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Case Report

CASE REPORT

A case of metastatic adrenocortical carcinoma

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Abstract

Adrenocortical carcinoma is a rare endocrine malignancy with poor prognosis. Adrenocortical carcinoma can be seen in familial syndromes such as multiple endocrine neoplasia 1(MEN-1), Li–Fraumeni syndrome, Beckwith–Wiedemann syndrome and Carney complex (Kjellman, M, Roshani, L, The, BT *et al*. Genotyping of adrenocortical tumours: very frequent deletions of the MEN1 locus in 11q13 and of a 1-centimorgan region in 2p16. *J Clin Endocrinol Metab* 1999;84:730-5). Treatment options for adrenocortical carcinoma are limited. We report a case of adrenocortical carcinoma in a 50-year-old lady who subsequently underwent adrenalectomy. She was started on mitotane as adjuvant therapy and chemotherapy after the metastatic lesions were found. Due to the rarity of the tumour, the understanding and experience of management modalities is limited. New treatment options may be available in the coming years to improve outcome. Early identification of tumour is key to increase the chances of progression free survival.

INTRODUCTION

Adrenocortical carcinoma is a rare endocrine malignancy with an annual incidence of 0.5–2 cases per million people [2]. Adrenocortical carcinoma is more common in females and had a bimodal age distribution with a peak at <5 years and a second peak between the forties and fifties [1]. Although most adrenocortical carcinomas produce features of hormone hypersecretion, some may present just as an abdominal mass. Despite current treatment modalities the 5-year survival rates are only ~35% [2].

CASE REPORT

A 50-year-old lady was admitted to hospital with multiple non-specific symptoms which included generalised weakness, numbness on both upper limbs associated with spasms and loss of appetite. She had a past medical history of cervical and lumbar spondylosis. She was not taking any prescribed or over the counter medications. Vitals were stable except for elevated blood pressure of 160/100 mmHg. Physical examination was grossly normal. She did not have any signs of hypercortisolism or virilisation.

Her potassium was 1.7 mmol/L and sodium 144 mmol/L (Table 1). ECG showed ST segment depression in leads V5 and V6. Urine potassium to urine creatinine ratio was elevated (>1.5) indicating urinary losses of potassium. She was started on potassium supplementation.

The full adrenal screen performed on this patient showed an elevated aldosterone to renin ratio.

The patient was sent for computed tomography (CT) adrenal scan which revealed a left adrenal mass of 6 cm × 5 cm with irregular edges and central calcification. However, the tumour density and contrast washout were non-specific and was not able to further aid in characterising the adrenal mass. A CT scan of the brain, thorax, abdomen and pelvis performed to detect any evidence of metastases was negative.

Due to the size of large adrenal mass which raises the suspicion of malignancy, the patient subsequently underwent laparoscopic left adrenalectomy. The 6 cm × 5 cm adrenal mass was removed with adequate resection margin. Her blood pressure

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Table 1: Investigation results

Haemoglobin	10.4 g/dL	(13–18)
White blood cells	11.9 × 10^9/L	(4–11)
Platelets	413 × 10^9/L	(150–400)
Sodium	144 mmol/L	(135–145)
Potassium	1.7 mmol/L	(3.5–5)
Urea	7.9 mmol/L	(2.5–6.7)
Creatinine	112 mmol/L	(70–150)
9 am cortisol	384 nmol/L	(180–620)
ACTH	6.6 pmol/L	(2.2–17.6)
9 am cortisol (post 1 mg dexamethasone)	39 nmol/L	(<50)
Renin (supine)	0.9 ng/mL/h	(1.1–2.7)
Aldosterone (supine)	827 pmol/L	(100–450)
DHEAS	2.33 μmol/L	(0.96–6.95)
Urine potassium	72 mmol/L	
Urine creatinine	8.3 mmol/L	
Urine normetadrenaline	3.1 mmol/24 h	(<4.5)
Urine metadrenaline	1.4 mmol/24 h	(<1.9)

Table 2: Weiss criteria and patient's histology results

Components of Weiss criteria	Patient's histology results
1. High Fuhrman nuclear grade:	Present
2. >5mitoses/ 50 hpf:	33/50 hpf
3. Atypical mitotic figure:	Present
4. <25% of tumour cells are clear cells:	Tumour shows <10% of clear cells
5. Diffuse architecture (>33% of tumour):	Tumour shows mainly broad trabecular architecture with some areas showing sheet formation
6. Necrosis:	Focal necrosis is identified
7. Venous invasion:	Present
8. Sinusoidal invasion:	Present
9. Capsular invasion:	Present

and potassium levels normalised after surgery and she remained clinically well. Histology of the adrenal mass showed tumour cells positive for synaptophysin and inhibin. The tumour cells were arranged predominantly in a trabecular pattern with some areas showing sheet formation. A few clear tumour cells were seen. The tumour cells had large nucleoli and were pleomorphic. Mitotic activity was 33/50 hpf. There were areas of focal necrosis with vascular, sinusoidal and capsular invasion. The histology fulfilled more than three aspects of the Modified Weiss criteria to support the diagnosis of adrenocortical carcinoma (Table 2).

The patient was commenced on 3 g of mitotane daily which was gradually titrated in 1 g increments weekly to 8 g of mitotane daily in divided doses. At 8 weeks she achieved a plasma mitotane concentration of 16 mg/L. Hydrocortisone replacement was started at 10 mg twice a day. The adequacy of replacement was monitored using adrenocorticotrophic (ACTH) levels. She had CT scans 2 monthly to look for metastasis. A positive emission tomography (PET) scan done 2 months after surgery showed no suspicious focal fludeoxyglucose (FDG)-avid lesion. Unfortunately the patient presented 2 months later (4 months after surgery) with acute abdominal pain.

CT scan showed ruptured hypervascular nodule along the omentum raising the possibility of a metastatic nodule. No further investigations could be performed as the nodule was not amenable to biopsy. Her abdominal pain resolved and she was closely monitored. CT scan done 10 months after the adrenalectomy raised possibility of disease progression with new pulmonary and liver nodules suspicious of metastasis. She then was referred to medical oncology and underwent radiotherapy for 2 months. Four cycles of chemotherapy (Cisplatin, Etoposide and Doxorubicin) was given. Further chemotherapy could not be given due to episodes of neutropenic sepsis.

The patient continued to deteriorate despite chemotherapy and was subsequently referred to palliative care. She died 28 months after her initial presentation to hospital.

DISCUSSION

Despite the absence of signs and symptoms, patients with an adrenal mass need to be evaluated for possible Cushing's syndrome, phaeochromocytoma and hyperaldosteronism. An adrenal mass which is <2 cm in size is very likely benign [3]. Only 2% of tumours <4 cm have been found to be adrenocortical carcinoma. Masses larger than 5 cm are most probably malignant. Other features of malignant masses seen on CT and MRI scans include irregular edges, heterogeneity, central necrosis and calcification [4]. Unenhanced CT scan density of <10 HU indicates the mass if most probably benign [3]. Delayed contrast washout of <50% in 15 min is classically seen in malignant masses [4].

Adrenal scintigraphy can be performed to gain information on the functionality of the tumour [6]. Newer imaging modalities such as FDG-PET-CT have 95% sensitivity and specificity for the diagnosis of adrenocortical carcinoma [7].

The role of fine needle aspiration for adrenal nodules has not been investigated thoroughly. As it has a high false negative rate, fine needle aspiration is generally not recommend [9].

At the point of presentation the patient in this case had no evidence of metastases. As such, the gold standard treatment for adrenocortical carcinoma is surgery as it is the only potentially curative modality available. Indications for surgery are tumour size more than 4 cm, functional tumour and imaging features such as Hu more than 20, delayed contrast washout, internal haemorrhage, central necrosis and peripheral enhancing nodules which suggest a malignant mass [4].

The surgeons opted to perform a laparoscopic resection as the patient requested minimally invasive surgery with shorter hospitalisation. However current experience indicates that laparoscopic resection remains controversial due to the possible risks of tumour seeding leading to local recurrences and peritoneal carcinomatosis [5].

Surveillance of recurrence post-surgery may need to continue for as long as 10–12 years [9] as up to 50–80% of patients with R0 resection have recurrence or metastatic disease [6]. Protocols in specialist centres suggest 3 monthly PET or CT scan for the first 2 years post-surgery and 6–2 monthly thereafter for at least the subsequent 5 years [9].

Current histological assessment of adrenocortical carcinoma is based on the Weiss scoring system which consists of nine morphological features seen on light microscopy. A score of <3 defines benign adenomas and scores of more than 6 suggests adrenocortical carcinoma [5].

The use of mitotane in the treatment of adrenocortical carcinoma was reported in 19 59 [7]. Mitotane inhibits 11-β hydroxylase leading to reduced steroid synthesis and destruction of mitochondria causing necrosis of the adrenocortical cells [8]. As mitotane inhibits the synthesis of steroids, hydrocortisone replacement should be started after 2–4 weeks of mitotane therapy. Mitotane should be instituted early as adjuvant therapy after resection of the primary tumour and before local extension or distant metastases occur. Studies have shown that adjuvant mitotane improves disease free survival following surgery [9].

The two common chemotherapy regimens used in metastatic adrenocortical carcinoma are a combination of cisplatin, etoposide and doxorubicin or streptozocin. The FIRM-ACT trial showed significantly higher response rates and longer median progression free survival with cisplatin, etoposide and doxorubicin regime compared to streptozocin (23 vs 9%) [10].

CONFLICT OF INTEREST STATEMENT

No conflict of interests.

FUNDING

No funding was acquired for this case report.

ETHICAL APPROVAL

Ethical approval was not required.

CONSENT

Consent was gained from patient prior to her demise.

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