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**Adrenal metastasis from endometrial cancer: A case report**

Da Dalt G *et al*. Adrenal metastasis from endometrial cancer

Gianfranco Da Dalt, Alberto Friziero, Andrea Grego, Simone Serafini, Ambrogio Fassina, Stella Blandamura, Cosimo Sperti

**Gianfranco Da Dalt, Alberto Friziero, Andrea Grego, Simone Serafini, Cosimo Sperti,** Department of Surgery, Oncology and Gastroenterology, 3rd Surgical Clinic, University of Padua, Padua 35128, Italy

**Ambrogio Fassina, Stella Blandamura,** Department of Medicine, Surgical Pathology and Cytopathology, University of Padua, Padua 35128, Italy

**ORCID number:** Gianfranco Da Dalt (0000-0002-4246-9128); Cosimo Sperti (0000-0002-7869-8715); Alberto Friziero (0000-0003-0431-6566); Andrea Grego (0000-0002-7217-3184); Simone Serafini (0000-0001-8392-7714); Stella Blandamura (0000-0002-0466-6948); Ambrogio Fassina (0000-0002-5737-2249).

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**Corresponding author: Cosimo Sperti, MD, Professor,** Department of Surgery, Oncology and Gastroenterology, 3rd Surgical Clinic, University of Padua, via Giustiniani 2, Padua 35128, Italy. cosimo.sperti@unipd.it

**Telephone:** +39-49-8218845

**Fax:** +39-49-8218821

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**Abstract**

***BACKGROUND***

Metastases to adrenal glands originate principally from lung, breast, or gastrointestinal cancers, followed by malignant melanoma and thyroid neoplasms. We present an unusual case of uterine cancer metastasizing to the adrenal glands with a review of the English literature on the management of this rare disease.

***CASE SUMMARY***

A 53-year-old Caucasian woman with a history of endometrial cancer (grade 2; International Federation of Gynecology and Obstetrics III A) was hospitalized in November 2017 for a left adrenal mass found on a follow-up computed tomography scan 3years after her gynecological surgery. Laboratory test results were normal. A laparoscopic left adrenalectomy was performed. The postoperative course was uneventful, and no chemotherapy was administered. The pathological report confirmed an adrenal endometrioid metastasis. At 36 mo of follow-up, the patient is alive and well, with no evidence of recurrent disease. A literature review identified only 11 previously-published cases of adrenal metastases from uterine cancer.

***CONCLUSION***

Adrenal metastasis from uterine cancer is very rare. Laparoscopic adrenalectomy may be an effective treatment in selected cases of localized adrenal metastasis.

**Key words**: Adrenal gland; Adrenal neoplasms; Uterine cancer; Laparoscopy; Laparoscopic surgery; Case report

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**Core tip:** Isolated adrenal metastasis from endometrial cancer is uncommon but should be suspected in patients with history of gynecological cancer. We report a case of large, metachronous adrenal metastasis from endometrial cancer successfully treated with laparoscopic resection. Mini-invasive surgery is safe and feasible with good oncological results also for metastatic lesions of adrenal gland.

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**INTRODUCTION**

Secondary tumors are the second most common cause of adrenal cortex neoplasms, and carcinoma (especially in the advanced stage) accounts for more than 90% of secondary tumors[1]. In order of frequency, the most common primary sites of the metastatic carcinoma are: lung cancer, breast cancer, and gastrointestinal cancers, followed by malignant melanoma and thyroid neoplasms. The metastatic involvement of adrenal glands by endometrial carcinoma is rare, and there is some controversy over the most appropriate treatment due to the lack of specific guidelines. The prognosis for patients with secondary tumors involving the adrenal glands is generally poor, but survival rates seem to improve in some cases after surgical resection. The National Comprehensive Cancer Network (NCCN) guidelines on malignancies of the adrenal glands recommend a direct open approach, while laparoscopic adrenalectomy is the gold standard in Europe, and the open approach is reserved for masses more than 6-8 cm in diameter, cases of extra-adrenal tissue invasion, or patients with contraindications to laparoscopy[2,3].

We present an unusual case of metachronous uterine cancer metastasizing to an adrenal gland that was successfully treated with laparoscopic resection. A review of cases previously reported in the English literature was undertaken to ascertain what is currently known about the treatment of this unusual condition. A comprehensive search was run in PubMed (Medline) and Scopus as at December 2018 using the keywords: “adrenal gland neoplasms”, adrenal metastasis”, “uterine cancer”, “endometrial cancer”. The “related articles” function was used to widen the search and all abstracts, studies, and citations retrieved were reviewed.

**CASE PRESENTATION**

***Chief complaints***

A 53-year-old Caucasian woman was admitted in November 2017 for an adrenal mass.

***History of present illness***

In 2014 she had undergone total hysterectomy, bilateral oophorectomy and pelvic lymphadenectomy for a grade 2, International Federation of Gynecology and Obstetrics (FIGO) stage III A endometrioid endometrial cancer (EEC). Postoperatively, she was treated with six cycles of carboplatin-paclitaxel chemotherapy. She had no known family history of colon cancer, and endometrial cancer related to Lynch syndrome was ruled out.

***History of past illness***

The patient had a history of laparoscopic uterine myomectomy and tonsillectomy when she was younger.

***Physical examination***

Physical examination revealed abdominal tenderness with moderate palpation of the left mid-quadrant of the abdomen.

***Imaging examinations***

Computed tomography (CT) of the chest and abdomen revealed a solid left adrenal mass with malignant features (6 cm in diameter, with parenchymal invasion) (Figure 1).

***Laboratory examinations***

Laboratory test findings, including hormonal assays, were unremarkable.

**FINAL DIAGNOSIS**

Macroscopic examination of the resected specimen showed the left adrenal gland (7 × 4 × 3 cm) almost entirely substituted by a solid, off-white neoplastic mass (6.8 cm in largest diameter). Microscopic sections showed massive adrenal and peri-adrenal endometrioid metastasis (Figure 2). Immunohistochemical staining was positive for progesterone and estrogen receptors (Figure 3).

**TREATMENT**

Laparoscopic adrenalectomy was performed.

**OUTCOME AND FOLLOW-UP**

The postoperative course was uneventful and the patient was discharged 5 d after the surgical procedure. Two months later, 18-FDG positron emission tomography showed no pathological uptake, so no adjuvant therapy was administered. At the latest follow-up (December 2018), the patient was in good clinical condition with no recurrent disease.

**DISCUSSION**

Endometrial cancer is the most common gynecological cancer in developed countries. Most endometrial cancers are diagnosed at an early FIGO stage, and the most common histological type is EEC. These patients are generally considered at low risk, with 5-year survival rates of 95%; however, survival drop considerably to 69% and 13%, respectively, in the event of regional or distant metastases. Patients with endometrioid cancer in FIGO stages II to III, or with non-endometrioid cancer are at high risk of relapse[4]. The adrenal gland is a rare site of metastases from endometrial cancer. To our knowledge, only 11 previous cases have been reported in the English literature (Table 1), including: 8 cases of metachronous single-site metastases, 2 of metachronous multiple-site metastases, and one synchronous metastasis. Nakano *et al*[5] were the first to report a case of adrenal metastasis from endometrial cancer in 1975. On reviewing all the studies listed in Table 1: the patients’ median age was 62 years (range 39-77 years). There were two patients with FIGO stage I disease, two with FIGO stage II, two with FIGO stage III, and two with FIGO stage IV, while the stage was not stated in three cases. Six patients had an endometrioid histology, four had a non-endometrioid type, and no histology was available for one. When stratified according to the European Society of Medical Oncology 2016 Consensus Conference recommendations, nine patients were at high risk of recurrence or distant metastases[4].

In most cases, the adrenal lesions were identified on CT scans. Laboratory tests revealed no hormone overproduction in any of the patients.

Gynecological and oncological societies have no shared approach to the adjuvant treatment of “high-risk” endometrial cancer. While the value of external beam radiotherapy and/or vaginal brachytherapy for local recurrence control is accepted almost worldwide, any use of chemotherapy to prevent distant relapses is at the clinician’s discretion[15]. Our review identified seven cases treated with adjuvant therapy after gynecological surgery: 4 patients were administered radiotherapy at least; 3 were treated with chemotherapy alone.

Disease-free survival after hysterectomy naturally varied considerably, given the marked differences between the cases reviewed in terms of disease stage and grade, histology, and adjuvant therapy. It ranged from 6 mo to 108 mo with a median disease-free survival in the series of 15 mo.

The surgical approach to adrenal gland metastases is controversial. Following the NCCN guidelines, many authors treat adrenal metastases directly with open surgery[16], but laparoscopic adrenalectomy has been used successfully for a variety of secondary tumors[17,18].

Our review found that only three of eight cases of single-site adrenal metastases from endometrial cancer (5.7-7.5 cm in diameter) were treated mini-invasively (laparoscopy or robotic surgery). The largest tumor (7.5 cm in diameter) was treated by Rekhi *et al*[13] with robotic adrenalectomy. Five patients underwent open adrenalectomy, and the largest tumor was reportedly 5 cm in diameter (range 3.5-5 cm). Our patient was successfully treated using a laparoscopic approach with no operative complications and with a good survival. A good outcome after mini-invasive surgery was reported by other Authors too. Izaki *et al*[8] and Choi *et al*[9] reported two similar cases, both high-risk patients with FIGO stage IIIC primary endometrial cancer and metachronous single-site adrenal metastases (5.7 and 6.0 cm in diameter, respectively); both patients were treated laparoscopically and had a long follow-up (82 and 45 mo, respectively).

So, despite the small number of patients considered, our review suggests that a laparoscopic approach is a valid alternative to open surgery for isolated adrenal metastases from endometrial cancer.

Finally, there is no general consensus regarding chemotherapy after surgery for adrenal metastases. Izaki *et al*[8] described a patient who underwent laparoscopic adrenalectomy followed by three cycles of carboplatin-based chemotherapy, with a complete response at 67 mo. Other Authors[10,13,14] administered adjuvant chemotherapy after surgery for adrenal secondary tumors, but provided no follow-up data.

Only one of the cases emerging from the literature review was managed with no surgery or oncological treatment. Zaidi *et al*[11] reported giving only palliative therapy to a patient with a low-stage uterine cancer and an early adrenal gland metastasis, and the outcome was very poor (she survived only 3 mo after her metastasis was diagnosed).

**CONCLUSIONS**

Adrenal metastasis from uterine cancer is rare, but should be suspected whenever an adrenal mass is detected in the follow-up after the resection of gynecological cancer. Although the number of cases reported in the literature is very small, laparoscopic resection seems to be feasible and safe, with good oncological results.

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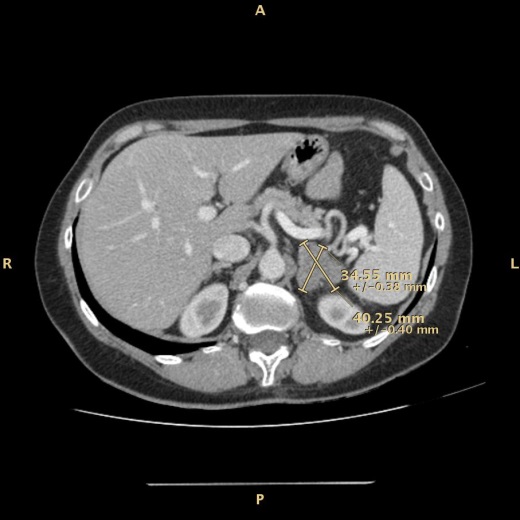
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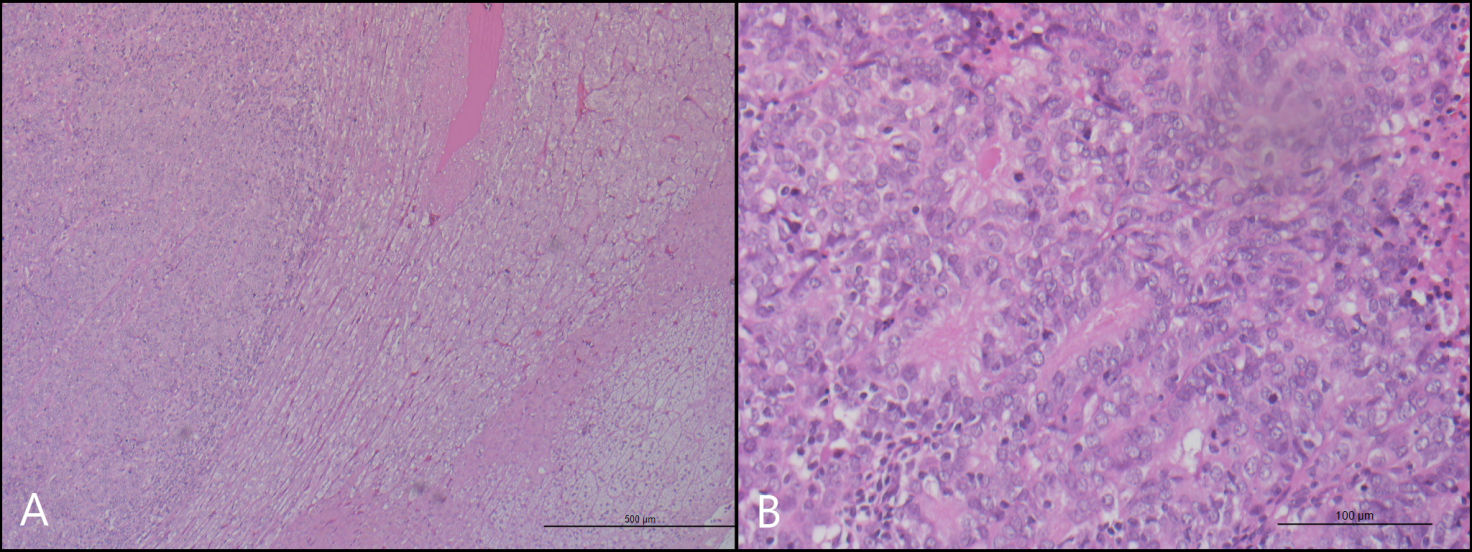
**Table 1 Patients with adrenal metastases from endometrial cancer**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Case reports** | **Age** **(yr)** | **Histology** **of primary** | **Stage (FIGO)** | **Adjuvant treatment** | **DFS (mo)** | **Site** | **Treatment** | **F-U** **(mo)** |
| Nakano *et al*[5], 1975 | 77 | Mixed  (clear cell-squamous) | Na | Na | 26 | Metachronous multiple sites | Whole brain irradiation and supportive care | 28 |
| Lam *et al*[6], 2001 | Na | Na | Na | Na | Na | Metachronous single site | Laparotomic adrenalectomy | Na |
| Baron *et al*[7], 2008 | 76 | Endometrioid G1 | IV B | EBRT | 9 | Metachronous single site | Laparotomic partial adrenalectomy | 24 |
| Baron *et al*[7], 2008 | 62 | Endometrioid G1 | Na | VBT + 6 adriamycin- cisplatin cycles | 108 | Metachronous multiple site | Supportive treatment | 110 |
| Izaki *et al*[8], 2010 | 55 | Endometrioid | III C | 7 carboplatin paclitaxel cycles | 15 | Metachronous single site | Laparoscopic adrenalectomy + CT (3 carboplatin cycles) | 82 |
| Choi *et al*[9], 2011 | 62 | Squamous | III C | 6 cisplatin cycles | 10 | Metachronous single site | Laparoscopic adrenalectomy | 45 |
| Berretta *et al*[10], 2013 | 67 | Mixed (anaplastic-endometrioid) | IV B | Na | Na | Synchronous multiple sites | One-time laparotomic adrenalectomy + hysterectomy and salpingectomy + taxol and carboplatin chemotherapy | Na |
| Zaidi *et al*[11], 2013 | 75 | Endometrioid G3 | I B | Na | 6 | Metachronous single site | Supportive treatment | 9 |
| Singh Lubana *et al*[12], 2015 | 60 | Serous | II | EBRT + C + CT: 3 paclitaxel carboplatin cycles | 66 | Metachronous single sites | Laparotomic  adrenalectomy | 90 |
| Rekhi *et al*[13], 2015 | 39 | Endometrioid G2 | II | VBT + EBRT | 24 | Metachronous single site | Robotic adrenalectomy + CT | Na |
| Mouka *et al*[14], 2016 | 58 | Endometrioid G3 | I B | 6 CT | 12 | Metachronous single site | Laparotomic  adrenalectomy + CT | Na |
| Present case, 2019 | 53 | Endometrioid G2 | II B | No treatment | 36 | Metachronous single site | Laparoscopic adrenalectomy | 45 |

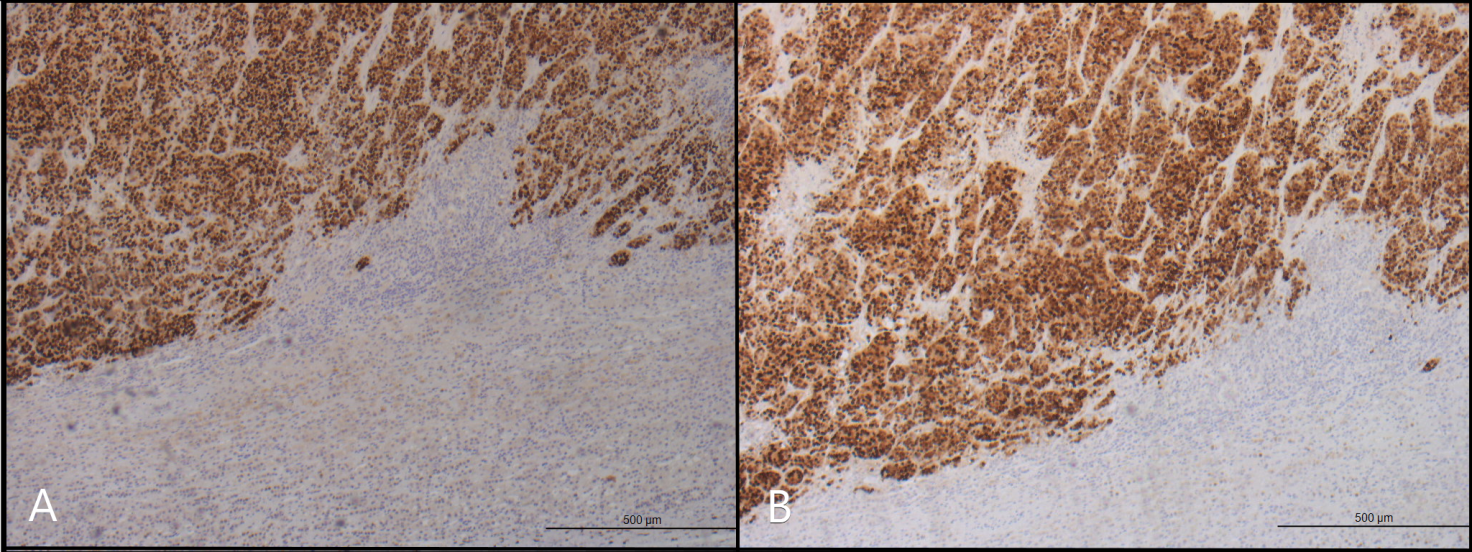
FIGO: International Federation of Gynecology and Obstetrics; DFS: Disease-free survival; F-U: Follow-up; Na: Not available; EBRT: External beam radiation therapy; VBT: Vaginal brachytherapy; CT: Chermotherapy.



**Figure 1 Computed tomography scan of abdomen showing left adrenal mass measuring 40 mm × 34 mm.**



**Figure 2 Hematoxylin and eosin stain of endometrial endometrioid carcinoma.** A: panoramic view of left adrenal gland; B: high magnification showing the glandular pattern of neoplastic cells.



**Figure 3** **Immunohistochemical staining.** A, B: Immunohistochemical staining positive for estrogen receptors (A) and progesterone receptors (B) shows high reactivity in metastatic cells.