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CASE REPORT

Remission of Recurrent Endometrial Cancer with Hormonal Therapy : Case Report and Review of Literature

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ABSTRACT

A case of stage II endometrial cancer which had recurred after radiotherapy and hysterectomy was manipulated with hormonal therapy. Oral megestrol acetate 160 mg per day induced partial response of measurable lesion. The duration of response was appreciated, 41 months. Later tamoxifen 40 mg per day orally also stabilized the progressive disease for another 18 months. Hormonal therapy has modest activity, low toxicity and should be considered in selected case of recurrent endometrial cancer

Key words : recurrent endometrial cancer, hormonal therapy

Recurrent and metastatic endometrial carcinoma has very poor prognosis. Currently, systemic therapy with either hormonal or cytotoxic agents has a palliative role only. Progestogen has been a major hormone used in advanced or recurrent endometrial carcinoma. Different progestogens, such as medroxy progesterone acetate (MPA), megestrol acetate (Megace) and hydroxy progesterone caproate (Delalutin), produce equivalent anti-tumour activity.[1,2] The

overall response rate, the duration of response and duration of survival on progestogen therapy are modest. However, occasional sustained remission and prolonged survival has been reported.[3]

Tamoxifen, the non-steroidal antiestrogen, can induce progestogen receptors in endometrial carcinoma.[4,5] Furthermore, it has anti-tumour activity in endometrial cancer.[6] It may be used as second line hormonal therapy when progesterone therapy fails.

We report a case of recurrent endometrial carcinoma who had prolonged remission of her disease with megestrol acetate. When her disease progressed, she was treated with tamoxifen which stabilized her progressive disease.

Case Report

A 67 year old white woman, para 5, abortion 1, developed recurrent endometrial cancer. Her tumour history began in March of 1990 when she presented to her gynaecologist with vaginal bleeding for one week. Pelvic examination revealed enlarged uterus, size equal to eight weeks' pregnancy. The cervix was 4 cm in diameter. There was a fungating tumour mass 1.5 cm in size filling the cervical os. The endometrial cavity sounded to 9.3 cm. Endometrial and cervical biopsies revealed endometrioid adenocarcinoma of the endometrium, grade II. The metastatic investigation showed no evidence of cancer outside the uterus. She was diagnosed as stage II, grade II, endometrial adenocarcinoma. The treatment consisted of whole pelvis radiation, 45 Gy divided into 27 fractions over 5 weeks, followed by single intracavitary Radium insertion. In July of 1990 (seven weeks after the completion of radiotherapy) she underwent exploratory laparotomy with extrafascial hysterectomy and bilateral salpingo-oophorectomy. Exploration of intraperitoneal cavity showed no evidence of tumour and no lymphadenopathy. The pathological examination revealed residual adenocarcinoma along the endometrial lining. The depth of myometrial invasion was less than 2 mm The other resected tissues were unremarkable.

In February, 1991 she began to have right flank pain. An intravenous pyelogram showed bilateral hydronephrosis and hydroureter. A computed tomography (CT) of abdomen and pelvis showed small amount of ascites. There was a soft tissue mass along the left side of the anterior abdominal wall. A CT guided fine needle aspiration of this mass revealed metastatic adenocarcinoma. Bilateral ureteral stents were placed to relieve the ureteral obstruction. She was then referred to the University of Texas M.D. Anderson Cancer Centre. On our initial evaluation, she reported mild intermittent right sided flank pain. Physical examination revealed fullness on both sides of the mid abdomen and minimal discomfort on deep palpation, which might represent residual bilateral hydronephrosis. There was no lymphadenopathy. Pelvic and rectal examinations were unremarkable. All pathology was reviewed and reported as well differentiated adenocarcinoma of endometrium with mucin production. The serum CA 125 and CEA were 1335.7 U/ml and 2292 ng/ml respectively. The serum creatinine was normal. The therapy was initiated with oral megestrol acetate 160 mg in four divided doses.

Two months later the serum CA125 and CEA dropped to 370 U/ml and 751 ng/ml respectively. The CT of abdomen and pelvis showed more than 50% decrease in the size of the metastatic tumour in the abdomen. She had no symptoms. She was in remission for 41 months with a good quality of life. Periodic physical examination and CT of abdomen and pelvis were

used to follow the persistent partial remission. She also had a good serologic response. The CA 125 level ultimately dropped to normal and the serum CEA remained at 120 - 180 ng/ml.

In September of 1994, a follow up CT scan of abdomen and pelvis demonstrated progression of the tumour. However she remained asymptomatic. Her CA125 level was normal, but the serum CEA became elevated to 300 ng/ml. Because of the good initial hormonal response of her disease, her treatment was changed to tamoxifen 20 mg orally twice a day. Her disease has again stabilized with no further progression for another 18 months.

Discussion

Generally, the therapeutic approach in recurrent metastatic endometrial carcinoma is based on the degree of tumour differentiation, inferred status of steroid receptors and the patients' performance status. The patient who has minimal disease with no symptoms, well differentiated tumours and positive steroid receptors is a good candidate for hormonal therapy. The advantages of this therapy are patients' tolerance, ease of administration, low toxicity and low cost.

Various types of progestogens have been tried in advanced or recurrent endometrial carcinoma with the overall response rate of 34%, as reviewed by Kauppila.[1] The duration of response ranged from 16 to 28 months and the average survival time was 18 to 33 months. Subsequent studies revealed lesser overall response rates due to the high proportion of patients with high grade tumours and differences in response criteria.[2,7,8] Thigpen et al[7,8] reported 14, 18 and 26% objective response rates with oral MPA 150, 200 and 1,000 mg/d respectively. The median duration of survival was 10.4 months. Podratz et al[2] performed a retrospective review of 155 patients and found objective response rates of 11, 9 and 12% for megestrol acetate, hydroxy progesterone caproate and medrogestone respectively. Interestingly, almost 40% of the patients had stabilization of their disease for three months or longer. Forty percent of patients with low grade tumours had an objective response. Overall, the 5 year survival rate was 8%.

Tamoxifen has been used in endometrial carcinoma with a widely variable response rate. The pooled data from Moore et al[6] revealed 22% response rate (range 0-53%) when 20 to 40 mg/d orally was used. The patients with low grade tumours, presence of steroid receptors, and prior response to progestin therapy had a higher response rate to tamoxifen than patients without these characteristics.[9] A downregulation of the progesterone receptor from prolonged progestogen therapy was considered as the cause of acquired progestogen resistance. Tamoxifen can increase the level of progesterone receptors but the clinical data failed to demonstrate the benefit of adding tamoxifen to progestogen in treating advanced or recurrent endometrial carcinoma.[9,10]

Gonadotropin releasing hormone (GnRH) analogs represent another hormonal modality which has been studied in various gynaecologic malignancies. Of 17 patients with progestogen resistant advanced or recurrent endometrial cancer, 6 patients (35%) had an objective response including 1 patient with a complete response. The median duration of response was 24 months.[11]

The advanced age, poor performance status and coexisting illness in patients with endometrial cancer frequently limit the use of chemotherapy. Single agent trials which demon-

strated objective responses of more than 20% were Cisplatin,[12] Doxorubicin,[13] and Carboplatin.[14,15] The median time to progression and median duration of survival were short lasting only 2 to 4 months and 4 to 8 months respectively. The combination of Cisplatin, Doxorubicin and Cyclophosphamide with or without progestogen was most active with an objective response rate of up to 53% but the duration of response was only 4-6 months and the survival duration was less than 12 months.[16,17] Furthermore, moderate to severe toxicity occurred in almost half of the patients treated with this combination chemotherapy.

Current systemic therapy for recurrent metastatic endometrial carcinoma is palliative. Though hormonal therapy has modest activity, selection of patients may respond and maintain good quality of life. Accordingly, hormonal therapy should be considered in patients with advanced or recurrent endometrial carcinoma.

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