Multiple primary cancer in the female genital system
Two rare case reports and a literature review

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Abstract

Rationale: Multiple primary cancer (MPC) refers to tumors that occur in one or multiple organs within the same patient at the same time or at different periods. MPC often occurs in the head and neck, but is rarely reported in the female genital system.

Patient concerns: In the present study, we report 2 rare cases that presented with tangible lower abdominal tumors.

Diagnoses: Laboratory tests, pelvic ultrasound (US), computed tomography (CT), and fast histopathological examinations during surgery indicated a diagnosis of MPC.

Interventions: The 2 patients all received radical resections of multiple tumors.

Outcomes: Postsurgical histopathological and immunohistochemical examinations further confirmed primary endometrial cancer and right ovarian cancer in Case 1, and primary cervical cancer and left ovarian cancer of Case 2. The 2 patients all recovered well without obvious complications.

Lessons: Our study demonstrated that female genital MPC should be noted for patients with multiple genital tumors. In addition, accurately diagnosis and radical surgical treatment should be well performed.

Abbreviations: CA-125 = carbohydrate antigen-125, CEA = carcino-embryonic antigen, CK20 = cytokeratin 20, CK7 = cytokeratin 7, CT = computed tomography, ER = estrogen receptor, H&E = hematoxylin and eosin, MPC = multiple primary cancer, PR = progesterone receptor, US = ultrasound, WBC = white blood cell.

Keywords: female genital system, multiple primary cancer

1. Introduction

Multiple primary cancer (MPC) refers to more than one primary tumor that occurs at the same time or in succession in one or multiple organs within the same individual. The pathogenic mechanism of MPC is not fully understood, even though its incidence is increasing. There are obvious differences between MPC and metastatic tumors in the treatment method and prognosis; therefore, a lot more attention should be paid to the diagnosis and treatment of MPC. Unlike metastatic neoplasms, MPC is usually found in the neck and head, but it is rarely reported in the female genital system.

In the present study, we present 2 rare case reports with MPC in the female genital system. In addition, the clinical features, examination, and treatment methods are also discussed.

2. Case report

This study was approved by the Ethics Committee and institutional Review Board of the First Hospital of Jilin University, Changchun, China.

2.1. Case 1

A 45-year-old woman came to our hospital after suffering from intermittent abdominal pain for 1 year, a palpable pelvic mass for 20 days, and menstrual extension. This patient denied any other medical history. Physical examination revealed uterine tenderness and a painful mass in the right lower abdomen. Laboratory tests showed a plateletcrit of 0.43, platelet count of $4 \times 10^{11}/L$, and carbohydrate antigen-125 (CA-125) of 41.7U/mL. Pelvic ultrasound (US) showed uneven echoes in the endometrium, which was 2.4 cm in thickness, many flake materials without any echo, and blood signals (Fig. 1A). In addition, a 9.2 cm mass with uneven echoes in the right uterine adnexa was also found (Fig. 1B). Pelvic enhanced computed tomography (CT) examination also showed a thickened endometrium and a 5.8 × 7.4 cm tumor with uneven enhancement shadow in the right uterine adnexa (Fig. 2).

After careful consideration, the patient underwent a laparotomy. During surgery, we found that the right ovary was significantly enlarged, with a size of $10.0 \times 8.0$ cm, and the left ovary was about $3.0 \times 2.0$ cm with tubal thickening. Furthermore, the appendix was...
congested and swollen. As a result, we performed a partial hysterectomy, right adnexectomy, left fallopian tube resection, left ovarian cyst removal, and appendectomy. Fast pathological examination indicated right ovarian cancer, endometrial cancer, and a left ovarian cyst with salpingitis. A total hysterectomy and left ovarian resection were further performed. Postsurgical histopathological (Fig. 3) and immunohistochemical (Fig. 4) examinations confirmed the diagnoses of primary endometrial cancer and right ovarian cancer. Figure 3 shows the hematoxylin and eosin (H&E) staining of the endometrial cancer and right ovarian cancer. Immunohistochemical examinations indicated positive expressions of the estrogen receptor (ER), Ki67, P16, and the progesterone receptor (PR), which represented primary endometrial cancer (Fig. 4A). In addition, positive expressions of CA-125, ER, P16, and cytokeratin 7 (CK7) indicated primary right ovarian cancer (Fig. 4B). This patient recovered well, did not show any complications, and was approved to receive subsequent chemotherapy.

2.2. Case 2

A 47-year-old woman came to our hospital because of vaginal contact bleeding after sex for about 1 month. The patient underwent a cervical biopsy in another hospital and the examination reported cervical cancer. She denied any relevant medical history. Through physical examination, we found an obvious pelvic mass that was about 15.0 × 12.0 cm in size. Laboratory tests showed a carcino-embryonic antigen (CEA) level of 73.3 ng/mL, a CA-125 level of 5474.0 U/mL, and a white blood cell (WBC) count of 1.6 × 10^10/L. Pelvic US indicated that the cervix was swollen, full of blood, and was 4.4 × 3.6 cm in size (Fig. 5A). In addition, a 4.2 × 3.6 cm mass in the left uterine adnexa and a 14.5 × 12.1 cm mass in the pelvic cavity (Fig. 5B) were also found. CT examination showed a small mass with low density in the left cervical side wall (Fig. 6A) and large tumor mass with low density in the pelvic cavity (Fig. 6B).

Our clinical team agreed that the diagnosis of cervical carcinoma of this patient was clear, and the pelvic masses seemed to be ovarian tumors, which needed to be confirmed by the clinical team. Figure 2. Pelvic enhanced computed tomography (CT) examination of case 1. Black arrow showing the thickened endometrium and white arrow showing a 5.8 × 7.4 cm tumor with uneven enhancement shadow in the right uterine adnexa.

Figure 1. Ultrasound (US) examination of uterine and right uterine adnexa of case 1. (A) US showing a thickened endometrium with uneven echoes and blood signals (black arrow). (B) US showing a 9.2 × 7.4 cm mass with uneven echoes in the right uterine adnexa (black arrow).

Figure 3. Hematoxylin and eosin (H&E) staining of the endometrial cancer (A) and right ovarian cancer (B) (magnification × 200).
laparotomy and histopathological examination. During surgery, we found a 15.0 × 15.0 × 13.0 cm cystic mass in the pelvic cavity that was derived from the left ovary, and a 4.0 × 4.0 × 3.0 cm hard mass in the left sidewall of cervix that was confirmed to be cervical connective tissues. There was nothing wrong in the right uterine adnexa. In addition, appendecal congestion and greater omentum adhesion were also found. The left uterine adnexa were first resected and fast pathological examination confirmed left ovarian cancer. Total hysterectomy, right uterine adnexa resection, partial greater omentum excision, and appendectomy

Figure 4. Immunohistochemical staining of primary endometrial cancer (A) and right ovarian cancer (B) (magnification × 200).

Figure 5. Ultrasound (US) examinations of the cervix and right uterine adnexa of case 2. (A) US showing a swollen cervix with enhanced echoes and blood signals (white arrow). (B) US showing a 14.5 × 12.1 cm mass in the right uterine adnexa (white arrow).

Figure 6. Pelvic computed tomography (CT) examination of case 2. (A) A small mass with low density in the left cervical side wall (white arrow). (B) A large tumor mass with low density in the pelvic cavity (white arrow).
were then performed. Postsurgical histopathological and immuno-
histochemical examinations were also performed to confirm
the diagnoses of primary cervical adenocarcinoma and left
ovarian cancer. Figure 7 shows the H&E staining of the cervical
cancer and left ovarian cancer (Fig. 7). Immunohistochemical
staining showed positive expressions of CA-125, P16, and paired
box gene-8, which represented primary cervical adenocarcinoma
(Fig. 8A). Furthermore, positive expressions of CA-125,
cytokeratin 20 (CK20), P16, and CK7 indicated primary ovarian
cancer (Fig. 8B). This patient also recovered well and received
further radiotherapy and chemotherapy treatment.

3. Discussion

MPC mainly occurs in head and neck, but is rarely reported in the
female genital system. Two or more primary tumors can happen
in 1 individual at the same time or at different periods. The age of
onset of MPC is similar to that of single cancer, which usually
happens in patients between 50 and 70 years. When multiple
primary tumors occur at the same time, MPC can be easily
misdiagnosed. However, when these primary tumors occur at
different times, MPC can be mixed with recurrent and metastatic
cancer. As a result, accurate diagnoses and appropriate treatment
of MPC are necessary.

The etiology of MPC in the female genital system is not fully
known; however, it may be associated with the following factors:
During the embryo development period, ovaries, fallopian tubes,
and the uterus are all derived from coelomic epithelium. Therefore,
when these different tissues are affected by the same
carcinogenic factor, it is possible for primary malignant
neoplasms to occur in these organs. However, this incidence is
pretty low. It is reported that the possibility of simultaneous
occurrence of ovarian cancer and uterine cancer is 1.4% to
3.8%.[4] In another study, Dragoumis et al[5] found that the
possibility of the simultaneous occurrence of ovarian cancer and
uterine cancer was 2.9%. In our study, ovarian cancer and
endometrial cancer occurred in the first case, and cervical cancer
and ovarian cancer occurred in the second case. MPC usually
occurs in families with a variety of genetic abnormalities.[6] The
female genital system, including the breast, ovaries, uterine, and
fallopian tubes, possess large amounts of ERs. MPC may occur in
the female genital system when patients take too much estrogen.

Figure 7. Hematoxylin and eosing (H&E) staining of the cervical cancer (A) and right ovarian cancer (B) (magnification x 200).

Figure 8. Immunohistochemical staining of primary cervical cancer (A) and right ovarian cancer (B) (magnification x 200).
Some patients with hypoimmunity possess increased susceptibility to MPC.

Diagnosis of MPC is difficult, especially distinguishing it from metastatic cancer. Many patients have lost the chance of radical treatment because of misdiagnosis. As a result, some rules should be noted for the diagnosis of female genital MPC. Each kind of tumor should be confirmed to be malignant. Each tumor should possess its own specific pathological form. During diagnosis or follow-up of cancer patients, if there are more than 2 cancer masses, and MPC should be suspected. Tumor markers, such as CA-125 and CEA, should be referenced. In this study, multiple primary genital tumors were diagnosed accurately by histopathological staining during laparotomies in both cases. Tumor markers and US examinations were also performed and carefully referenced before surgery.

Compared with recurrent and metastatic tumors, the treatment methods for MPC are different. Radical surgical treatment should be better performed for MPC, while palliative therapies are always chosen for recurrent and metastatic tumors. In addition, compared with recurrent and metastatic tumors, the prognosis of MPC is better. In our study, when diagnosed with genital MPC, the 2 patients immediately received radical surgical treatment.

In the present study, the 2 patients were accurately diagnosed with genital MPC and received radical surgical therapy. Our study demonstrated that for patients with multiple tumors who also have a history of cancer, a family history of cancer, hypoimmunity, or positive expressions of multiple tumor markers, MPC should be suspected. In addition, accurate diagnosis and suitable treatment methods should be performed for patients with genital MPC.

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