Successful salvage treatment of recurrent endometrial cancer with bulky central tumor and extensive lymph node metastasis. A case report

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Summary

Recurrent endometrial cancer with both local and distant metastasis is very difficult to treat. A 55-year-old endometrial adenocarcinoma patient with bulky central recurrences and pelvic and inguinal lymph node metastases underwent laparotomy and paraaortic, pelvic and inguinal lymphadenectomy followed by concurrent chemoradiation (with cisplatin) to the paraaortic and inguinal lymph nodes as well as the whole pelvis. Neck and mediastinal lymph node metastasis emerged during treatment. Neck-node radiation and epirubicin was added followed by paclitaxel and carboplatin. Complete remission was achieved. Ten months later, isolated central re-recurrence happened and total pelvic exenteration was performed. The patient has survived without further recurrence for more than five years after the exenteration. Therefore, a multimodality approach with a combination of radical resection (even pelvic exenteration), radiotherapy and chemotherapy could be offered to well-selected patients with recurrent endometrial cancer despite out-of-field progression during therapy and in-field local failure to initial salvage treatment.

Key words: Endometrial cancer; Lymph node metastasis; Recurrence; Chemoradiation; Exenteration.

Introduction

Endometrial carcinoma is the most common gynecologic malignancy and is characterized by early diagnosis and long-term survival for most patients. The salvage rates of recurrent endometrial carcinoma in different series vary enormously. The prognosis of recurrent endometrial carcinoma is generally poor except for isolated vaginal relapse [1-3]. Recurrences associated with disseminated disease or distant metastasis are usually not easily treatable. Aalders *et al.* noted a two percent 5-year survival rate among patients with both local recurrences and distant metastasis [1]. However if failure appears at sites that have already been radiated, further treatment options are even more limited.

Pelvic exenteration is a viable option for gynecologic malignancies with pelvic recurrence not involving the pelvic sidewall. However, such radical procedures are rarely performed for endometrial cancer because disseminated disease usually coexists [4, 5].

Here, we report a case of recurrent endometrial cancer treated with concurrent chemoradiation and postradiation adjuvant chemotherapy for extensive lymph node metastasis including the inguinal, pelvic, para-aortic and neck lymph nodes. Pelvic exenteration was subsequently performed for localized re-recurrence with a good outcome.

Case report

A 55-year-old woman presented with an exophytic mass at the suburethral area. She had undergone a subtotal hysterectomy for uterine leiomyoma 18 months before at a local hospital. The final pathology turned out to be endometrioid adenocarcinoma of the endometrium. No additional therapy was advised.

Pelvic examination disclosed a suburethral tumor measuring 3 x 4 x 2 cm and an apparently cancer-infiltrated cervical stump. Enlarged confluent right inguinal lymph nodes were also palpable. Biopsy of the suburethral lesion revealed poorly differentiated adenocarcinoma (Figure 1) consistent with the previous uterine pathology through histology slide review.

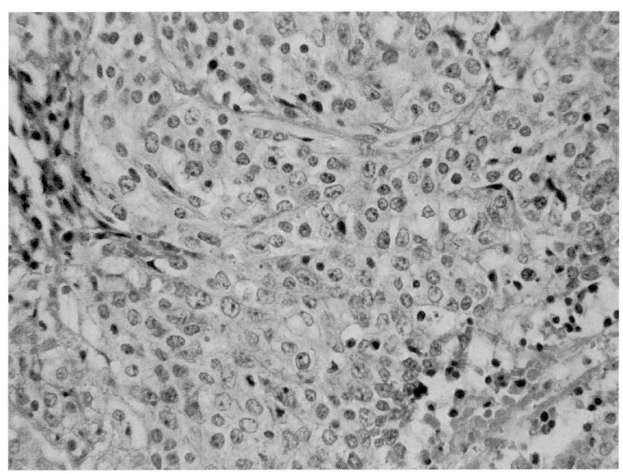

Figure 1. — Poorly differentiated adenocarcinoma (hematoxylin & eosin, original magnification x 400).

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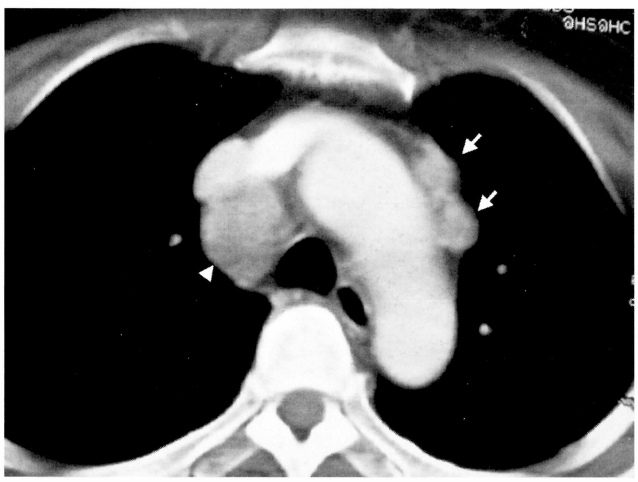
Fig. 2A

Fig. 3A



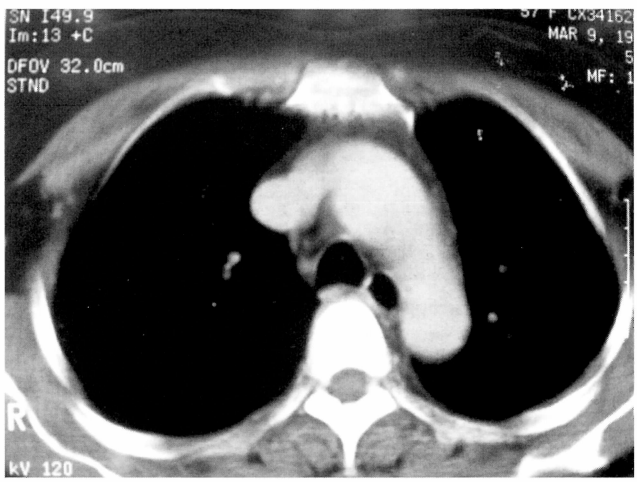


Figure 2A. — Bilateral heterogeneously enhanced iliac nodes (3.5 x 3.5 cm) compatible with metastasis.
Figure 2B. — Enlarged right inguinal lymph node with homogeneous enhancement (1); thickened anterior vaginal wall with irregular margin compatible with central recurrence (2).
Figure 3A. — Enlarged paratracheal (arrow head) and anterior mediastinal (arrows) lymph nodes were noted when neck node metastasis was proven.
Figure 3B. — Previously enlarged paratracheal and anterior mediastinal lymph nodes resolved.

Computed tomography (CT) of the abdomen and pelvis showed bulky pelvic (Figure 2A), inguinal lymph node metastases and central tumor (Figure 2B) with unremarkable paraaortic lymph nodes. The other oncologic survey studies, including chest X-ray, lower gastrointestinal series and cystoscopy, were all negative. Cancer antigen 125 (CA-125) was 84 U/ml (normal < 35 U/ml) and carcinoembryonic antigen (CEA) was 150 ng/ml (normal < 5 ng/ml).

The patient underwent restaging laparotomy and cytoreductive surgery with bilateral paraaortic, pelvic lymph node dissection and right inguinal lymph node excision, omentectomy and multiple intra-abdominal biopsies. Paraaortic, pelvic and right inguinal lymph node metastases were documented. The central recurrences at the cervix and suburethral site were left for postoperative radiotherapy with concurrent cisplatin (60 mg/m^2) per two weeks. External radiation with ten megavoltage X-ray by four-field box beam was given in a daily fraction size of 1.8 Gray (Gy) at five fractions per week. Total dose was 41.4 Gy to the whole pelvis, inguinal, and para-aortic area.

Unfortunately, enlarging left supraclavicular lymph nodes were palpable during the course of chemoradiation. Echo-guided biopsy of the lesion confirmed the diagnosis of metastatic adenocarcinoma. Mediastinal and paratracheal lymph nodes were also enlarged by chest CT scan (Figure 3A). Owing to progression during salvage therapy, curative radiation was shifted to palliation, yet left neck lymph nodes were encompassed in the radiation field while intracavitary brachytherapy was omitted.

Nevertheless, chemotherapy was changed to combining cisplatin (60 mg/m^2) with epirubicin (60 mg/m^2) per three weeks. Two courses of adjuvant chemotherapy with paclitaxel (135 mg/m^2) and carboplatin (area under the curve = 5) per three weeks were administered after completion of radiotherapy. After these treatments, complete remission was achieved. Tumor markers (CA-125 and CEA) returned to normal.

A rapidly growing suburethral tumor measuring 4 x 2.5 x 2 cm was found ten months after cessation of chemotherapy. One posterior vaginal wall tumor about 1.5 cm close to rectal mucosa was also palpable. Local re-recurrence was confirmed. A series of restaging examinations, including chest X-ray and CT scan, magnetic resonance imaging (MRI) of the abdomen and pelvis, lower gastrointestinal series, cystoscopy and proc-

toscopy, were again performed. All the other studies were negative for metastasis (Figure 3B) except bone scan, in which sacral bone metastasis was suspected. Biopsy of the sacral bone lesion was negative. Since no other distant or regional diseases were controlled, a total pelvic exenteration was performed. Postoperative recovery was uneventful. She has remained without further recurrence for more than five years after the re-recurrence.

Discussion

Little information is available regarding the optimal treatment of recurrent endometrial cancer. Generally, there is a hope for cure if all gross diseases can be irradiated [2, 3] or surgically removed [4, 5]. Patients who develop recurrences in the previously irradiated area or distant/disseminated disease have limited treatment options, although anecdotal cases have long-term survival with hormone therapy [1, 6, 7].

Chemotherapy with cisplatin/carboplatin or doxorubicin had response rates around 15-25%. The median survival time was approximately four to ten months [7]. Several phase II studies demonstrated that paclitaxel is an active agent (response rates of 36 to 43%) for recurrent endometrial cancer, but the median survival time was also short [8, 9]. Hoskins *et al.* observed a high response rate (56%) with paclitaxel and carboplatin alone to 18 recurrent endometrial cancer (non-papillary serous) patients. The median failure-free survival was six months, and all eventually died from their disease [10].

The clinical significance of maximal cytoreductive surgery for recurrent endometrial cancer is unknown. Scarabelli *et al.* reported a series of 20 recurrent endometrial cancers, eight of which had adjuvant radiotherapy in the initial treatment. Residual tumor at the end of cytoreductive surgery was the only significant variable for prognosis. For those with gross residual tumor, 0% survival rate was noted at nine months [11]. In contrast, the central recurrences at the cervix and suburethral site of this case were left for postoperative chemoradiation to avoid an initial pelvic exenteration in the presence of coexistent extensive lymph node metastasis. Eventually, all the extrapelvic diseases were controlled, and pelvic exenteration was inevitable and feasible.

Patients who develop pelvic relapse in the radiation field have a dismal prognosis. The only subset of patients potentially curable are those whose pelvic recurrence is centrally located. Morris *et al.* reported on 20 patients who underwent pelvic exenteration for advanced (n = 14) or recurrent endometrial cancer (n = 6). The 5-year disease-free survival rate for the whole series was 45%, with a complication rate of 60% [4]. Barakat *et al.* reported a 20% 5-year survival rate in 44 patients undergoing pelvic exenteration for recurrent endometrial cancer with a major complication rate of 80% [5].

For this case, surgical staging and cytoreduction of retroperitoneal lymph nodes was performed with an end to define the disease extent and accurate radiation field prescription. Unfortunately, disease progressed with the presentation of documented neck-node and probable mediastinal-node metastases during chemoradiation. However, with extension of the radiation field to the neck lymph node region and adding epirubicin for concurrent chemoradiation, and adjuvant chemotherapy with paclitaxel and carboplatin, complete clinical remission was achieved. Progression on treatment does not totally negate a hope for cure, and a patient who has been put on palliation can be shifted back to curative intent based on the individual response to initial treatment.

Despite extensive lymph node metastasis at first relapse and out-of-radiation-field progression during salvage therapy, this reported case was successfully treated with extended chemoradiation followed by adjuvant chemotherapy and subsequent pelvic exenteration. We are not able to tell how this excellent result was achieved for this particular patient. However, we are certain that multimodality approaches can be applied to achieve complete surgical resection or curative radiotherapy for all gross tumors in combination with concurrent/adjuvant chemotherapy, and such option should be opened to well-selected patients with recurrent endometrial cancer.

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