Case Report

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Rare case of uterine neoplasm: cervical sarcoma with endometrial carcinoma

Ying Ma[1], Jie-Qiong Cao[3], Yan Yin[2], Li-Ting Yao[3], Xiao Han[3], Qiu-Man Wang[3] and Ye Zhao[1]

Abstract

Multiple primary malignant tumors (MPMTs) refer to two or more primary malignant neoplasms that simultaneously or successively occur in one or more organs in the same individual. Cervical sarcoma concomitant with endometrial carcinoma is rare. A 46-year-old woman was admitted because of increased menstrual volume for 4 years and irregular vaginal bleeding with discharge for 6 months. The diagnosis of endometrial carcinoma at stage II was made on the basis of results of ultrasound, pelvic magnetic resonance imaging, and hysteroscopic curettage. Extensive total abdominal hysterectomy + bilateral adnexectomy + bilateral ovarian arteriovenous high ligation + pelvic adhesion separation + pelvic lymphadenectomy + abdominal aortic lymphadenectomy via the abdomen were performed. Postoperative diagnosis of cervical sarcomas with endometrial carcinoma in stage IIIC1 was made according to the results of pathology and immunohistochemistry. Six cycles of cisplatin-epirubicin-isocyclophosphamide treatment were provided after the operation. Most clinical manifestations of cervical sarcomas are abnormal vaginal bleeding. Use of preoperative imaging and hysteroscopy is difficult for diagnosing cervical sarcomas, and postoperative pathological examinations and immunohistochemical diagnosis are mainly used instead. The possibility of MPMTs should be considered for endometrial carcinoma, especially if the cervical lesion is larger than that of the uterine cavity.

[1]Department of Gynecology, The First Hospital of Shanxi Medical University, Taiyuan, China
[2]Department of Pathology, The First Hospital of Shanxi Medical University, Taiyuan, China
[3]First Clinical Medical College, Shanxi Medical University, Taiyuan, China

Corresponding author:
Ye Zhao, Department of Gynecology, The First Hospital of Shanxi Medical University, No. 85 Jiefang South Street, Yingze District, Taiyuan 030001, China.
Email: zhaoy6520134@163.com

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Introduction

Multiple primary malignant tumors (MPMTs)[1] refer to two or more primary malignant neoplasms that simultaneously or successively occur in one or more organs in the same individual, but are not correlated with each other. The incidence of MPMTs in the female reproductive system is only 1% to 2%, most of which are ovarian tumors and endometrial carcinoma. Uterine sarcoma accounts for only 3% to 4% of uterine malignant neoplasms. Among them, uterine leiomyosarcoma and endometrial stromal sarcoma account for the majority,[2] while cervical sarcoma is rare.[3] Cervical sarcoma concomitant with endometrial carcinoma is even more rare. At present, only a few cases of cervical sarcoma concomitant with endometrial carcinoma have been reported worldwide.[4] In the present study, we report a case of cervical sarcoma with endometrial carcinoma, with the aim of improving the understanding of gynecological MPMTs.

Case presentation

This study was conducted in accordance with the Declaration of Helsinki and with approval from the Ethics Committee of The First Hospital of Shanxi Medical University. Written informed consent was obtained from the participant.

The female patient was 46 years old, G3P2. The patient was admitted to our hospital on January 3 2018, with a complaint of increased menstrual volume for 4 years and irregular vaginal bleeding with discharge for 1 year. In the past, the patient's menstrual cycle was regular with a moderate menstrual volume. Since February 2014, the patient's menstrual volume had increased, accompanied by anemia. Endometrial thickness was shown by ultrasonography, but diagnostic curettage was not performed. Irregular vaginal bleeding and vaginal discharge accompanied by paroxysmal lower abdominal pain occurred 3 months before admission. There was no major abnormality in pelvic ultrasonography. The ThinPrep® cytological test (Hologic, Boston, MA, USA) was negative for intraepithelial lesions or malignancy and human papillomavirus (HPV) was negative. On October 23 2017, pelvic B-ultrasound showed an inhomogeneous echo mass measuring 3.1×2.5 cm in the middle and lower segments of the uterine cavity. On December 12 2017, a gynecological examination showed that the cervix was enlarged and hard in texture. Ultrasound showed that there were hydrometra and isoechoic areas in the cervical canal without an obvious blood flow signal, and the size of the mass was 5.2×3.8 cm. The results of a physical examination were as follows. The cervix had barrel-shaped enlargement approximately 6 cm in size, the external cervical orifice was difficult to expose, the uterus was in anteposition, and there was no lifting pain or swing pain. The fundus of the uterus reached the umbilical pubic space. Accessory examinations showed that the carcinoembryonic antigen (CA-125) level and chest computed tomography were normal. The ThinPrep cytological test showed that the cells were atypical

adenocytes with a negative result for HPV. B-ultrasound of the pelvic cavity showed that there was a hyperechoic mass in the uterine cavity with a size of 27.4 × 12.9 mm and a hypoechoic mass in the lower part of the uterine cavity with a size of 88.4 × 56.2 mm (Figure 1a). Magnetic resonance imaging of the pelvis showed that a giant solid mass was in the uterine cavity and cervix. Endometrial cancer (International Federation of Gynecology and Obstetrics stage II) accompanied by multiple lymph node metastasis in the bilateral iliac vessels was considered (Figure 1b). Hysteroscopy was then performed, and a cauliflower-like lesion on the left side of the posterior wall of the uterine cavity was found, which extended into the cervical canal. No tissue was scraped out of the cervical canal by segmented curettage. The material that was scraped out of the uterine cavity was fragile. Postoperative pathology showed that the lesion was a malignant neoplasm that tended to be poorly differentiated into endometrioid carcinomas. Preoperative diagnosis of endometrial carcinoma (stage II) was made.

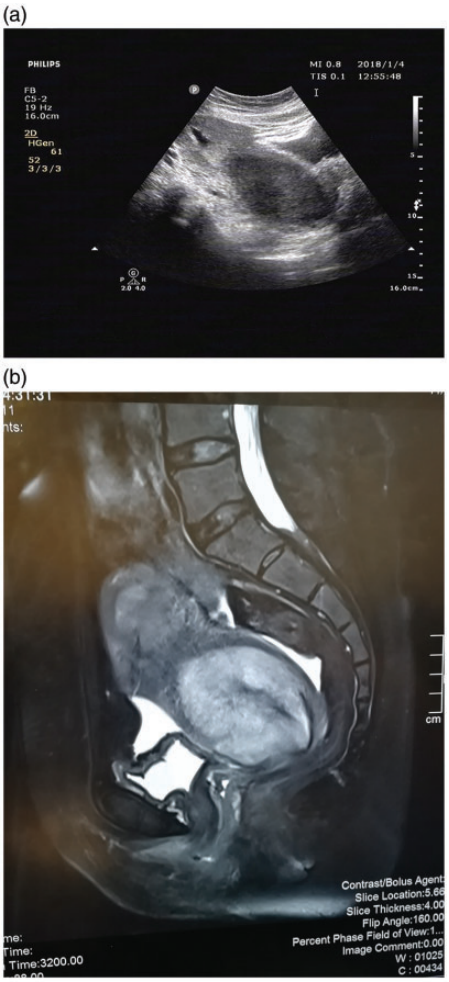

Figure 1. Imaging of the pelvis. (a) B-ultrasound of the pelvic cavity shows that there is a hyperechoic mass in the uterine cavity with a size of 27.4 × 12.9 mm. There is also a hypoechoic mass in the lower part of the uterine cavity with a size of 88.4 × 56.2 mm. (b) Magnetic resonance imaging of the pelvis shows a giant solid mass in the uterine cavity and cervix. Endometrial cancer (International Federation of Gynecology and Obstetrics stage II) accompanied by multiple lymph node metastasis in the bilateral iliac vessels was considered.

On January 26 2018, extensive total abdominal hysterectomy + bilateral adnexectomy + bilateral ovarian arteriovenous high ligation + pelvic adhesion separation + pelvic lymphadenectomy + abdominal aortic lymphadenectomy via the abdomen were performed. Intraoperative findings were as follows. A 4 × 3.5-cm cauliflower-like mass was on the endometrium and a 10 × 7-cm mass was on the lower segment of the uterus in which the mass was gray-yellow and fragile. Postoperative pathology of the material from the endometrium showed a high-grade endometrial carcinoma invading into less than half of the myometrium. Immunohistochemical staining showed that IMP3-P53, MutL homolog 1, post-meiotic segregation 2, cluster of differentiation 10 (CD10), Wilms tumor protein 1 (WT1), phosphatase and tensin homolog, synembryn, P16, CD99, inhibin, and estrogen receptor (ER) were negative. MutS protein homolog 2, MutS protein homolog 6, visceral larva migrans foci, paired box gene 8 foci,

and progesterone receptor (PR) were positive. Local Ki-67 was approximately 30% positive (Figure 2). Material from the lower segment of the uterus showed that cytokeratin, CD10, P16, WT1, mucin 1, CD99, P63, napsin A, inhibin, synembryn, PR, AE1/3, carcinoembryonic antigen, paired box gene 8, epithelial membrane antigen, CD45, smooth muscle actin, ER, and CD20 were negative, while vimentin was positive, and local Ki-67 was approximately 70% positive. The results of morphology and immunohistochemistry were in accordance with the diagnosis of cervical sarcoma (stage IIIC1, Figure 3). Pelvic lymph nodes were considered to have sarcoma metastasis. No invasion of cancer cells was found in other parts of the uterus and pelvic lavage fluid. The diagnosis of cervical sarcoma (stage IIIC1) and endometrial carcinoma was finally made, which indicated that the patient had MPMTs.

Six cycles of cisplatin-epirubicin-isocyclophosphamide (PEI protocol) treatment were provided after the operation, and repeated once every 28 days. The tumor markers of the patient were normal after the operation. Up to the time the present manuscript was written (1 year after the operation), no recurrence or progression had occurred.

Discussion

MPMTs have an incidence ranging from 0.4% to 2.4% in China and from 0.73% to

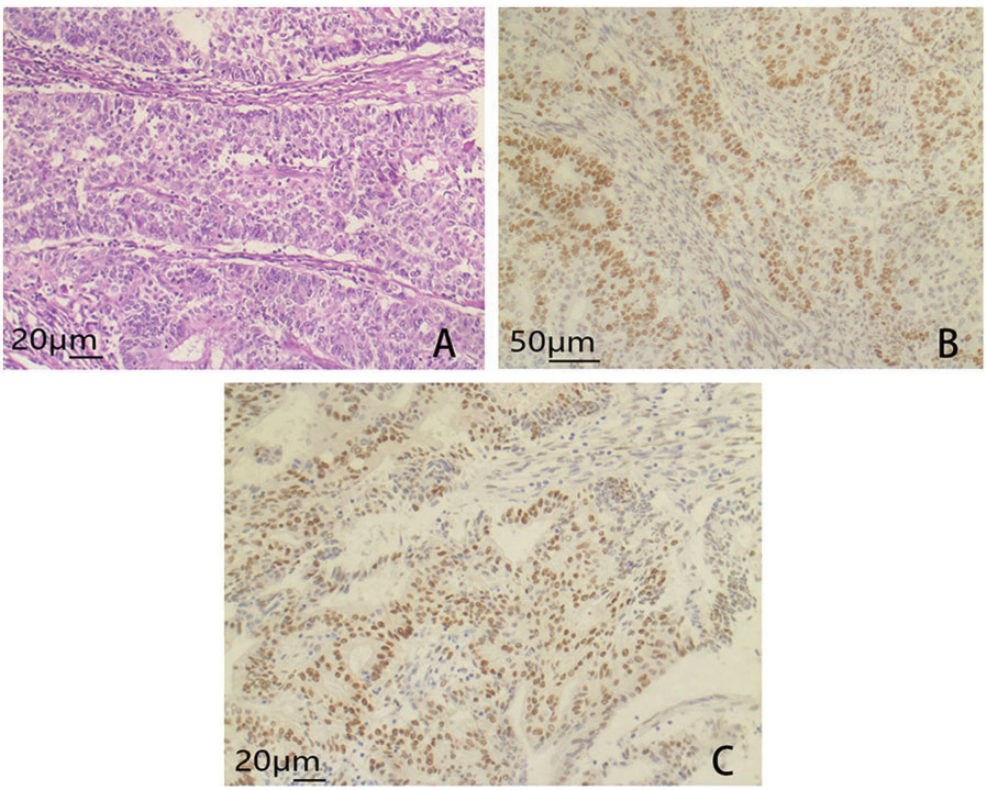

Figure 2. (a) Postoperative pathology of material from the endometrium shows a high-grade endometrial carcinoma invading into less than half of the myometrium. (b) Immunohistopathological analysis of the lesion shows positive staining for progesterone receptor and (c) Ki-67.

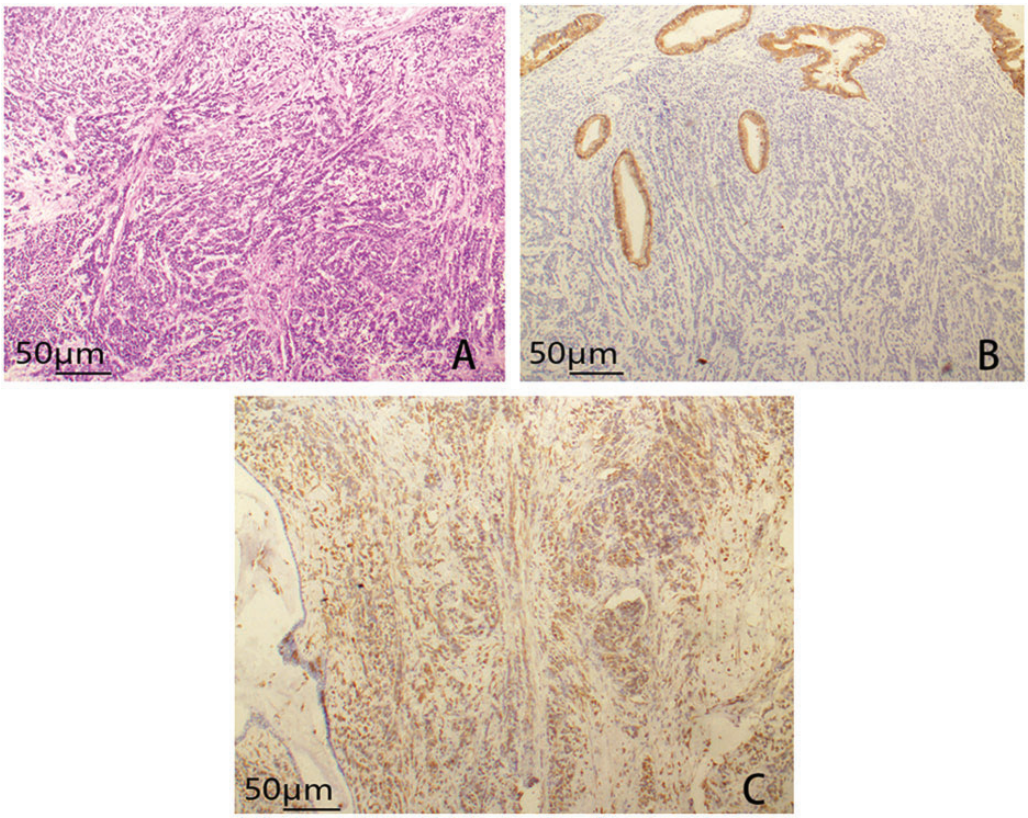

Figure 3. (a) Postoperative pathology of material from the lower segment of the uterus is in accordance with the diagnosis of cervical sarcoma. (b) Immunohistopathological analysis of the lesion shows positive staining for vimentin and (c) Ki-67.

11.70%[5] in other countries. This disease with an interval between onset of multiple malignant neoplasms of less than 6 months is called simultaneous MPMTs, while disease with an interval greater than 6 months is called asynchronous MPMTs. However, simultaneous MPMTs are rare and account for merely approximately 10% of MPMTs. The mechanism of MPMTs remains unclear. The mechanism of MPMTs may be related to persistence of carcinogenic factors, genetic factors, host susceptibility, immune deficiency, and other factors. The present patient did not have high-risk factors of endometrial cancer, such as hypertension, diabetes, obesity, and polycystic ovary, and she did not have a family history of cancer. The test for high-risk HPV was also negative. Furthermore, there were no pathogenic or suspected pathogenic gene mutations detected in the patient's peripheral blood samples.

Rosenberg et al.[6] reported that cervical sarcoma accounted for 0.005% of all malignant cervical neoplasms. MPMTs are rare in cervical sarcomas with other tumors of the reproductive system (e.g., endometrial and fallopian tube cancers), and only one case has been reported to date.[7] Most of the clinical manifestations are menstrual changes and/or irregular vaginal bleeding. In our case, the patient had similar clinical

symptoms, such as abnormal uterine bleeding, fluid secretion, and secondary moderate anemia. Simple endometrial thickening and cervical lesions were detected by ultrasound. Additionally, the cervical part of the tumor was larger than that of the uterine cavity. These findings provide a basis for studying development of MPMTs. When cervical lesions are larger than uterine lesions, invasion of primary tumors should be considered, and the possibility of MPMTs should be considered to avoid misdiagnosis.

After admission, hysteroscopy clearly showed that the lesions spread throughout the uterine cavity and invaded the cervical canal. However, the results of curettage did not suggest that there was a difference between cervical canal neoplasms and endometrial carcinoma. Magnetic resonance imaging showed that the tumor of the cervix was caused by invasion of endometrial carcinoma, but it did not suggest that the tumor was a primary tumor of the cervix. As previously reported, imaging examinations are not able to easily identify MPMTs.[4,5] Furthermore, the preoperative diagnostic rate of MPMTs is low and its clinical misdiagnosis rate is high. The diagnosis of MPMT mainly relies on pathological results and early diagnosis is difficult to achieve. However, Pang et al.'s study[8] showed that the sensitivity and specificity of fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography in preoperative diagnosis of MPMT could be increased.

The pathological diagnosis of MPMTs follows the diagnostic criteria established by Warren and Gates in 1932 as follows:[9] (1) every neoplasm should be a primary malignant neoplasm; (2) every neoplasm should have its own unique pathological morphology; (3) the neoplasm should occur at different parts of the body or organ (including different sites of the same organ), without consequence with each other; and (4) each neoplasm has its own manner of metastasis. Metastasis and recurrence should be excluded in the diagnosis. The main points of our patient's diagnostic criteria are as follows: (1) gross pathological features of different appearances and typical neoplasms were observed in the specimens. Endometrial cancer was located in the uterine cavity and was cauliflower-like. Furthermore, a solid neoplasm was observed in the cervix, it was grayish yellow, and there were visible borders in the section. (2) Distinct organizational characteristics were also present between these two types of neoplasms under a microscope. There were totally different immunological features of immunohistochemistry between the two types of neoplasms. (3) Metastasis in the lymph nodes was typical sarcoma metastasis without epithelial components.

MPMTs should be differentiated from malignant mixed Müllerian tumors (MMMTs). According to the World Health Organization classification, MMMTs[2] are called carcinosarcoma occurring in the female genital tract, and onset is at the uterus or ovaries. Furthermore, MMMTs are malignant uterine neoplasms that consist of a mixture of malignant epithelial and mesenchymal components. Based on all of the above-mentioned points, MPMTs of endometrial carcinoma complicated by cervical sarcoma was the correct diagnosis for the present patient.

MPMTs in the female reproductive system belong to rare diseases with complex types, which lack unified therapeutic protocols in the clinic. Individualized treatments for MPMTs are advocated. The present patient received six cycles of cisplatin–doxorubicin–isocyclophosphamide chemotherapy after radical surgery. The 5-year survival rate after this treatment method is only approximately 30%.[10,11] The survival rate of patients with MPMTs with cervical sarcomas is not optimistic. Up to the time

the present manuscript was written, no recurrence had occurred during follow-up.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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ORCID iD

Ye Zhao https://orcid.org/0000-0002-3115-4585

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