A malignant looking “renal” mass is not always renal cancer

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1. Introduction

Neuroendocrine tumours are rare and may exist for years before final diagnosis. They are frequently diagnosed incidentally and occasionally following surgery for unrelated conditions.1 We describe the rare occurrence of a 20cm malignant neuroendocrine tumour encapsulating a normal kidney and adrenal gland. This was originally diagnosed radiologically as renal cell carcinoma (RCC) and surgical excision was performed. The subsequent post-operative period was very complicated, most likely due to the absence of pre-operative alpha blockade.

This patient had a documented history of resistant hypertension, a common manifestation of catecholamine excess. Current guidelines for management of renal masses do not discuss criteria for investigating catecholamine excess.2 This case highlights the importance of awareness around situations in which to consider screening for catecholamine excess during pre-operative assessment of “renal” masses.

2. Case presentation

A 58-year-old caucasian female presented to her general practitioner with a distended abdomen, right sided pain and swollen legs. She had a nine-year history of severe hypertension, managed with six anti-hypertensives, and type 2 diabetes.

Computed tomography (CT) scan of the thorax, abdomen and pelvis reported a 20cm right renal mass with areas of calcification (Fig. 1). The report also stated that the ipsilateral adrenal gland was difficult to visualise but the left kidney and adrenal appeared normal. Following a multidisciplinary team discussion involving both urologists and radiologists, the diagnosis of RCC was agreed. A radical nephro-adrenalectomy was performed without any intra-operative complications.

Immediately after surgery she became hypoglycaemic, hypotensive and oliguric despite aggressive intravenous fluid resuscitation. By day 3, she had developed hypoxia, pneumonia, persistent oliguria with deteriorating renal function and pain control difficulties prompting admission to critical care. She improved rapidly and returned to the surgical ward but the hypoglycaemic episodes continued and she developed difficulty swallowing which was felt to be secondary to intubation trauma.

Six days later she again became hypoxic with, on this occasion, tachycardia and hypertension so required another 5-day admission to critical care for non-invasive ventilation. Chest X-ray suggested pulmonary oedema and echocardiogram demonstrated significantly impaired left ventricular function (pre-operative echocardiogram was normal).

In the following two weeks she had more episodes of hypotension, acute kidney injury and hypoglycaemia. On her 28th post-operative day, she became hypercalcaemic prompting referral to the endocrinology team. The 9am cortisol level was profoundly low given her stressed state and intravenous hydrocortisone was commenced. Remarkably, from this point onwards her blood pressure and blood glucose levels normalised.

She was subsequently switched to oral hydrocortisone and eventually, after a 48-day admission, discharged home without any antihypertensive or diabetes medications. Dynamic function testing performed a month following discharge demonstrated profound adrenal insufficiency (Table 1), thus hydrocortisone was continued. Blood pressure and HbA1c remained normal off medications.

The full histological analysis of the excised tumour reported a normal kidney and adrenal gland within a large malignant...
neuroendocrine carcinoma. The tumour cells stained strongly for synaptophysin and CD56 but showed no reactivity for S100 (Fig. 2). Vaso-active amines were also present leading to the conclusion that the carcinoma had arisen from a pre-existing phaeochromocytoma.

Functional imaging two months after discharge did not demonstrate any evidence of residual disease or metastasis, however six months later her symptoms returned and imaging revealed a new liver metastasis. She is currently undergoing chemotherapy treatment.

3. Discussion

Phaeochromocytoma is a rare neuroendocrine tumour with an incidence of 2–8 per million/year. The majority are benign, however around 10–17% are malignant. Diagnosis is challenging due to the range of non-specific features which include hypertension, palpitations, sweating and hyperglycaemia. Although surgical excision is the only definitive treatment, it can be dangerous and patients should undergo a period of stabilisation with β-blockade therapy pre-operatively to prevent the development of intra-operative complications. Patients are also prone to major postoperative complications such as hypotension and hypoglycaemia and this risk increases if the phaeochromocytoma is undiagnosed.

We present this rare case of a malignant neuroendocrine tumour surrounding a normal kidney and adrenal gland, originally diagnosed as an RCC. For several preceding years the patient had been suffering with resistant hypertension and hyperglycaemia which are common features of catecholamine excess. Had this been considered, the correct diagnosis would have been reached and appropriate pre-operative stabilisation would have occurred.

Unfortunately, the patient did not receive pre-operative β-blockade therapy and thus developed several post-operative complications. Hypotension is a common complication arising from abrupt reduction in alpha-adrenergic stimulation. Hypoglycaemia also results from sudden removal of alpha (predominantly alpha2) receptor stimulation causing rebound hyperinsulinaemia. In addition, she developed an episode of acute pulmonary oedema – which has been described following surgery in patients with undiagnosed phaeochromocytoma and hypercalcaemia, a recognised feature of adrenal insufficiency.

The adrenal insufficiency was unexpected but could be explained by co-secretion of adrenocorticotropic hormone (ACTH). This phenomenon is rare and fewer than 50 cases have been described. It has been postulated that ACTH secreted from the tumour cells stimulates cortisol release from the cortical cells within the same gland. This would suppress the contralateral

| Sample         | Serum cortisol |
|----------------|----------------|
| Basal          | <25 n mol/L    |
| 30 minutes     | 44 n mol/L     |
| 60 minutes     | 59 n mol/L     |
adrenal resulting in insufficiency following radical resection. Unfortunately, the histological analysis did not comment on the presence of any features of ACTH secretion so there is no way to confirm this.

4. Conclusion

This is a rare but important case of a large malignant neuroendocrine tumour misdiagnosed as a renal cell carcinoma which had severe consequences for the patient concerned. Cases of phaeochromocytoma originally diagnosed as RCC have been described, however it is rare for a neuroendocrine tumour to grow to such a large size and surround a structurally normal kidney.

Current guidelines for the management of renal masses do not discuss when to consider screening for catecholamine excess, particularly in the context of resistant hypertension. Had this possibility been considered pre-operatively, the post-operative complications this patient suffered could have been minimised.

Renal masses are becoming increasingly common in urological practice and although the vast majority are RCC, this case highlights that awareness of more uncommon causes is essential.

References

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