Endometrial stromal sarcoma in a 29-year-old patient. Case report and review of the literature

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Summary

Objective: Endometrial stromal sarcomas are rare tumors accounting for about 0.2% of all genital tract malignancies. They are considered to occur more often in premenopausal women. Endometrial stromal sarcomas are hormone sensitive tumors. A state of hyper-estrogenemia could act as a growth stimulus. Given the rarity of these tumors there are limited reports in the literature referring to the clinical management and final outcome of these cases. *Case:* The patient, a 29-year-old woman, had a surgical history of myomectomy in another hospital three months before her referal to our department. The histological examination of the removed myoma showed an endometrial stromal sarcoma. Total abdominal hysterectomy, with bilateral salpingo-oophorectomy, omentectomy and elective pelvic lymphadenectomy were then performed as a second radical surgical approach. *Conclusion:* Endometrial stromal sarcomas are uncommon and their differential diagnosis from typical submucosal uterine myomas or benign endometrial polyps could be difficult. The hysteroscopic features of uterine sarcomas are often similar to those of endometrial polyps or submucosal myomas. The histological examination of the specimen is necessary to exclude malignancy and establish the final diagnosis. Total abdominal hysterectomy, bilateral salpingo-oopherectomy with pelvic lymphadenectomy is the optimal treatment in cases of endometrial stromal sarcomas.

Key words: Endometrial sarcoma; Leiomyoma; Myomectomy.

Introduction

Endometrial stromal sarcomas (ESS) are extremely rare malignant tumors that represent approximately 10% of all uterine sarcomas but only around 0.2% of all uterine malignancies [1-3]. The annual incidence of ESS is 1-2 per million women accounting for 400 to 700 new cases each year in Europe [4].

The differential diagnosis of ESS from other lesions such as leiomyomas is often preoperatively difficult and the final diagnosis is mainly postoperatively given after histological examination [5, 6]. The typical gross appearance of ESS includes a single nodule, multiple solid and cystic masses, and a poorly demarcated lesion with occasional cystic degeneration, or rarely a cystic multilocular lesion [7].

The staging of uterine sarcomas is based on the International Federation of Gynecology and Obstetrics (FIGO) Staging System for uterine corpus cancer [8, 9]. According to the World Health Organization's (WHO) classification, uterine sarcomas are classified into four main histological subtypes in an order of decreasing incidence: carcinosarcomas, leiomyosarcomas, endometrial stromal sarcomas and other sarcomas [10, 11]. Unfortunately, clinical-trial reports and literature reviews often include a broad range of histological subtypes of sarcoma which restrict interpretation and application of results. Response rates from protocols with multiple subtypes should consequently be interpreted with caution; therefore the effort to tailor the approach to patients seems mandatory.

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We report a case of a 29-year-old patient diagnosed with ESS together with a literature review based on pubmed databases.

Case Report

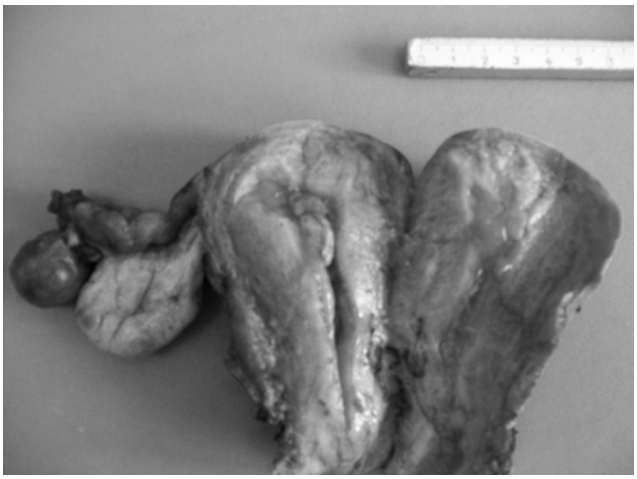
The patient, a 29-year-old nulliparous woman with a history of abnormal uterine bleeding and surgical removal of a uterine leiomyoma three months before, was referred to our department. After receiving three cyclus of gonadotrophin releasing hormone (GnRH) analogues the patient underwent (in another hospital) surgical excision of a uterine tumor with a maximum diameter of 6 cm which was located in the frontal region of the uterus and had ultrasound characteristics of a typical leiomyoma. Histological examination of the lesion revealed an endometrial stromal sarcoma with 10 mitotic figures (MF)/10 high power fields (HPF). Immunohistochemistry showed: CD 10 (+), SMA (-), caldesom (-), desmin (-), PanCK (±), vimentin (+) and ER (+ ≥ 80%), PGR (+ ≥ 90%).

A more radical surgical treatment of the disease was considered necessary and the patient was re-operated in our department. The serous neoplasmatic markers were within normal ranges.

Total abdominal hysterectomy with bilateral salpingo-oopherectomy, omentectomy and elective pelvic lymphadenectomy were performed. The final histological examination revealed an endometrial stromal sarcoma. Within the uterine cavity, a yellowish polypoid lesion measuring 1 x 0.4 x 0.3 cm was detected. At microscopic examination the tumor was characterized by the presence of multi nodule lesions throughout the myometrium trying to penetrate to the myometrium vessels. The cervix was found to have no malignancy but histology revealed lesions of chronic cervicitis and tubal metaplasia.

The adnexae, omentum and all removed pelvic lymph nodes were negative for malignancy. Immunhistological markers were as follows: CD10 (+), vimentin (+), SMAlocally (+), MSA (-), caldesom (-) and ER (+) > 90%, PGR (+) > 90%.

Fig. 1



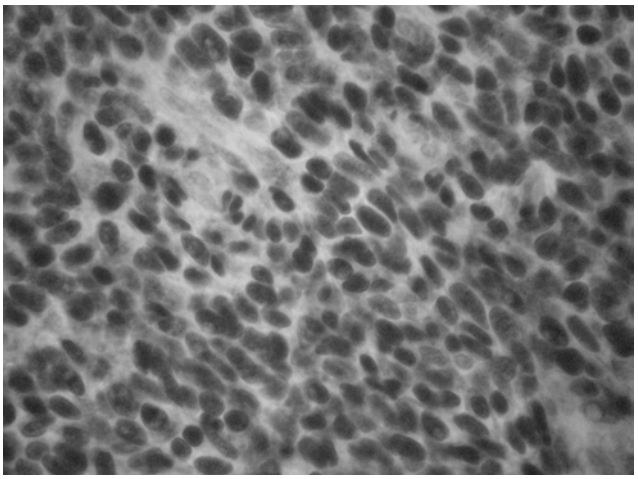


Fig. 2

Figure 1. — Yellowish polypoid lesion in the uterine cavity.
Figure 2. — Microscopic examination of the endometrial cavity (stain positive for ER) x400.

The patient had an uneventful recovery. Follow-up 24 months after initial diagnosis and surgical treatment with clinical examination and magnetic resonance imaging (MRI) showed no signs of recurrence.

Discussion

Uterine sarcomas are relatively rare tumors of mesodermal origin representing 2-6% of all uterine malignancies [12]. Depending on mitotic activity, vascular invasion or prognosis there are three categories of endometrial stromal tumors: endometrial stromal nodule, high-grade endometrial stromal sarcoma and indifferentiated endometrial sarcoma. ESS represents a very rare class of malignant tumors that comprises approximately 10% of all uterine sarcomas but only around 0.2% of all uterine cancers [13]. The typical gross appearance of ESS includes a single nodule, multiple solid-cystic masses and a poorly demarcated lesion with occasional cystic degeneration, or rarely cystic multilocular lesion [14].

Endometrial stromal sarcoma is characterized by proliferative lesions composed of cells with endometrial stromal cell differentiation and typically extensive worm-like vessel invasion [15]. Treatment of ESS is surgical [16, 17]. It includes total abdominal hysterectomy, bilateral salpingo-oophorectomy, omentectomy and cytological examinations of washings from the abdominal cavity [18, 19]. If the tumor is palpable in the parametrium, a more extensive procedure such as a radical hysterectomy should be performed [20].

Lymphatic invasion is well established and pathognomic for ESS formally designated as endolymphatic stromal myosis [21]. Despite this, lymph node involvement is not considered as a clinical problem and pelvic lymphadenectomy is not generally added to hysterectomy as the cornerstone of the treatment [22]. However recent data reported a higher incidence of lymph node metastases, showing the need for an extensive lymph node sampling.

Due to the high recurrence risk even with localized tumors, many clinicians advocate adjuvant chemotherapy, radiation therapy and/or hormones to suppress tumor growth [23]. There is no firm evidence coming from a prospective study that adjuvant chemotherapy or radiation therapy is of substantial benefit for patients with uterine sarcoma [24]. Postoperative pelvic radiotherapy reduces local recurrence but has not been consistently shown to prolong survival [25].

Low-grade endometrial stromal sarcomas are estrogen and progesterone receptor-positive tumors [26, 27]. In the past, hormonal therapy consisting of progestins was given for advanced or recurrent metastatic ESS. Hydroxy-progesterone acetate (MPA) and megestrole acetate are synthetic derivates of progesterone receptor [28]. Aromatase inhibitors and GnRH analogues have become new effective alternatives for first- and second-line treatment [29-31]. Recently, hormonal therapy has been introduced for the prevention of recurrences.

Uterine sarcomas have a poor prognosis and survival is much worse than that reported for endometrial adenocarcinoma, with an overall 2-year survival less than 50% even when presenting at an early stage [32]. A higher survival probability for patients with ESS is often reported [33]. Prognostic factors in patients with ESS are still controversial [34]. The negative prognostic influence of a high mitotic index was revealed in previous studies [35]. In the present study survival probabilities have been calculated by the product limit method of Kaplan and Meier which showed patients with no myometrial invasion and low mitotic count ≤ 5 MF/HFP to have longer disease-free survival but the p value was not statistically significant.

Conclusions

ESS is a malignant tumor that shows endometrial stromal differentiation and is histologically characterized by uniform small to medium sized cells and a distinctive

arterial vasculature that resembles spiral arteries of the normal endometrium. The clinical presentation of ESS is usually abnormal uterine bleeding in premenopausal women and shows an indolent clinical behavior.

Optimal therapy of ESS is not well established. The standard surgical procedure includes total abdominal hysterectomy, bilateral salpingo-oopherectomy and radical cytoreductive surgery of extra uterine disease.

Moreover, despite traditional recommendations to include bilateral salpingo-oopherectomy in the primary surgical management of ESS, same investigators have advocated preserving ovarian function, particularly in younger women. The role of pelvic, paraaortic lymphadenectomy and adjuvant treatment with radiation therapy, chemotherapy or hormonal treatment remains controversial.

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