SHORT COMMUNICATION

SYNCHRONOUS OCCURRENCE OF PRIMARY NEOPLASMS IN THE UTERUS WITH SQUAMOUS CELL CARCINOMA OF THE CERVIX AND ADENOCARCINOMA OF THE ENDOMETRIUM

Cheng-Kuo Lin, Mu-Hsien Yu, Ta-Wei Chu1, Hung-Cheng Lai*

Department of Obstetrics and Gynecology, Tri-Service General Hospital, National Defense Medical Center, Taipei, and
1Department of Obstetrics and Gynecology, Armed Forces Tao-Yuan General Hospital, Tao-Yuan, Taiwan.

SUMMARY

Objective: Synchronous primary malignant neoplasms of the uterus are uncommon. Patients with synchronous cervical and endometrial cancers are even rarer. We describe a case of cervical squamous cell carcinoma and endometrial endometrioid adenocarcinoma occurring simultaneously in a 47-year-old woman presenting with massive menstrual bleeding. The concept of synchronous primary malignancies of the genital tract is also reviewed in this report.

Case Report: A 47-year-old overtly obese female presented with menometrorrhagia of over 6 months’ duration. Pelvic examination detected a large cervix but apparently normal externals. Magnetic resonance imaging revealed a mass over the cervical region and endometrial lesions in the uterine cavity. Surgical exploration disclosed a cervical tumor and erosion of the endometrium. The pathologic findings were compatible with synchronous occurrence of primary neoplasms in the uterus with squamous cell carcinoma of the cervix and adenocarcinoma of the endometrium.

Conclusion: Synchronous genital tract neoplasms are rare but cause more clinical problems than a single neoplasm. It is practical to pay more attention to the differential diagnosis of primary and metastatic tumors. The second primary cancer that occurs in an individual with endometrial cancer may offer an opportunity for early detection. The prognosis for a patient with synchronous gynecologic malignancies does not seem to be worse.

Key Words: cervical cancer, endometrial cancer, synchronous primary malignancies

Introduction

Synchronous multiple malignant neoplasms of the female genital tract are somewhat rare. For the most part, concomitant malignancies in the genital system are frequently diagnosed as metastatic disease. For patients with more than one gynecologic neoplasm, most cases are reported as synchronous endometrial and ovarian cancers. However, synchronous primary malignancies of the uterus are relatively rare. The prognoses of patients with synchronous primary cancers are related to the stage of disease at the time of diagnosis. We herein present an unusual case of cervical squamous cell carcinoma and endometrial endometrioid adenocarcinoma occurring simultaneously and presenting with massive vaginal bleeding.

Case Report

A 47-year-old overtly obese (body mass index, 36) female, gravida 3, para 3, had a history of poorly controlled non-insulin-dependent diabetes mellitus. Also,
she had never been part of a cervical screening program in the past 10 years. She had endured menometrorrhagia with her menstrual cycles for more than 6 months. She was referred to our emergency service due to massive vaginal bleeding during the procedure of diagnostic dilatation and curettage for potential endometrial lesions at a regional hospital. The endometrial biopsy tissues were carried with her and sent for histopathologic examination.

On examination, she was initially found to have a blood pressure of 78/61 mmHg with impending hypovolemic shock. Emergency blood transfusion and resuscitation were carried out. Physical examination revealed a soft abdomen and palpable enlarged uterus as at 12 gestational weeks in size. Rectovaginal bimanual examination revealed a large movable cervix with grossly smooth appearance, well supported smooth vagina, free parametrium and movable uterosacral ligaments. Magnetic resonance imaging (MRI) demonstrated a lobulated mass over the cervical region and multifocal cystic lesions in the uterine cavity with asymmetrical thickening of the upper-third portion of the corpus (Figure 1). Subsequent cystoscopic and proctoscopic examinations were both normal. The Pap smear was deferred due to uterine bleeding. According to the imaging interpretation, we applied Lugol’s iodine solution to stain the cervix and took a biopsy from the prominent region even though the cervix looked normal. The cervical specimen showed poorly differentiated cervical carcinoma. The pathology of the endometrial tissues was well differentiated endometrioid adenocarcinoma.

Due to the cervical cancer being at clinical stage Ib2, a radical hysterectomy, bilateral salpingo-oophorectomy, bilateral pelvic and common iliac and paraaortic lymph node dissection, and partial omentectomy were carried out. In addition, we measured the preoperative serum levels of tumor markers CA125, SCC and CEA, which were 128.10 U/mL, 6.0 ng/mL and <1.0 ng/mL, respectively. Macroscopically, the uterus was enlarged, measuring 17 × 10 × 8 cm, with a large cervix. Both adnexa and parametrium were unremarkable. On cutting, an ulcerative tumor could be seen to have replaced the whole layer of the cervix (Figure 2). In the uterine cavity, there was a fungating tumor, 4 × 4 × 1 cm, over the endometrium with superficial myometrial invasion (Figure 3). Microscopic examination showed squamous cell carcinoma of the cervix and endometrioid adenocarcinoma of the endometrium, grade II, with
myometrial invasion (invasive depth, 0.5 cm; full thickness of myometrium, 4 cm) (Figure 4). Histopathology of the cervix showed that non-keratinized squamous cell carcinoma had invaded almost the whole layer of the cervix, and there was stromal invasion and positive lymph–vascular space invasion (LVSIs). The bilateral ovaries, tubes, omentum, parametrium and vaginal surgical margins were all free. Surgical vaginal cuff and cutting end were free of tumor invasion (4.2 cm total length of vagina). Also, there was no LVSIs of the endometrial cancer. The lymphadenopathy was as follows: metastatic carcinoma with the same patterns as the cervical carcinoma, including right common iliac (1/8), right pelvic (4/8) and left pelvic (5/12) lymph nodes. The left common iliac (0/8) and paraaortic (0/10) lymph nodes were announced free of tumor metastasis. This patient was thoroughly evaluated and the FIGO stages were cervical cancer stage Ib2 with lymph node metastases and endometrial cancer stage Ib, grade II. Standard therapies include surgery and/or radiation therapy and/or adjuvant chemotherapy. Management with radical hysterectomy and adjuvant concurrent chemoradiation therapy (CCRT) appears to be the treatment of choice. Thus, we performed CCRT with a regimen of cisplatin and 5-fluorouracil. The radiation programs were started with initial teletherapy followed by brachytherapy. The first course of adjuvant chemotherapy with cisplatin (75 mg/m², day 1) and 5-fluorouracil (1,000 mg/m², day 2 to day 5) were given on the 16th day after surgery. The whole process was smooth and the patient tolerated it well. She was discharged and will be admitted next time for a further course of CCRT.

Discussion

Multiple primary cancers associated with gynecologic malignancies are observed infrequently. The incidence of synchronous primary tumors of the female genital tract is only 1–6% of all genital neoplasms. Further, endometrial cancer with simultaneous ovarian malignancy is the most commonly occurring [1,2]. In a retrospective study of 3,863 patients with female genital malignancies, 26 (0.7%) patients with synchronous primaries were identified [3]. Eisner et al found that the most frequently documented synchronous malignancies were coexistence of endometrial and ovarian cancers, which were seen in 11 patients, although four patients had a primary malignancy of the cervix and endometrium. These patients all had squamous cell carcinomas of the cervix, three associated with adenocarcinoma of the endometrium and one with a mixed müllerian tumor of the endometrium. Ayhan et al showed that 29 patients diagnosed as having synchronous tumors constituted 1.7% of all patients with genital malignancies (29/1,690) [2]. The most common cancer was

Figure 3. Fungating masses about 4 cm in size over the endometrium with superficial myometrial invasion.

Figure 4. (A) Invasive squamous tumor nests adjacent to the endocervical gland (hematoxylin and eosin, 100×). (B) Infiltrating endometrioid adenocarcinoma with glandular tumor cell invasion to almost half of the myometrium (hematoxylin and eosin, 40×).
Multifocal lesions may be expressed by the fact that, at the time of diagnosis, the majority of patients have low-stage disease. The association of low-grade histologies indicates that they may have arisen as synchronous separate, multifocal primary lesions rather than metastasis [3]. The prognosis in these patients is more favorable when compared to metastatic lesions of individual tumors [1]. Ayhan et al reported similarly favorable outcomes in the endometrial and ovarian cancer group as well as the other synchronous tumor groups [2]. The survival of patients with synchronous primary cancers is related to the stage of disease of either of the two tumors at the time of diagnosis [4]. Endometrial cancer usually produces early symptoms with abnormal bleeding. Nevertheless, early invasive cervical carcinoma may be asymptomatic. While the cervical tumor grows and presents exophytically, vaginal bleeding and abnormal discharge may be signs. The clinical features of squamous cell carcinomas are that they are substantially exophytic, obvious growth tumors of polypoid or papillary excrescence. However, a portion of squamous cell carcinomas may be endophytic, deeply infiltrating into the surrounding structures without visible surface lesions. They contribute to diffuse enlargement of the cervix (a barrel-shaped cervix) and act like certain types of adenocarcinoma of the cervix.

Our patient had never been part of a cervical screening program. Furthermore, the cervical lesion was confined to the endocervix so that diagnosis of cervical cancer might not have been considered if no manifestation of abnormal vaginal bleeding had derived from the endometrial cancer.

References