

Uterine Serous Carcinoma Arising From Endometrial Polyp: A Case Report

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Serous carcinoma is the prototype of type II endometrial carcinoma. A 71-year-old woman who had history of smoking, diabetes mellitus and hypertension admitted to the hospital with postmenopausal uterine bleeding. Curettage material was diagnosed as adenocarcinoma. Hysterectomy specimen revealed a uterine polypoid mass which afterwards was histopathologically proven to be a serous carcinoma arising from an endometrial polyp. Immunohistochemically, tumor cells showed diffuse reaction for p53 and c-erbB-2, and focal reaction for estrogen and progesterone receptors. In addition to history of diabetes mellitus and hypertension, our case shared some clinical and immunohistochemical characteristics of type I endometrial carcinoma, such as focal expression of estrogen and progesterone receptors. Overexpressions of p53 and c-erbB-2 in this tumor type should be considered.

Key Words: Serous carcinoma, Endometrial polyp, P53, C-erbB-2.

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Introduction

Endometrial carcinoma is the leading malignant neoplasm of female genital tract and the fifth most common cancer in women.¹ Endometrioid adenocarcinoma (type I cancer), the most common type of endometrial carcinoma, is associated with hyperestrogenism and atypical endometrial hyperplasia. In contrast, serous carcinoma (so-called type II cancer) is less common and associated with neither hyperestrogenism nor atypical endometrial hyperplasia. Instead, endometrial intraepithelial carcinoma is the precursor of uterine serous carcinoma (USC).^{1,2} The prevalence of endometrial polyp in general population is about 24% in which 5% includes carcinoma.¹ Endometrioid adenocarcinoma is the most common malignant neoplasm in endometrial polyps, while serous carcinoma occurs rarely.³ In this case report, USC arising from endometrial polyp were presented and clinical and immunohistochemical findings were discussed.

Case Report

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The patient was a 71-year-old gravida 7, para 7 woman presented with postmenopausal uterine bleeding. She had regular menses from her first menarche at age 13 until her menopause at age 51. She had a history of smoking as well as diabetes mellitus and hypertension. Serum tumor markers (AFP, CEA, β hCG, CA-125) were in normal range. Uterine body and cervix were normal by gynecological examination. Transvaginal ultrasonography revealed hemorrhage within the uterine cavity. Cervicovaginal smear exhibited atrophic ectocervical and endocervical epithelial cells. Histopathologic examination of the endometrial curettage material revealed adenocarcinoma with focally papillary and glandular growth patterns. The patient underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy with bilateral pelvic and para-aortic lymphadenectomy, as well as appendectomy and omentectomy. Peritoneal washing was also performed during the operation.

On macroscopic examination, the uterus contained a 3x2x0.8 cm polypoid mass. Histopathological examination revealed a malignant tumor with prominent solid, glandular and partially papillary patterns growing in an endometrial polyp with cystically dilated glands settled in a fibrovascular stroma (Figure I). Tumor cells had eosinophilic and clear cytoplasm containing pleomorphic nuclei with prominent nucleoli. There were also focal areas of tumor necrosis (Figure IIA). The mitotic index was 28 in 10 high power fields. No psammoma bodies were observed. Endometrial intraepithelial carcinoma was noted in the surface of tumor (Figure IIB). The remainder

endometrium outside the polyp was atrophic and there were foci of adenomyosis in the myometrium. Histochemically, mucicarmine stain was focally positive, but periodic acid-Schiff was negative. Immunohistochemical staining for p53 and c-erbB-2 showed diffuse nuclear and cytoplasmic reactivity in the tumor cells, respectively (Figure IIIA and 3B). Estrogen receptor expressed focal but strong nuclear reactivity (Figure IIIC). Progesterone receptor showed weak positive nuclear reactivity in a minority of tumor cells (Figure IIID). Additionally, tumor cells were reactive for epithelial membrane antigen (EMA) and vimentin, and focally for carcinoembryonic antigen (CEA), but smooth muscle actin, chromogranin and CD34 were negative. A final diagnosis of serous carcinoma arising from endometrial polyp was given. Tumor superficially invaded myometrium, and lymphovascular space invasion and two metastatic lymph nodes were identified. Cervical, adnexal, omental and appendical involvements were not observed. Inclusion cysts and endosalpingiosis were detected in bilateral ovarian tissues. Peritoneal washing cytology was negative for malignant cells. The USC was staged as FIGO stage IIIC. The patient was treated with six cycles of Carboplatin and Paclitaxel every 3 weeks. The patient has been well without metastasis at 9 months follow-up.

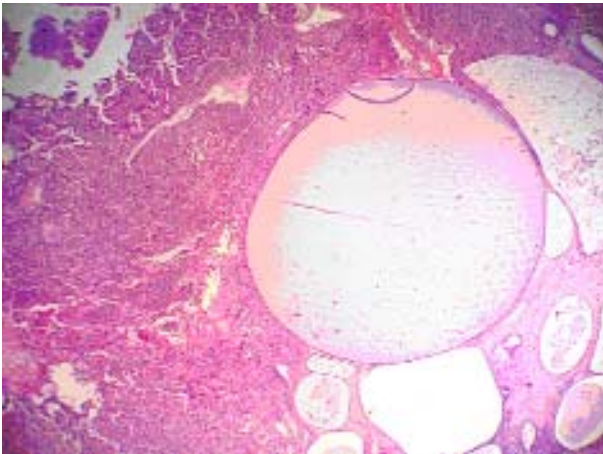


Figure 1: A part of endometrial polyp involved (left) by serous carcinoma (HE, x100).

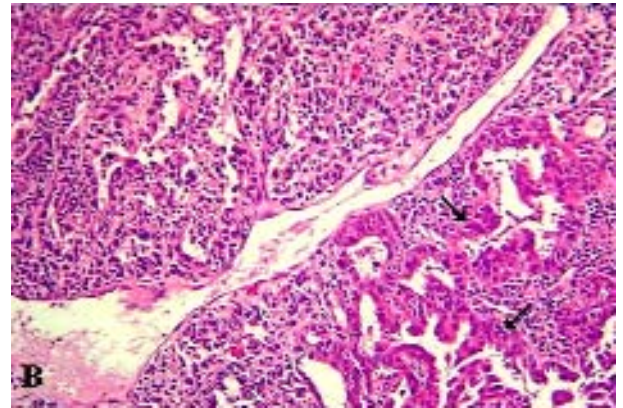
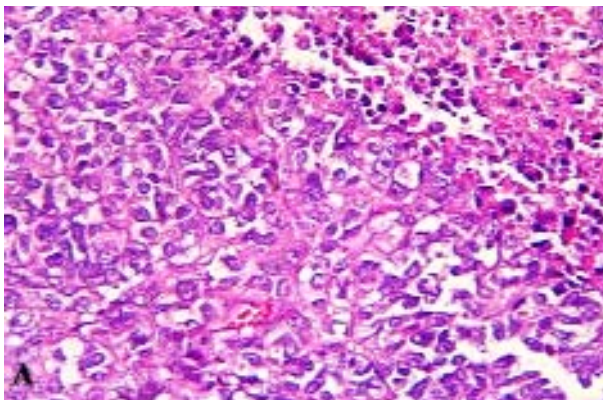


Figure 2: The tumor cells have eosinophilic and clear cytoplasm which contains pleomorphic nuclei. Necrotic area seen at upper right (HE, x400) (A), an appearance of endometrial intraepithelial carcinoma in the surface of tumor (arrow) (HE, x200) (B).

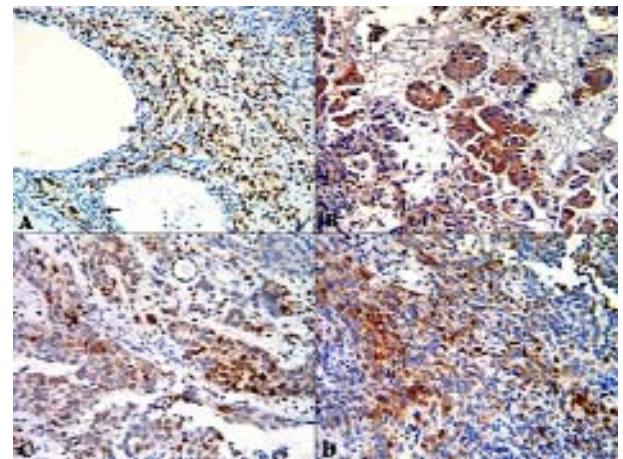


Figure 3: Strong positivity of serous carcinoma cells for p53 and negative staining of benign glandular epithelial cells (arrow) (A), expression of c-erbB-2 (B), focal nuclear expression of estrogen (C), and progesterone (D) receptors in the serous carcinoma (Immunoperoxidase, x200).

Discussion

Endometrial polyps are considered benign proliferative lesions and are commonly encountered in routine surgical pathology practice. Endometrial polyps may range from atrophic to hyperplastic and to carcinomatous. Although endometrioid adenocarcinoma is the most common malignant neoplasm, USC is less common in endometrial polyps.³ USC is an uncommon variant of endometrial carcinoma and constitutes approximately 10% of all endometrial glandular tumors. It occurs in postmenopausal elderly women, and arises in a background of atrophic endometrium from a precursor known as endometrial intraepithelial carcinoma. It is estrogen independent and negative for estrogen receptor. In contrast, endometrioid adenocarcinoma is associated with hyperestrogenism and estrogen receptor positivity. Patients with USC do

not have the usual clinical risk factors for endometrioid adenocarcinoma, such as obesity, diabetes mellitus, hypertension, and hormone replacement therapy.^{1,2,4} Cases with USC associated with tamoxifen therapy were reported.⁵

Molecular mechanisms underlying type I and II endometrial cancer are different. Endometrioid carcinoma may be associated with microsatellite instability and mutations in the PTEN, K-ras, and B-catenin genes, whereas USC is usually (80%) associated with p53 gene mutation. Overexpression of c-erbB-2 and gene amplification were found in about 45% and 70% of USC, respectively. The accumulation of p53 and c-erbB-2 in USC can immunohistochemically be detected in tumor nuclei (6,7). In our case, the malignant tumor in the endometrial polyp exhibited the solid, glandular and papillary morphology of serous carcinoma. Endometrial intraepithelial carcinoma was present adjacent to the serous carcinoma. USC and endometrial intraepithelial carcinoma showed strong reactivity for p53 and c-erbB-2. There were, however, some clinical and immunohistochemical findings that were consistent with a type I endometrial carcinoma, such as focal expression of estrogen and progesterone receptors and history of smoking, diabetes mellitus and hypertension. Estrogen and progesterone receptor positivity in USC have been reported in a few previous studies but significance of these expressions are not known.^{5,8} These studies suggested that the serous morphology could represent tumor progression from an initial endometrioid adenocarcinoma. Furthermore, USC with estrogen and progesterone receptor positivity may contain endometrioid adenocarcinoma component.^{5,8}

USC is an extremely aggressive cancer and has a high risk for recurrence, metastasis, and death.^{9,10} Histopathologically, these tumors are high grade and often deeply myoinvasive with lymphovascular space involvement. In the present case, superficial myometrial invasion, lymphovascular space invasion and two metastatic lymph nodes were identified as reported in the previous cases. USC and endometrial intraepithelial carcinoma arising in endometrial polyps have been reported in the literature.^{5,10-13} Studies assessing the behavior of serous carcinoma in the endometrial polyps are limited, and their results are controversial, although some cases without myometrial invasion have been reported to show extrauterine extension.^{9,10,12,13} Therefore, it has been suggested that even patients with stage 1A disease might be treated with adjuvant chemotherapy.⁹ However, it has been also reported that the clinical outcome is excellent when the tumor is confined to endometrial polyp or endometrium.¹¹ Advanced stage, the degree of myometrial invasion, lymphovascular space invasion, lymph node metastasis, invasion of omentum and positive cytology were poor prognostic factors in USC (1,2,11,14). Current patient has been treated with chemotherapy and well without metastasis at 9 months follow-up.

In summary, we have described a case of USC arising in the endometrial polyp. These tumors are unresponsive to hormonal treatment, because they almost always lack expression of hormone receptors. The clinical and prognostic significance of estrogen and progesterone receptor positivity are not known. p53 and c-erbB-2 may be overexpressed in USC and be used as a supportive diagnostic tool.

Endometrial Polipden Gelişen Uterin Seröz Karsinom: Olgu Sunumu

Seröz karsinom, tip II endometrial karsinomun tipik bir örneğidir. Sigara içme, diabetes mellitus ve hipertansiyon hikayesi olan 71 yaşındaki kadın hasta postmenapozal kanama şikayeti ile başvurmuştur. Küretaj materyalinde adenokarsinom tanısı almıştır. Histerektomi materyalinde uterusu polipoid kitle belirlenmiştir. Histopatolojik olarak endometrial polipden gelişen seröz karsinom gözlenmiştir. İmmünohistokimyasal olarak tümör hücrelerinde p53 ve c-erbB-2 ile diffüz, östrojen ve progesteron reseptörü ile fokal reaksiyon saptanmıştır. Olgumuz, diabetes mellitus ve hipertansiyon hikayesine sahip olmasının yanı sıra östrojen ve progesteron reseptörleri ile fokal reaksiyon vermesi ile tip 1 endometrial karsinoma ilişkili klinik ve immünohistokimyasal bulguları paylaşmaktadır. Bu tümörde p53 ve c-erbB-2'nin aşırı ekspresyonu göz önünde bulundurulmalıdır.

Anahtar Kelimeler: Seröz karsinom, Endometrial polip, p53, c-erbB-2.

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