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Cytologic Features of Endometrial Papillary Serous Carcinoma*

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=Abstract=

Endometrial papillary serous carcinoma (EPSC) is a distinct variant of endometrial adenocarcinoma that histologically resembles ovarian serous papillary adenocarcinoma and has an aggressive clinical course. Usually, the tumor is diagnosed at the advanced stage. The tumor has well confused with metastatic ovarian tumor of identical histology. Dignosis of EPSC should be considered when the cervico-vaginal smear reveals numerous papillary clusters of tumor cells with macronucleoli and psammoma bodies.

Recently, we have experienced two cases of EPSC diagnosed on cervico-vaginal smears, which revealed characteristic cytologic features including numerous papillary clusters of tumor cells with macronucleoli. The cytologic diagnoses were confirmed on histologic sections.

Key Words : Endometrial adenocarcinoma, Endometrial papillary serous carcinoma, Cytologic features, Cervico-vaginal smear

INTRODUCTION

Endometrial adenocarcinoma comprises a morphologically heterogeneous group of neoplasm[1]. About 80% of endometrial carcinomas exhibit typical adenocarcinoma closely resembling normal or hyperplastic endometrial glands[2]. The remainder comprises different histologic types of müllerian derivatives. Among them, endometrial papillary serous carcinoma (EPSC) is a distinct variant which histologically resembles that of ovarian papillary serous carcinoma[3].

Grading of endometrial carcinoma depends upon architectural pattern and cytologic features, and the latter has more significance concerning prognosis[4]. EPSC has distinct architectural and cytologic features. There is about twice high positive detection rate on cervico-vaginal smears than that of conventional endometrial carcinoma[5]. This makes diagnosis of this rare tumor easy on the simple screening procedure if the pathologist is alert to find this

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peculiar cytologic features.

We described cytologic features of two cases of EPSC, which were later confirmed on histologic examination of hysterectomy specimens.

CASE PRESENTATION

CASE 1 : A 57-year-old obese woman, gravida 2 and paragravida 2, presented with low abdominal pain for 6 months. Menopause occurred 13 years before. Vaginal bleeding or discharge was absent. The cervicovaginal smear and punch biopsy from the cervix were interpreted as a papillary adenocarcinoma. Radical hysterectomy with bilateral salpingo-oophorectomy was performed. The uterus was not enlarged and weighed 90 gm. The endometrial cavity was filled with granular, soft, papillary tumor. which extended to the endocervical canal. The microscopic features were those of an EPSC. The tumor had infiltrated up to a half of the myometrium. The pathologic stage was Ib by FIGO classification. The patient received five cycles of combined chemotherapy after the surgery. The patient was alive and well for 3 years and 2 months with no evidence of metastasis.

CASE 2 : A 47-year-old obese woman, gravida 10 and paragravida 3, complained of abrupt abdominal distension for 2 weeks. Menorrhagia was present for 3 months. The abdominal sonography and CT scan revealed diffuse peritoneal seedings of a malignancy. The primary site of the tumor was thought to be the right ovary because of a slight enlargement. Upper gastro-intestinal barium study and gastrofiberscopy failed to reveal any malignancy. The cervico-vaginal smear and curettage of the endometrium showed papillary adenocarcinoma. Radical hysterectomy revealed the low segment of the endometrium filled with residual tumor nodules, the largest measuring 1 cm in diameter. Although myometrial invasion was limited to the superficial layer, numerous lymphatic tumor emboli were found in whole thickness of the myometrium and perimetrium. The omentum and surface of ovaries and salpinges were studded with multiple metastatic nodules. The pathologic stage was stage IV in FIGO. The patient received three cycles of combined chemotherapy for 4 months.

CYTOLOGIC FEATURES

The cervico-vaginal smears from both cases showed identical cytologic features. There was an increase in the number of exfoliated tumor cells on the background of necrotic and bloody smears (Fig. 1). The tumor cells were usually arranged in three dimensional papillary clusters (Fig. 2). The cells were relatively large in size. The cytoplasm of individual cells was scanty and basophilic, and had small vacuoles and indistinct borders (Fig. 3). There was absence of phagocytosis in tumor cells, unlike that of conventional adenocarcinoma. Molded nuclei of the tumor cells showed marked pleomorphism with moderate hyperchromatism. The nuclear chromatin was finely clumped. Prominent, acidophilic macronucleoli were observed (Fig. 4). No psammoma bodies were present in both cases.

HISTOPATHOLOGIC EXAMINATION

Case 1 : On the examination of hysterectomy specimen, the endometrial cavity was filled with exophytic, irregular, and friable masses which extended into the endocervical canals. Sections from the endometrium showed complex papillary arrangement of tumor cells with broad, coarse and edematous fibrous stalks (Fig. 5). The lining epithelium of papillae was focally tufted. The tumor cells had acidophilic macronucleoli (Fig. 6). However, psammoma body was not present. The tumor had invaded the myometrium up to a half of the thickness. The

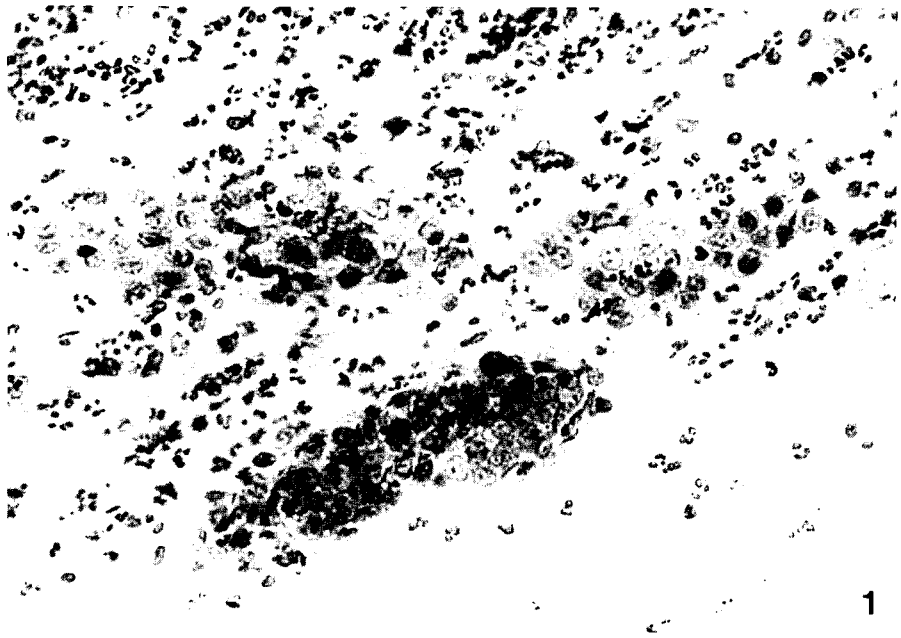

Fig. 1. Many clusters of tumor cell papillae are smeared on the necrotic, hemorrhagic background (Papanicolaou, ×200).

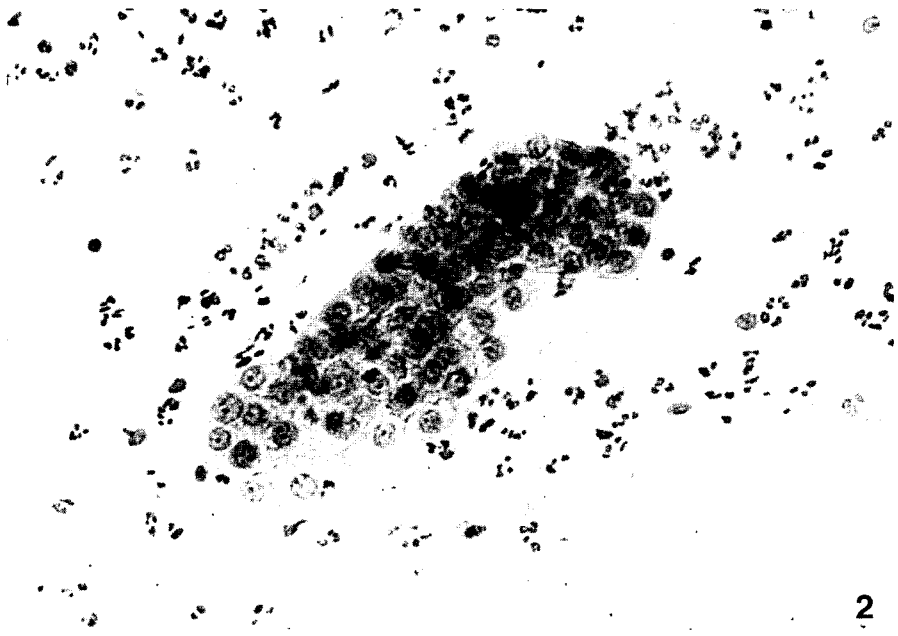

Fig. 2. Three dimensional papillary cluster of tumor cells is characteristic of this tumor (Papanicolaou, ×200).

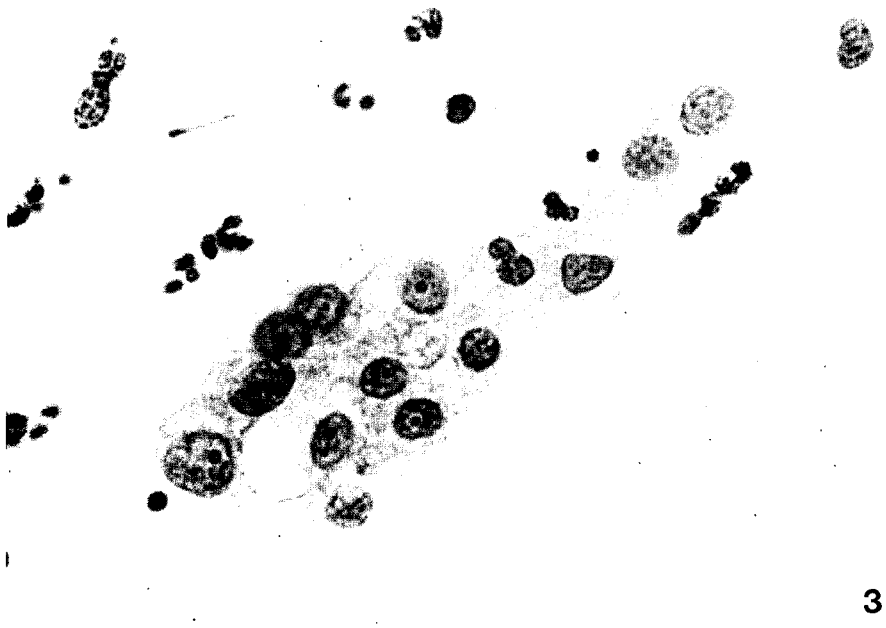

Fig. 3. Individual tumor cells are relatively large and finely vacuolated. The borders of cytoplasm are indistinct (Papanicolaou, ×400).

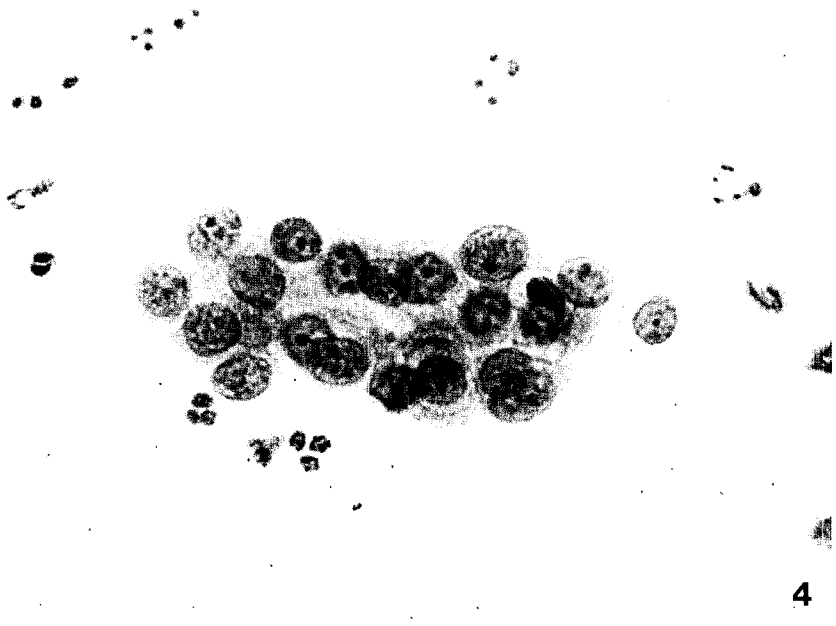

Fig. 4. Tumor cells have acidophilic macronucleoli and finely stippled chromatin (Papanicolaou, ×400).

Fig. 5. The endometrial papillary carcinoma has complex papillae of tumor cells with fibrous stalks (H-E, ×100).

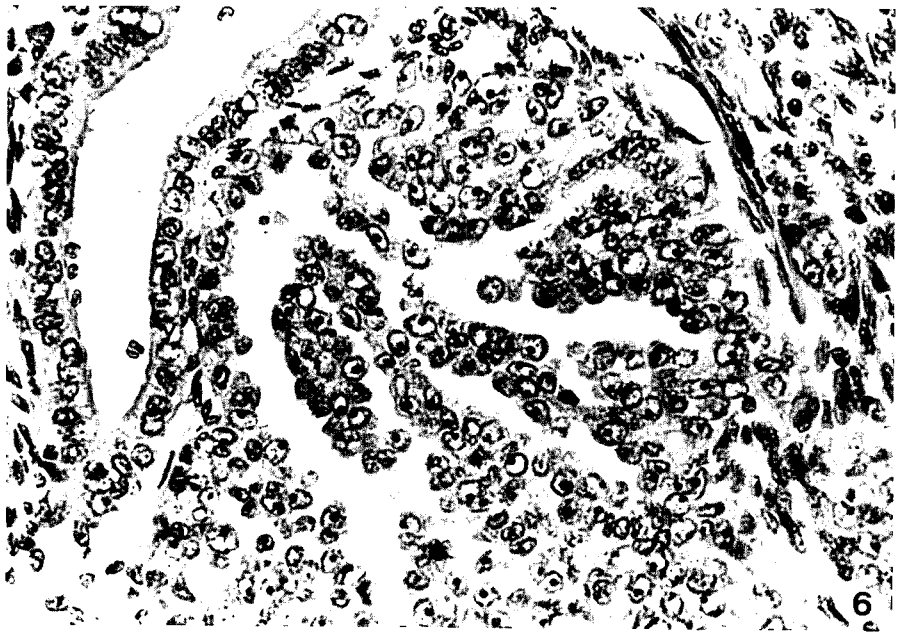

Fig. 6. Individual tumor cells contain macronucleoli with perinucleolar halo (H-E, ×200).

numerous lymphatic tumor emboli were noted in the myometrium. Both ovaries and salpinges were free of tumor invasion.

Case 2 : Sections from the curetted endometrial tissue revealed a papillary tumor made up of large cells. In many areas, tumor exhibited solid nests or cribriform pattern. The tumor cells had acidophilic macronucleoli. Radical hysterectomy specimen revealed a residual mass on the low uterine segment measuring 1 cm in diameter. The histologic features of residual tumor were similar to those of the previous curetted specimen. Although the myometrium was focally invaded by tumor, lymphatic emboli of the tumor were numerous in the endocervix, myometrium, and perimetrium. Sections from both ovaries, salpinges, and the omentum showed multiple papillary excrescences on the serosal surfaces.

DISCUSSION

In 1963, Karpas and Bridge first reported on a patient with an endometrial adenocarcinoma that contained psammoma bodies[6]. Subsequent several reports during the last two decades documented that psammoma bodies were present in adenocarcinoma of the endometrium that were histologically identical to the serous papillary carcinoma of the ovary[7-12]. Since the endometrium develops from the müllerian system, an adenocarcinoma of the endometrium can histologically resemble that of the upper vagina, the cervix, the fallopian tube and the surface mesothelium of the ovary[13]. In 1982, Hendrickson et al. described a type of highly malignant variant of endometrial adenocarcinoma as uterine papillary serous carcinoma. This paper first outlined the microscopic criteria for diagnosis, cytologic features and clinical course of the tumor[3].

A few reports described the cytologic features of this tumor on the cervico-vaginal smear[5, 14, 15]. The smears showed numerous papillary clusters with malignant appearing epithelial cells on the necrotic and bloody background. The epithelial cells had acidophilic macronucleoli, fine chromatin and clear cytoplasm which were distinct features of EPSC, especially differentiated from the other adenocarcinoma of the endometrium. Phagocytosis of nuclear debri was not conspicuous in most cases, which was frequently noted in usual endometrial adenocarcinoma. There were no pasmmoma bodies or phagocytosis in our cases. All these findings were compatible with EPSC. Tumor cells were cytologically characterized by marked nuclear pleomorphism, nuclear hyperchromatism, large or giant nuclei, and acidophilic macronucleoli. Numerous mitotic figures could be encountered. Psammoma bodies were present in 30% of cases reported[3, 14, 15].

Histologically, the architectural unit consisted of complex papillary fronds with broad, coarse and edematous stroma. Tufted stratification of lining epithelium occurred. Solid area was not uncommon and correlated with high grade. Myometrial invasion (70%) and permeation of lymphatic vessels (37%) were characteristic pattern of the tumor spread. The ovarian involvement was present in 19% of cases[3, 9]. Both cases under discussion also revealed myometrial invasion of tumor cells and frequent lymphatic emboli. Case 2 showed multiple nodules studded on the surface of the ovaries, salpinges and omentum, which were metastatic from the endometrial primary.

The differential diagnosis of EPSC in cervicovaginal smear includes usual endometrial adenocarcinoma, endocervical adenocarcinoma and mestastasis from the ovary, salpinx and other distant sites. EPSC is distinguished from the usual endometrial adenocarcinoma in that the EPSC shows higher celluearity and numerous papillary clusters of the tumor cells with acidophilic macronucleoli. The phagocytosis of polymorphonuclear leukocytes are frequently noted in usual endometrial adenocarcin-

oma, but could not seen in EPSC[5, 16]. Adenocarcinoma of the endocervix may have same findings of EPSC that the neoplastic cells are larger and more numerous in number on the smears. However, papillary clusters with nuclear pleomorphism and macronucleoli so characteristic of EPSC are not seen in endocervical adenocarcinoma. The columnar cells with abundant cytoplasm are often seen in endocervical adenocarcinoma. There are little degeneration, contrary to that found in the cell from an endometrial neoplasm[16, 17]. It may be difficult to distinguish EPSC from metastatic carcinoma of the surface of the ovary and salpinx. All three entities show identical histologic features which arise from the müllerian duct. These entities are characterized by numerous papillary clusters with prominent macronucleoli and occasionally associated with psammoma bodies. However, the cervico-vaginal smears from metastatic tumor generally show the absence of necrotic and bloody background and a smaller number of malignant cells[16, 18, 19].

The cytologic diagnosis of EPSC should be considered when numerous papillary clusters of tumor cells with macronucleoli are present on the necrotic and hemorrhagic background of the cervico-vaginal smear.

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국문요약

자궁 내막의 유두상 장액성 암종의 세포학적 소견

한양대학교 의과대학 병리학교실

공 구·홍 은 경·이 중 달

자궁내막의 유두상 장액성 암종은 자궁 내막에서 발생하는 매우 희귀한 선암종의 한 형태로, 동명의 난소 암종과 조직학적으로 동일하며, 매우 불량한 예후를 나타낸다. 대개 이 종양은 말기에 진단되며, 같은 조직학적 소견을 보이는 전이성 난소암종과 혼돈되기 쉽다.

최근, 저자들은 자궁경부-질 도말 표본에서 2예의 유두상 장액성 암종을 진단 하였는데, 그 세포학적 소견은 종양 세포의 유두상 구조가 풍부하게 도말되었고, 종양 세포들은 거대한 핵소체를 가지고 있었다. 도말배경은 괴사성 및 혈성으로 종양소인을 잘 반영하고 있었다. 이 세포학적 진단은 자궁 절제 표본의 조직학적 검사로 확인 되었다.