Clinical Case Report

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Primary squamous cell carcinoma of the endometrium in a woman of perimenopausal age

A case report

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Abstract

Rationale: Primary squamous cell carcinoma of the endometrium (PSCCE) is a rare entity, and only sporadic cases have been reported in the literature since the 1st report in 1892. This report describes a case of a perimenopausal woman with PSCCE.

Patient concerns: A 47-year-old, human papilloma virus type 16-positive, perimenopausal woman was admitted to our hospital with irregular vaginal bleeding for 6 months and secondary anemia.

Diagnoses: The patient was diagnosed with stage IIIc primary and moderately differentiated endometrial squamous cell carcinoma.

Interventions: The patient underwent diagnostic curettage twice and cold knife conization (CKC). Following this total abdominal hysterectomy combined with bilateral adnexectomy and pelvic lymph node, dissection was performed. After the surgery, the patient was treated with radiotherapy and chemotherapy. Tumor markers were followed up regularly after the operation to monitor tumor recurrence and therapeutic effect.

Outcomes: Ninety-two days after the operation, there was tumor recurrence of the left pelvic cavity and the patient died after 11 months of follow-up.

Lessons: Intrauterine pathology after the 1st diagnostic curettage suggests that high-grade squamous intraepithelial lesion should make the clinician vigilant and investigate the origin of the lesion. Magnetic resonance imaging scans and tumor markers can be used to confirm the diagnosis as soon as possible and avoid unnecessary interventions like CKC.

Abbreviations: CDK = cell division protein kinase, CKC = cold knife conization, HPV = human papilloma virus, HSIL = high-grade squamous intraepithelial lesion, ISGP = International Society of Gynecological Pathology, MRI = magnetic resonance imaging, PSCCE = primary squamous cell carcinoma of the endometrium, PRb = retinoblastoma gene product, SCC = squamous cell carcinoma antigen.

Keywords: endometrium, primary squamous cell carcinoma

1. Introduction

Primary squamous cell carcinoma of the endometrium (PSCCE) is a rare entity. The 1st case of primary endometrial squamous cell carcinoma (SCC) was reported in 1892.[1] In 1928, Fluhmann[2] established the strict pathologic and clinical criteria for PSCCE. The 3 criteria for diagnosis were as follows: no co-existence of adenocarcinoma of the endometrium with PSCCE; no connection between the tumor in the endometrium and cervical squamous epithelium; no co-existence of primary SCC of the cervix with PSCCE. This report describes the whole process of the patient from diagnosing a lesion to a radical operation, after which, the patient received docetaxel combined with carboplatin chemotherapy and local radiotherapy.

2. Case report

A 47-year-old Chinese female in perimenopause, Gravida 7 Para 4, with irregular vaginal bleeding for 6 months was referred to the department of gynecology in the Affiliated Hospital of Jining Medical University. The maximum amount of vaginal bleeding was about 100 mL with large blood clots. She was obese and had anemia. Gynecologic examination revealed the soft velvet cervix, and the uterus was as large as 12 weeks of pregnancy, abdomen was soft, no tenderness and masses, and no other special positive signs. The Bai-fluid-base thin-preparation cytologic test was negative, while the human papilloma virus (HPV) E6/E7 mRNA test showed HPV type 16-positive. Transvaginal ultrasound was performed and the results showed a large uterus with an

Editor: N/A.

CZ, HZ and LY contributed equally to this work.

This study was financially supported by a grant from the Shandong Provincial Department of Education Postgraduate Tutor Mentoring Ability Enhancement Plan (no: SDYY17123), Young Teacher Research Support Fund of Jining Medical University (no: JY2017FS015).

The authors have no funding and conflicts of interest to disclose.

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Medicine (2018) 97:48(e13418)

Received: 17 June 2018 / Accepted: 1 November 2018

http://dx.doi.org/10.1097/MD.0000000000013418

abnormal endometrial thickness of 11.0 mm, and no substantial masses. Except for laboratory examination indicating hemoglobin of 54 g/L, no other abnormalities were found in other biochemical indexes. Unfortunately, we did not conduct tumor marker detection study markers before surgery.

The patient subsequently underwent cervical biopsy and 1st diagnostic curettage. The results of 1st diagnostic curettage revealed intrauterine high-grade squamous intraepithelial lesion (HSIL). Cervical biopsy pathology showed that 6 and 12 points were HSIL. To determine the degree of cervical lesions, we performed a cold knife conization (CKC) to excise a $2.5 \times 2.0 \times 1.5$ cm cervical tissue and then performed 2nd diagnostic curettage. Postoperative pathology reported chronic inflammation of the cervix with HSIL of the focal lesion and involvement of the glandular, negative margin. The 2nd diagnostic curettage revealed intrauterine HSIL with focal SCC.

After the 2nd diagnostic curettage we had a magnetic resonance imaging (MRI) scan and the result showed a bulky uterus, with enlarged pelvic and para-iliac, perivascular multiple lymph nodes (Fig. 1). The serosal layer of the bladder and uterus were not disrupted and appeared smooth (Fig. 2). The cervix appeared normal except for the nabothian cysts and the left ovary had a cyst with a diameter of 3 cm. According to the MRI results, differential diagnoses included malignant lymphomas and urologic tumors. However, according to the laboratory examination and pathologic findings, the lesion still originated from the uterus. The patient underwent total abdominal hysterectomy combined with bilateral adnexectomy and pelvic lymphadenectomy. The specimens were taken for peritoneal washing cytology. Gross examination showed (Fig. 3): a large uterus associated with severe pelvic adhesion; the left ovary had a smooth surface, filled with clear fluid, and complete envelope with a diameter of about 3 cm cyst; the left tube and the right adnexae appeared normal; no metastatic tumor was found in the abdomen and pelvic cavity; and the swollen lymph nodes appeared palpable around the stiffened iliac vessels on both sides.

Twenty-seven days after the radical surgery, the patient was transferred to the urogenital oncology department to receive 3 cycles of docetaxel (75 mg/m^2, day 1, pump in) combined with carboplatin (200 mg/m^2, day 1, drop in) chemotherapy. During the chemotherapy period, the patient did not have bone marrow suppression and severe damage to liver and kidney function. However, 92 days after the operation, the tumor recurrence of the left pelvic cavity and the patient was treated with local radiotherapy (180 cGy/session; total dose, 5040 cGy) to control the tumor progression. The patient relapsed during the 11-month follow-up period. The last laboratory examination of our hospital in May 18, 2018 showed that the tumor-associated material was 127.22 U/mL, the SCC antigen was 10.2 ng/mL and the carcinoembryonic antigen was 1.57 ng/mL. Finally, the patient died at home in June 2018.

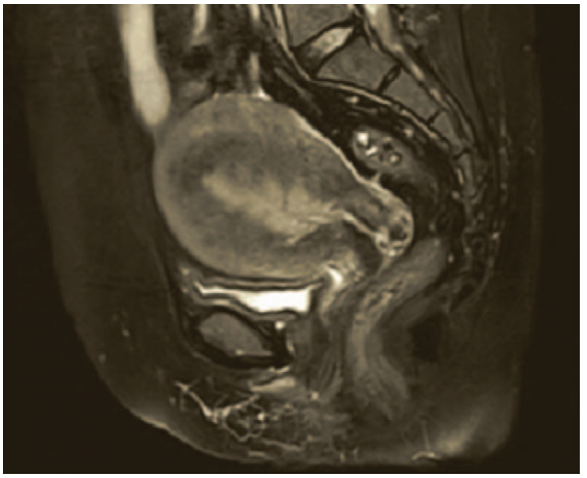

Figure 2. Magnetic resonance imaging scan showing normal bladder and cervix (except for the nabothian cysts).

3. Results

Tumor heteromorphic cells were not found during peritoneal washing. On sectioning the uterus, the myometrium and cervical canal were invaded by tumors measuring $6 \times 5 \times 3$ cm. Histology confirmed the lymph vascular space involvement and pelvic lymph nodes metastasis. The vaginal cutting, tube margin, and ovaries appeared normal. Microscopically, the endometrial tissue showed moderately differentiated SCC cells, forming nests, and keratin

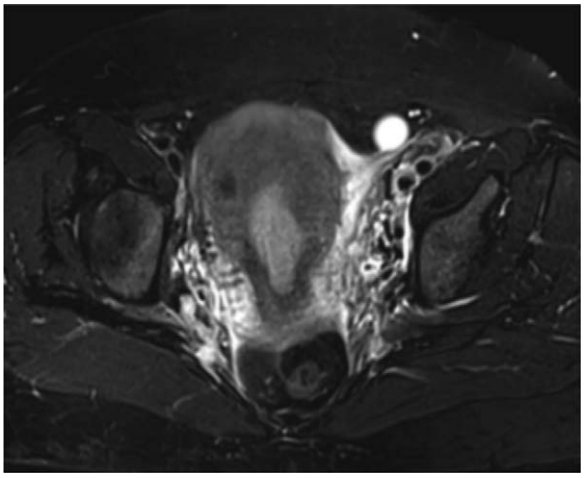

Figure 1. Magnetic resonance imaging scan showing enlargement of multiple pelvic and para-iliac, perivascular lymph nodes.

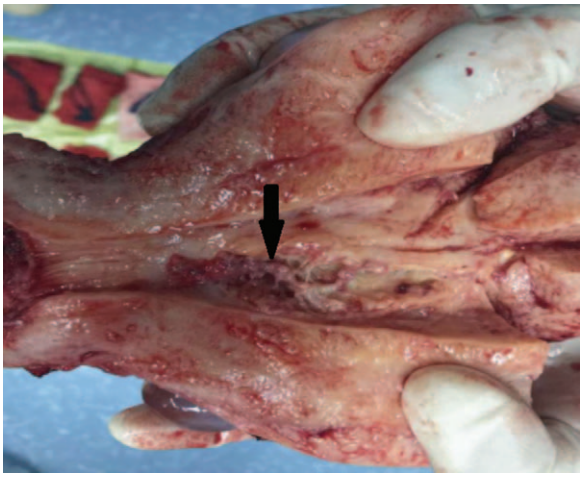

Figure 3. Gross examination showing a bulky uterus with an abnormal endometrial lesion, but not connected with the cervix (as indicated by the arrow).

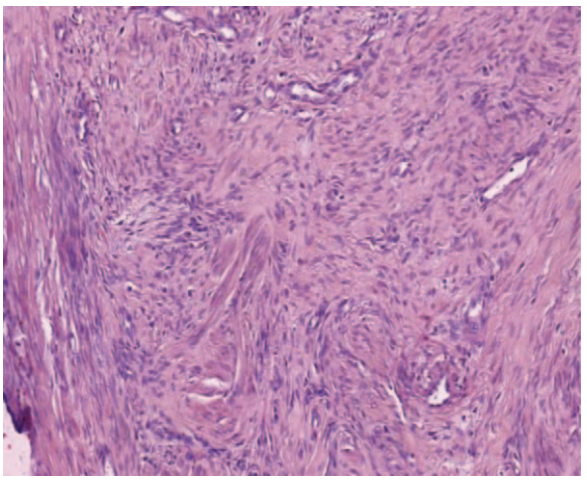

Figure 4. Low power view of tumor showing moderately differentiated squamous cell carcinoma cells (hemotoxylin and eosin ×100).

pearl (Figs. 4 and 5). Although we did not do immunohistochemical analysis, none of the sections showed existence of an adenocarcinoma. The final diagnosis showed primary and moderately differentiated endometrial SCC (stage IIIc).

4. Discussion

The diagnostic curettage after admission was performed to exclude the malignant lesion of endometrium. However, pathology results of the 1st curettage suggested no malignant lesions of the endometrium, leading to the receiving of unnecessary CKC for the patient. We did not have a reasonable explanation for this. Almost all types of endometrial cancer are adenocarcinomatous,[3] and most of the endometrial squamous carcinomas originate from the SCC of the cervix[4] or endometrial stem cell, and squamous metaplasia of the normal endometrium.[5] Primary endometrial SCC is a rare entity. However, this type of endometrial cancer has a high degree of malignancy and poor prognosis, and the 5-year survival rate was very low except for individual cases.[6,7] The common treatment methods include surgical hysterectomy with adnexectomy and radiotherapy.[8] According to Goodrich et al's[9] report, after the radical surgery, their 2 patients received external beam radiation with cisplatin chemosensitization, followed by vaginal brachytherapy and have obtained good clinical result.

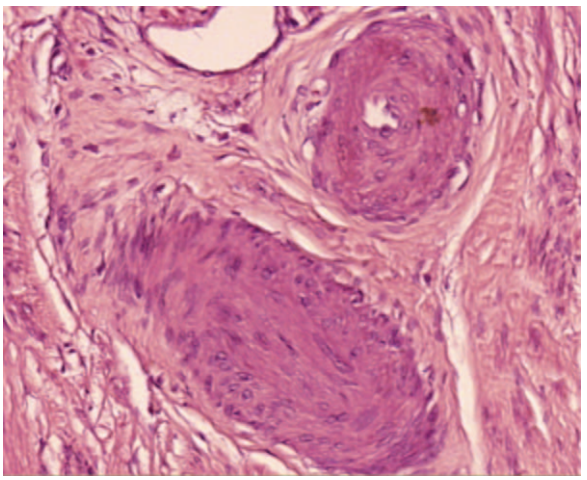

Figure 5. High power view of tumor showing keratin pearl (hemotoxylin and eosin ×200).

The PSCCE is differentiated from the endometrial adenocarcinoma with squamous differentiation,[10] the latter included adenoacanthoma, and adenosquamous carcinoma. Adenoacanthoma is a benign squamous metaplasia of the endometrial adenocarcinoma, but the adenosquamous carcinoma caused by the simultaneous presence of endometrial adenocarcinoma and SCC.[11] However, in 1987, the International Society of Gynecological Pathology (ISGP) no longer uses the concepts of adenoacanthoma and adenosquamous carcinoma, and they were collectively referred to endometrial adenocarcinoma with squamous differentiation. As Zaino et al's[12] research has shown that the difference in squamous components of endomentrial carcinoma is closely related to the histologic differentiation of the glandular component in most tumors. Whether there is squamous epithelial differentiation and differentiation degree has no significant differences in prognosis for adenocarcinoma.[13] This is particularly important for diagnosis and differential diagnosis of PSCCE.

However, the pathogenesis and etiology of PSCCE are poorly investigated and incompletely understood. Various scholars have speculated that the etiology could be related to bidirectional differentiation of pluripotent endometrial precursor cells,[14] heterotopic cervical tissue,[15] chronic pelvic inflammatory, radiation therapy,[16] or HPV infection.[17] Generally, high-risk HPV subtypes are the major cause of cervical SCC.[18] Recently, other scholars have tried to explain the relationship between HPV infection and PSCCE, but it still remained controversial. A study conducted by Bures et al[19] suggested that the pathogenesis of PSCCE involves overexpression of p19, pRb, CDK6, and Cyclin D1, but no expression of p16, p18, CDK4, and HPV E7.

In conclusion, we believe that our case fulfils the strict criteria for the diagnosis of PSCCE as defined by Fluhmann.[2]

The results of 1st diagnostic curettage suggesting HSIL in the uterus should alert the clinician to investigate the source of the lesion. So it is important that early diagnosis and early treatment of this malignancy is needed in clinicians daily practice. Currently, there is no universally accepted optimal treatment method that would improve the prognosis and chances of a longer life. Early diagnosis followed by prompt surgical operation remains the best treatment for patients at present.

Acknowledgment

The authors thank our department colleagues and the devotion of this patient, and the patient has signed the informed consent form.

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Writing – review & editing: Chao Zhang.

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