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Persistent low-grade endometrial stromal tumor during two consecutive pregnancies – a case report and review of literature

M.W. Lui[1], P.P.C. Ip[2], E.Y.P. Lee[3], K.Y. Tse[1], H.Y.S. Ngan[1]

[1]Department of Obstetrics and Gynaecology, [2]Department of Pathology, [3]Department of Diagnostic Radiology, Queen Mary Hospital, the University of Hong Kong (Hong Kong)

Summary

The authors report a case of persistent endometrial stromal tumour during two consecutive pregnancies. The diagnosis of endometrial stromal sarcoma (ESS) is difficult by fragmented tissue. There were a total of 19 reported cases of pregnancy after conservative management of endometrial stromal sarcoma. Monitoring of disease during pregnancy is challenging, although most patients remain in a stable condition with a follow-up duration of 2-60 months. Although the present patient had a favorable disease outcome despite having co-existing ESS sustained throughout two term pregnancies, the current evidence on the safety of this approach is still scarce and thorough counseling is mandatory if any young patients wish to retain their fertility potential.

Key words: Endometrial stroma tumour; Fertility-sparing surgery; Pregnancy.

Introduction

Endometrial stromal sarcoma (ESS) is a rare tumour, accounting for around 1% of all uterine malignancies [1, 2]. It is typically slow-growing with late relapse. The mean age at presentation is 50 years [1]. Sixty percent of patients present with International Federation of Gynecology and Obstetrics (FIGO) Stage I disease, and the five-year survival is nearly 90%. The standard treatment is total hysterectomy and bilateral salpingo-oophorectomy with or without lymphadenectomy [3]. However, late recurrence is common and occurs in up to 14-60% of patients [4]. Although fertility-sparing treatment has been reported in the literature, its safety is still controversial. In this case report, a patient with concurrent and persistent ESS in two consecutive pregnancies are described.

Case Report

A 37-year-old nulliparous woman presented with lower abdominal pain and foul smelling vaginal discharge for two weeks. She enjoyed good past health with regular monthly periods. On examination, a 5-cm necrotic polyp protruding from cervical os was identified. Detached part of the polyp was sent for histology and endometrial stromal tumor was suspected. MRI of pelvis showed a 2.4×1.9×0.8-cm uterine mass breaching of junctional zone (Figure 1). Because the diagnosis of ESS was not yet confirmed due to the limited amount of tissue, hysteroscopic resection was performed. Intra-operatively, a 2-cm polyp was seen arising from the right posterior wall and it was resected. However, after multidisciplinary review with pathologist, endometrial stromal nodule cannot be differentiated from low-grade endometrial stromal sarcoma due to the fragmentation of the tissues. Postoperative ultrasonography (USG) of pelvis showed a 0.76×0.43-cm echogenic focus at fundus, suspicious of residual tumour. In order to obtain a definitive diagnosis and in view of possibility of incomplete resection in case of ESS, total hysterectomy was suggested. The limitation of monitoring by imaging and risk of recurrence were fully informed. Patient had a strong desire to retain her uterus and she refused hysterectomy as she was nulliparous. She was initially scheduled for a repeat MRI scan six months afterwards.

Patient became pregnant spontaneously four months after the first presentation. The pregnancy was complicated by gestational diabetes mellitus. Gynaecologic oncology team was consulted and

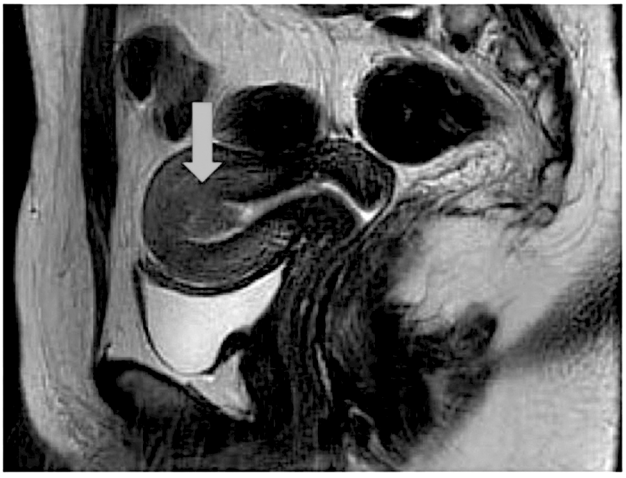

Figure 1. — MRI performed at the time of diagnosis. Sagittal T2 MRI shows a mildly hyperintense polypoid endometrial mass arising from the fundal region (red arrow).

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Table 1. — *Summary of the case reports of pregnancy after conservative management of ESS.*

Case	Age	Primary operation	Adjuvant treatment	Interval (months)	Pregnancy outcome	Recurrence	Further treatment	Follow-up duration (months)	Condition
Present patient	37	Hysteroscopic resection	Nil	4/15	NSD at 41w CS at 35w	No	TH, BSO	60	Remission
Koskas 2009 [7]	34	Hysteroscopic resection	Nil	6	NSD at 39w	Yes	TH, BSO/ letrozole	6	Alive with disease
Yan 2010 [8]	25	Open myomectomy	Etoposide/ cisplatin	40	CS at 39w	Nil	Nil	60	Remission
Delaney 2012 [9]	16	Open myomectomy	Megestrol acetate	96	CS at 34w	Nil	Nil	N/A	N/A
Sánchez-Ferrer 2013 [10]	32	Open myomectomy	Megestrol acetate	16	CS at 32w	Nil	TH 6m + Megace	60	Remission
Jain 2014 [11]	23	Open myomectomy	Nil	12	TH, LSO at term	Yes	Nil	32	Recurrence, require operation/ chemotherapy
Dong 2014 [15]	25	Open myomectomy	Medroxy-progesterone	18	CS at term	Nil	Nil	2	Remission
Noventa 2015 [12]	34	Laparoscopic myomectomy	Nil	12	Pregnant at 11w	N/A	N/A	N/A	N/A
Bai 2014 [13]	8 patients pregnant after myomectomy - 5 had CS at term (details not known)								
Lissoni 1997 [14]	3 patients pregnancy after myomectomy (uncertain of the route) - 2 had delivery at term; 1 ended up in miscarriage (details not known) - All in remissions with mean FU of 51 months (12-84 months)								

TH: total hysterectomy, BSO: bilateral salpingo-oophorectomy, N/A: not available, CS: cesarean section, NSD: normal spontaneous delivery. PN: postnatal.

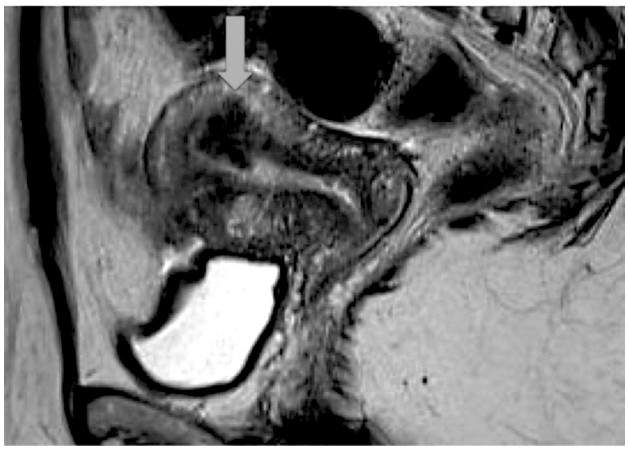

Figure 2. — MRI performed after first pregnancy. Sagittal T2 MRI shows a hypointense mass corresponding to previous known endometrial mass (red arrow).

follow-up was arranged after delivery. Serial ultrasound examinations during the antenatal period did not show any obvious uterine mass. She delivered a baby girl weighing 3,265 grams vaginally at term. MRI of pelvis was repeated three months after delivery and a 2-cm uterine tumour with disruption of the junctional zone and myometrial invasion at fundus was noted (Figure 2). Because of the suspicious features, hysterectomy was recommended again. However the patient insisted to preserve her uterus as she desired to become pregnant again. She became pregnant spontaneously again three months later. Her second pregnancy was unremarkable and the tumour was not detectable on serial ultrasound scans. The pregnancy was complicated by breech presentation and premature prelabour rupture of membranes at 35 weeks of gestation. The baby was delivered by lower segment cesarean section. Intraoperatively, a 2-cm yellowish polypoid tumour was identified densely adherent to the right fundal region of the uterus. Gynaecologic oncologist was consulted. Cesarean hysterectomy was not performed at the time of operation due to increased operative risks. Detached tissue was sent for histology and confirmed to be endometrial stromal tumour.

The patient underwent total laparoscopic hysterectomy three months after her delivery, which was around three years after first presentation. The operation was uneventful. Intraoperatively a 2-cm tumour was identified at the left fundal region. Pathology report confirmed low grade endometrial stromal sarcoma. Megestrol acetate was given postoperatively and the patient remains disease- free 60 months after first presentation.

Discussion

Endometrial stromal tumor refers to tumour resembling endometrial stromal cells from a proliferative endometrium. It is further classified into non-invasive endometrial stromal nodule and invasive ESS. Invasion into myometrium and lymphovascular spaces are distinctive features of invasive ESS. There is only mild nuclear atypia and tumour cell necrosis that rarely occurs . However, it would be difficult to differentiate invasive ESS from endometrial stromal nodule using specimen after

hysteroscopic resection or uterine curettage, due to the fragmented nature of the tissues [1, 5].

ESS is regarded as a hormone-sensitive tumour, where estrogen receptors and progesterone receptors were over-expressed in around 70% and 95% of cases, respectively [2]. It was controversial whether ovarian-sparing surgeries would affect the overall survival in young patients with early stage of disease [4, 6]. In review of English literature, there were 19 patients, including the present patient, who achieved pregnancy after conservative management of ESS [7-15]. The details of the patients are summarized in Table 1. The interval between first diagnosis and pregnancy ranged from six to 96 months. The follow-up duration ranged from two to 84 months. All except two patients remained in remission after pregnancy. The present patient was the first report in the literature whose ESS was persistent throughout two consecutive pregnancies. While it appeared that there was no immediate detrimental effect of the hormonal environment during pregnancy on the disease outcome of the patient, the true effect on the disease recurrence and overall survival is still unclear.

Because estrogen- and progesterone- receptors are highly expressed in ESS, adjuvant hormonal therapy, including progestins and aromatase inhibitors, has been commonly used after fertility-sparing surgery after ESS [1, 3] to prevent disease recurrence. Only three reported cases have received postoperative adjuvant hormonal treatment. The patients were prescribed megestrol acetate 80-100 mg daily [9, 10] or medoxyprogesterone 250 mg daily [15]. The optimal duration and regimen of the adjuvant hormonal therapies is not clear but high-dose progestins had been used for up to eight years before contemplating pregnancies. The relationship of adjuvant hormonal treatment and recurrent cannot be established due to the limited number of cases. As total hysterectomy is still recommended after completion of family, use of adjuvant hormonal treatment may further prolonged the interval.

As being hormonal sensitive, use of ovarian stimulation was another concern. Postoperative hormonal treatment given during in-vitro fertilization with ovarian stimulation has been performed in the case reported by Sánchez-Ferrer *et al.* [10] and Koskas *et al.* [7]. Though the first patient remained disease-free five years after delivery, the second patient was unfortunate, as she had recurrence shortly after delivery and required chemotherapy. Nevertheless, the safety of ovarian stimulation needs further evaluation as the evidence is still limited.

Monitoring of the disease during pregnancy by ultrasound and MRI is challenging, as the uterine tumor may be obscured by the fetuses and the fetal movement may cause artifact in MRI [7]. In the present patient, the 0.76×0.43 cm uterine mass could not be detected by ultrasound in her first pregnancy. The tumour grew to 2 cm as shown on MRI three months after her pregnancy. However, it was not revealed again on serial ultrasounds throughout her second pregnancy. Regarding mode of delivery, it should depend on the extent and nature of any previous myomectomy and obstetrics indications. In the first pregnancy of the present patient, despite the presence of residual tumour, a trial of vaginal delivery was discussed, as the serosa was not breached during hysteroscopic resection and the residual tumor was less than 1cm.

In conclusion, although the present patient had a favorable disease outcome despite having co-existing ESS sustained throughout two term pregnancies, the current evidence on the safety of this approach is still scarce and thorough counseling is mandatory if any young patients wish to retain their fertility potential, and because the risk of recurrence is up to 56% even for Stage I disease and it can occur 20 years later [1], hysterectomy is still the treatment of choice and should be recommended after completion of family.

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Corresponding Author:
MAN WA LUI, F.H.K.A.M. (O&G)
Department of Obstetrics & Gynaecology
The University of Hong Kong
Queen Mary Hospital
102 Pokfulam Road (Hong Kong)
e-mail: luimanwa@gmail.com