Clinical Case Report

Medicine®

OPEN

Concomitant endometrial and cervical adenocarcinoma

A case report and literature review

Mengfei Xu, MM[a], Feng Zhou, MD[a,*], Lili Huang, MD[b]

Abstract

Rationale: Concomitant malignancy of the endometrium and cervix is extremely rare.

Patient concerns: A 56-year-old female presented to the Women's Hospital, School of Medicine, Zhejiang University, complaining of irregular vaginal bleeding. The human papillomavirus test (type 18/45) was positive. We performed dilation and curettage; pathology revealed moderately differentiated endometrial carcinoma exhibiting squamous differentiation. The epithelium of the cervical uterus was atypical upon biopsy.

Diagnoses: Histological and immunochemical tests confirmed a diagnosis of endometrial carcinoma concomitant with cervical adenocarcinoma.

Interventions: She underwent laparoscopic staging surgery.

Outcomes: The patient fully recovered with only surgery.

Lessons: Endometrial carcinoma concomitant with cervical adenocarcinoma is very rare. It is imperative to schedule adequate examination, and to perform careful preoperative diagnosis and appropriate treatment to minimize relapse.

Abbreviations: AFP = alpha-fetoprotein, CA125 = carbohydrate antigen, CA199 = carbohydrate antigen, CEA = carcinoembryonic antigen, ER = estrogen receptor, HPV = human papillomavirus, PR = progesterone receptor.

Keywords: cervical adenocarcinoma, concomitant malignancy, endometrial carcinoma

1. Introduction

Concomitant primary malignant tumors of the female genital tract are rare. Most such cases are combined endometrial and ovarian cancer[1] of unknown etiology and pathogenesis. It has been suggested that when embryologically similar tissues are concomitantly exposed to carcinogens or irritants, synchronous neoplasms may develop.[2] In addition, the expression of the p53 tumor suppressor gene may increase the risk of a secondary tumor.[3,4] We present a rare case of concomitant malignancy of the endometrium and cervix.

2. Case report

A 56-year-old female (gravidity 2; parity 2) with no significant medical history or any physical finding other than irregular vaginal bleeding presented to us for careful evaluation. Menopause had commenced at the age of 54 years. Physical examination revealed a soft abdomen, cervical atrophy, no contact bleeding, and no tenderness on palpation of the bilateral adnexa. The serum levels of carbohydrate antigen (CA)125, CA199, alpha-fetoprotein, and carcinoembryonic antigen were all within normal limits. The human papillomavirus (HPV) test (type 18/45) was positive. We performed dilation and curettage; pathology revealed a moderately differentiated endometrial carcinoma accompanied by squamous differentiation in the uterine cavity. The epithelium of the cervical uterus was atypical upon biopsy. We scheduled laparoscopic staging surgery including radical hysterectomy, bilateral adnexectomy, and pelvic lymphadenectomy. No dispersal of a malignant endometrial tumor was observed in the abdominal cavity. Both the pelvic and periaortic lymph nodes were normal when palpated.

Macroscopically, the uterus was approximately 7.5 × 4.5 × 3 cm in dimension; an endometrial tumor 1.2 × 1.0 × 0.5 cm in dimension was evident in the uterine cavity. On cutting, the tumor surface was predominantly solid in nature and gray in

Editor: N/A.

Ethics approval and consent to participate: This study was approved by the ethics committee of the Women's Hospital, School of Medicine Zhejiang University.

Consent for publication: Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Availability of data and material: The datasets during and/or analyzed during the present study available from the corresponding author on reasonable request.

Authors' contributions: Drafting the manuscript and revising it critically for important intellectual content: XM. Final approval to the version to be published: ZF. All authors made substantial contributions to conception and design, or acquisition of data, or analysis/interpretation of data, and read and approved the final manuscript.

The authors have no conflicts of interest to disclose.

[a] Department of Pathology, [b] Department of Obstetrics, Gynecology Women's Hospital, School of Medicine, Zhejiang University, Hangzhou, Zhejiang Province, People's Republic of China.

[*] Correspondence: Feng Zhou, Women's Hospital, School of Medicine, Zhejiang University, Hangzhou, Zhejiang Province, People's Republic of China (e-mail: fungchew@zju.edu.cn).

Copyright © 2018 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

Medicine (2018) 97:1(e9596)

Received: 24 November 2017 / Accepted: 20 December 2017

http://dx.doi.org/10.1097/MD.0000000000009596

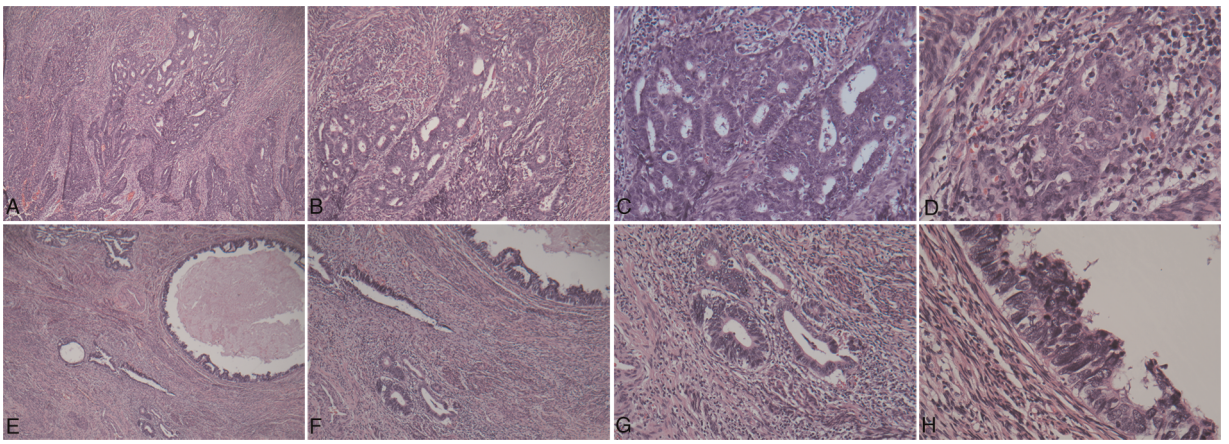

Figure 1. Microscopic photograph of endometrial and cervical adenocarcinoma. The endometrial carcinoma comprised crowded, complex, branching glandular structures (A 50×, B 100×, C 200×) with moderate uclear atypia (D 400×). The cervical adenocarcinoma invaded the stroma (E 50×, F 100×). The neoplastic epithelium contained atypical neoplastic glands (G 200×) with enlarged, elongated hyperchromatic nuclei (H 400×).

color, accompanied by obvious hemorrhage and necrosis, and invaded the superficial myometrium. No cervical mass was apparent. The bilateral adnexa were macroscopically normal.

Microscopically, the uterine cavity mass exhibited areas of crowded, complex, branching glandular structures, lined by stratified columnar epithelium. The extent of nuclear atypia was only moderate; the cytoplasm was eosinophilic and granular. Elsewhere, focal squamous differentiation was apparent. Histologically, the cervical pattern was complex; atypical neoplastic glands invaded the stroma. The neoplastic epithelium contained atypical neoplastic glands with enlarged, elongated hyperchromatic nuclei (Fig. 1). The cervical canal was normal, as were both fallopian tubes and ovaries. The pelvic lymph nodes were negative.

Immunohistochemically, the tumor in the uterine cavity was positive for the estrogen receptor (ER), progesterone receptor (PR), and vimentin; and was partial positive for p16, with a high ki67 index. However, the tumor in the uterine was diffusely positive for p16, but was negative for ER, PR, and vimentin (Fig. 2). Thus, we diagnosed the patients with endometrial carcinoma (Grade 2) concomitant with cervical adenocarcinoma (of the usual type).

3. Discussion

Tumors are defined as synchronous when they develop concomitantly. Synchronous primary genital cancers are rare, constituting only 1% to 6% of all genital tract neoplasms.[5] Single neoplasms or metastatic tumors of the cervix, endometrium, or ovary are more common. To date, only 6 cases of concomitant endometrial and cervical cancer have been reported.[5,6,11]

We report a case of mixed endometrial carcinoma in a 56-year-old female, accompanied by cervical adenocarcinoma, which is unusual. Patients with endometrial cancer are at markedly higher risk of concomitant breast, fallopian tube, ovarian, cervical, and colon cancer.[7] Accurate differential diagnosis of primary and metastatic tumors is essential, because both the treatment and outcomes significantly differ.

The treatment strategy depends on age, initial cancer stage and grade, the extent of myometric lymphatic invasion, and lymphatic metastasis status. Tumor staging is the most important factor when evaluating the prognosis of endometrial cancer. FIGO recommends that when endometrial carcinoma attains the cervix, the cancer should be staged as II.[8] The standard treatment for endometrial cancer is hysterectomy, bilateral

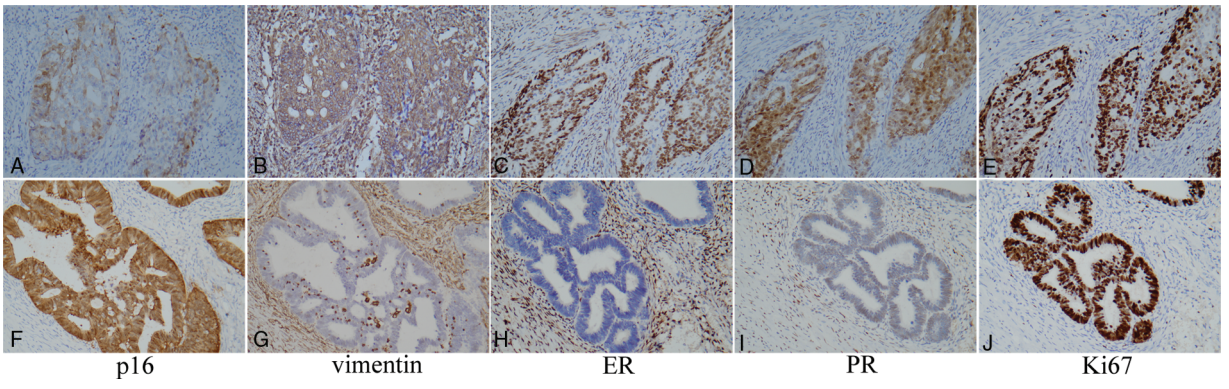

Figure 2. The immunochemical photograph of endometrial and cervical adenocarcinoma. P63 (A, F 200×), vimentin (B, G 200×), ER (C, H 200×), PR (D, I 200×), Ki67 (E, J 200×) stained in the tumor cells of endometrial adenocarcinoma (A–E). The different staining pattern was observed in the neoplastic glands of cervix (F–J). ER = estrogen receptor, PR = progestrogen receptor.

salpingo-oophorectomy, and further surgical staging. Grade 1 or 2 cancers with minimal myometrial infiltration are low risk, and no treatment is required. Those with suspected cervical stromal invasion and lymphovascular involvement may require adjuvant radiation therapy.[9]

Malignant cervical glandular lesions are less common than squamous cell carcinoma, and are difficult to diagnose upon routine inspection.[10] Although the tumor may attain the uterine cavity, neither tumor staging (IB1) nor prognosis is affected. Both the optimal treatment for cervical adenocarcinoma and prognosis remain unclear. Radical hysterectomy has been recommended for those with stage IB1 cervical cancer.[11] Patients with high-level risk factors require extensive adjuvant radiotherapy.

Most reported contemporaneous primary neoplasms are of early stage and low-grade, as in our case.[6] Many studies have shown that patients with contemporaneous early/low-grade endometrial and ovarian carcinomas survive better than those with more advanced metastatic malignancies.[12,13] One patient with both endometrial and cervical cancer exhibited no recurrence over 2 years of follow-up after comprehensive treatment. If preoperative diagnosis of a cervical glandular lesion fails, radiotherapy after surgery is required as rescue treatment[14]

However, the origin of the tumor of our present case remains debatable because of the histological features. In endometrial cancer, ER status may be the predominant element increasing the underlying risk for multiple cancers, whereas HPV is associated with the development of cervical and vaginal lesions.[15] The expression of ER, PR, and vimentin indicated that the tumor was of endometrial origin. However, the absence of hormone receptors from the cervix accompanied by diffuse p16 reactivity favored a cervical origin. Moreover, the low-grade histology indicated a multifocal, primary sporadic cancer. Therefore, we considered that the patient had contemporaneous malignancies of the endometrium and cervix.

4. Conclusion

In conclusion, our patient had independent primary endometrial and cervical tumors distinguishable both clinicopathologically and immunohistochemically. Concomitant primary gynecological cancers are uncommon; thus, more case reports are required to define the most appropriate treatment.

References

[1] Gutiérrez-Palomino L, Romo-de Los Reyes JM, Pareja-Megía MJ, et al. Triple synchronous primary gynaecological tumours. A case report. Cir Cir 2016;8469–72.
[2] Woodruff JD, Solomon D, Sullivant H. Multifocal disease in the upper genital canal. Obstet Gynecol 1985;65:695–8.
[3] Ohel G, Schwartz Z, Birkenfeld A, et al. Second primary genital malignancies associated with endometrial cancer. Arch Gynecol 1986;239: 75–80.
[4] Kimura K, Shinmura K, Hasegawa T, et al. Germline p53 mutation in a patient with multiple primary cancers. Jpn J Clin Oncol 2001;31:349–51.
[5] Eisner RF, Nieberg RK, Berek JS. Synchronous primary neoplasms of the female reproductive tract. Gynecol Oncol 1989;33:335–9.
[6] Sun HD, Lai CR, Yen MS, et al. Synchronous occurrence of primary neoplasms of the uterus with mucinous carcinoma of the cervix and endometrioid carcinoma of the endometrium. Taiwan J Obstet Gynecol 2011;50:377–8.
[7] Bongers V, Braakhuis BJ, Tobi H, et al. The relation between cancer incidence among relatives and the occurrence of multiple primary carcinomas following head and neck cancer. Cancer Epidemiol Biomarkers Prev 1996;5:595–8.
[8] Hui P, Baergen R, Cheung ANY. Kurman RJ, Carcangiu ML, Herrington CS, Yong RH, et al. Gestational trophoblastic neoplasms. WHO Classification of Tumors of Female Reproductive Organs IARC, Lyon:2014;158–61.
[9] Orezzoli JP, Sioletic S, Olawaiye A, et al. endometrioid adenocarcinoma of the endometrium: clinical implications of cervical stromal invasion. Gynecol Oncol 2009;113:316–23.
[10] McCluggage WG. New developments in endocervical glandular lesions. Histopathology 2013;62:138–60.
[11] Lv S, Xue X, Sui Y, et al. Synchronous primary malignant neoplasms of the cervix and endometrium. Mol Clin Oncol 2017;6:661–4.
[12] Zaino R, Whitney C, Brady MF, et al. Simultaneously detected endometrial and ovarian carcinomas-a prospective clinicopathologic study of 74 cases: a gynecologic oncology group study. Gynecol Oncol 2001;83:3553–62.
[13] Soliman PT, Slomovitz BM, Broaddus RR, et al. Synchronous primary cancers of the endometrium and ovary: a single institution review of 84 cases. Gynecol Oncol 2004;94:456–62.
[14] Atasever M, Yilmaz B, Dilek G, et al. Synchronous Primary Carcinoma in 5 different organs of a female genital tract an unusual case and review of the literature. Int J Gynecol Cancer 2009;19:802–7.
[15] Tong SY, Lee YS, Park JS, et al. Clinical analysis of synchronous primary neoplasms of the female reproductive tract. Eur J Obstet Gynecol Reprod Biol 2008;136:78–82.