

Secondary small cell carcinoma of the endometrium after concurrent chemoradiotherapy for cervical cancer: a rare case

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Summary

Background: Small cell carcinoma of the endometrium is extremely rare. There is no reported case of secondary small cell carcinoma of the endometrium after concurrent chemoradiotherapy for cervical cancer. **Case Report:** A 48-year-old woman was diagnosed with squamous cell carcinoma of the cervix Stage IIIB (T3bN0M0) and treated by concurrent chemoradiotherapy. After five years and nine months' post-treatment, the woman was diagnosed with small cell carcinoma of the endometrium Stage IIIA (pT3aNXM0). Although the patient received chemotherapy combining paclitaxel and carboplatin postoperatively, she developed a recurrence with pelvic tumor three months after operation. After recurrence, she received one course of chemotherapy combining cisplatin and irinotecan. Although a remarkable reduction of recurrent tumor was found as autopsy findings, she died of disease two months after this chemotherapy. **Conclusion:** In case of small cell carcinoma of the endometrium, chemotherapy regimen used for small cell lung cancer such as chemotherapy combining cisplatin and irinotecan should be considered.

Key words: Secondary small cell carcinoma of the endometrium; Concurrent chemoradiotherapy; Cervical cancer.

Introduction

Cervical cancer patients often received initial radiotherapy, either alone or in combination with chemotherapy. Therefore, several studies have reported a correlation between radiotherapy for cervical cancer and subsequent cancer risk such as endometrial cancer. In previous reports, the relationships between radiotherapy and the risk of secondary endometrial cancer was controversial [1-4]. Small cell carcinoma in the female genital tract is rare, and most reported cases were found in the uterine cervix and ovary. Primary small cell carcinoma of the endometrium is extremely rare, and approximately less than 100 cases have been reported in the English-language literature [5-7]. There is no reported case of secondary small cell carcinoma of the endometrium after concurrent chemoradiotherapy for cervical cancer. Here, the authors present a rare case of secondary small cell uterine carcinoma after concurrent chemoradiotherapy for cervical cancer.

Case Report

A 48-year-old woman without a past medical history of interest was diagnosed with squamous cell carcinoma of the cervix Stage IIIB (T3bN0M0) and treated by concurrent chemoradiotherapy (six cycles of weekly cisplatin, 40 mg/m²), achieving a complete response. Radiation therapy performed at that time was as followed; 45 Gy of whole-pelvic external beam radiotherapy (EBRT) was administered, followed by 10 Gy of central shielding

EBRT, up to a total EBRT of 55 Gy. After EBRT, 10 Gy of intracavitary brachytherapy (ICBT) using high-dose rate (HDR) was administered. After five years and nine months' post-treatment, she was referred to the present hospital with lower abdominal pain. No other symptoms were observed. Examination of the pelvis, which demonstrated a normal uterine cervix and an enlarged uterine body with a necrotic tissue and bleeding, suggesting endometrial cancer. Ultrasonography revealed a uterine corpus tumor without ascites. MRI examination of the pelvis, which demonstrated a large endometrial mass with an internal focus of bleeding, suggesting an endometrial cancer (Figure 1). CT examination of the abdomen and chest demonstrated no metastasis. Laboratory investigations showed no remarkable findings. Serum tumor markers were as follows: CA125: 49 U/mL, SCC: 0.8 ng/mL, CA19-9: 36 U/mL, and neuron-specific enolase (NSE): 16.2 ng/mL. The cytological examination of cervix showed no abnormality. The histological examination of endometrium showed small cell carcinoma. Therefore, primary endometrial cancer was initially considered the most likely diagnosis.

The patient underwent an exploratory laparotomy. Macroscopically, there were a moderate amount of bloody serous ascites in the peritoneal cavity. There was enlarged uterine body (size: 12×8 cm) which presented a carcinomatous tumor with necrotic lesions in the endometrium. There were very strong adhesions between the uterine cervix and the bladder. The ovary was unremarkable (Figure 2). There were no other remarkable findings in the peritoneal cavity. At this time, the authors diagnosed the patient with primary endometrial cancer and performed supra vaginal hysterectomy and bilateral salpingo-oophorectomy. For massive adhesion and bleeding, systematic pelvic lymphadenectomy and para-aortic lymphadenectomy were not performed.

The pathological examination showed that the tumor was densely cellular, and the tumor cells had scanty cytoplasm and

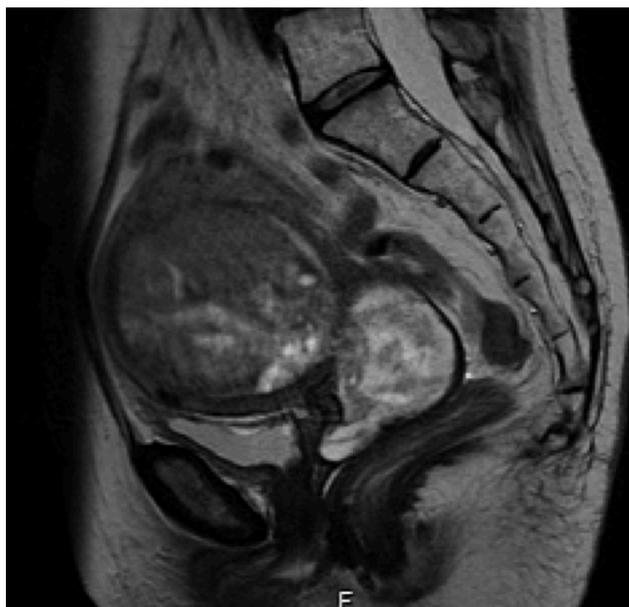


Figure 1. — MRI examination of the pelvis which demonstrates a large endometrial mass with an internal focus of bleeding, suggesting endometrial cancer.

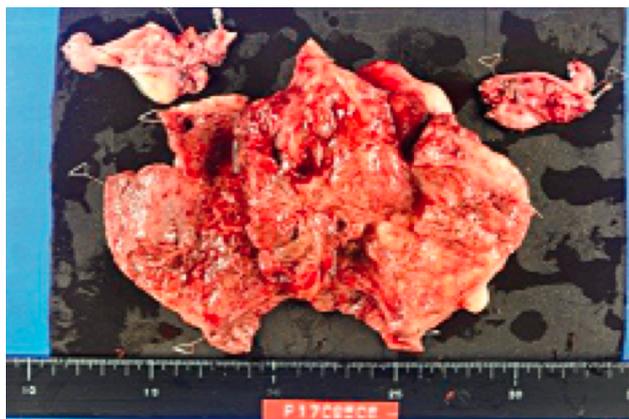


Figure 2. — Macroscopic image of resected specimen. The uterine body size of 12×8 cm presents a carcinomatous tumor with necrotic lesions in the endometrium.

spindle-shaped. There was a metastatic tumor in right ovary. The cytological examination of ascites showed abnormality. The tumor cells showed strong positivity by immunohistochemistry for cluster of differentiation 56 (CD56), synaptophysin, and AE1-AE3, although chromogranin A, p40, WT1, estrogen receptor (ER), and vimentin were negative (Figure 3). Finally, the pathological examination showed a small cell carcinoma. The authors confirmed the diagnosis of primary endometrial cancer Stage IIIA (pT3aNXm0) according to the International Federation of Gynecology and Obstetrics (FIGO) surgical staging system.

Although the patient received three courses of chemotherapy combining paclitaxel (175 mg/m²) and carboplatin (AUC6) ad-

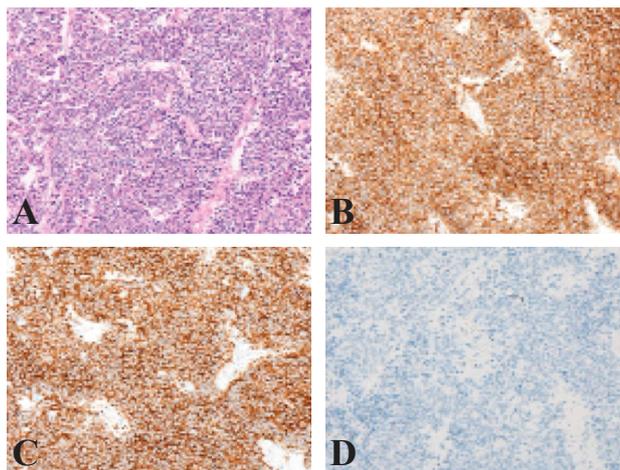


Figure 3. — A) Microscopic image of tumor cells (Hematoxylin and Eosin, ×200), which shows scanty cytoplasm and small- to medium-sized hyperchromatic nuclei. B) Image of CD56-positive tumor cells (×200). C) Image of synaptophysin-positive tumor cells (×200). D) Image of ER-negative tumor cells (×200).

ministered every three weeks postoperatively, she developed a recurrence three months later with a large tumor in pelvic cavity. After recurrence, the woman received one course of chemotherapy combining cisplatin (60 mg/m², Day 1), and irinotecan (60 mg/m², Days 1, 8, and 15) administered every four weeks. Although a remarkable reduction and necrosis of recurrent tumor was found at autopsy, the patient died of disease two months after this chemotherapy.

Discussion

Cervical cancer patients often receive initial radiotherapy, either alone or in combination with chemotherapy. Cervical cancer survivors, however, often live with long-term consequences of the disease, including a risk of developing alternative primary cancers. Therefore, several studies have reported a correlation between radiotherapy for cervical cancer and subsequent cancer risk, such as endometrial cancer [1-4]. Curtis *et al.* reported that significant lower risk was seen in patients in USA with cancers of the endometrium, the breast, and melanoma of the skin [1]. Ohno *et al.* reported that there was no significant risk of secondary primary uterine malignancies in 2,167 cervical cancer patients who had underwent radiotherapy [3]. Chaturvedi *et al.* reported that cases of secondary endometrial cancer did not show a statistically significant increase during a follow-up study of 104,760 one-year survivors of cervical cancer in northern Europe and USA [2]. On the other hand, Teng *et al.* reported that a significantly higher risk was observed for secondary cancers of the endometrium [4]. Therefore, the relationship between the radiotherapy and the risk of secondary endometrial cancer was controversial.

Small cell carcinoma is a type of neuroendocrine cancer,

which arises most commonly in the lungs, accounting for 15% to 20% of all lung cancers [5-7]. Small cell carcinoma in the female genital tract is rare, and most of reported cases were found in the uterine cervix and ovary. It resembles small cell carcinoma of the lung. Primary small cell carcinoma of the endometrium is extremely rare, and approximately less than 100 cases have been reported in the English-language literature [5-7]. There is no reported case of secondary small cell carcinoma of the endometrium after concurrent chemoradiotherapy for cervical cancer. Therefore, this case is the first reported.

Small cell carcinoma of the endometrium is often seen at advanced stage and has a poor prognosis. There are no established treatment guidelines for this tumor [5, 7]. Chen *et al.* reported that patients with Stage IB small cell cancer underwent both surgery and postoperative TC therapy composed of paclitaxel and carboplatin, which achieved satisfactory results [7]. Matsumoto *et al.* reported that patients with Stage IIIC small cell cancer underwent both surgery and postoperative TC therapy, which achieved unsatisfactory results [5]. Although the present patient received three courses of chemotherapy combining paclitaxel (175 mg/m²) and carboplatin (AUC6) administered every three weeks postoperatively, she developed a recurrence three months later with a large tumor in pelvic cavity. Some reports conclude that treatment of small cell ovarian carcinoma of the pulmonary type should be based on the therapy used to treat other small cell carcinomas [5, 7]. In the present case, the patient received only one course of chemotherapy as a second-line chemotherapy combining cisplatin (60 mg/m², Day 1), and irinotecan (60 mg/m², Days 1, 8, and 15) administered every four weeks. In spite of only one course of chemotherapy for a large recurrent tumor after a first-line chemotherapy, a remarkable reduction and necrosis of recurrent tumor was found at autopsy. This regimen seems to be effective for patients with small cell carcinoma

of the endometrium. In case of small cell carcinoma of the endometrium, chemotherapy regimen used for small cell lung cancer, such as chemotherapy combining cisplatin and irinotecan, should be considered.

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