Conservative Management of Low-grade Endometrial Stromal Sarcoma Followed by Pregnancy and Severe Recurrence

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Abstract. Background: Since low-grade endometrial stromal sarcoma (LGESS) has the most favourable prognosis in comparison to other sarcomas, fertility-sparing surgery in young women has been reported in rare cases. However, such tumours almost always show positive sex steroid receptors and their evolution in the hormonal milieu of pregnancy remains unpredictable. Case Report: We report the case of a 34-year-old woman treated conservatively for LGESS who conceived rapidly after hysteroscopic resection of the tumour. In the post partum period, pelvic pain motivated a laparoscopic exploration which revealed severe peritoneal recurrence. Conclusion: This case report highlights the possible dramatic evolution of LGESS after pregnancy and suggests that definitive surgery should not be postponed but performed as soon as the diagnosis of ESS has been made.

Endometrial stromal sarcomas (ESS) are rare tumours of the uterus, accounting for 0.2 to 1% of all uterine malignancies (1-4). Such tumours may occur in young women in whom classical treatment consisting of total abdominal hysterectomy and bilateral salpingo-oophorectomy is called into question. In particular, since low-grade ESS has the most favourable prognosis in comparison to other sarcomas (5), conservative, fertility-sparing surgery in young women has been reported (6-9).

Case Report

A 34-year-old woman presented to her physician for primary infertility lasting for 13 months. Medical and surgical histories were unremarkable. Previous Papanicolaou smears and pelvic examinations were normal.

Infertility explorations included hysterosalpingography and ultrasonad examination which revealed an intrauterine lesion. Abdomino-pelvic tomodensitometry and magnetic resonance imaging (MRI) showed focal hypertrophy and hypointense infiltration of the endometrium, without enhancement after gadolinium injection, consistent with sarcoma. Laparoscopy was normal. In particular, no extension of disease outside the uterine body and no serosal lesion were diagnosed. Peritoneal cytology was performed first followed by temporary tubal occlusion to avoid malignant cell dissemination during hysteroscopy. Hysteroscopy revealed a 15 mm polyp in the left cornual area which was resected using monopolar electrocoagulation. Before the end of surgery another peritoneal cytology was performed and the temporary proximal tubal occlusion was removed.

The histological examination of the polyp revealed a low grade ESS (6 mitoses per 10 high power fields) with focal infiltration of the myometrium. On pathological examination, both peritoneal cytologies showed no malignant cells. On immunohistochemistry, the cells were strongly positive for oestrogen and progesterone receptors (Figure 1). Growth fraction determination with Ki-67 antibody showed that 5% of the tumoral cells were proliferative. Immunostaining for p53 was negative whereas immunostaining for CD10 was strongly positive.

Because of the patient’s wish to become pregnant and nulligravity, conservative management was elected by the gynaecological oncology staff. The patient was then referred to the Reproductive Medicine Unit and the decision was taken for the patient to undergo hysteroscopic examination with endometrial cytology and biopsy every 3 months. No other cause of infertility was found on basic infertility investigations (typical biphasic temperature, bilateral tubal permeability on hysterosalpingography performed before the diagnosis of ESS and normal spermcytogram). Ovarian reserve assessed by anti-Müllerian hormone, follicular...
stimulating hormone and antral follicle count on ultrasonography were also normal. Intracytoplasmic sperm injection (ICSI) with spontaneous natural cycles was preferred in order to avoid tumoral stimulation. On the second cycle, one oocyte was retrieved and fertilized. The embryo obtained was transferred on day two and the patient became pregnant. Thus, pregnancy occurred 6 months after the initial diagnosis of ESS and after the first and only hysteroscopic examination showing no malignant cells on endometrial biopsy and cytology.

MRI examination of the pelvis at 24 weeks of gestation was proposed but refused by the patient. Third trimester ultrasonography did not reveal any abnormal uterine or adnexal findings. Pregnancy was uncomplicated and vaginal delivery occurred at 39 weeks of gestation after spontaneous onset of labour, giving birth to a healthy boy of 3,140 g.

The post partum period was marked by right iliac fossa pain. Ultrasonography revealed a bilateral pelvic mass. Serum markers (cancer antigen 125 and carcino-embryonic antigen) were normal and hysteroscopy did not reveal tumoral recurrence on either visual or pathological examinations (cytology and biopsy).

The MRI confirmed the existence of bilateral pelvic mass and laparoscopy was performed after the patient was convinced to undergo surgery (she first refused it). Exploration revealed two tumours (Figure 2). The first one measured 3 cm and was localized in the right iliac fossa, between and in contact with both the round ligament and the last ileal loop. The second was similar, localized in the Douglas pouch and measured 2 cm. The exploration was otherwise normal. Peritoneal cytology, endometrial curettage and excision of the mass in the Douglas pouch were performed. Because of the proximity of the right iliac fossa mass with the last ileal loop and the related risk of digestive injury with subsequent ileostomy, excision of the right iliac fossa mass was not performed immediately. Pathological examination of the Douglas mass revealed peritoneal recurrence of a low grade ESS. Other pathological examinations did not reveal other tumoral processes.

One month later, a new laparoscopy with prior bowel preparation was performed. Exploration revealed increasing size of the right iliac fossa mass, two new tumours (both on the peritoneum, one at the anterior side of the rectum and the other one in the left iliac fossa) and multiple ileal infracentimetric granulations. Peritoneal cytology, excision of the two recurrent tumours and biopsy of two ileal granulations without digestive injury were performed. Pathology examination of the masses and ileal granulations revealed peritoneal recurrence of a low grade ESS. Peritoneal cytology was negative. Because the patient still refused to undergo hysterectomy, decision was taken to treat her using non-steroidal aromatase inhibitors (Letrozole). Last radiological explorations using MRI (3 and 6 months after the beginning of medical treatment) showed good response to the treatment with near disappearance of the granulations on the last MRI examination.

Discussion

Considering the good prognosis of low-grade ESS, several authors have proposed conservative management to preserve fertility in young women (6-9) and rare cases of pregnancy after such management have been reported (7). In Lissoni et al.’s study (7), conservative management of ESS allowed three pregnancies (50% of the patients), without recurrences but with a relatively short follow-up. The authors postulated that “the increased level of steroid hormones during pregnancy might even result in a protective role against further development of the tumor”. The underlying mechanism for this could be the existence of positive sex steroid receptors on most tumoral ESS cells (positive rates for oestrogen and progesterone receptors of 71% and 95%, respectively (10)) and high levels of circulating estrogens and progesterone during the pregnancy. Unfortunately, in their study, expression of sex steroid receptors was not reported.

In our case, evolution of the tumour was less favourable. Although a live birth was achieved, a large extension of the primary tumour was also observed. Despite various precautions to avoid tumour recurrence and dissemination (temporary tubal occlusion, regular hysteroscopic and histological examinations of the uterine cavity, avoidance of ovarian stimulation protocols), the post partum laparoscopy revealed a serious progression of the low-grade ESS. The interval between treatment and recurrence of these tumours is particularly variable, reported from 3 months to 23 years, with a median interval of approximately 3 years (6). In our case, this delay was particularly short (10 months) and we can assume that the pregnancy itself favoured recurrence of the ESS as previously reported (11). Such a relapse is in accordance with the increased proliferation rate of endometrial stromal tumours due to the hormonal stimuli of pregnancy already reported by Karpe et al. (12). In a recent retrospective study based on 11 cases of low-grade ESS treated by hormonal treatment (eight cases with progestins, two cases with aromatase inhibitor, and one case with the combination progestin’s/aromatase inhibitor), Dahhan et al. (13) concluded that hormonal treatment for measurable residual or recurrent low-grade ESS has a high response rate. In consequence, aromatase inhibitor should be considered as the treatment of choice for patients in which recurrent disease cannot easily be resected. In our case report, early response to the aromatase inhibitor Letrozole was good. But since radical surgery could not be performed, long term response to aromatase inhibitor remains uncertain.
This case report highlights the possible dramatic evolution of low-grade ESS after pregnancy and suggests that definitive surgery should not be postponed but performed as soon as the diagnosis of ESS has been made, whatever its grade is.

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**References**


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