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Endometrial stromal sarcoma of the uterus

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Uterine sarcomas are rare tumors constituting 1–3% of all uterine malignancies. These tumors are characterized by aggressive growth and by poor overall prognosis. There is much controversy concerning diagnostic criteria and the great variation in histology, as well as the role of radiotherapy and chemotherapy in the management of these tumors. We report a case of endometrial stromal sarcoma of the uterus in a 45-year-old woman. Total abdominal hysterectomy, bilateral salpingo-oophorectomy and pelvic lymphadenectomy was performed, followed by adjuvant radiotherapy and tamoxifen treatment. The patient has now been seen regularly for 2 years from the start of the treatment and at present there is no evidence of disease.

Key words: Adjuvant therapy, chemotherapy, radiation therapy, uterine sarcoma.

Introduction

Sarcomas of the uterus are rare tumors. They account for 1–3% of all malignant uterine growths and 2% of all malignancies of the female genitalia.[1–3] In view of the aggressive growth of the tumor and the early onset of metastatic spread through the bloodstream and lymphatics, uterine sarcomas are among the most malignant tumors of the female reproductive tract, and have a correspondingly unfavorable prognosis.

There is no universally agreed approach to the therapy of these tumors at present; in the following observations, we describe our own experience in a patient with endometrial stromal cell sarcoma of the uterus.

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Case report

A 45-year-old woman, gravida 2, para 2, was admitted to hospital for surgical treatment of uterine myomas and menometrorrhagia. Previous curettages had not shown any histological abnormalities. Abdominal hysterectomy was performed without complications and no specific intra-abdominal features were seen to suggest the presence of a tumor.

Histological examination revealed an actively growing invasive endometrial stromal sarcoma (ESS), with infiltration of blood vessels and lymphatics (Figures 1–3). An intramural myoma was also confirmed. Repeat laparotomy was conducted, with bilateral adnexectomy and removal of pelvic lymph nodes. Histological examination of the samples confirmed metastatic spread to two lymph nodes (left obturator fossa, right iliac node) but otherwise lymph nodes, adipose and adnexial tissues were normal. No suspect findings were found on exploration of the entire abdominal cavity, including cytological diagnosis of smears. Further oncological diagnosis showed no abnormal features (computer tomography of the whole abdomen, iv urogram, abdominal sonography, chest X-ray examinations, tumor markers CEA, CA 125, CA 15-3, CA 19-9). The case was therefore diagnosed as ESS stage $T_1N_1M_0$ G 3, estrogen receptor positive, progesterone receptor positive.

External whole pelvis irradiation and vaginal brachytherapy was given following surgery (46.6 Gy bilaterally to true pelvis and paraortically, plus 9 Gy each in the parametrium on both sides, 16 MeV photons, and 15 Gy in two fractions by vaginal afterloading administration of ^{192}Ir).

The patient received tamoxifen adjuvant therapy (Nolvadex, ICI) at a dose of 30 mg/day. The

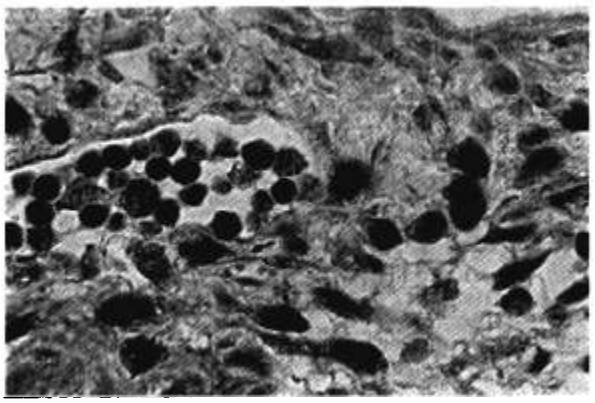

Figure 1. An invasive stromal sarcoma in growth, showing uniformly intensive progesterone-receptor-positive (red) cell nuclei. Receptor-negative lymph cells are shown on the left (internal control). Magnification × 430. Stain: alkaline phosphatase–anti-alkaline phosphatase (APAAP) reaction. Monoclonal antibody (Dianova Co.).

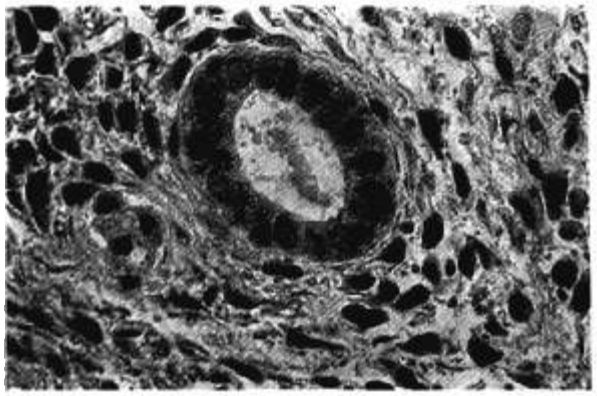

Figure 2. Stromal sarcoma, showing largely uniformly receptor-positive nuclei. An endometrial mucosal gland with only minimally positive nuclei is visible in the centre. Magnification × 430. Stain: alkaline phosphatase–anti-alkaline phosphatase (APAAP) reaction. Monoclonal antibody (Dianova Co.).

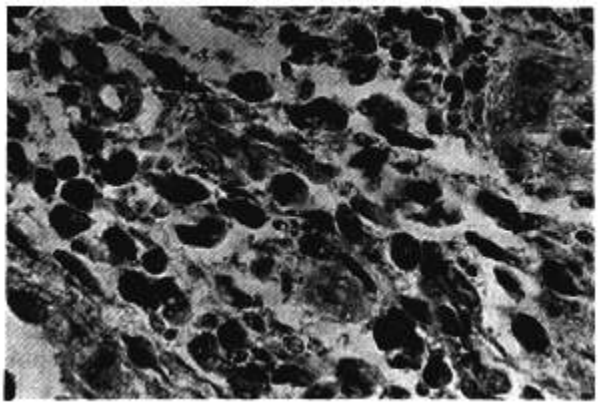

Figure 3. Marginal area of necrotic zone of a stromal sarcoma. Receptor concentration still largely uniform. All the tumor cells display a strong red stain. Magnification × 430. Stain: alkaline phosphatase–anti-alkaline phosphatase (APAAP) reaction. Monoclonal antibody (Dianova Co.).

post-operative course was complicated by a deep vein thrombosis in the left leg, confirmed by phlebography (on day 4 after the repeat laparotomy); episodes of diarrhea occurred during radiotherapy but the dose of tamoxifen did not need to be reduced. The patient has now been under observation for 2 years; she continues to receive tamoxifen and has been free of symptoms or recurrence.

Discussion

ESSs account for 1–32% of all uterine sarcomas.[1–7] In a retrospective analysis of 119 patients who have been treated at the Göttingen University Hospital Gynaecological Clinic, ESS accounted for 18% of cases.[8] The disease mostly appears in peri- or post-menopausal patients.[3,5,9–16] The peak age for ESS in our own patient population is 59 years.

Abnormal uterine bleeding, particularly in the post-menopause, is a diagnostic symptom.[5,9,15,17] In contrast to leiomyosarcoma, ESS is usually confined to the true pelvis[9,15,18] when first diagnosed.

Prognosis depends almost entirely on the stage of the disease when diagnosed[2,4,15] and this has been confirmed by our own experience.

Rapid progression is characteristic of all sarcomas. Most women develop local recurrence or distant metastases within two years. The 5-year survival[9] is approximately 16%, irrespective of stage.

Initial therapy consists of abdominal hysterectomy and bilateral adnexectomy. Mantravadi *et al.*[14] and Piver and Lurain[2] also recommend selective removal of pelvic and para-aortal lymph nodes. According to DiSaia *et al.*[10] 35% of stage I patients have pelvic node metastases and 14.3% have para-aortal lymph node metastases. In stage II Wertheim hysterectomy with extirpation of pelvic nodes should be considered.[2,7,9]

Exact definition of the extent of the tumor is particularly important in planning therapy. In this context, there is no generally valid recommendation for routine infracolic omentectomy[19] and we did not perform this operation in the case reported here.

Radiotherapy as sole treatment is to be considered only in patients who are generally inoperable cases, or where parametrial metastases are present.[6,7,11,14,15]

Where adjuvant radiotherapy is used in stage I ESS, the risk of local recurrence and distant metastases is reduced,[19] but there is no improvement in survival.[6,7,19,20]

The place of adjuvant chemotherapy in uterine sarcoma, particularly in stage I, has yet to be clarified; the most frequently used agents are adriamycine, vincristine, actinomycine D and cyclophosphamide, or cyclophosphamide, vincristine, adriamycine and DTIC.[2,19,21,22]

Partial remissions following adjuvant chemotherapy have been described in 20–30% of cases, and complete remissions in 10–15%, but no improvements in survival time have been achieved with this therapy.[9] Sutton *et al.*[23] found estrogen receptors in 55.5%, and progesterone receptors in 55.8% of uterine sarcomas. ESS was found to have the highest concentration of receptors, compared with other histological forms of sarcomas.

There are few data available which relate to adjuvant hormonal therapy. Good results have been achieved in occasional cases of metastatic ESS using progestagens at high dose.[13] Even pulmonary metastases have responded favorably, after tamoxifen therapy had failed.[24]

Given the poor prognosis of ESS, tamoxifen is in our opinion indicated as an adjuvant treatment following surgical primary therapy and radiotherapy. Chemotherapy should be reserved for cases of recurrence, or distant metastases, since the efficacy of adjuvant chemotherapy in stage I remains unproven.

Opinion is divided as to the treatment to be given in such cases, and we therefore draw attention to the treatment which was adopted in the present case, where we implemented a protocol in accordance with national and international recommendations.

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