

Case Report

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A Case Report of Solitary Adrenal Metastasis from Early Stage Endometrial Carcinoma

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ABSTRACT

Although Type I endometrial cancers are generally associated with a good prognosis, specific histopathological features portend worse outcomes. Compared to type II tumours which have increased metastatic potential, this phenomenon is seldom seen in type I counterparts at presentation. Moreover, adrenal metastatic sites are rarer still with only one case report describing this pattern of dissemination to date. To our knowledge this is the first case report of an isolated adrenal metastasis from early stage type I endometrial cancer and highlights the heterogeneity which exists in this disease.

KEYWORDS: Endometrial cancer; Endometrioid adenocarcinoma; Adrenal metastasis.

INTRODUCTION

The worldwide prevalence of endometrial carcinoma was 280,000 cases in 2008.¹ Clinico-pathologic and molecular data suggests the existence of two distinct types of endometrial carcinomas. Type I endometrial carcinoma comprise the endometrioid adenocarcinomas, which are often preceded by premalignant disease and express the oestrogen receptor and progesterone receptor.² Furthermore, they are predominantly low grade and rarely metastasise. The prognosis of type I cancers are favourable if diagnosed at an early stage, with a 5 year survival of >97% in stage I and >80% in stage II.³ Type II endometrial carcinomas are those of non-endometrioid histology, in particular serous or clear-cell morphology. These tumours are considered to be of high histological grade, arise in the background of atrophic endometrium and are not driven by oestrogenic signalling.⁴ Despite the higher prevalence of type I cancers, type II tumours account for a high proportion of endometrial cancer-related deaths (44%), as they have a higher proclivity for extra uterine spread, are associated with poor prognosis and, if treated at an early stage, carry a higher risk of recurrence.⁵ Although type I cancers generally have a good prognosis, deaths do occur with these tumours, hence tumour heterogeneity must have a significant part to play.

Endometrial cancer recurrence is frequently loco-regional with distant metastases usually found in lungs, liver, and more rarely, bone and brain. Metastatic spread to the adrenal gland is common with carcinomas of the lung, breast, kidney, gastrointestinal tract in addition to melanoma. However, the dissemination of endometrial cancer to the adrenal gland is a rare occurrence. To the best of our knowledge, only four such cases have been reported in the literature. Here we report a case of a solitary adrenal metastasis from early stage type I endometrial

carcinoma.

CASE REPORT

We report the case of a 62-year-old female who presented with twelve months of progressively worsening postmenopausal per-vaginal bleeding in November 2011. Physical examination was within normal limits. She initially underwent a pelvic ultrasound scan which was unremarkable. Subsequently a dilatation and curettage procedure was performed which revealed grade 3 endometrial adenocarcinoma (Type I).

A CT thorax, abdomen and pelvis performed in December 2011 showed no evidence of metastatic disease. A laparoscopic modified radical hysterectomy; bilateral salpingo-oophorectomy and peritoneal lymph node dissection were performed. Histopathological diagnosis revealed an endometrioid adenocarcinoma invading 5mm of the myometrium with focal lymphovascular invasion considered to be FIGO Stage 1B disease. She went on to have brachytherapy.

A progress CT scan performed in March 2012 revealed a new left adrenal nodule measuring 17mm in size which was monitored. A subsequent CT adrenal gland performed in May 2012 showed an increase in the size of the adrenal nodule to 20mm. A laparoscopic adrenalectomy was performed in September 2012 and subsequent histology revealed malignant cells in keeping with endometrial adenocarcinoma to the adrenal gland and focal squamous metaplasia was evident. The tumour cells were positive for cytokeratin (CK) 7 and negative for TTF1, napsin A, CK20, CDX2 and villin. Immunohistochemistry on tumour cells revealed strong expression for oestrogen receptors and weak to moderate staining of progesterone receptors (Figure 1).

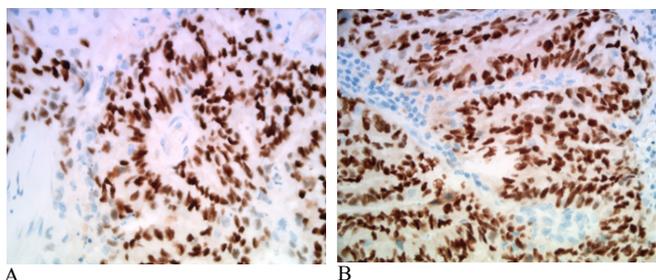


Figure 1: Immunohistochemical staining confirming strong oestrogen receptor (A) and weak to moderate progesterone receptor expression (B) in approximately 70% of tumour cells.

DISCUSSION

Women with early (FIGO stage 1) type I endometrial cancer have a low risk of recurrence of their disease. This risk is significantly higher for some women with risk factors including high grade, deep myometrial invasion (>50%), extrauterine spread, lymphovascular invasion and certain histological subtypes (e.g. papillary serous carcinoma, endometrioid carcinoma and clear cell carcinoma).⁶

Adrenal metastasis following endometrial carcinoma is rare. To date, four cases have been reported describing adrenal metastasis from endometrial cancer. The first case described a 76-year-old women with FIGO stage 4, well differentiated endometrial cancer and pathological right acetabular fracture.

The patient underwent transabdominal hysterectomy (TAH), bilateral salpingo-oophorectomy (BSO) with pelvic lymph node dissection followed by post-operative pelvic radiation. Surveillance CT performed 9 months later revealed a 50mm right suspicious adrenal mass. Laparotomy and partial resection was performed due to direct extension to adjacent organs. The patient was given medroxyprogesterone 500mg daily. She subsequently developed lung recurrence and died two years after initial surgery.⁷

The second case was a 62-year-old female with well-differentiated adenocarcinoma with no evidence of metastasis. The patient was given uterovaginal brachytherapy and underwent TAH/BSO and pelvic node dissection with cleared resection margins. At 7 years follow up the patient was found to have localised lung metastasis confirmed by biopsy. The patient received 6 cycles of adriamycin and cisplatin followed by medroxyprogesterone 500mg daily. After 2 years of remission she was found to have disease recurrence with lung metastasis and bilateral adrenal masses, as well as presumed malignant ascites. The patient died 2 months later, 9 years after initial diagnosis.⁷

The third case involved a well-differentiated, stage 3C endometrial cancer involving pelvic lymph nodes, treated with TAH and BSO followed by adjuvant carboplatin and paclitaxel for seven cycles. Fourteen months later she developed a 30mm right adrenal tumour which was laparoscopically resected, and a further 3 cycles of adjuvant carboplatin and paclitaxel were administered. There was no evidence of recurrence 5 years later.⁸

The fourth case involved a patient with progesterone positive, moderate-poorly differentiated stage 3C endometrial carcinoma who underwent a laparoscopic hysterectomy/BSO and pelvic lymphadenectomy and subsequently received six cycles of adjuvant cisplatin. A 60mm left adrenal mass was detected on PET-CT ten months later and was laparoscopically resected. Several months later the patient developed a new liver lesion.⁹

Laparoscopic adrenalectomy is considered to be the treatment of choice in solitary adrenal metastasis. The locoregional recurrence rate after laparoscopic adrenalectomy of primary adrenal cancer is 60%, usually occurring 1-2 years after resection.¹⁰ In a 12-year series of 30 patients undergoing surgery for adrenal metastasis from all cancers, the overall median survival was 23 months with a 5-year survival rate of 23%. Other studies reported similar survival rates.¹¹⁻¹³ In gen-

eral, the prognosis of patients with metastatic disease is poor, with few survivors at 5 years.

According to the literature, metastatic spread to the adrenal glands tends to occur in advanced stage endometrial carcinoma. Metastatic spread from a type I early stage endometrial cancer is rare. Although the second aforementioned case report potentially describes a type I cancer, in view of well-differentiated histopathological features, the disease free survival was several years. This is in stark comparison to our case whereby the patient had a type I cancer that relapsed within 6 months of definitive surgery. Hence, highlighting that there is indeed a significant degree of heterogeneity, which exists in a subtype that is usually deemed to have an excellent prognosis.

There is increasing evidence that stage IC endometrial carcinoma patients should be regarded separately due to an increased risk of pelvic and distant metastases with lower survival rates.¹⁴ The 5-year vaginal and pelvic relapse rate of this particular cohort has been reported at 13%, substantially higher than the other stage I patients who had excellent pelvic control rates after pelvic radiotherapy (97-99%).¹⁵ The overall survival at 5 years was 58% for the IC grade 3 patients, compared to 74% for those with IB grade 3, and 83-86% for IB grade 2 and IC grade 1 and 2 disease ($p < 0.001$).

Whether or not surgical staging has been performed, pelvic radiotherapy is generally recommended for grade 3 tumours with deep myometrial invasion.^{5,7-10} In view of the increased risk of distant relapse and cancer related death, adjuvant chemotherapy is currently being investigated in the PORTEC-3 study (Clinicaltrials.gov Identifier NCT00411138).

CONCLUSION

The notion that type I tumours have a predominantly good prognosis is for the most part true. However, more scrutiny is required for treatment of endometrial cancers with poor histological features. This paves the way to develop novel biomarkers to predict type I tumours with poor prognosis that may potentially benefit from adjuvant chemotherapy or targeted agents.

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