Survey of adjuvant hormone therapy in patients after endometrial stromal sarcoma

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Summary

Introduction: We surveyed the use of adjuvant hormonal therapy in patients with endometrial stromal sarcomas.

Material and methods: A questionnaire was circulated among the 130 members of an Internet-based endometrial stromal sarcoma support group. The questions pertained to age at diagnosis, organs involved at diagnosis, recurrences, metastases, current disease status, and treatment protocols, with special focus on hormonal therapy.

Results: The questionnaire was returned by 64 of 120 women (49%). At the time of the study 48 patients (mean follow-up 2.4 (range, 1-9) years) had no evidence of disease (NED) and 16 (mean follow-up 6.2 (range, 1-22) years) were alive with disease (AWD). Of the 16 women AWD, 15 (95%) were being treated with hormones as opposed to ten of 48 (21%) women with NED. Hormone treatment consisted of progestins (15 patients), aromatase inhibitors [9], aromatase inhibitor plus GnRH analog [1], or tamoxifen [1].

Discussion: Adjuvant hormonal therapy presently appears to be used predominantly in women with advanced or recurrent endometrial stromal sarcomas but is also a potential option for patients after surgery without residual tumor.

Key words: Endometrial stromal sarcoma; Hormonal therapy.

Introduction

Endometrial stromal sarcomas (ESS) are rare uterine tumors that account for about 0.2% of all genital tract malignancies [1]. At time of hysterectomy over 80% of ESS are limited to the uterus [2]. ESS are estrogen-dependent tumors and most women with ESS undergo bilateral salpingo-oophorectomy for hormonal ablation as part of the primary treatment. However, pelvic or abdominal recurrences develop in one-third to one-half of patients [2, 3]. Residual or recurrent disease is managed with repeated debulking, occasionally followed by hormonal therapy. The therapeutic value of adjuvant hormonal therapy for patients who have no residual tumor after primary surgery is unclear. In the present study, we analyzed the current treatment regimes of 64 patents with ESS with special attention given to adjuvant hormonal therapy.

Material and Methods

A questionnaire was circulated among the 130 members of an Internet-based ESS-support group [4]. The questions pertained to age at diagnosis, organs involved at diagnosis, recurrences, metastases, current stage of ESS, and treatment protocols, with special focus on hormonal therapy.

Results

The questionnaire was returned by 64 of 130 women (49%) (57 from the U.S.A., two from Canada, two from Australia, two from the U.K. and one from New Zealand). At diagnosis 58 patients were premenopausal and six were postmenopausal. The average age at diagnosis was 42 years (range, 26-72 years). Sixteen patients (25%) were younger than 40 years at diagnosis. At diagnosis 47 patients had had Stage I, four Stage II, six Stage III and seven Stage IV disease. At the time of the study 48 patients (mean follow-up 2.4 (range, 1-9) years) had no evidence of disease (NED) and 16 (mean follow-up 6.2 (range, 1-22) years) were alive with disease (AWD). Of the 16 women AWD, 15 (95%) were being treated with hormones. In contrast only ten of 48 (21%) women with NED were being treated with hormones. Among the 25 patients with hormonal treatment 15 (60%) received progestins. Four patients had received progestin but had stopped due to side-effects. Dosage of progestin ranged from 40 to 320 mg medroxyprogesteroneacetate/day. Nine of 25 patients (36%) were receiving aromatase inhibitors, mainly non-steroidal formulations (letrozole n = 4, anastrozole n = 4). Only one patient was receiving a steroidal aromatase inhibitor (exemestane). One of the patients treated with oral aromatase inihibitors additionally received a GnRH analog every three months. Only one patient (4%) was on tamoxifen (Figure 1).

Discussion

This survey suggests that hormonal therapy is well established for advanced ESS or recurrent ESS. In contrast, only 21% of patients with NED were receiving adjuvant hormonal therapy (Figure 1). The high recurrence rates after surgical treatment in ESS, even in young patients with early stage disease, suggest that surgical treatment alone is ineffective in preventing recurrences of

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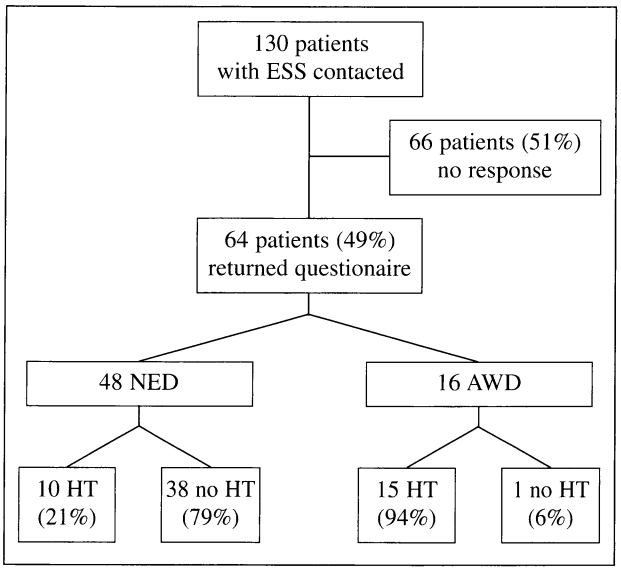

Figure 1. — Characteristics of 130 patients with surgically treated endometrial stromal sarcomas who were contacted. NED = no evidence of disease; AWD = alive with disease; HT = hormonal therapy.

ESS. In other hormone-dependent tumors, e.g. breast carcinoma, postoperative hormonal therapy following complete excision of the primary tumor significantly reduces recurrence rates. Similar treatment strategies have not been established for ESS, mainly due to the rarity of the condition.

Adjuvant hormonal treatment is a potential option for patents after surgery of ESS without residual tumor. Indicators and predictive factors for treatment success of hormonal therapy could be the immunohistochemical demonstration of progesterone-receptors, gonadotropin-releasing hormone receptors and the enzyme complex aromatase, which have been demonstrated in the majority of ESS [5-7].

Clinical responses to endocrine therapy in patients with recurrent ESS have been reported for progestins, aromatase inhibitors and GnRH-analogs. Katz *et al.* [8] reported four complete or partial responses with hormonal therapy and all four patients were alive and free of disease or alive with stable disease two to six years after initial diagnosis. Recurrent disease has been successfully treated with progestins [9-18]. Spano *et al.* [19] followed two patients with metastatic ESS who had complete tumor remission after treatment with an aromatase inhibitor. Mesia and Demopoulos [20] observed incomplete regression in one patient with Stage I ESS after treatment with the leuprolide acetate. Scribiner and Walker [21] treated a woman with inoperable ESS with leuprolide acetate and progesterone and achieved marked tumor shrinkage.

Progestins are the most used agents in hormonal therapy for ESS. Side-effects include prothrombotic effects and hot flashes. Aromatase inhibitors appear particularly suitable for long-term therapy because they inhibit intratumoral and peripheral aromatase and thereby lower systemic estrogen levels. However, patients receiving aromatase inhibitors require osteoporosis prophylaxis. An interesting approach is the combination of aromatase inhibitors with GnRH-analoga [6, 7]. Tamoxifen is contraindicated in women with ESS because it appears to have a proliferative effect on the endometrial stroma [22].

The duration of adjuvant hormonal therapy for patients with ESS is unknown. In a clinico-pathologic study on ESS, the median time between hysterectomy and relapse was 5.4 years for ESS Stages I and nine months for ESS Stage III-IV [2]. In a series by Piver *et al.* [3], time to recurrence varied between three months and 23 years, with a median of three years. In light of these experiences, it would seem reasonable to consider adjuvant hormonal therapy of five years or more following primary surgery for ESS, particularly for patients with early-stage disease.

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