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# Letters

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## Autologous Bone Marrow Transplantation for Uterine Sarcoma. Case Report

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UTERINE SARCOMAS are rare tumours and, although they account for only 6% of all uterine neoplasms, they are responsible for more than 15% of deaths from malignancy in women [1]. According to their histogenesis, they can be divided into three main subtypes: malignant mixed mülleran tumours, leiomyosarcomas and endometrial stromal sarcomas. The latter arise from endometrial stroma, account for 0.2% of all uterine malignancies and approximately 7–15% of all uterine sarcomas [2]. Stromal tumours are seen most frequently between the ages of 45 and 50 years. Approximately 10% of cases present with metastatic disease, localised predominantly in the lungs [3]. Surgery remains the treatment of choice for all sarcomas arising from the uterus both with respect to the primary tumour and to localised pulmonary metastases [4].

Hormonal therapy is ineffective, even though half the tumours have positive oestrogen receptors [5]. Chemotherapy remains the treatment of choice in patients with advanced disease, but results are scanty. Here we report on a case of metastatic uterine sarcoma treated with surgery and both conventional dose and high dose chemotherapy.

After an episode of vaginal bleeding, our patient was diagnosed to have a large uterine mass and bilateral pulmonary metastases. In August 1988, she underwent abdominal hysterectomy and unilateral oophorectomy for a 45 × 65 mm low grade uterine endometrial stromal sarcoma with negative oestrogen and progesterone receptors. Pelvic nodes were negative. The small cells of this low grade tumour extensively infiltrated the myometrium up to the serosa (Figure 1). Mitotic figures were 10–12 high power fields and there were haemorrhagic and necrotic foci. CT scan of the chest showed bulky bilateral pulmonary metastases. In October 1988 she underwent resection of the two larger pulmonary metastases

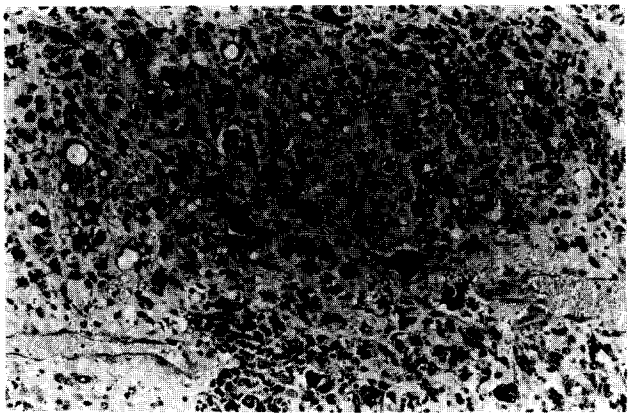

**Figure 1. Low grade uterine endometrial stromal sarcoma. Immunochemistry showed negative oestrogen and progesterone receptors. The small cells extensively infiltrated the myometrium until the serosa. Mitotic figures were 10–12 HPF and there were foci of haemorrhage and necrosis.**

in the right lung. She underwent six courses of CYVADIC chemotherapy (doxorubicin 50 mg/m$^2$ day 1, cyclophosphamide 700 mg/m$^2$ day 1, vincristine 1.4 mg/m$^2$ day 1, dacarbazine 1000 mg/m$^2$ day 1 to day 3). A repeated CT scan showed a partial remission. On June 1989, she underwent a median sternotomy for resection of residual disease: a diffuse metastatic spread was found in both lungs. On July 1989, she had three further courses of chemotherapy with ifosfamide 7500 mg/m$^2$ and cisplatin 125 mg/m$^2$; both drugs were administered in 5 days. Chest CT scan showed a minor response. She had autologous bone marrow pull on January 1990 and in February she underwent high dose chemotherapy with: carboplatin 800 mg/m$^2$, etoposide 800 mg/m$^2$, and cyclophosphamide 5000 mg/m$^2$ in 3 days, followed by infusion of $2 \times 10^8$ autologous marrow cells/kg. During the time of engraftment, she had neutropenic fever with negative blood cultures and a perianal abscess. During the month following ABMT, she received thymopentin 1 mg/kg every other day. The time taken to reach $1 \times 10^3$ neutrophils and $50 \times 10^5$ platelets was 17 and 19 days respectively; the CD4+/CD8+ lymphocyte ratio improved in a few months. At the last follow-up visit, 66 months after ABMT (August 1995), she is still in complete remission with no evidence of disease.

Little progress has been made in the treatment of metastatic uterine sarcoma and median survival of less than 6 months has been described [3]. Piver and Rose, in a retrospective study of 78 patients with uterine sarcoma, noted single agent activity with doxorubicin, cisplatin and methotrexate with responses between 5% and 11%; and effective multi-agent therapy with CYVADIC (23% response rate); cisplatin and dacarbazine (21% response rate), and vincristine, dactinomycin and cyclophosphamide (18% response rate). Another phase II trial performed on 18 patients with mixed mesodermal sarcomas of the uterus with single agent cisplatin, obtained a 42% response rate, but the progression free survival and overall survival were short [6].

Our patient, after debulking surgery, received six courses of CYVADIC regimen, and showed a partial remission. After the second debulking surgery, she still had disease in both lungs, as established during surgery. She showed also a minor response to a cisplatin–ifosfamide combination. In contrast

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she had a complete response to high dose carboplatin, etoposide and cyclophosphamide. Our patient had received a total of nine previous chemotherapy courses and three operations in 2 years: this was the reason for not employing higher doses of chemotherapy. Furthermore, since at that time, growth factors were not commercially available, we administered thymopentin after ABMT for its pleiotropic properties and, in particular, for its stimulation of T cell function [7]. The present case demonstrates that metastatic low grade uterine sarcoma can be considered a chemotherapy-sensitive neoplasm. Further experiences should be performed with high dose carboplatin, cyclophosphamide and etoposide in the setting of metastatic uterine sarcoma.


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# Skin Lesions and G-CSF in Patients with Malignant Diseases. Malignancy or Cutaneous Side-effect?

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TREATMENT WITH haematopoietic colony-stimulating factors is occasionally associated with neutrophilic dermatoses and vasculitis [1, 2]. Furthermore, pre-existing factors may be exacerbated during such therapy.

We report 2 patients who illustrate a diagnostic problem which may arise during G-CSF treatment of cancer patients: metastases to the skin or a cutaneous side effect of G-CSF?

*Case I.* A 26-year-old man with an angiosarcoma of the right atrium and bilateral pulmonary metastases was treated with cycles of etoposide/doxorubicin/ifosfamide (VIGA) and support with filgrastim (Neupogen®, Roche). The pulmonary metastases gradually decreased during treatment. After the sixth course of VIGA, he noticed a 1 cm indurated plaque in the skin of his right forearm. The leucocyte count was 36.8 × $10^9$/l. A fine needle aspiration was performed and the cytological picture was described as "probable mesenchymal malignant tumour with numerous mature neutrophil granulocytes". The mesenchymal cells were similar to the malignant cells in the primary biopsy. Immunochemistry of these cells was not carried out. Neither was a biopsy performed, but the patient's treatment was changed to high dose ifosfamide. The tumour disappeared gradually. A subsequent review of the cytological report altered the diagnosis to "possible inflammatory process combined with mesenchymal cells of uncertain origin".

*Case II.* A 33-year-old man with a non-seminomatous germ cell tumour of the right testicle and metastases to the retroperitoneum, stomach and left supraclavicular fossa was treated with bleomycin/etoposide/cisplatin (BEP) every 3 weeks. After the third course he received filgrastim 390 μg subcutaneously from day 6 to 14 because of severe leucopenia. On day 17, he noticed a tumour under his right mandibula, and on day 21, the tumour was erytematous and 6 cm in diameter. His leucocyte count was 6.8 × $10^9$/l with neutrophil count 4.8 × $10^9$/l. A fine needle aspiration was performed, and the cytologist's conclusion was "dominance of mature neutrophil granulocytes with a few groups of confluent large malignant cells" (Figure 1). The malignant cells were assumed to represent metastatic spread from his non-seminomatous germ cell tumour. No biopsy was performed. As there was no other clinical or serological suspicion of progression of the patient's malignancy, the treatment was not altered. The skin lesion was treated with benzylpenicillinnatrium and metronidazol, and the tumour diminished in size. A new fine needle aspiration 5 days later displayed the picture of a typical inflammatory disorder.

The cells with malignant appearance in our patients were not immature myeloid cells, but they could have been large

**Figure 1. Large undifferentiated and multinucleated cell with a background of mature neutrophil granulocytes. Diff Quick stain, oil immersion lense (×100).**

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