Synchronous clear cell adenocarcinoma of the cervix and endometrioid carcinoma of the endometrium

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Summary

Synchronous primary malignant neoplasms of uterus are uncommon. Patients with synchronous cervical and endometrial cancers are even rarer. We describe a case of cervical clear cell carcinoma and endometrial adenocarcinoma occurring simultaneously in a 54-year-old woman presenting with intermittent vaginal bleeding. The concept of synchronous primary malignancies of the genital tract is also reviewed in this report.

Key words: Cervical carcinoma; Endometrial carcinoma; Synchronous tumor.

Introduction

Multiple synchronous malignant neoplasms in the female genital tract are rare. Most of them are diagnosed as metastatic disease. Most cases of more than one gynecologic neoplasm are reported as synchronous endometrial and ovarian cancer. Synchronous primary malignant tumors of the uterus are exceptional, though. In this paper, a case is reported of synchronous clear cell adenocarcinoma of the cervix and endometrioid carcinoma of the endometrium.

Case Report

A nulliparous 54-year-old postmenopausal female was admitted to hospital with intermittent vaginal bleeding of one year's duration. She had very little bleeding at first, but the bleeding lasted longer and became heavier in time. The patient did not have a history of coitus or gynecological problems. Her left foot had been operated on for poliomyelitis when she was a child, after which she underwent osteomyelitis treatment three to four times. Otherwise, she had a relatively unremarkable medical and surgical history. Her family history revealed no evidence of cancer among her first-degree relatives.

A punch biopsy of the patient's vaginal protruding mass revealed clear cell adenocarcinoma with extensive necrosis, and colposcopy confirmed a bleeding protruding mass. A pelvic computed tomography (CT) and magnetic resonance imaging (MRI) scan revealed widening of her endometrial cavity, and right corneal area; her endometrial cavity was occupied by an intermediate-signal-intensity mass that extended and protruded to the vagina and widened her cervix; she had no suspected lymph node or distant metstasis (Figure 1). The results of the subsequent cystoscopic and sigmoidoscopic examinations were normal. The results of all the blood tests, which included tumor markers (SCC, CEA, CA125, and CA19-9), were within normal values.

Because the cervical cancer was at the IB2 clinical stage, a radical hysterectomy, bilateral salpingo-oophorectomy, bilateral pelvic and common iliac and paraaortic lymph node dissection, and partial omentectomy were performed four days after the patient's admission. A small amount of ascites was found in the pelvic cavity. The cytologic evaluation of the ascites revealed that they were non-malignant. Both ovaries were atrophied. Macroscopically, the size of the uterus was 11 x 6 x 4.2 cm, it weighed 160 g, and it had the usual serosal surface. When it was opened, a 4.5 x 1.0 cm large friable mass was found in the fundus, and 1.5 cm apart from it, in the endocervix, was a 5.5 x 4.0 cm large polypoid mass. The latter mass protruded into the vagina. There was no gross lymphadenopathy in the pelvic lymph nodes or the paraaortic lymph nodes. The other internal organs were grossly free.

Histologic examination showed that the endometrial mass was characterized by well formed glands that resembled those of normal endometrium. The tumor cells showed mild nuclear atypism and invaded more than half of the myometrium. The endometrial lesion was diagnosed histologically as grade 1 endometrioid adenocarcinoma (Figure 2). The endocervical mass showed a solid and tubule-papillary growth pattern with extensive necrosis. The tumor cells were characterized by abundant clear cytoplasm and hobnail cells with marked cytological atypia. The endocervical mass was histologically diagnosed as clear cell adenocarcinoma (Figure 3). A total of 45 pelvic lymph nodes and paraaortic lymph nodes were retrieved, but no lymph node metastasis was observed.

The patient was thoroughly evaluated, and the FIGO stages were found to be IB2 clear cell carcionoma of the cervix and Stage IB adenocarcinoma of the endometrium. Concurrent chemoradiation therapy (CCRT) with a cisplatin (60 mg) regimen was performed post-operatively at the outpatient department. During the 5th cycle, the whole process was smooth and the patient tolerated it well.

Discussion

Billroth first reported the development of different primary malignant tumors in the same patient in 1879 [1]. Warren and Gates [2] defined the criteria for the diagnosis of multiple primary tumors as follows: (1) each of the

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Fig. 1

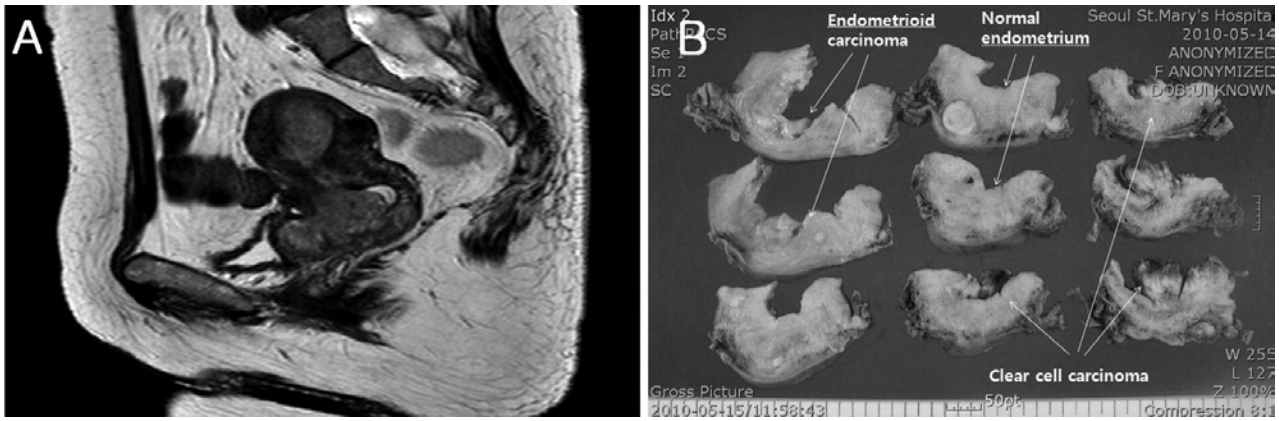

Fig. 2

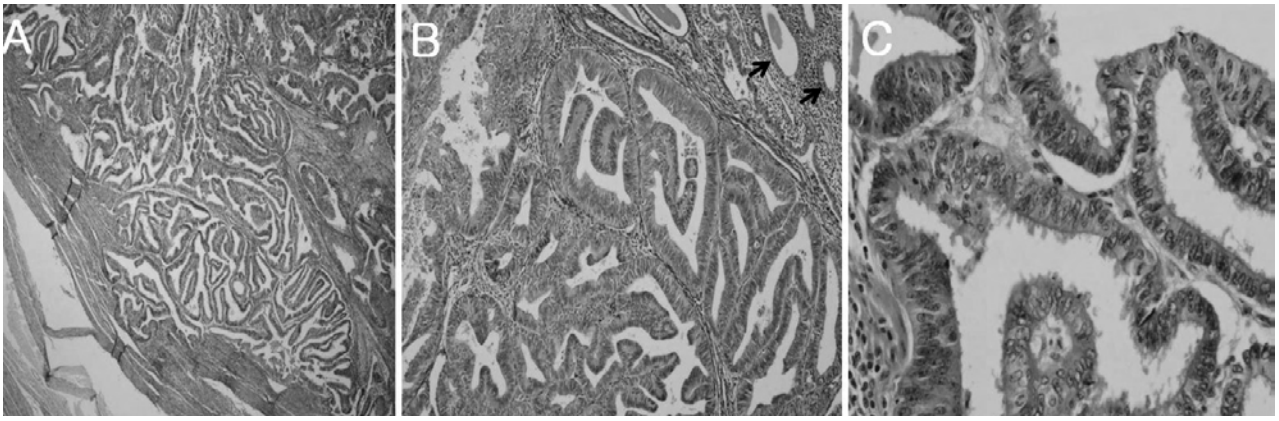

Figure 1. — (A) Sagittal T2-weighted magnetic resonance imaging shows widening of the endometrial cavity and a mass which is extended and protruding to the vagina and widening cervix. (B) Solid tumor originating in the endometrium and the cervix

Figure 2. — (A) Endometrioid adenocarcinoma (x40): well formed glands that resemble those of the normal endometrium, invading into the myometrium. (B) Well formed glands that resemble those of the normal endometrium. Black arrow; normal endometrial glands (x100). (C) Columnar tumor cells with pseudostratification and mild nuclear atypism (x400).

tumors must present a definite picture of malignancy; (2) each tumor must be clinicopathologically distinct; and (3) the probability of one tumor being a metastasis or recurrence must be excluded. The incidence of synchronous primary tumors of the female genital tract is only 1-6% of all genital neoplasms. The most frequently associated tumors are endometrial and ovarian carcinomas [3, 4]. Concurrent neoplasms of the cervix and endometrium are rarer. Ayhan et al. showed that 29 patients who were diagnosed as having had synchronous tumors constituted as 1.7% of all patients with genital malignancy (29/1,690) [4]. The most common cancer was that of the ovary concomitant with other gynecologic malignancies, and the endometrial and ovarian cancer group consisted of 15 patients. Furthermore, three patients had concurrent squamous carcinoma of the cervix and adenocarcinoma of the endometrium. To the best of our knowledge, only 13 cases of synchronous cervical and endometrial carcinoma have been published. Most of them were squamous cell carcinoma of the cervix and adenocarcinoma of the endometrium. This is the first report of synchronous primary clear cell carcinoma of the cervix and adenocarcinoma of the endometrium [5].

The etiology of a synchronous neoplasm is not clear. It has been postulated, however, that embryologically simliar tissues of the genital tract, when simultaneously subjected to hormonal influences or to carcinogens, may develop a synchronous neoplasm [6]. An association between in-utero DES exposure and clear cell carcinoma of the cervix and the vagina was especially identified in the early 1970s, but in this case, the patient's mother had no history of DES exposure. HPV is also well known to have oncogenic potential. HPV DNA is detected in > 90% of cases of squamous cell carcionoma of the cervix. It could not be detected in the surgical specimen in this study, though. This is consistent with the demonstration of Pirog et al. of the lack of association of HPV with clear cell adenocarcinoma [7].

The prognosis of synchronous neoplasm is more favorable than that of metastatic lesions of individual tumors [3]. Because of the early symptoms of endometrial cancer such as vaginal bleeding, the second primary cancer that occurs in an individual with endometrial cancer may have a more favorable prognosis. Ayhan et al. reported similarly favorable outcomes in the endometrial and ovarian cancer group and in other synchronous tumor groups [4].

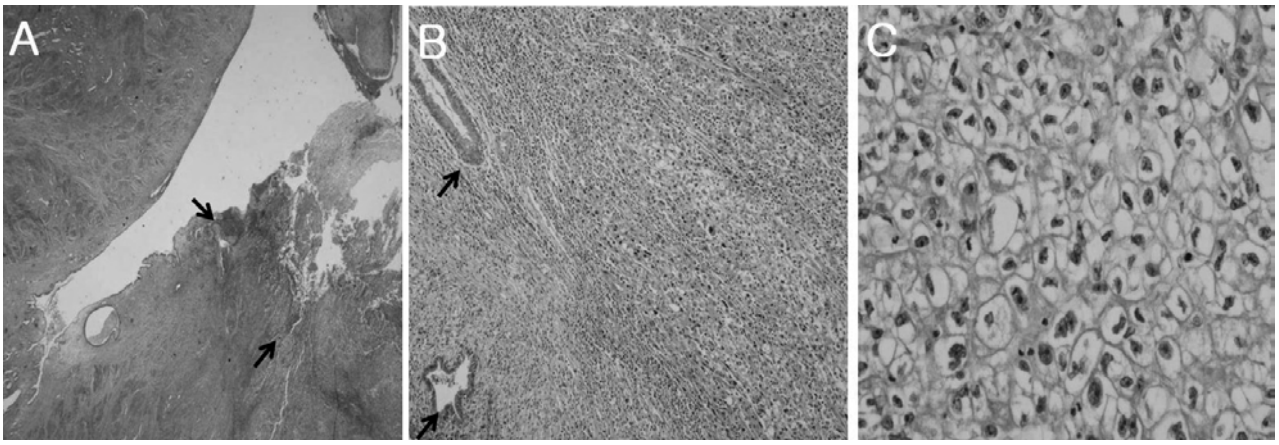

Figure 3. — (A) Clear cell carcinoma (x10): Scanning power field showed clear cell carcinoma. (B) Solid sheet of tumor cells with plump clear cytoplsm. Black arrow; normal endocervical glands (x100). (C) The tumor cells were characterized with abundant clear cytoplasm and hobnail cells by marked cytological atypia (x400).

Lin *et al*. reported a favorable prognosis in adenocarcinoma of the endometrium and squamous cell carcinoma of the cervix [8]. The clinical characteristics associated with clear cell carcinoma of the cervix (CCCC) differ from those associated with squamous cell carcinoma of the cervix, including advanced age, lack of smoking history, and lower frequency of abnormal cervical cytology. A clear cell histology alone, however, does not appear to portend a poor prognosis. Many studies have reported a similar case of survival from early CCCC [9, 10]. Hanselaar *et al*. reported negative prognostic factors similar to those of patients with squamous cancers. In the case in this study, the size of the clear cell carcinoma of the cervix was > 4 cm. CCRT was performed as an adjuvant treatment which is the same as the treatment of squamous cell carcinoma of the cervix.

In summary, a rare case of synchronous clear cell carcinoma of the cervix and endometrial adenocarcioma was presented in this study. The etiology and pathogenesis were not clear. Despite the use of the recently introduced advanced diagnostic technique, it is still difficult to detect synchronous neoplasms. Therefore, the possibility of a synchronous neoplasm should be kept in mind.

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