Neuroendocrıne Small Cell Carcinoma of the Endometrium: A Case Presentation

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To present a case of neuroendocrine differentiated small cell carcinoma of the endometrium with postmenopausal bleeding and its clinical, histological and immunohistochemical features are discussed. A 54-year-old woman (gravida 4, para 1), admitted to our clinic with a chief complaint of postmenopausal bleeding for 1 months. She has been in menopause for 10 years. On pelvic examination, she had 3 months-sized, firm, large, hard, and anteverted uterus. Cervicovaginal smear was normal. A subsequent endometrial curettage was suspicious for carcinoma. The patient underwent total abdominal hysterectomy with bilateral salpingooophorectomy and pelvic lymphadenectomy. Malignancy was confirmed from frozen section. The final pathology report confirmed neuroendocrine differentiated small cell carcinoma of the endometrium. The postoperative course was uneventful and the patient received chemotherapy including cisplatin and etoposide. These tumors have a propensity for systemic spread and poor prognosis; therefore, the stage of the tumor is an important prognostic factor. Early detection provides the only opportunity for long-term survival in patients with small cell carcinoma of endometrium.

Key Words: Endometrium, Small cell carcinoma, Neuroendocrine differentiation.

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Introduction

Small cell carcinoma is one of the most aggressive tumors that arise in the female genital tract. Although it occurs elsewhere, it is most commonly found in the cervix. Small cell carcinoma of the endometrium is extremely rare.[1] This tumor may exhibit evidence of neuroendocrine differentiation and has a high propensity for systemic spread and poor prognosis.[2]

The mean age for patients with small cell carcinoma of the endometrium is 60 years.[1] Common clinical findings are abnormal vaginal bleeding and pelvic pain. They may produce and secrete a variety of metabolically active substances (amines and peptides) and cause distinct clinical syndromes.[3]

Currently, the diagnosis of neuroendocrine tumors (NET) mainly relies on the positive assessment of markers of NE differentiation by immunohistochemistry. The mainstay of treatment is surgery.[3]

We present a case of neuroendocrine differentiated small cell carcinoma of the endometrium with postmenopausal bleeding and its clinical, histological and immunohistochemical features are discussed.

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Case Presentation

A 54-year-old woman (gravida 4, para 1), admitted to our clinic with a chief complaint of postmenopausal bleeding for 1 months. . She had been in menopause for 16 years. In her medical history she had hypertension and hypertyroidism. On physical examination, she had 3 months-sized, hard, firm, and anteverted uterus. Direct inspection did not reveal cervical mucosal abnormalities. On transvaginal ultrasonography uterus was 91x95x99 mm sized and endometrial thickness was 7.8 mm. There was no mass lesion in uterus and the overies were atrophic. The cervicovaginal smear was normal, endometrial biopsy result was suspicious for carcinoma of the small cell type. Tumor markers were all in normal ranges. The patient underwent a total abdominal hysterectomy, bilateral salpingo-oophorectomy, and pelvic lymph node dissection.

On gross examination, the uterus was 3 months-sized, firm, large, hard and overies were atrophic. Malignancy was confirmed from frozen section. The final pathology report confirmed small cell carcinoma of the endometrium The tumor involved the full thickness of the myometrium and extended to the uterine serosa. On macroscopic examinations, the uterus was bulky, hard and histopathologically, the tumor had invaded the endometrium, myometrium and serosa of uterus and the case was solely small cell. Lymphovascular invasion, lymph node and ovarian metastases were observed. Tumor cells had infiltrated the parametrium on both sides

Histologically, tumor cells were round, without significant pleomorphism, hyperchromatic nuclei, ill-defined cytoplasm and separated by fibrous bands, high mitotic rate and zonal necrosis (Figure 1). The patient was surgically staged as IIIC1 (Current FIGO). Immuno-histochemical staining for neuron-specific enolase, synaptophysin, LMW-cytokeratin and S-100 was positive in tissue sections (Figure 2). Vimentin, CD 20, CD 99, CD 10, glial fibrillary acid protein, common leukocyte antigen and chromogranin were negative.

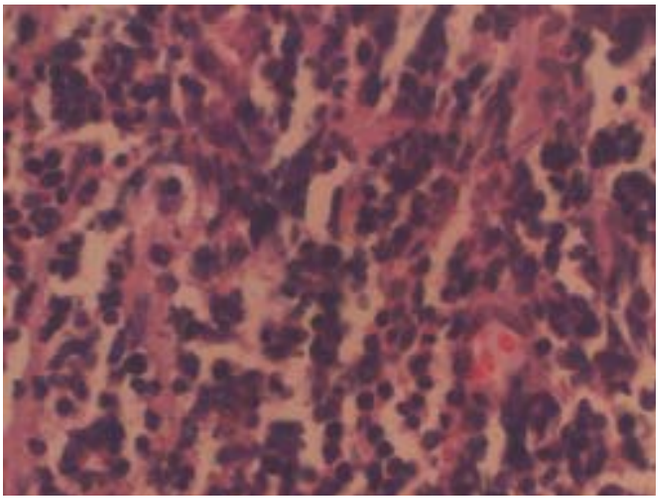

Figure 1: Histopatology of small cell carcinoma of the uterus with hematoxylin-eosin staining: a lot of small cells monotonously proliferate and the tumor cells have hyperchromatic round nuclei and scanty cytoplasm (X100).

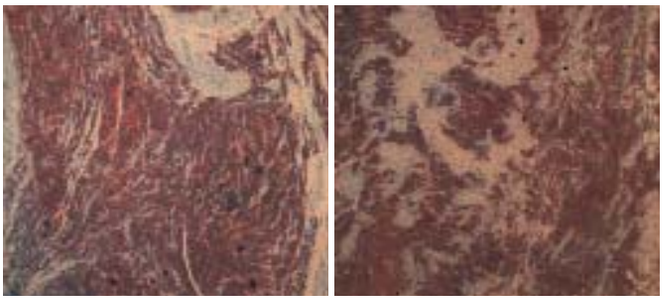

Figure 2: Immunohistochemical profile of the tumor. NSE immunoreactivity is detected in tumor cells. (right). Synaptophysin immunoreactivity is observed in tumor cells (left). (X4 right, X4 left)

Three months later at the first control visit, thorax tomography was normal, , implants of 1cm size were observed in the pelvic area in abdominopelvic tomography. The patient was scheduled for chemotherapy in form of cisplatin and etoposide.

Discussion

Squamous cell carcinoma is reported most often in the uterine cervix and the ovary, it occurs very rarely in vagina and endometrium.[3] Primary small cell carcinoma of the endometrium (SCCE) is a rare entity that represents only 0.8% of the endometrial cancers.3 This tumor may exhibit evidence of neuroendocrine differentiation and has a high propensity for systemic spread and poor prognosis.[2] Neuroendocrine (NE) SCCE is a very rare disease.[3]

Clinical presentations include postmenopausal bleeding, lower abdominal mass, chronic abdominal pain and menorrhagia.[4] Our patient presented with postmenopausal bleeding, no pelvic pain or abdominal mass.

Small cell neuroendocrine carcinomas are found in pure form or combined with endometrioid adenocarcinoma, adenosquamous carcinoma, or malignant mullerian mixed tumors. The aggressive clinical behavior of these endocrine neoplasms has been well documented. In this case, the presence of another accompanying tumor could not be determined.

In a series of ten cases of SCCE, Hoeven et al. have reported that on macroscopic examination, most of the tumors were bulky and the intraluminal masses invaded at least half of the myometrial wall.3.5 Majority of the SCCE were admixed elements of mostly adenocarcinoma (five), adenosquamous carcinoma (two), or heterologous mesodermal-mixed tumor (one). Only two of the cases were solely small cell.

In the case series presented by Huntsman et al. they found sheets, cords, and nests of small or intermediate-sized cells with scanty cytoplasm, hyperchromatic nuclei, and a high mitotic rate on microscopic examination.[6] Single-cell and zonal necrosis and vascular invasion were typically present.

In our case, histologically, tumor cells were round, without significant pleomorphism, hyperchromatic nuclei, ill-defined cytoplasm and separated by fibrous bands, high mitotic rate and zonal necrosis. The patient was surgically staged as IIIC1 (FIGO).

The following diagnostic criteria for SCC of the endometrium have been proposed: 1) unequivocal evidence of endometrial origin, 2) dense sheet-like growth of morphologically similar small to intermediate- sized tumor cells in standard hematoxylin and eosin-stained sections, and 3) immunohistochemical staining for one or more neuroendocrine markers (NE).[7]

The most commonly used markers are general NE markers (applicable to all NE cells) either in the cytosol such as NSE (neuron-specific enolase) or in the granular markers such as chromogranin A (CgA) and synaptophysin. In immunohistochemical studies, high frequency of reactivity for NSE has been detected in 79% of SCCE cases; positive rates for other NE markers synaptophysin and CgA are 42% and 38%, respectively.[8] In our case, Immuno-histochemical staining for neuron-specific enolase, synaptophysin, Pancytokeratin and

S-100 was positive in tissue sections. Vimentin, CD 20, CD 99, CD 10, glial fibrillary acid protein, common leukocyte antigen and chromogranin were negative.

Clinical reports are limited to only case studies; therefore, clinical behavior and optimal treatment modalities are not well defined. The standard modality of treatment is like in endometrial carcinoma, and it consists of aggressive surgical resection, radiation therapy, and hormonal treatment followed by chemotherapy at the time of progression.[3]

In this case; our patient, underwent total abdominal hysterectomy with bilateral salpingooophorectomy and pelvic lymphadenectomy. At the first control visit, in abdominopelvic tomography there were tumoural implantations in pelvic area. Because of this, the patient received chemotherapy including cisplatin and etoposide.

These tumors have a propensity for systemic spread and poor prognosis; therefore, the stage of the tumor is an important prognostic factor.[3] Early detection provides the only opportunity for long-term survival in patients with small cell carcinoma of endometrium.1 Immunohistochemical analyses are helpful in diagnosing and differentiating primary Neuroendocrine (NE) small cell carcinoma of the endometrium from benign and malignant diseases of the endometrium.[9]

Endometriumun Nöroendokrin Küçük Hücreli Karsinomu: Olgu Sunumu

Postmenopozal kanamalı bir olguda endometriumun nödoendokrin differensiasyon gösteren küçük hücreli karsinonomunun kliniği, histolojik ve immünhistokimyasal özellikleri sunulması. 54 yaşında bayan hasta (gravida 4, para 1), 10 yıldır menopozda olup, 1 aydır devam eden postmenopozal kanama şikayeti ile kliniğimize başvurdu. Pelvik muayenesinde, 3 aylık cesamette sert, büyük ve antevert uterus palpe edildi. Servikovajinal smear normal ve endometrial küretaj sonucu ise karsinom açısından şüpheli olarak geldi. Hastaya total abdominal histerektomi-bilateral salpingoooferektomi ve pelvik lenfadenektomi yapıldı. Frozen sonucu malignite olarak doğrulandı. Son patolojisi endometriumun nöroendokrin differansiasyon gösteren küçük hücreli karsinomu olarak rapor edildi. Postoperatif dönem sorunsuz olup, hastaya cisplatin ve etoposid kemoterapisi verildi. Bu tümör sistemik yayılıma eğilimli ve kötü prognozludur, bu sebeple tümörün evresi en önemli prognostik faktördür. Endometriumun küçük hücreli karsinomu olan hastalarda erken teşhis uzun süreli sağkalım için tek şanstır.

Anahtar Kelimeler: Endometrium, Küçük hücreli karsinom, Nöroendokrin differansiasyon.

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