# Cervicovaginal Smear Findings of Endometrial Serous Carcinoma: A Case Report

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An endometrial serous carcinoma case which is a variant of endometrial carcinoma exhibiting an agressive course that has been detected by cervicovaginal smear, is presented in this report in light of the datas of the related literature.

No particular sign has been observed during the gynecological examination of the 77-year-old patient who applied to university hospital with the complaints of vaginal discharge and perineal pruritus. Cervicovaginal smear showed atypical glandular cells, exhibiting seldom bare nuclei and papillary clusters in most of the areas with a necrotic background. By the help of those cytopathological findings, the diagnosis was "Epithelial cell abnormality: atypical glandular cells (AGC) in favour of neoplasia and atypical squamous cells of undetermined significance (ASCUS) and due to "possiblity of an adenocarcinoma", cervical and/or endometrial biopsy was recommended. The result of the endometrial biopsy was reported as "serous papillary adenocarcinoma". Postoperatively, examination of hysterectomy material revealed an infiltration of "endometrial serous carcinoma" extending towards cervix, myometrium, and serosa, and full filling the endometrial cavity. The case, regarded as Stage IV died on postoperative 13th day.

Although cervicovaginal smear generally is not a sensitive screening test for endometrial carcinomas, it played an important role in determining serous carcinoma. This may be related with advanced stage and/or aggressive features of the neoplastic process.

**Key Words:** Endometrial serous carcinoma, Cervicovaginal smear, Atypical glandular cells

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## Introduction

Currently, endometrial carcinoma is the most common malignancy of the female genital tract, accounting for almost one half of all gynecologic cancers in the United States. It is the fourth most common cancer, ranking behind breast, lung, and bowel cancers, and the eighth leading cause of death from malignancy in women. Aging, obesity, hypertension, diabetes, and estrogens have been hold responsible earlier in the development endometrial cancer. According to World Health Organization (WHO), endometrial cancer is divided into histopathological subgroups as follows: endometrioid adenocarcinoma, serous adenocarcinoma, clear cell adenocarcinoma, mucinous adenocarcinoma, adenosquamous, squamous, mixed type, and undifferentiated carcinoma.[1,2]

Endometrial serous carcinoma which is also called as "papillary serous carcinoma" and "serous adenocarcinoma", is a histopathologically distinct variant of endometrial carcinoma which shows an aggressive clinical course. Endometrial papillary serous carcinoma, which has been first described by Hendrickson et al. in 1983, constitutes approximately 10% of all endometrial glandular tumors.[1,3,4]

Though conventional cervicovaginal smear is a sensitive and effective screening test for early diagnosis of cervical cancers, its contribution in determining malignant cells of endometrial origin, is known to be limited.[5]

In cervicovaginal smears, due to its histopathologic features, endometrial serous carcinoma can be more easily detected compared to the classic endometrioid variant. Detecting this variant of endometrial carcinoma which shows an aggressive clinical course and poor prognosis, bears importance in terms of clinical treatment planning.[3,4]

In this study, an endometrial serous carcinoma case which is a rare variant of endometrial carcinoma and detected preoperatively by cervicovaginal smear, is reported.

## Case Report

No particular sign has been observed during the gynecological examination of the 77-year-old postmenopausal patient who applied to our hospital with the complaints of vaginal discharge and perineal pruritus. Pelvic ultrasound revealed a

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pelvic mass of 54x33 mm that is adjacent to the uterus and having solid-cyctic components. Hypercellular cervicovaginal smear showed pleomorphic atypical glandular cells on a necrotic background between ectocervical and endocervical epithelial cells, which exhibit seldom bare nuclei, diffuse papillary structures, dense clusters, and irregular nuclear membranes as well as prominent nucleoli, hyperchromatic nuclei, and eosinophilic cytoplasm (Figure 1-3).

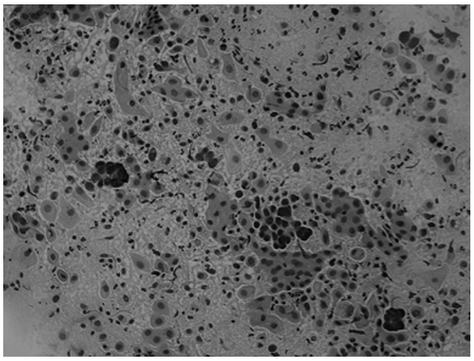

*Figure 1: Hypercellular cervicovaginal smear revealing atypical glandular cells (AGC) forming papillary clusters and atypical squamous cells of undetermined significance (ASCUS) on the tumor diathesis background (H&E, X200)*

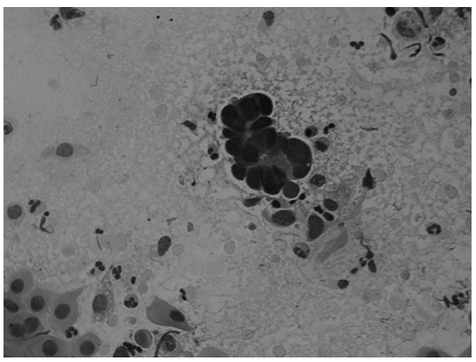

*Figure 2: Papillary structure composed of pleomorphic atypical glandular cells with distinct nucleoli, irregular nuclear membranes, hyperchromatic nuclei, and eosinophilic cytoplasms (H&E, X400)*

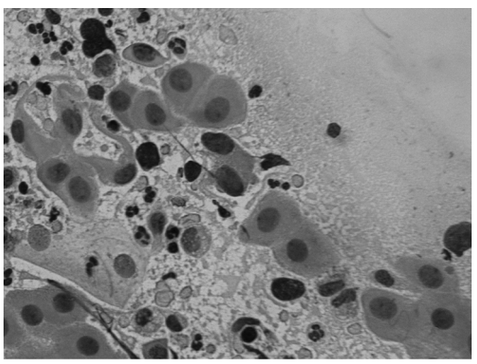

*Figure 3: Atypical cells with bare nuclei among cervical epithelial cells (H&E, X400)*

In the light of those cytopathologic results; the diagnosis was, epithelial cell abnormality: atypical glandular cell (AGC) in favour of neoplasia and atypical squamous cells of undetermined significance (ASCUS); and due to a "possible adenocarcinoma", cervical and/or endometrial biopsy was recommended. The microscopic examination of the cross sections of the endometrial biopsy displayed large pleomorphic atypical epithelial cell groups exhibiting eosinophilic cytoplasm, distinct nucleoli, seldom hyperchromatic nuclei, mainly vesicular nuclei, forming complex papillary structures, and having thin fibrovascular core in many areas, among the blood and fibrin mass (Figure 4).

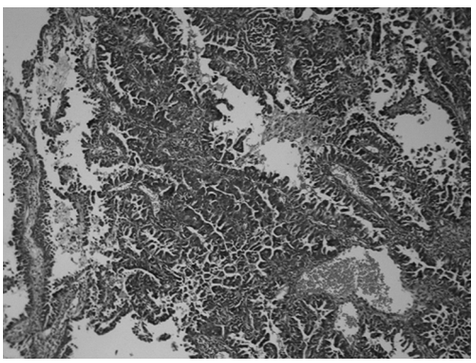

*Figure 4: Pleomorphic atypical epithelial cell clusters forming papillary structures and having fibrovascular cores (H&E,X200)*

Endometrial biopsy was reported as "serous papillary adenocarcinoma". In the light of this result; the patient had undergone surgical intervention including total abdominal hysterectomy and salpingo-oopherectomy, omentectomy and appendectomy. Gross examination of the hysterectomy material which is atrophic in appearance, revealed a tumoral infiltration which was completely filling the endometrial cavity and extending towards cervix, myometrium, and serosa. Histopathological examination revealed the tumor as consisted of large atypical epithelial cells displaying hyperchromatic and vesicular nuclei, prominent nucleoli, eosinophilic cytoplasms, forming complex papillary structures, and denoting thin branching around the fibrovascular core (Figure 5).

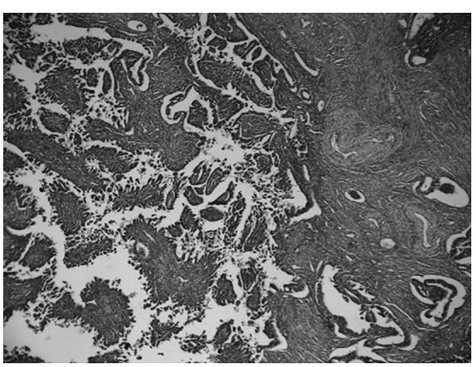

*Figure 5: Serous carcinoma forming deep myometrial invasion (H&E, X200)*

"Psammoma body" was not observed neither in cervicovaginal smear and nor in histopathological cross sections. There was lymphovascular space invasion in this tumor diagnosed as "endometrial serous carcinoma". There was also carcinoma infiltration in the right and left ovarium-tuba, appendix serosa and omentum, besides malignant epithelial cells detected in peritoneal cytology. The case, regarded as Stage IV, died on the postoperative 13$^{th}$ day due to cardiopulmonary failure.

## Discussion

In general, endometrial carcinoma is looked over in two subgroups. First group of these tumors are usually well-differentiated, mainly displaying superficial invasion, and have good prognosis and good response to progestagen treatment. The best example for this group of tumors is endometrioid type adenocarcinoma which derivates from atypical endometrial hyperplasia that arises due to unopposed estrogen stimulation. The characteristics of this second group of tumors are, tendency to make deep invasion, high rate of pelvic lymph node metastasis, poor response against progestagen treatment, poorly differentiated and poor prognosis. The perfect example for the second group is serous carcinomas which originate from atrophic endometrium frequently encountered among elderly women and possessing none of the classical risk factors for this carcinoma.[1,2]

It is generally possible to detect the endometrial cells during the first 12 days of menstrual cycle on cervical smears physiologically.[5] But it is abnormal to observe those cells in the cervicovaginal smears during second half of the menstrual cycle or in any time of postmenopausal period, then abnormal endometrial desquamation should be considered.[6] While Ng et al. reported the presence of adenocarcinoma in 3,2% of the 662 patients exhibiting such cells and Cherkis et al. reported adenocarcinoma in 11,2% of 179 cases with the same smear characteristics.[6-8] Moreover, it has been reported that this feature becomes more significant with age, with increase in the degree of cytological atypia and with accompanying advanced stage detected postoperatively and it is also reported that the detection of malignant cells in cervicovaginal smears increases. Malignant cervical smear rate was found to be high in endometrial serous carcinoma cases having poor prognosis and displaying an agressive clinical course as in our case.[6,7]

Endometrial serous carcinoma is an uncommon neoplasia which exhibits well-differentiated tubuloglandular morphology associated with or without papillary growth pattern. Serous carcinomas that have such histomorphological features, are commonly seen in postmenopausal women like our case.[1,4] Psammona bodies are encountered in 20% of tumors.4 No "psammoma body" was observed in both histopathological sections and cervicovaginal smears of the presented case. This neoplasia should be distinguished from classic endometrioid type endometrial carcinoma due to differences in the treatment.[3,4]

In 1999, Wright et al. reported that endometrial serous carcinoma and endometrioid adenocarcinoma may be distinguished by investigating some parameters in cervicovaginal smear. Detecting cytomorphological findings similar to the features observed in our case such as hypercellular smears, tumor diathesis on the background, papilary clusters, bare nuclei, presence of large cells with pleomorphic nuclei and bulky dense eosinophilic cytoplasms, suggest endometrial serous carcinoma first.[4,6] Besides endometrioid adenocarcinoma, serous carcinoma of endocervix, ovarium, and tuba uterinas must be taken in consideretion for differential diagnosis.[4,6,8] Serous carcinomas of ovarium and tuba uterina may be characterized less cellular smears and a clean background without tumor diatesis and retraction rings around the cell clusters.[3,4,8] It can not be distinguished from serous carcinoma of endocervix by only morphology and supportive techniques are required to distinguish them.[3,8]

In the present study, although generally cervicovaginal smear is not a sensitive screening test for endometrial carcinomas, it has played an important role in determining serous carcinoma. This may be due to advanced stage of the neoplastic process as well as the agressive nature of the tumor and its histopathological features. Due to clinical importance in behalf of planning the appropriate treatment, when malignant cells originating from endometrium are detected and papillary clusters and/or bare nuclei are denoted in cervicovaginal smears, endometrial serous carcinoma with poor prognosis should be suspected.

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## Endometrial Seröz Karsinomun Servikovajinal Yayma Bulguları: Olgu Sunumu

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Servikovajinal yaymada saptadığımız endometrial karsinomun agresif klinik seyir gösteren varyantı olan endometrial seröz karsinom olgusu, literatür bilgileri ışığında sunulmaktadır.
Vajinal akıntı ve perineal kaşıntı şikayetiyle hastanemize başvuran 77 yaşındaki hastanın jinekolojik muayenesinde bir özellik izlenmemiştir. Servikovajinal yaymada; nekrotik zeminde, yer yer çıplak nükleuslu, çoğu alanda papiller kümeler oluşturan atipik glandüler hücreler izlendi. Bu sitopatolojik bulgularla "Epitelyal hücre anomalisi: atipik glandüler hücreler (AGC), neoplazi lehine ve önemi belirlenemeyen atipik skuamöz hücreler (ASCUS) tanısı verildi ve "olası adenokarsinom" nedeniyle olguya servikal ve/veya endometrial biyopsi önerildi. Endometrial biyopsi sonucu "seröz papiller adenokarsinom"

olarak rapor edildi. Operasyon sonrası histerektomi materyalinde; endometrial kaviteyi tamamen dolduran, servikse, miyometriuma ve serozaya doğru uzanım gösteren "endometrial seröz karsinom" infiltrasyonu gözlendi. Evre–IV olarak kabul edilen olgu, postoperatif 13. günde eksitus olmuştur.
Servikovajinal yayma genel olarak endometrial karsinomlar için duyarlı bir tarama testi olmamasına rağmen seröz karsinom olgusunun saptanmasında önemli rol oynamıştır. Bu durum neoplastik sürecin ileri evrede olmasına ve/veya agresif niteliğine bağlanabilir.

**Anahtar Kelimeler:** Endometrial seröz karsinom, Servikovajinal yayma, Atipik glandüler hücreler

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