Small cell carcinoma of the endometrium: A report of three cases

Endometriyumun küçük hücreli karsinomu: Üç vakanın sunumu

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Abstract

Small cell carcinoma (SCC) is a tumour that occurs mostly in the lung, but may be found in any organ in the body. Since SCC of the endometrium is rare, clinical behaviour and management of the disease is not well-defined. The only known prognostic factor is the stage of the disease. Here, we reported three patients with SCC of the endometrium, their management and the follow-up period.

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Key words: Small cell carcinoma, endometrium, chemotherapy

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Özet

Küçük hücreli karsinom vücutta her organda görülebilir, ancak en sık akciğerde bulunur. Endometriyumun küçük hücreli karsinomu nadir görüldüğü için klinik davranışı ve tedavisi net tanımlanmış değildir. Bilinen tek prognostik faktör hastalığın evresidir. Bu yazıda endometriyumun küçük hücreli karsinomu olan üç hastayı, tedavisini ve takip sürecini sunduk. (J Turkish-German Gynecol Assoc 2013; 14: 113-5)

Anahtar kelimeler: Küçük hücreli karsinom, endometriyum, kemoterapi

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Introduction

Small cell carcinoma (SCC) is a tumour that occurs mostly in the lung, but may be found in any organ of the body. The cervix is the most common site in the female genital tract, whereas SCC of the endometrium is quite rare (1). To our knowledge, 80 cases of small cell carcinoma of the endometrium have been reported up to now. Since it is rare, clinical behaviour and management of the disease is not well-defined. It has a more miserable course compared to the endometrioid carcinoma of the endometrium, which is diagnosed at an advanced stage and has a poor prognosis (2). Here, we reported three patients with SCC of the endometrium and their management, one of which had an unusual course.

Case Reports

Case 1

A 52-year-old G3/P3 woman presented with postmenopausal vaginal bleeding. Her medical history was unremarkable. Pathological evaluation of her endometrial biopsy specimen revealed a poorly differentiated adenocarcinoma. Her preoperative Ca-125 was 42. During surgery, frozen section analysis of the total abdominal hysterectomy and bilateral salphingo-oophorectomy specimen was reported as an 11x6x5 cm polypoid tumour filling the entire endometrial cavity that may be uterine sarcoma or a malignant mix mullerian tumour. Therefore, bilateral pelvic and paraaortic lymph node dissection up to the left renal vein and total omentectomy were performed. Final histological examination of the specimen showed SCC of the endometrium; stage IC (International Federation of Gynaecology and Obstetrics staging [FIGO], 1988). The tumour was characterised by atypical small cells with scant cytoplasm, and some with salt and pepper chromatin configuration, forming glandular and cribriform structures (Figure 1). Immunohistochemically, the tumour cells were strongly and diffusely positive for neurone-specific enolase (NSE), strongly and focally positive for pancytokeratin and low-molecular weight keratin (LMWCK) and negative for synaptophysin, chromogranin A and S100 (Figures 2-4). She received six cycles of chemotherapy with cisplatin (80 mg/m^2, first day) and etoposide (120 mg/m^2, first three days) every 21 days. Following chemotherapy, she received external radiotherapy. Since then, the patient has been followed-up without evidence of disease for 58 months.

Case 2

A 35-year-old G1/P1 woman presented with abnormal vaginal bleeding. Her medical history was unremarkable. Pathological evaluation of her endometrial biopsy specimen revealed poorly differentiated adenocarcinoma. Her preoperative Ca-125 was 10. Total abdominal hysterectomy, bilateral salphingo-oophorectomy, bilateral pelvic and paraaortic lymph node dissection

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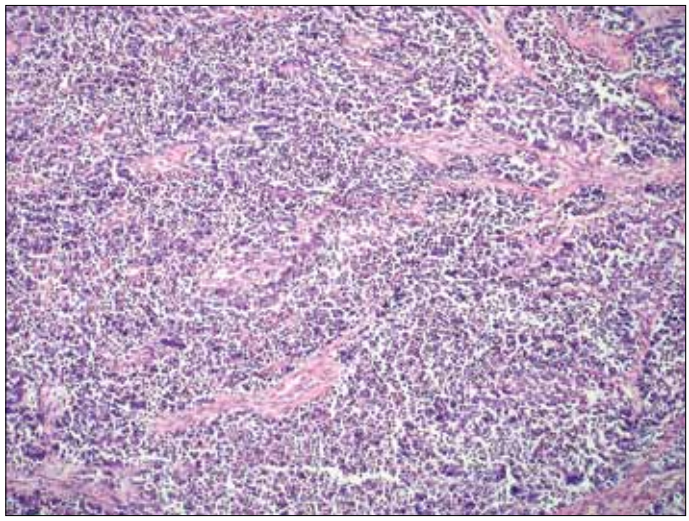

Figure 1. Small Cell Carcinoma: Atypical round small cells with scant cytoplasm and unnoticeable nucleolus; some have a salt and pepper chromatin configuration showing a diffuse growth pattern. (HEx40)

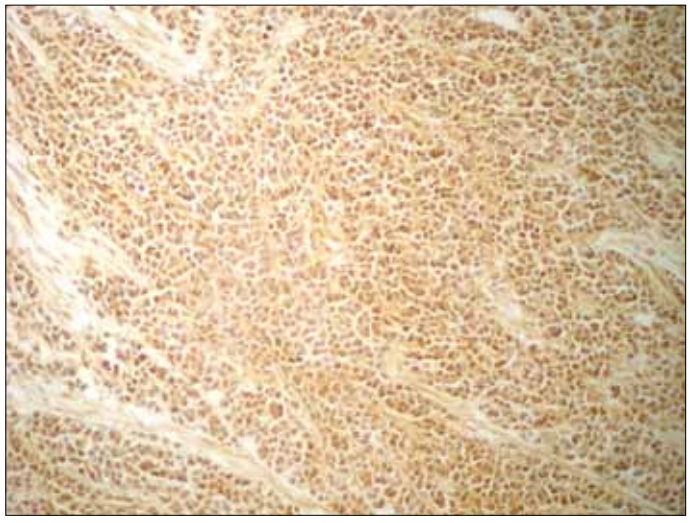

Figure 2. Small Cell Carcinoma: The tumour cells were strongly and diffusely positive for neuron-specific enolase (NSE) (x200)

up to the left renal vein and total omentectomy were performed. Final histological examination of the specimen showed undifferentiated endometrioid carcinoma of the endometrium with neuroendocrine differentiation; this was considered stage IIIC (FIGO 1988), since there was pelvic lymph node involvement. The details of immunohistochemical staining could not be obtained. She received pelvic radiotherapy and six cycles of chemotherapy with cisplatin (75 mg/m^2) and adriamycin (50 mg/m^2) following radiotherapy. She has been free of disease for 13 years.

Case 3

A 45-year-old G3/P2 woman presented with abnormal vaginal bleeding. Her medical history showed mitral stenosis, mitral insufficiency and tricuspid insufficiency. Pathological evaluation of her endometrial biopsy revealed undifferentiated carcinoma. Her preoperative Ca-125 was >500 IU/mL. During surgical exploration, massive ascites, a 100x100 mm

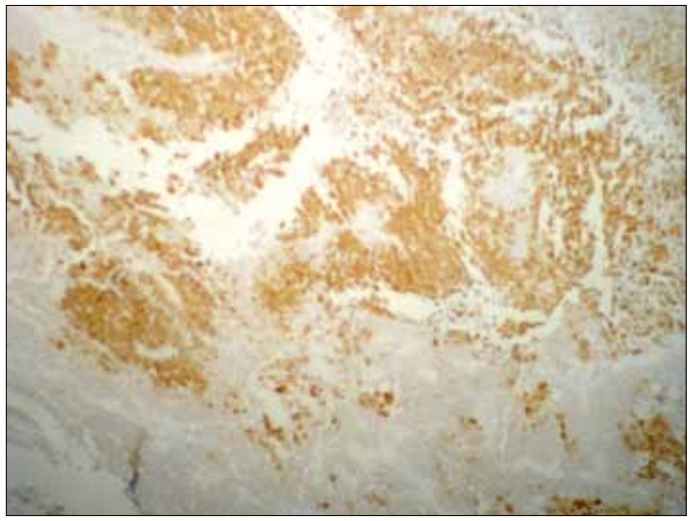

Figure 3. Small Cell Carcinoma: The tumour cells were strongly and focally positive for pancytokeratin (x100)

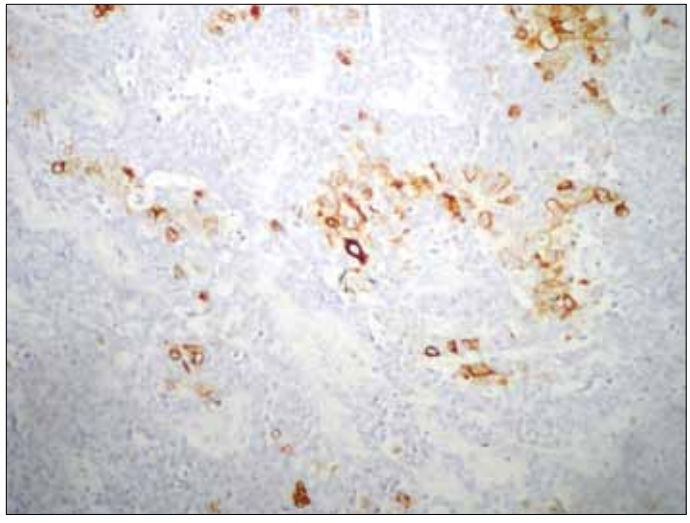

Figure 4. Small Cell Carcinoma: The tumour cells were focally positive for low-molecular weight keratin (LMWCK) (x200)

hemorrhagic omental mass that was adherent to the transverse colon, a 60x60 mm semi-solid metastatic mass in the right lower quadrant, and multiple tumoural implants up to a size of 30x30 mm on the intestinal serosal surfaces were observed. Maximal debulking was achieved by performing a type 2 hysterectomy, bilateral salphingo-oophorectomy, bilateral pelvic and paraaortic lymph node dissection up to the left renal vein, total omentectomy, and mass extraction from serosal surfaces of intestines. Pathological evaluation showed grade III endometrial carcinoma with a small cell carcinoma component, myometrial invasion, bilateral ovarian involvement, metastasis on the omentum, metastasis in the right pelvic lymph nodes and metastasis on the intestinal serosal surfaces, indicating a stage IVB endometrial carcinoma (FIGO 1988). The details of immunohistochemical staining could not be obtained. She received three cycles of chemotherapy with endoxan (1000 mg/m^2), doxorubicin (50 mg/m^2) and vincristine (1 mg/m^2). After the third cycle of chemotherapy, a 2 cm mass in the cuff

was detected upon vaginal examination. Her control abdominal tomography revealed multiple metastatic masses including spleen and liver, since her thorax tomography did not show any pathology. Concurrently, she was diagnosed with a right femoral vein embolism and underwent embolectomy. Since the disease progressed during chemotherapy, she was considered to be refractory to chemotherapy and her chemotherapy treatment was changed. She received three cycles of cisplatin (80 mg/m^2, first day) and etoposide (120 mg/m^2, first three days) every 21 days. She died of the disease seven months after surgery, following the third cycle of chemotherapy.

Discussion

SCC is a rare tumour of the endometrium with a prevalence of 1% of all endometrial carcinomas (2). The mean age of patients presenting with SCC of the endometrium is 60 years (1); however, our patients were younger. The most common complaint is abnormal vaginal bleeding (3), similar to endometrioid endometrial carcinoma. The diagnosis of SCC of the endometrium needs evidence of endometrial origin, dense sheet-like growth of morphologically similar small tumour cells and immunohistochemical staining for at least one neuroendocrine marker (4). Some of the most common neuroendocrine markers that have been reported to be positive in these tumours are NSE, synaptophysin, chromogranin A and cytokeratin (1, 5, 6). In the first case, the tumour cells were strongly and diffusely positive for NSE, strongly and focally positive for pancytokeratin and LMWCK and negative for synaptophysin, chromogranin A and S100.

Polypoid feature was suggested to be a good prognostic factor for small cell carcinoma of the endometrium in the study by Albores-Saavedra et al. (7), although the series was small. In the first case, the tumour was polypoid, but related data of the second and third cases could not be obtained.

Small cell carcinoma of the endometrium may accompany other types of endometrial carcinoma, most commonly endometrioid and adenosquamous types (2, 4, 8, 9), with similar prognoses in comparison with sole SCC of the endometrium. SCC of the endometrium may be rarely associated with paraneoplastic syndromes. These may be seen as Cushing syndrome, hypoglycaemia, visual disturbances and membranous glomerulonephritis (7), whereas a specific syndrome has not been defined peculiar to SCC of the endometrium. There were no symptoms of paraneoplastic syndrome in the three cases presented here.

Among the 80 cases of endometrial SCC that have been reported up to now, more than half of the patients with available data had stage III and IV disease (6). Two of the patients reported here had stage III and IV disease. Due to the rarity of SCC of the endometrium, management of the disease is not well-established. Actually, most of the information about the management of this cancer comes from SCC of the lung, since the behaviour of this tumour is similar. Recently, Matsumoto et al. (1) analysed the patients diagnosed up to now. What has been learned from the cases in the literature is that if diagnosed earlier, the prognosis of this cancer is better than cases with advanced disease (1). Since SCC has an aggressive growth pattern and a tendency for systemic metastasis wherever it occurs, systemic chemotherapy for metastasis and radiotherapy for local control seem logical, certainly following surgery. In terms of chemotherapy, the combination of cisplatin and etoposide has been most widely used, and it is also the preferred regimen for SCC of the lung.

The only known prognostic factor is the stage of disease. The patient in the first case had a stage IC tumour and she was free of disease for 58 months in accordance with the literature. The third case had a stage IVB tumour and died of the disease seven months after surgery. The second case does not have any evidence of disease 13 years after diagnosis, which is surprising considering that she had stage IIIC disease identified at diagnosis. More patients and more data are required to define the prognostic factors and to form a general treatment modality for SCC of the endometrium.

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References

1. Matsumoto H, Takai N, Nasu K, Narahara H. Small cell carcinoma of the endometrium: a report of two cases. J Obstet Gynaecol Res 2011; 37: 1739-43. [CrossRef]
2. Huntsman DG, Clement PB, Gilks CB, Scully RE. Small-cell carcinoma of the endometrium. A clinicopathological study of sixteen cases. Am J Surg Pathol 1994; 18: 364-75. [CrossRef]
3. Katahira A, Akahira J, Niikura H, Ito K, Moriya T, Matsuzawa S, et al. Small cell carcinoma of the endometrium: report of three cases and literature review. Int J Gynecol Cancer 2004; 14: 1018-23. [CrossRef]
4. Van Hoeven KH, Hudock JA, Woodruff JM, Suhrland MJ. Small cell neuroendocrine carcinoma of the endometrium. Int J Gynecol Pathol 1995; 14: 21-9. [CrossRef]
5. Kurtay G, Taşkin S, Kadan E, Sertçelik A. Primary endometrial small cell carcinoma. J Obstet Gynaecol 2012; 32: 104-6. [CrossRef]
6. Korcum AF, Aksu G, Ozdogan M, Erdogan G, Taskin O. Stage I small cell carcinoma of the endometrium: survival and management options. Acta Obstet Gynecol Scand 2008; 87: 122-6. [CrossRef]
7. Albores-Saavedra J, Martinez-Benitez B, Luevano E. Small cell carcinomas and large cell neuroendocrine carcinomas of the endometrium and cervix: polypoid tumors and those arising in polyps may have a favorable prognosis. Int J Gynecol Pathol 2008; 27: 333-9. [CrossRef]
8. Manivel C, Wick MR, Sibley RK. Neuroendocrine differentiation in Müllerian neoplasms. An immunohistochemical study of a 'pure' endometrial small-cell carcinoma and a mixed Müllerian tumor containing small-cell carcinoma. Am J Clin Pathol 1986; 86: 438-43.
9. Shaco-Levy R, Manor E, Piura B, Ariel I. An unusual composite endometrial tumor combining papillary serous carcinoma and small cell carcinoma. Am J Surg Pathol 2004; 28: 1103-6. [CrossRef]