine locations, classically described as arising in foci of endometriosis. Approximately 70 cases of extrauterine ESS have been reported in the literature and sites of origin include the ovary, omentum, rectovaginal septum, endocervix and peritoneum [2, 3].

Our objective was to describe the clinical and pathological findings of one case of low-grade endometrial stromal sarcoma arising in the endocervix in a 44- year-old woman and to review the literature.

## Case Report

A 44-year-old woman presented with a 4-week history of abnormal vaginal secretions and occasional bleeding. Her medical history was unremarkable. Physical examination revealed a soft, hemorrhagic mass on the posterior cervix, approximately 7 x 4 x 3 cm, looking like a degenerated fibromyoma. There was no evidence of parametrial invasion.

Ultrasonography (US) studies revealed a solid mass on the posterior cervix, of heterogeneous constitution and approximately 70 x 40 mm in dimension (Figure 1). Doppler examination showed a tumor with a rich vascular pattern and vessels of high resistance (PI = 1.16). The Papanicolaou smear revealed mild atypia of glandular cells. In the laboratory work-up decreased hemoglobin (9.4 g/dl) and hematocrit levels (29.7%) were found. The tumor markers (CA15-3, CA19-9, CA125, CEA, SCCA) were within normal limits. Since the presumed clinical diagnosis was "degenerated cervical leiomyoma", transvaginal excision of the cervical mass was initially performed along with a curettage (D&C) of the endocervix and the endometrium.

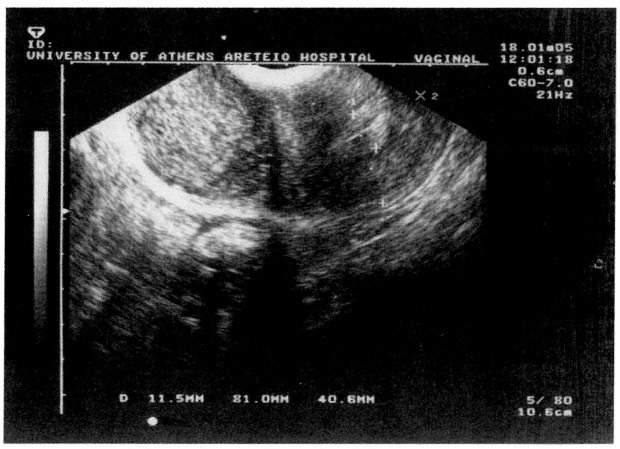
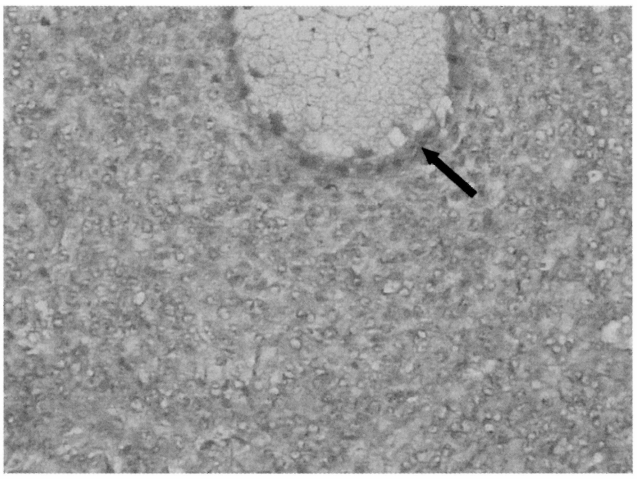



Figure 1. — Transvaginal ultrasonogram demonstrating a solid mass of heterogeneous constitution on the posterior cervix, measuring 70 x 40 mm in dimension.

Revised manuscript accepted for publication January 11, 2007

Fig. 1



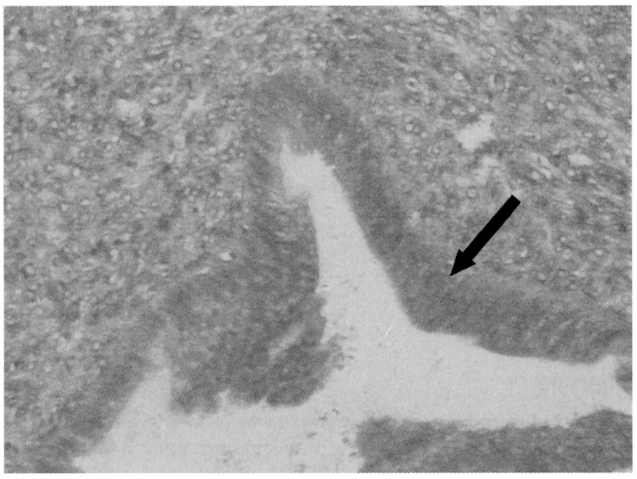


Fig. 2

Figure 2. — Histological section of the endometrial stromal sarcoma of the cervix showing part of a benign gland (arrow) (hematoxylin-eosin x 160).
Figure 3. — Histological section of the endometrial stromal sarcoma of the cervix showing an association with a focus of endometriosis (arrow) (H-E x 160).

On histopathological examination, multiple sections of the neoplasm presented the morphology of an endometrial stromal tumor with a low degree of mitotic activity (1-3 mitoses/10 HPF). Benign looking glands of endocervical type were present in the stromal component and the diagnosis of adenosarcoma was included in the differential diagnosis (Figure 2).

Based on the above findings, radical surgery was planned. The preoperative work-up, abdominal and chest CT included, was negative for metastatic disease. A small increase of the uterine dimensions and low density areas were the only findings on the abdominal CT. A Piver II radical hysterectomy with bilateral salpingo-oophorectomy along with systematic pelvic lymphadenectomy up to the level of the common iliac vessels was performed. Abdominal exploration did not reveal either any signs of abdominal endometriosis or metastatic disease. However the peritoneal washings were positive for malignancy (presence of cells in the uterine stromal sarcoma). The patient had an uneventful postoperative course and was discharged on the seventh postoperative day.

The histopathological examination of the surgical specimen confirmed the diagnosis of endometrial stromal sarcoma of low-degree malignancy. The immunohistochemical study showed the neoplastic cells to be vimentin (+), actin (-) and desmin (-). Estrogen and progesterone receptors were stained positive. The glands observed in the neoplasm were benign. There were also endocervical glands entrapped and in close relation to the superficial endocervical epithelium. The tumor was in close relation with endometriotic foci (Figure 3). Extensive cervical endometriosis and uterine adenomyosis were observed as well. The fallopian tubes and ovaries were free of disease. Twenty-eight excised lymph nodes were negative for metastatic tumor.

The case was discussed at the tumor board meeting and the tumor was classified as Stage IIIA, according to the FIGO surgical staging system for endometrial cancer. Although peritoneal cytology was positive, no adjuvant treatment was recommended. The patient has been followed-up regularly for one year without any signs of recurrence.

## Discussion

Cervical sarcomas are rare entities comprising 0.5% of all primary cervical malignancies. Endometrial stromal sarcomas belong to the homologous uterine sarcomas. Most ESSs are low-grade tumors, although some of them appear to be of higher grade, based on the nuclear size, degree of nuclear atypia, or mitotic activity. The former have traditionally been designated as low-grade ESS and the latter as high-grade ESS. The criteria for differentiating between LGSS and HGSS are controversial, and some pathologists believe that it would be more appropriate to classify HGSS as undifferentiated sarcoma rather than as a type of ESS. Norris and Taylor initially proposed the use of mitotic count to differentiate LGSS from HGSS. Tumors with less than 10 MF/10 HPF were classified as LGSS and those with 10 or more as HGSS [1]. However, Chang *et al.* [2] have shown that neither mitotic count nor cytologic atypia were statistically valid methods for dividing ESS into low- and high-grade types.

The most common symptom of the patients at presentation is abnormal vaginal bleeding, which occasionally is accompanied by abdominal discomfort and pain. The uterus is typically enlarged. Few women have bulky polypoid tumors that protrude from the cervical os. Although often indolent in behavior, ESS is a malignant tumor, and up to 30% of women with low-grade ESS have extrauterine disease at presentation [4]. Women with ESS generally do not have the usual risk factors for endometrial cancer, but a few patients occasionally present a history of prior pelvic irradiation [1]. A few cases of LGSS have been reported in women treated with tamoxifen for breast cancer [4]. LGSS usually cannot be detected on Papanicolaou smears because the cells lack sufficient atypia to permit their differentiation from benign endometrial stromal cells [1]. In our case, the Papanicolaou smear revealed only mild atypia of the glandular cells.

Low-grade ESS may arise in extrauterine locations, as in our case. More than 70 cases of extrauterine ESS have been reported in the literature. Chang *et al.* [2] reported 20 cases of such sarcomas and their sites of origin included the ovary, the fallopian tube, the pelvic cavity, the abdominal cavity and the retroperitoneum. Fukunaga

*et al.* [3] reported three more cases of extrauterine low-grade ESS, arising from the ovary, pelvic and abdominal cavities, two of which were associated with endometriosis. Endocervical stromal sarcoma (ECSS) is a quite rare neoplasm with less than 30 cases reported in the literature [5, 6]. Due to the limited number of reported cases, the natural history and optimal treatment for this disease are not clearly defined. The natural history of extrauterine ESS is probably best described by Chang *et al.* [2] and best characterized by prolonged disease-free intervals with late recurrences.

The role of endometriosis in the development of extrauterine ESS remains controversial. Fukunaga *et al.* [3] reported two cases of low-grade extrauterine ESS, which were associated with endometriosis. Clement *et al.* [7] differentiated between stromal endometriosis and ESS, stating that the former is characterized by an exclusive component of endometrial stroma and does not exhibit invasion. Chang *et al.* [2], however, argued that endometriosis is not a necessary prerequisite for the development of extrauterine ESS and instead proposed that the origin of this tumor may be related to the origin of endosalpingiosis and primary peritoneal carcinoma. In our case, the pathological evaluation revealed foci of endometriosis in the endocervix, closely associated with the tumor.

The main imaging findings of uterine sarcomas are large masses with extensive hemorrhage and necrosis. Heterogeneous echo patterns of uteri containing solid and cystic components have been described as non specific ultrasonographic findings of ESS [8]. Color Doppler US findings are not helpful in these tumors, since both low- and high-resistance flows have been described [8]. Although a low density mass with necrosis and hemorrhage are the most common CT and MRI findings of uterine sarcomas, there are no specific CT and MRI features to aid in the differential diagnosis [8, 9]. Endometrial carcinoma, uterine lymphoma, adenomyosis and myomas with secondary degeneration have been described as mimickers of uterine sarcomas on CT and MRI [9]. In our case, the clinical and US findings were misleading and the initial diagnosis was leiomyoma. The final diagnosis was based on pathologic findings. Amant *et al.* [10] reported that in 6/15 women suffering from ESS, the diagnosis was initially missed and the first diagnosis was leiomyoma in five cases.

Since ESS exhibits local extension and invasion into lymphatic and vascular spaces radical hysterectomy may be preferable although its advantage over simple hysterectomy has not been proven prospectively. Also, as these tumors are hormone responsive, oophorectomy has been recommended to decrease the recurrence rate. In one study, patients with LGESS and retained ovaries had a recurrence rate of 100%, but the recurrence rate was 43% for patients who had oophorectomies at the initial surgery [11]. The value of lymph node resection is controversial. A study by Riopel *et al.* [12] reported lymph node metastasis in five (33%) of 15 patients with endometrial stromal sarcoma undergoing lymph node dissection. The authors concluded that the incidence of lymph node involvement in ESS is higher than expected and the high recurrence rate may be due to occult lymph metastases. In our case, a radical hysterectomy (Piver II) with bilateral salpingo-oophorectomy along with systematic pelvic lymphadenectomy was performed.

The role of adjuvant treatment in ESS is not clear. The therapeutic effect of chemotherapy has been studied in some series and no potentially useful regimen was identified [13]. Chemotherapy did not decrease the progression of ESS. Postoperative radiotherapy has been shown to reduce central tumor but not distal recurrence and has not improved overall survival [14]. In our case, although positive cells were found in the peritoneal washings no adjuvant treatment was applied due to the low grade of malignancy and the absence of other signs of extrauterine disease. Also, hormonal therapy has been used, since these tumors are characterized by high levels of estrogen and progesterone receptors. There are studies which report that adjuvant progestin therapy can be effective in treating disease recurrence in low-grade ESS [15].

In conclusion, although the overall survival rates for patients suffering from uterine sarcoma are poor, low-grade ESS is associated with a good prognosis and long overall and disease-free survival. ESS has an indolent growth pattern associated with 80-100% 5-year survival, but about 37-60% of patients eventually recur after a very long time and 15-25% die of disease [1]. Our case represents an extrauterine low-grade ESS arising in the endocervix, where a problem in the differential diagnosis was encountered and which was finally treated only with surgery.

## References

[1] Zaloudek C., Hendrickson M.R.: "Mesenchymal tumors of the uterus". In: Kurman R.J. (ed.): "Blaustein's Pathology of the Female Genital Tract". 5th edition, New York, Springer, 2002, 586.

[2] Chang K.L., Crabtree G.S., Lim-Tan S.K., Kempson R.L., Hendrickson M.R.: "Primary extrauterine endometrial stromal neoplasms: a clinicopathologic study of 20 cases and a review of the literature". *Int. J. Gynecol. Pathol.*, 1993, *12*, 282.

[3] Fukunaga M., Ishihara A., Ushigome S.: "Extrauterine low-grade endometrial stromal sarcoma: report of three cases". *Pathol. Int.*, 1998, *48*, 297.

[4] Boardman C.H., Webb M.J., Jefferies J.A.: "Low-grade endometrial stromal sarcoma of the ectocervix after therapy for breast cancer". *Gynecol. Oncol.*, 2000, *79*, 120.

[5] Abdul-Karim F.W., Bazi T.M., Sorensen K., Nasr M.F.: "Sarcoma of the uterine cervix: Clinicopathologic findings in three cases". *Gynecol. Oncol.*, 1987, *26*, 103.

[6] Rotmensch J., Rosenshein N.B., Woodruff J.D.: "Cervical sarcoma: A review". *Obstet. Gynecol. Surv.*, 1983, *38*, 456.

[7] Clement P.B., Young R.H., Scully R.E.: "Stromal endometriosis of the uterine cervix. A variant of endometriosis that may stimulate a sarcoma". *Am. J. Surg. Pathol.*, 1990, *14*, 449.

[8] Gandolfo N., Gandolfo N.G., Serafini G., Martinoli C.: "Endometrial stromal sarcoma of the uterus: MR and US findings". *Eur. Radiol.*, 2000, *10*, 776.

[9] Rha S.E., Byum J.Y., Jung S.E., Lee S.L., Cho S.M., Hwang S.S. *et al.*: "CT and MRI of uterine sarcomas and their mimickers". *AJR*, 2003, *181*, 1369.

[10] Amant F., Moerman P., Cadron I., Neven P., Berteloot P., Vergote I.: "The diagnostic problem of endometrial stromal sarcoma: report on six cases". *Gynecol. Oncol.*, 2003, *90*, 37.

[11] Schwartz S.M., Thomas D.B.: "A case-control study of risk factors for sarcomas of the uterus. The World Health Organization collaborative study of neoplasia and steroid contraceptives". *Cancer*, 1989, *64* (12), 2487.
[12] Riopel J., Plante M., Renaud M.C., Roy M., Tetu B.: "Lymph node metastases in low-grade endometrial stromal sarcoma". *Gynecol. Oncol.*, 2005, *96*, 402.
[13] Huang K.T., Chen C.A., Tseng G.C., Chen T.M., Cheng W.F., Hsieh C.Y.: "Endometrial stromal sarcoma of twenty cases". *Acta Obstet. Gynecol. Scand.,* 1996, *75*, 551.
[14] Haberal A., Kayikcioglu F., Boran N., Caliskan E., Ozgul N., Kose M.F.: "Endometrial stromal sarcoma of the uterus: analysis of 25 patients". *Eur. J. Obst. Gynecol.*, 2003, *109*, 209.
[15] Keen C.E., Philip G.: "Progestogen-induced regression in low-grade endometrial stromal sarcoma. Case report and literature review". *Br. J. Obstet. Cynaecol.*, 1989, *96*, 1435.

Address reprint requests to:
A. KONDI-PAFITI, M.D.
Pathology Laboratory,
Aretaieion Hospital, School of Medicine
Vas Sofias 76, Athens, 11528 (Greece)