

Total Pelvic Exenteration for Recurrent Endometrial Sarcoma - A Case Report

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Rezumat

Exenterație pelvină totală pentru sarcom endometrial recurent - studiu de caz

Sarcoamele stromale endometriale sunt boli ginecologice rare caracterizate prin prezența unor celule asemănătoare cu cele ale stromei endometriale în timpul fazei proliferative a ciclului menstrual. Acestea sunt clasificate ca fiind tumori de grad scăzut sau înalt de malignitate în funcție de indexul mitotic, cele din urmă fiind de obicei considerate de prognostic rezervat și cu mari șanse de recurență. Prezentăm cazul unui pacient în vârstă de 46 ani care are în antecedent o intervenție chirurgicală pentru sarcom stromal urmată de radioterapie adjuvantă; după 18 luni a fost diagnosticat cu recurență pelvină ce invadează vezica urinară, trigonul vezical și rectosigmoidul pentru care s-a practicat exenterație pelvină totală.

Cuvinte cheie: sarcom stromal endometrial cu grad înalt de malignitate, histerectomie radicală, recurență pelvină, exenterație totală

Abstract

Endometrial stromal sarcomas are rare gynecologic malignancies characterized by the presence of cells that resemble those

of the endometrial stroma during the proliferative phase of the menstrual cycle. They are classified as low grade or high grade tumors depending on the mitotic index, the second one being usually associated with poor prognosis and high recurrence rate. We present the case of a 46-year-old patient who was previously submitted to surgery for an endometrial stromal sarcoma followed by adjuvant radiotherapy; 18 months later she was diagnosed with a pelvic recurrence invading the urinary bladder trigone and the rectosigmoid so she was submitted to a total pelvic exenteration.

Key words: high grade endometrial stromal sarcoma, radical hysterectomy, pelvic recurrence, total exenteration

Introduction

Uterine sarcomas are rare malignancies accounting for 3-8.4% of all uterine malignancies (1) classified by the World Health Organization (WHO) as mesenchymal tumors which include endometrial and smooth muscle tumors (2). Endometrial stromal sarcomas represent up to 15% of all uterine sarcomas and are composed by cells resembling those of the endometrial stroma during the proliferative phase of the menstrual cycle (3). Due to their different biological behavior, endometrial stromal sarcomas were classified in two groups according to the mitotic index: tumors with a mitotic count of less than 10 mitoses/10 high power field are considered low grade sarcomas (LGESS) while those with a higher mitotic count are classified as high grade tumors (HGESS) with a more aggressive biological behavior and a poorer overall prognosis (3,4). Standard management in

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both LGEES and HGEES consists of total hysterectomy with bilateral adnexectomy while the association of pelvic and para-aortic lymph node dissection still remains in question especially in patients with LGEES with presumed early stage disease (5-8).

Case report

A 46-year-old patient presented for abundant metrorragies associated with pelvic pain. The local examination and Papanicolaou test excluded the presence of a cervical tumor while the endometrial biopsy revealed the presence of an endometrial stromal sarcoma. The computed tomography revealed the presence of an uterine tumor with pelvic and para-aortic enlarged lymph nodes but with no signs of local invasion. The patient was submitted to surgery and a total radical hysterectomy with bilateral adnexectomy, pelvic and para-aortic lymph node dissection was performed. The histopathological examination confirmed the presence of a high grade endometrial stromal sarcoma with cervical extension and myometrial invasion but with negative resection margins; the pelvic and para-aortic lymph nodes were free of any tumoral involvement. Immunohistochemical studies showed positive staining for CD 10 and vimentine while Ki67 was positive in up to 60% of the tumoral cells. Actine was negative in the tumoral cells and positive in the blood vessels. Postoperatively the patient was submitted to adjuvant external beam radiotherapy for a month, the total dose of administrated radiation being 50 Gy, followed by two sequences of brachytherapy. At six months and one year follow up the patient was free of any recurrent disease (Fig. 1). Eighteen months after completing the adjuvant treatment the patient presented for pelvic pain, vaginal bleeding, polakiuria and constipation. The local examination revealed the presence of a large pelvic fixed tumor, invading the urinary bladder trigon and the anterior wall of the rectum. The computed tomography confirmed the presence of a pelvic recurrence originating from the vaginal stump invading the urinary

bladder trigon and the left ureteral ostium with grade III secondary ureterohydronephrosis, associated with delayed renal excretion. The imagistic studies also revealed the presence of multiple peritoneal tumors with possible invasion of the caecum, sigmoid colon and ileal loops. The patient was re-submitted to surgery and a palliative total pelvic exenteration was performed; the nodules of peritoneal sarcomatosis were also removed (Fig. 2-9). The postoperative course was uneventful, the patient being discharged in the 12th postoperative day. The histopathological studies confirmed the presence of a HGEES recurrent tumor. One month after surgery the patient was re-submitted to adjuvant chemotherapy.

Discussions

Initially, due to their different biological course, endometrial



Figure 2. Initial intraoperative aspect: large pelvic recurrence and peritoneal sarcomatosis

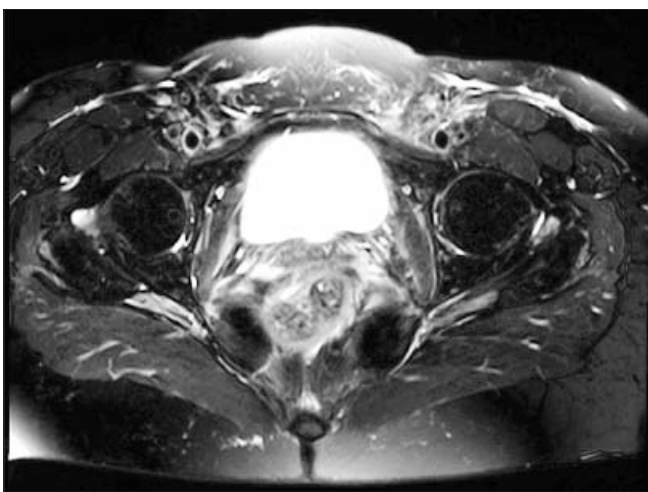


Figure 1. Six months follow-up: pelvic MRI revealed the absence of any pelvic recurrence



Figure 3. Disseminated lesions of sarcomatosis

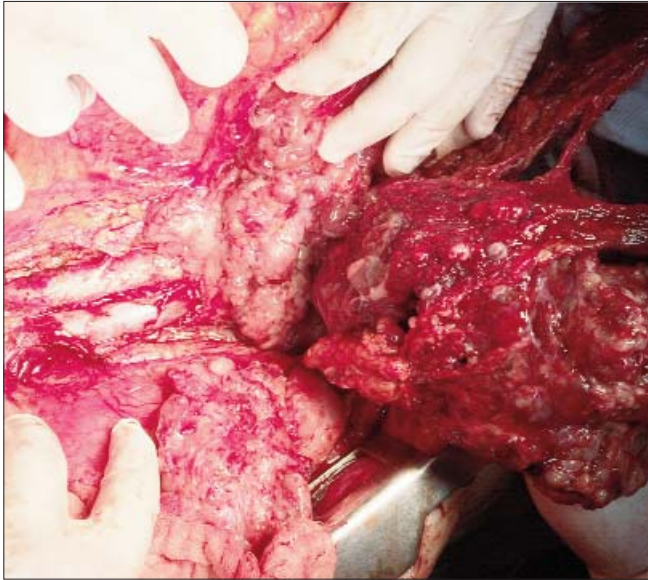


Figure 4. Mobilization of the pelvic recurrence

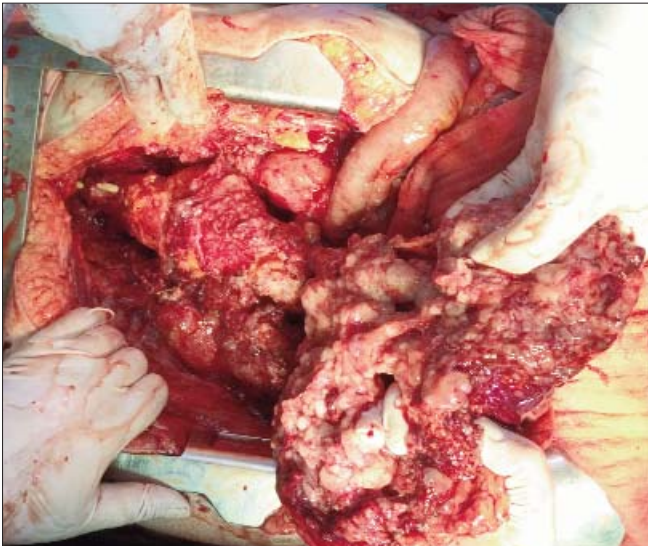


Figure 6. The pelvic recurrence is completely mobilized en bloc with total cystectomy and rectosigmoidian resection

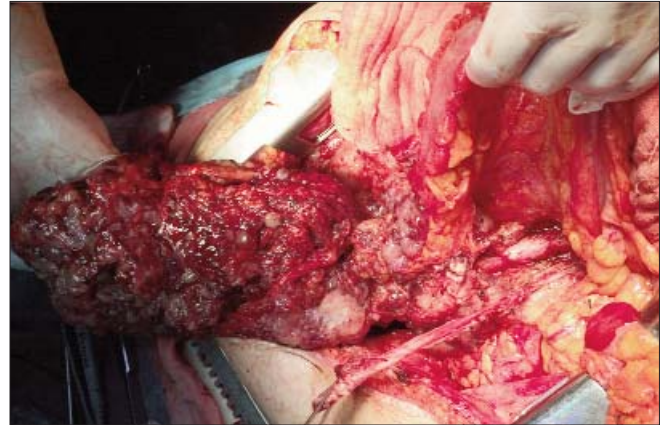


Figure 5. Dissection of the left ureter and rectosigmoidian mobilization

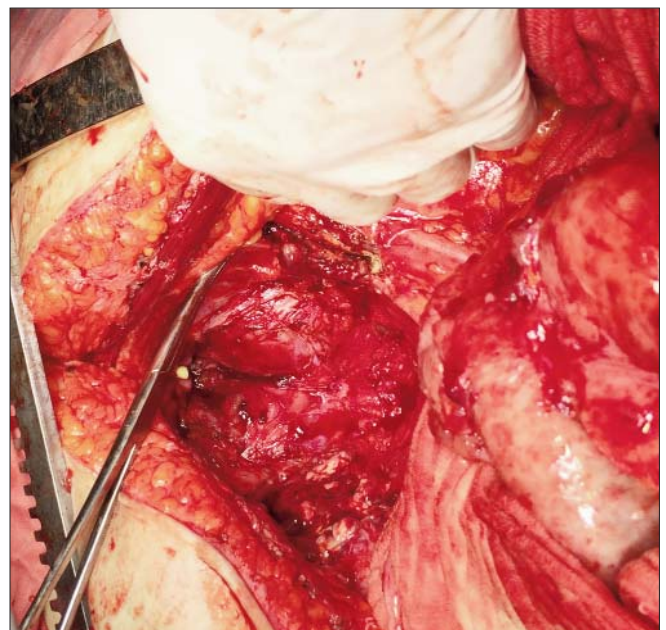


Figure 7. The final aspect after resection

stromal sarcomas were classified as LGESS and HGEES.

In order to determine which is the most efficient therapeutic strategy and which are the most important prognostic factors, Charles A Leath III and all conducted a study on 105 patients diagnosed with ESS: 72 cases with LGESS, 31 cases with HGEES and two cases with unclassified tumors. Patients with LGESS were diagnosed more frequently in an early stage of the disease when compared to cases with HGEES (68% of cases with LGESS and 39% of cases with HGEES were diagnosed in stages I,II, $p=0.002$). The incidence of positive pelvic and para-aortic lymph nodes was also higher among patients with HGEES while the median overall survival was 53 months for patients with HGEES and had not yet been reached for patients with LGESS (87.8% of cases being alive at 80 months, $p<0.0001$). Postoperatively six

patients with LGESS and 8 cases with HGEES were submitted to adjuvant radiation therapy. The median disease free survival among patients receiving adjuvant chemotherapy was significantly lower for patients with HGEES (21 months for HGEES versus 137 months LGESS, $p<0.0001$). Recurrence occurred in 37.5% of cases with LGESS and 38.7% of cases with HGEES, the most common site of recurrence being the pelvic cavity for the both groups (3).

In another study conducted by Yoon et al., 114 patients with ESS were included. The most important prognostic factors were the stage at diagnosis (FIGO stage I versus II-IV, $p=0.006$), the presence of positive estrogen receptors ($p=0.0027$) and the absence of lymph node metastases ($p=0.033$). The median follow up period was 46 months (range 0.5-251). The recurrence rate was 28.9%, while the location of

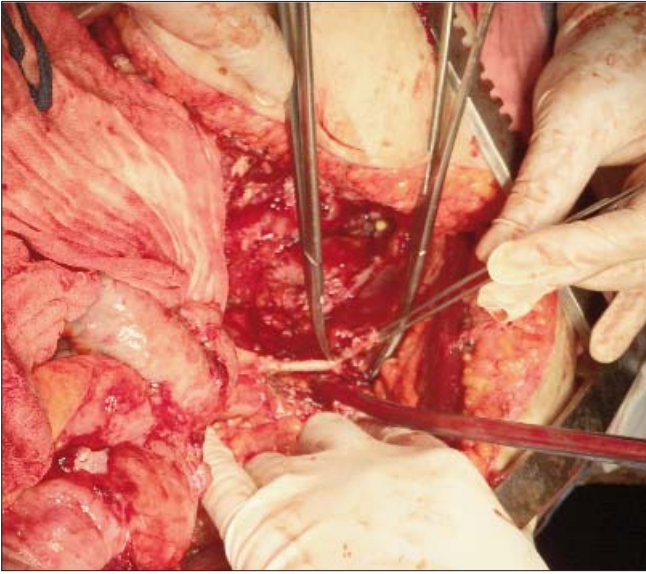


Figure 8. Dissection of the left external iliac artery

the recurrent disease was pelvic alone in 51.5%, extra-pelvic and/or pelvic recurrences in 48.5% and only extra-pelvic sites in 48.5%. When it comes to the postoperative follow-up after resection of the recurrent disease, the estimated median survival was 133 months, the most important prognostic factors being FIGO stage I at the moment of the initial diagnosis ($p=0.005$), positivity of hormone receptors ($p=0.001$) and cytoreductive resection of recurrent disease ($p=0.002$). In multivariate analysis the positivity of hormone receptors and performing cytoreductive surgery were independent prognostic factors for a better outcome after recurrence. Among the 28 patients submitted to cytoreductive surgery for recurrent disease six patients died of disease while the other 22 cases were successfully salvaged (9).

In order to evaluate the rate and time to recurrence as well as the role of different therapeutic strategies at the time of recurrence, Beck et al conducted a study involving 42 patients diagnosed with ESS. Recurrent disease was diagnosed in 16 cases, after a mean follow up of 100.5 months. Recurrence was found most often in pelvis (43.8% of cases) followed by lung (25% of cases). Although patients diagnosed in a more advanced stage of the disease reported recurrent tumors more often than those diagnosed in early stages, this fact was not statistically significant (67% versus 30%, $p=0.11$). Ovarian preservation was another factor associated with an increased risk of recurrence (the recurrence rate was 34.8% for patients in whom bilateral adnexectomy was performed and 80% in cases in which initial ovarian preservation was performed, $p=0.06$). In the same study seven patients were submitted to pelvic external radiotherapy or brachytherapy while chemotherapy was associated in three cases. However, due to the small number of cases submitted to different oncologic adjuvant treatment, it could not be concluded if association of adjuvant chemo-irradiation can provide a lower rate of recurrence (10).

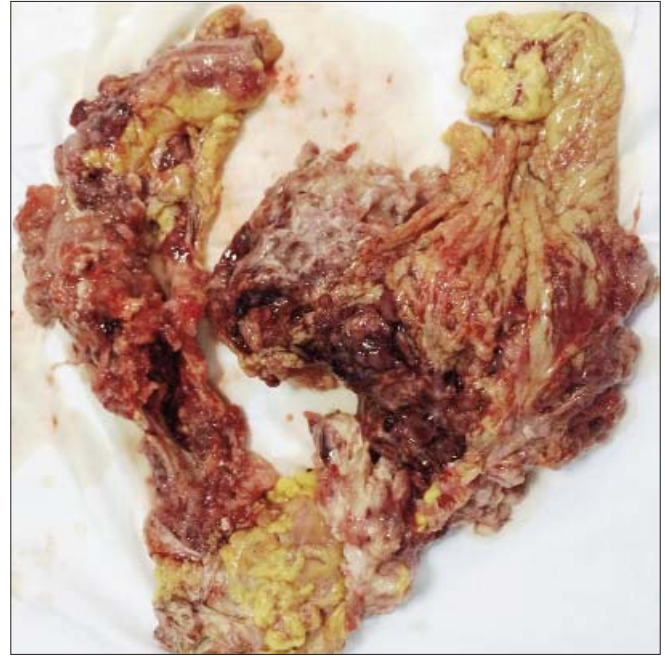


Figure 9. The specimen of total pelvic exenteration

In another study conducted by Cheng et al. involving 74 patients diagnosed with ESS recurrent disease was found in 47 cases, 16 of them being dead of disease at the moment of the last follow up. The location of the recurrent disease included pelvic recurrence in 43% of cases, extrapelvic recurrence in 34% of cases and both pelvic and extrapelvic recurrence in 23% of cases. At the moment of diagnosis of recurrent disease radiotherapy, chemotherapy and hormonal therapy were proposed; however radiation therapy was associated with stable disease in all cases submitted to irradiation, chemotherapy provided a stabilization of the disease in 40% of cases while progression of the disease was encountered in 60% of cases and hormone therapy provided a complete response in 17% of cases, partial response in 10% of cases, stable disease in 53% of cases and progression of the disease in 20% of cases. The median time to progression was 31 months for patients submitted to radiotherapy, 6.5 months for patients submitted to chemotherapy and 24 months for patients submitted to hormone therapy. The study concluded that whenever hormonal therapy might be taken in consideration, an improved outcome after recurrence should be expected (11).

In our case the absence of hormone receptors and the recent history of external and radiation therapy excluded these two options from the therapeutic armamentarium, the only feasible method to prolong survival being an aggressive surgical approach.

When it comes to the role of surgery in patients diagnosed with recurrent ESS, most authors sustain the role of secondary and even tertiary cytoreductive surgery with or without resection of distant lesions such as lung or cardiac metastases (12,13,14).

Conclusions

Although HGEES are aggressive gynecological malignancies with a high capacity of developing recurrent disease, surgery remains one of the most efficient therapeutic options. In our case the presence of large disseminated abdominal and pelvic recurrent tumors diagnosed 18 months after completing the adjuvant oncologic treatment pointed out the presence of an extremely aggressive malignancy which could not be managed otherwise than by an aggressive surgical approach. In the meantime, in this particular case surgery was the only treatment which might be performed; the absence of hormone receptors, the recent history of high dose external and vaginal irradiation and the impaired renal function due to the tumoral invasion of the left ureteral ostium with delayed left renal function formally excluded hormonotherapy, irradiation and chemotherapy respectively from the therapeutic plan.

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