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Endometrial intraepithelial carcinoma in the endometrial polyp coexistent with uterine papillary serous carcinoma

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Background: A 65-year-old woman presented with postmenopausal bleeding. Uterine papillary serous carcinoma (UPSC) and endometrial intraepithelial carcinoma (EIC) in a coexistent endometrial polyp was diagnosed.
Case: Macroscopic assessment of hysterectomy specimen showed a necrotic tumor in the endometrial cavity. An intact endometrial polyp was noted next to main tumor mass with foci of EIC. Immunohistochemistry revealed p53 antigen expression in the cells of EIC component.
Conclusion: The presence of EIC may imply the presence of high grade adenocarcinoma in extrauterine and peritoneal sites. EIC should specifically be explored in endometrial polyps, curettings and hysterectomy materials from postmenopausal woman..

Keywords: uterine serous carcinoma, endometrial intraepithelial carcinoma, polyp

Background

Uterine papillary serous carcinoma (UPSC) is a novel and attractive topic in gynecological pathology since its definition has deeply affected the clinicopathological concept of endometrial carcinogenesis. These tumors are usually accompanied with a superficial and assumable precursor lesion, i.e. endometrial intraepithelial carcinoma (EIC). We herein present a case which harbors UPSC, EIC and endometrial polyp.

Case

A 65-year-old female patient presented with postmenopausal uterine bleeding. A curetting was made and pathologic examination of this material was reported as uterine serous carcinoma. Patient underwent total abdominal hysterectomy, bilateral salpingoopherectomy with staging laparatomy. Patient was stage III and radiotherapy combined with platinum based chemotherapy was instituted. Despite the therapy patient died of extensive metastasis after 9 months.

Histological examination of preoperative biopsy material showed a necrotic tumor that is composed of papillary structures formed by anaplastic epithelial cells. Tumor cells have large, hyperchromatic, irregular nuclei with macronucleoli. The cytoplasm is dense and eosinophilic. Diagnosis of UPSC was made with these features (Figure 1).

Macroscopic assessment of hysterectomy specimen showed a necrotic tumor in the endometrial cavity extending from the fundus to the lower uterine segment. An intact endometrial polyp, which was 1 cm. in diameter was noted next to main tumor mass. Tumor was extending to the subserosa of uterus. Histological features of the tumor were similar to preoperative biopsy material.

Microscopic evaluation of polypoid lesion revealed foci of EIC in the otherwise conventional endometrial polyp. The polyp is composed of cystic glands lined by cuboidal to columnar epithelial cells

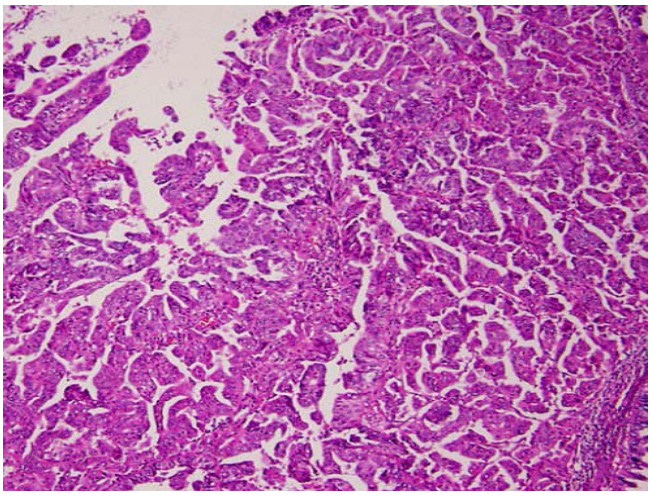

Figure 1. Uterine papillary serous carcinoma. Prominent pattern is papillary and shedding of cells into the lumen is seen.

and loose fibroblastic stroma. In microscopic areas close to the surface epithelium, we observed the EIC foci as complicated glandular structures that were lined by cells with enlarged hyperchromatic pleomorphic nuclei and prominent nucleoli (Figures 2, 3). No invasive component or desmoplasia was detected either around these glandular structures or in the polyp itself (Figure 4).

Immunohistochemistry revealed p53 antigen expression in the cells of EIC component (Figure 5). Underlying endometrium was atrophic, no hyperplasia was evident. The ovaries and fallopian tubes were unremarkable. Peritoneal washings were negative for tumor cells.

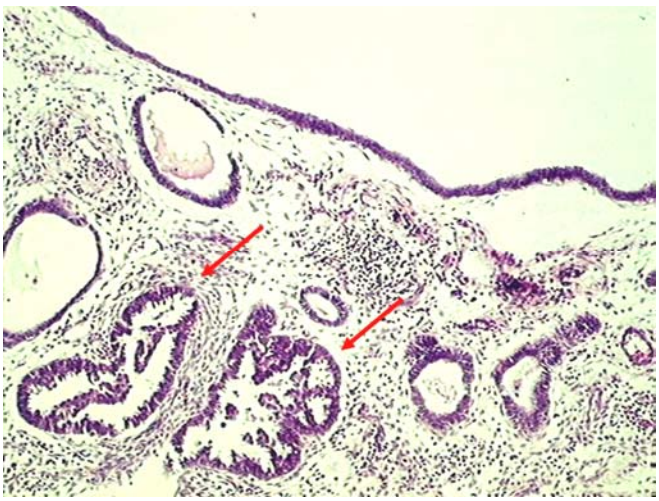

Figure 2. Endometrial intraepithelial carcinoma foci are visible underneath the surface epithelium in the endometrial polyp (arrows).

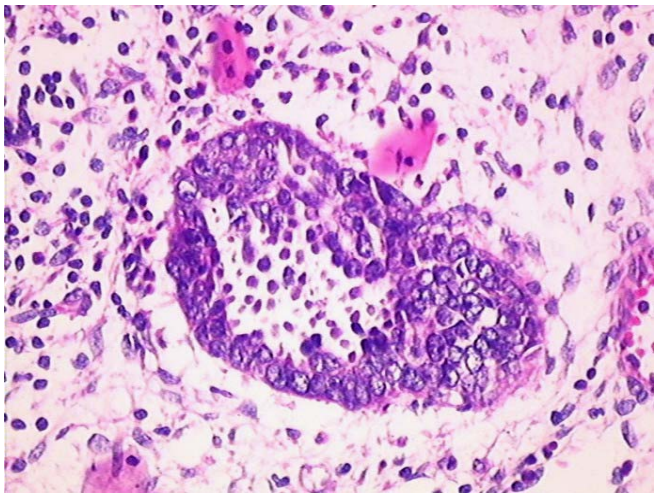

Figure 3. Endometrial intraepithelial carcinoma. Glandular epithelium replaced by atypical epithelial cells with high grade nuclei.

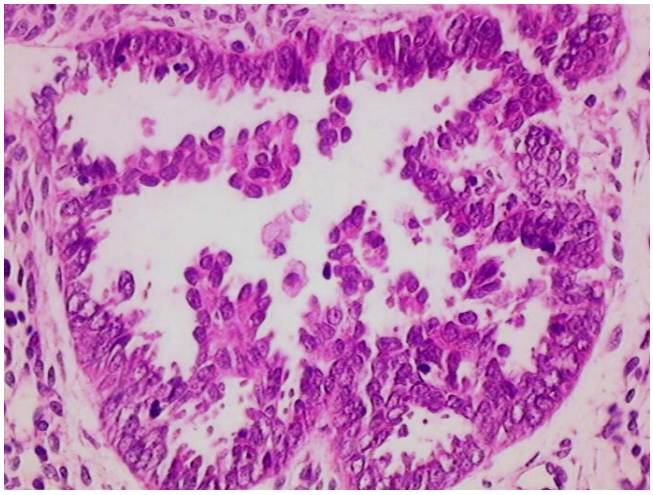

Figure 4. Endometrial intraepithelial carcinoma, micropapillary pattern. Glandular epithelium replaced by atypical epithelial cells with high grade nuclei. Although atypical epithelium formed bridges, basal membrane is intact and no invasive component is present.

Conclusion

We herein report a case of EIC in the endometrial polyp coexistent with UPSC. EIC is a recently described entity, characterized by the replacement of atrophic endometrial surface epithelium and glands by malignant cells resembling high-grade invasive endometrial carcinoma.[1,2] This lesion frequently accompanies UPSC and is thought to be the precursor lesion of USC.

EIC has different biological behavior from in situ carcinoma at other sites, which is not capable of metastasize before developing invasive component. Wheeler et al found that twenty percent of patients

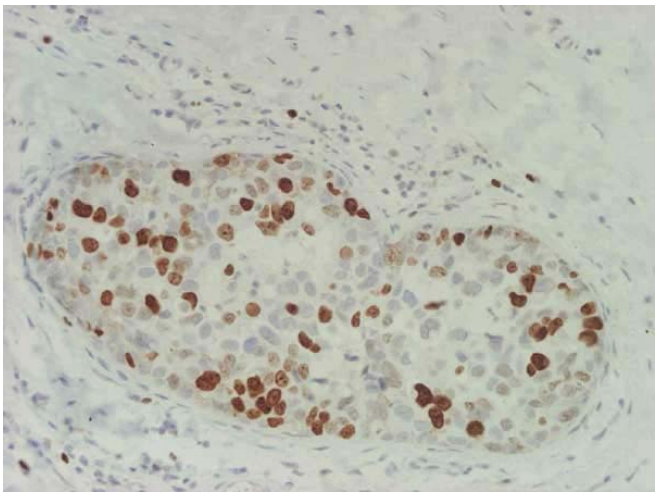

Figure 5. p53 expression in the EIC component.

with pure EIC (without coexistent serous carcinoma), an extrauterine disease was present and outcomes of such cases are poorer.[3] Soslow et al reported three cases of pure EIC associated with peritoneal carcinomatosis.[4] There were no intrauterine invasive tumors in these patients. Some authors believe that EIC should be interpreted as a malignant lesion and the most important predictor of outcome is presence or absence of extrauterine lesion.[4,5]

Since EIC may be focal in biopsies and curettings the histopathological diagnosis may be difficult. The most striking microscopic feature is the histological pattern. Several histological patterns have been described for EIC.[1,2,3] EIC may have a flat and a micropapillary pattern. In flat pattern, single or multiple cell layers line the glandular structures. In micropapillary pattern, atypical epithelial cells form intraglandular papillary projections. Both patterns of EIC may have cuboidal, columnar or hobnail cell types as well as mixed cell types.

EIC often involves benign endometrial polyps with extensive replacement of the surface epithelium and underlying glands.[1–4,6,7] The benign polyps with abnormal glandular crowding often display two features that complicate the diagnosis of invasion and also EIC. These features are cellular fibrotic stroma and foci of crowded glands. Specifically, cellular stroma may mimic a desmoplastic response to invasive tumor, and extensive EIC within preexisting glands may be confused with a confluent glandular pattern of stromal invasion. The differential diagnosis of glandular crowding in a polyp includes eosinophilic metaplasia, atypical hyperplasia, endometrioid carcinoma, and clear cell carcinoma. Eosinophilic metaplasia may demonstrate nuclear smudging, prominent nucleoli, and mitoses with reparative surface changes when associated with endometrial stromal breakdown. However, in contrast to eosinophilic metaplasia, EIC demonstrates more diffuse and severe cytologic atypia characterized by nuclei with coarse rather than smudged chromatin, larger eosinophilic nucleoli, and more numerous, occasionally abnormal mitoses. In difficult cases, immunohistochemical stains may be helpful. Although the literature is somewhat controversial, strong and diffuse immunostaining for p53 protein and Ki-67 supports the diagnosis of neoplasia.[6]

EIC is considered to be the precursor lesion of UPSC, since it can be found in nearly all uteri containing serous carcinoma.[8] In addition to histopathological observations, molecular studies support this hypothesis. Loss of heterozygosity (LOH) at the p53 locus is consistently identified in UPSC, whereas most EICs studied contain only one mutated p53 allele.[2,6] This observation suggests that UPSC develops from EIC and that p53 mutation is an early change in tumor progression in atrophic uteri.[6] It was also shown that pure EIC cases (without invasive tumor in uterus) and extrauterine tumor foci had identical unique p53 mutations.[5] These findings suggest that EIC is the putative precursor lesion of UPSC.

UPSCs have accounted less than 5% of endometrial carcinomas. These tumors tend to occur in patients who are older than patients with type 1 endometrial (EC) carcinomas. Estrogen use and obesity are not associated with UPSC. The usual clinical presentation is either postmenapausal bleeding or in serous-bloody vaginal discharge.[9,10]

Besides clinical presentation, UPSC differs from EC in regard to its clinical course. UPSC is one of the most aggresive malignant tumors of endometrium. Stage is the most important prognostic factor. However, even with smaller and superficial tumors, there may be extrauterine disease. Currently, all patiens with UPSC are being treated with staging laparatomy including peritoneal lavage and omentectomy.[11,12]

Prominent histological features of UPSC's are papillary pattern formed with high grade epithelial cells and shedding of these anaplastic cells. Nuclear features are high grade and necrosis is almost always present. Those features may be present partially in curreting materials. The diagnosis of UPSC with such cases may be challenging.[13,14]

The presence of EIC in uteri may imply the presence of high grade adenocarcinoma in extrauterine and peritoneal sites.[13,14,15] EIC should specifically sought in endometrial polyps, curettings and hysterectomy materials from postmenopausal woman.

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