The oncologic outcomes of endometrial cancer metastasizing to the adrenal gland and kidney: from case to analysis

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Abstract

Objective: To evaluate the oncologic outcomes of endometrial cancer metastasis to the adrenal gland and kidney, based on a case study and review of the literature.

Material and Methods: A systematic review of the medical literature was performed to identify articles about metastatic endometrial cancer to the adrenal gland and kidney from 1975 until 2021.

Results: A 55-year-old female patient was admitted to our center. On pelvic examination, a mass protruding out of the cervix was observed, which was shown to be endometrioid carcinoma on biopsy. Disease stage was IVB, based on radiological and pathological results and the International Federation of Gynecology and Obstetrics 2018 staging. Neo-adjuvant chemotherapy was given. After therapy, the patient underwent type 2 hysterectomy, bilateral salpingo-oophorectomy, total omentectomy and lymph node dissection. Left nephrectomy, left adrenalectomy and left hemicolectomy were also performed because the conglomerate tumor invaded the left kidney, left adrenal gland, and left colon mesentery. Pathological findings were consistent with metastasis of endometrioid carcinoma in the left adrenal gland, left kidney parenchyma and hilum.

Conclusion: Metastasis of endometrial cancer to the adrenal gland and kidney is extremely rare and metastasis to the kidney has been reported in only two previous cases. When there is an intraperitoneal spread of endometrial cancer, as well as ovarian cancer, cytoreductive surgery without leaving a residual tumor should be undertaken andshould include adrenalectomy and nephrectomy, if necessary. (J Turk Ger Gynecol Assoc 2023; 24: 172-6)

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Introduction

Endometrial cancer is the most common gynecological cancer in developed countries (1). Epithelial malignant neoplasms are the most frequent malignant neoplasms of the endometrium (approximately 80%). Although most cases are detected at an early stage, 3-13% of patients are diagnosed with stage IV disease (2). The estimated 5-year survival rate for stage IVB endometrial cancer according to the International Federation of Gynecology and Obstetrics (FIGO) is around 15% (3).

Aggressive histological subtypes also have a worse prognosis with serous and clear cell types having a worse prognosis than the endometrioid type (4). In a study in which the SEER database results were analysed, distant organ metastases were reported in 39.1% of patients with FIGO stage IVB endometrial cancer (5). Non-lymphatic distant metastases are most common in the lungs, and spread to the adrenal gland and kidney is extremely rare. To the best of our knowledge, to date, there have been only two reports of endometrial cancer spreading to the kidney. In this case report, we describe a patient with metastasis

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of endometrial cancer to the adrenal gland and kidney. In addition, the limited literature is reviewed.

Material and Methods

A systematic review of the medical literature was performed to identify articles about metastatic endometrial cancer to the adrenal gland and kidney. The electronic database search was conducted between the years 1975 and 2021 using PubMed/MEDLINE for English language abstracts. The search included metastatic endometrial cancer, adrenal metastasis from endometrial cancer, renal metastasis from endometrial cancer, renal metastasis, and metastatic tumours of the adrenal glands under medical subject headings or keywords. The study protocol was reviewed and approved by University of Health Sciences Turkey, Ankara City Hospital Ethics Committee (approval: E2-22-2358, date: 07.09.2022).

At the end of the search, 14 articles were eligible for further analysis. In accordance with these cases, and in conjunction with our case, 16 cases were evaluated for this study.

Statistical analysis

All statistical analyses were performed using the Statistical Package for the Social Sciences for Windows, version 22.0 (IBM Inc., Armonk, NY, USA). Descriptive values are expressed as arithmetic mean ± standard deviation, median and percent.

Results

Case Presentation

A 55-year-old female patient was admitted to our center with the complaint of vaginal bleeding. On pelvic examination, a mass protruding out of the cervix was observed. The physical examination was unremarkable. The results of complete blood count, kidney and liver function tests, and coagulation parameters were all normal. Among the tumor markers, CA125 107.4 IU/mL (normal <30), CA15-3 34.6 IU/mL (normal <32), and CA19-9 65.1 IU/mL (normal <30) were all high. Other tumor markers were normal. The biopsy of the mass protruding from the cervix was compatible with endometrioid carcinoma. F-18 fluorodeoxyglucose (FDG) positron emission tomography (PET)/computed tomography (CT) imaging revealed a 70x68x101 mm mass in the left adnexal area with indistinguishable borders from the uterus with a standardized uptake value (SUV_{max}) of 8.55. Involved lymph nodes were also observed in the left supraclavicular region (10x8 mm, SUV_{max} 4.63), in the paratracheal region (25x21x34 mm, SUV_{max} 10.96), and in the left paraaortic region (52x47 mm, SUV_{max} 12.33). The mass in the left paraaortic region invaded the left adrenal gland, left renal pelvis, and renal parenchyma (Figure 1). Fine needle aspiration biopsy of the left supraclavicular lymph node was consistent with endometrial carcinoma metastasis. The disease stage was IVB, based on radiological and pathological results and FIGO 2018 staging. Neo-adjuvant chemotherapy was administered to the patient. Supraclavicular and paratracheal lesions were not observed in the comparative analysis of FDG PET/CT performed after three cycles of carboplatin-paclitaxel chemotherapy, but the lesion in the left paraaortic region persisted. The decision to perform surgery was made by the gynecological-oncology team.

Under general anesthesia, the abdomen was entered through a midline incision from the xiphoid process to the pubis. In the intraoperative observation, peritoneal implants, bulky pelvic and paraaortic lymph nodes, and a 20 cm conglomerate mass including the uterus, left adnexa, and sigmoid colon were observed. Furthermore, a 10 cm mass was observed invading the inferior mesenteric artery and vein on the left side of the aorta, surrounding the renal vessels, and invading the left kidney and left adrenal gland. The patient underwent type 2 hysterectomy, bilateral salpingo-oophorectomy, total omentectomy, bilateral pelvic and paraaortic lymph node dissection. Left nephrectomy, left adrenalectomy and left hemicolectomy were also performed because the conglomerate tumor invaded the left kidney, left adrenal gland, and left colon mesentery (Figure 2). The operation was terminated with maximal cytoreduction. Intraoperative blood loss was approximately 1500 cc, and the operation lasted for about seven hours. The patient was discharged after six days without any early postoperative complications. The postoperative pathology was reported as grade 3 endometrioid carcinoma of the endometrium. The tumor size was 8x4x4 cm. Deep myometrial invasion, lymphovascular space involvement and cervical spread were observed. Histopathological findings were consistent with metastasis of endometrioid carcinoma in the left ovary, left adrenal gland, left kidney parenchyma and hilum, and pelvic and paraaortic lymph nodes (Figure 3, 4). The disease progressed one month after surgery. Unfortunately, the patient died due to disease progression before adjuvant therapy at four months after surgery.

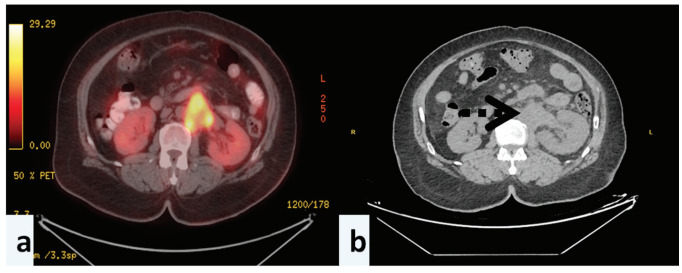

Figure 1. a) PET/CT scan of abdomen showing left adrenal mass in the left paraaortic region invaded the left adrenal gland, left renal pelvis and renal parenchyma; b) CT image of the same lesion

PET/CT: Positron emission tomography/computed tomography

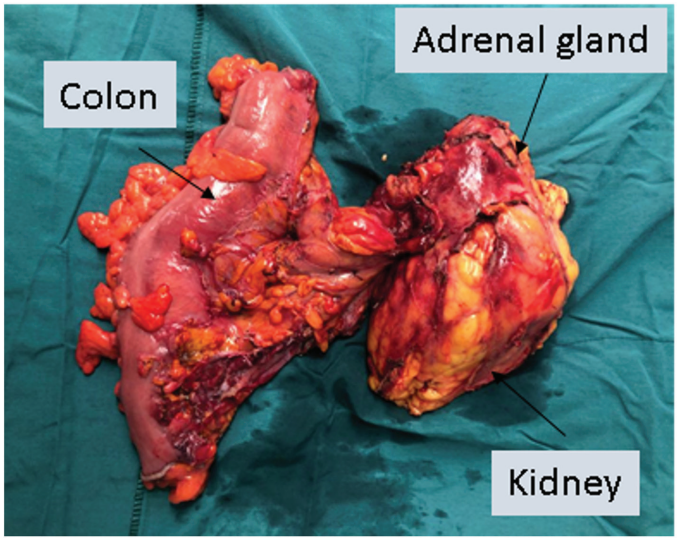

Figure 2. Surgical specimen of the left kidney, left adrenal gland, and left colon

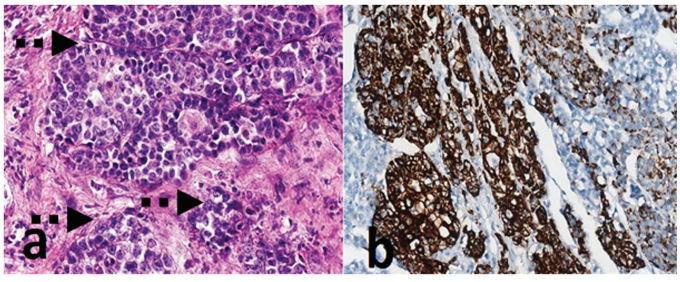

Figure 3. a) Tumoral areas in the adrenal (hematoxylin-eosin, x400); b) CK8-18 positivity in adrenal tumoral areas (x400) (tumor areas are marked with arrows)

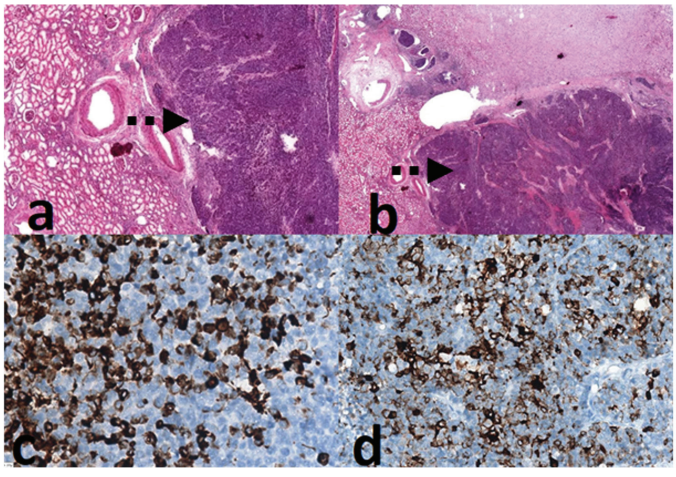

Figure 4. a) Tumoral areas in the kidney (hematoxylin & eosin, x400); b) Tumoral areas in the kidney with vascular tumor embolisms (hematoxylin & eosin, x100); c) CK8-18 positivity in renal tumoral areas (x400); d) Vimentin positivity in tumoral areas in the renal specimen (x400) (tumor areas are marked with arrows)

Discussion

In this case, a patient with endometrial cancer who had metastasis to the adrenal gland and kidney at the time of the diagnosis is described. Endometrial cancer spreads locally as well as through the lymphatic and vascular systemic circulation. Locally, it spreads mostly to the cervix, vagina, bladder and bowel. Rarely, hematogenous distant organ metastasis may also occur (6). The lung is the most common distant metastatic site. Having a distant metastatic site predicts overall survival (5). In the study of Blecharz et al. (7), in which 1,610 patients with hematogenous metastases were examined, 5-year survival rates were found to range from 0.6% to 7.2%. Survival rates also vary according to the location and the number of distant metastases (5).

Endometrial cancer that spreads to the adrenal gland is rare (8-11) and, to date, a total of 15 cases have been described (9,10,12) (Table 1). Twelve out of 15 cases presented with metachronous metastasis, while three had synchronous metastasis. Synchronous metastasis describes a concurrent tumor elsewhere, while metachronous metastasis describes a newly developing tumor after treatment. In the presented case, adrenal metastasis was also synchronous. When the tumor types of the patients in the literature were examined, endometrioid type was reported in nine patients, serous type in one patient, squamous type in one patient, dedifferentiated in one patient and mixed type in two patients (9,10,12). The patient in the presented case also had endometrioid type adenocarcinoma.

The described patient received three cycles of chemotherapy before surgery, and adjuvant therapy was planned after surgery but the disease progressed one month after surgery and the patient died before adjuvant therapy at four months after surgery. When the post-surgical management of the 15 patients in the literature was examined, the adjuvant treatment data was available for nine patients. Of these, seven were given chemotherapy as adjuvant therapy, and two were given external beam radiation therapy. Similar to our patient, adrenal metastases in patient 7, 14, and 15 (Table 1) were synchronous. However, there is insufficient data about survival in patients with these synchronous metastases. Similar to our patient, adrenalectomy was performed on patient 7 in primary cytoreduction but not performed in patient 14 or patient 15. Patient 15 underwent hysterectomy with bilateral salpingo-oophorectomy and adjuvant therapy was started after surgery. Due to the progression of the disease, patient 15 died in the sixth month after diagnosis before chemotherapy was completed. In the presented case, recurrence was observed in the first month, and the patient died in the fourth month.

Although the majority of adrenal metastases are asymptomatic, they may cause adrenal insufficiency depending on the size of the tumor and the extent to which it affects the adrenal gland (13). There were no signs of adrenal insufficiency in the present case despite the tumor being large. Diagnosis of adrenal metastases may be difficult with CT and magnetic resonance imaging examinations. Even though PET/CT isn't always recommended for endometrial cancer, it can help identify metastases in the adrenal glands (14).

Metastasis to the kidney was also present in the presented patient. Metastasis of endometrial carcinoma to the kidney is extremely rare and was described in only two previous case reports in the literature search (15,16). In one of these cases, a woman who underwent surgery for endometrial adenocarcinoma 24 years previously had recurrence in the kidney (15). After two-years of follow-up, it was highlighted that she remained alive. In the second case, a patient with uterine serous carcinoma and synchronous kidney metastases was reported (16).

In a study of 2,948 patients with stage IVB endometrial cancer, renal metastases were not identified (5). In another study examining kidney metastasis by Choyke et al. (17), the data of 27 patients was analyzed and no endometrial cancer was reported in these patients. Choyke et al. (17), reported, the most common types of cancer metastasis to the kidney were from lung and colon neoplasia, and the effect of renal metastasis on the survival of the patients was not reported.

Conclusion

Metastasis of endometrial cancer to the adrenal gland and kidney is extremely rare and metastasis to the kidney has been reported in only two earlier cases in the literature. These metastases to the adrenal gland and kidney may occur in patient management and care should be taken in terms of areas that may recur in patient follow-up. When there is an

Table 1. Patients with adrenal metastases from endometrial cancer on literature review

Author	Patient no	Age	Histology of primary	Adrenal metastasis	Stage	Adjuvant treatment	F-U (month)
Nakano and Schoene (18)	1	77	Mixed (clear cell + squamous)	Metachronous	NR	NR	28
Lam and Lo (19)	2	NR	NR	Metachronous	NR	NR	NR
Baron et al. (20)	3	76	Endometrioid	Metachronous	IVB	EBRT	24
	4	62	Endometrioid	Metachronous	NR	VBT + chemotherapy (adriamycin + cisplatin; 6 cycles)	110
Izaki et al. (21)	5	55	Endometrioid	Metachronous	IIIC	Chemotherapy (carboplatin + paclitaxel; 7 cycles)	82
Choi et al. (22)	6	62	Mixed (squamous + mucinous)	Metachronous	IIIC	Chemotherapy (cisplatin; 6 cycles)	45
Berretta et al. (11)	7	67	Mixed (anaplastic + endometrioid)	Synchronous	IVB	NR	NR
Zaidi et al. (8)	8	75	Endometrioid	Metachronous	IB	NR	9
Singh Lubana et al. (23)	9	60	Serous	Metachronous	II	EBRT + Chemotherapy (carboplatin + paclitaxel; 3 cycles)	90
Rekhi (24)	10	39	Endometrioid	Metachronous	II	VBT+EBRT	NR
Mouka et al. (25)	11	58	Endometrioid	Metachronous	IB	Chemotherapy (6 cycles)	NR
Da Dalt et al. (9)	12	53	Endometrioid	Metachronous	IIB	NR	45
Coward et al. (26)	13	62	Endometrioid	Metachronous	IB	NR	9
Ryan et al. (10)	14	68	Endometrioid	Synchronous	IVB	Chemotherapy (carboplatin + paclitaxel; 6 cycles)	6
Shiraishi et al. (12)	15	50	Dedifferentiated (undifferentiated + endometrioid)	Synchronus	IVB	Chemotherapy (carboplatin + paclitaxel; 4 cycles)	6
Present case	16	55	Endometrioid	Synchronous	IVB	no	4

NR: Not reported, EBRT: External beam radiation therapy, VBT: Vaginal brachytherapy, F-U: Follow-up

intraperitoneal spread of endometrial cancer, as in ovarian cancer, cytoreductive surgery without leaving residual tumor should be performed, and should include adrenalectomy and nephrectomy, if necessary.

Ethics Committee Approval: *The study protocol was reviewed and approved by University of Health Sciences Turkey, Ankara City Hospital Ethics Committee (approval: E2-22-2358, date: 07.09.2022).*

Informed Consent: *Due to the retrospective nature of the study, the ethic comittee did not request informal consent.*

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