JSM Endocrinology, Diabetes and Obesity

Case Report

Conn's Syndrome with Bilateral Renal Cell Carcinoma

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Abstract

Primary hyperaldosteronism, also known as Conn's Syndrome, is a cause of secondary hypertension, seen in approximately 11-16% of cases of resistant hypertension (1). Hyperaldosteronism due to an aldosterone-producing adrenal adenoma is the second commonest cause following bilateral adrenal hyperplasia (1).

Higher incidence of renal cell carcinoma (RCC) has been reported in primary hyperaldosteronism when compared to the general population and in hypertensive patients with alternative aetiologies (2,3,4) . We report the case of a 50-year-old gentleman with resistant hypertension and hypokalaemia, found to have a left-sided adrenal adenoma causing hyperaldosteronism. Work-up for this condition revealed synchronous bilateral renal tumours, with histology following partial nephrectomies indicating clear cell renal cell carcinoma. We identified no other cases in the literature reporting bilateral renal cell carcinoma in a patient with Conn's Syndrome in remission.

Background

Primary hyperaldosteronism, also known as Conn's syndrome after the clinician who first described it in 1955 (5), is a prevalent cause of resistant hypertension, seen in approximately 11-16% of cases (2). Hyperaldosteronism due to an aldosterone-producing adrenal adenoma, is the second commonest cause following bilateral adrenal hyperplasia (1). The incidence of adrenal adenomas is reported as being significantly higher in patients with renal cell carcinoma in comparison to the general population (2,3). While hypertension is itself recognised as a risk factor for developing renal cell carcinoma6, Lang et al have also reported a significantly higher incidence of malignancy in patients with primary hyperaldosteronism compared to hypertensive controls. In their review of 335 patients with primary hyperaldosteronism, 11.7% of patients had been diagnosed with a malignancy in their lifetime, of which 13% were RCC (2).

Bilateral renal cell carcinoma is a rare form of kidney cancer, with evidence suggesting bilateral RCC occurs in approximately 3-4% of renal cancer patients. Literature indicates that synchronous bilateral renal cell carcinoma may carry a more favourable prognosis to metachronous disease (7,8).

Submitted: 19 May 2021 | **Accepted:** 21 July 2021 | **Published:** 29 July 2021

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Citation: Feighan C, Ludgate S, Connolly S, McQuaid SE, Hatunic M (2021) Conn's Syndrome with Bilateral Renal Cell Carcinoma. JSM Endocrinol Diabetes Obes 4: 3.

Case report

A 50-year-old gentleman was referred to the Endocrinology outpatient department for evaluation of persistent hypertension and hypokalaemia. He was referred by the specialist stroke prevention and hypertension clinic who had seen him due to a 7-year history of hypertension. Medications included Lercanidipine 20mg and Telmisartan 80mg with Hydrochlorothiazide recently held due to hypokalaemia. Past medical history included hereditary spherocytosis managed with splenectomy at age 11, macular degeneration, cataracts and a left Baker's cyst. His potassium at the time of referral was 2.8mmol/l and potassium replacement was commenced. On examination in clinic blood pressure control was suboptimal at 140/88 mmHg despite therapy. Initial investigations revealed a potassium of 3.1mmol/l with oral replacement, a low-normal renin of 13.8mIU/l (9.0-103.5), high-normal aldosterone 644pmol/l (138-670) and raised aldosterone: renin ratio (ARR) of 47 (<30pmol/L:mIU/L). Thyroid function tests, renal, liver, bone profiles, plasma metanephrines and normetanephrines were normal. Initial renal ultrasound identified a 1.3 x 1.7cm simple appearing cyst in the right kidney and was otherwise unremarkable. Blood results indicated primary hyperaldosteronism, confirmed by a positive saline infusion test (initial aldosterone 553 and post infusion 249 pmol/L), carried out following cessation of Lercandipine and Telimisartan and commencement of Verapamil.

CT of the adrenal glands showed a 1 cm nodule arising from the lateral limb of the left adrenal gland with average Hounsfield units of this nodule on non-contrast imaging is 5, 56 on arterial phase and 47 on portal venous phase imaging. Incidental findings included a 2.7 cm enhancing mass arising from the posteromedial aspect of the lower pole of the left kidney and a 2.5cm enhancing mass arising from the posteromedial aspect of the lower pole of the right kidney not visualised on previous renal ultrasound and suspicious for bilateral renal cell carcinomas (Figure 1 & 2). No extension into the renal sinus or renal veins was identified on either side. Degenerative changes are identified within the

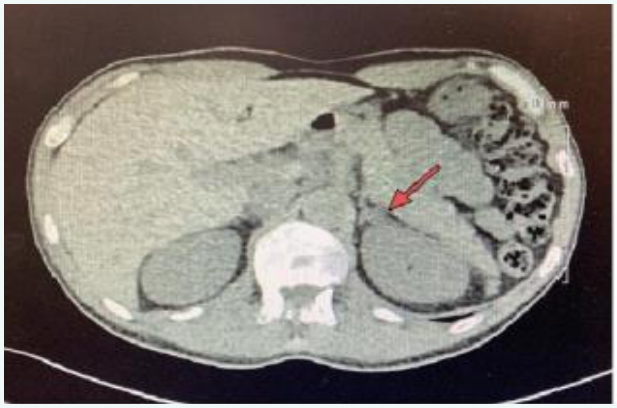

Figure 1 CT adrenals showing 1cm nodule in the left adrenal gland.

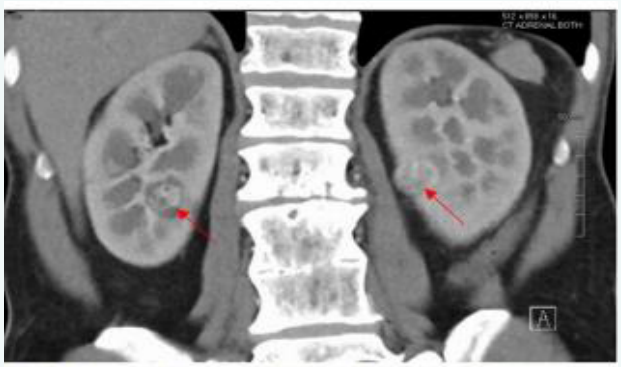

Figure 2 Coronal view of CT adrenals showing bilateral renal tumours, 2.5cm on the left and 2.7cm on the right.

lumbar spine. There were fusions of the L3 and L4 vertebral bodies

Following urology review and multidisciplinary team discussion a left-sided adrenalectomy and partial nephrectomy with surveillance of the right renal mass was advised. Adrenal vein sampling was not undertaken as definitive surgery was planned. The patient underwent a laparoscopic left adrenalectomy and partial nephrectomy with complete normalisation of serum potassium and blood pressure improvement, calcium channel blocker and oral potassium replacement were ceased Table. Histology confirmed a left adrenal cortical adenoma borders without a true capsule. The tumour cells are large and have round, regular nuclei with small nucleoli, negative for atypical mitotic figures. Immunohistochemical staining shows diffuse positivity with melan A. Inhibin shows patchy positivity. Focal AE13 staining. Calretinin is negative. MIB 1 <5%. The left 17 mm clear cell renal carcinoma stage PT1a. Tumour appears encapsulated with pushing invasion into the tumour capsule with the tumour cells are diffusely positive for CD10 and show patchy positivity for CK7.

Three months following the initial surgical procedure a right-sided laparoscopic partial nephrectomy was undertaken. Post-operative histology indicated clear cell renal cell carcinoma stage PT2a G2. Annual surveillance imaging has indicated no signs of recurrence up to three years following surgical resection. Blood pressure remains well-controlled with medications limited to Telmisartan 20mg once daily, with nocturnal dip now seen and stable normokalaemic blood results (Table 1). Annual clinic appointments are ongoing in Urology and Endocrine Outpatient Departments.

Conclusion

We report a case of Conn's syndrome presenting with resistant hypertension and hypokalaemia with imaging leading to identification of an adrenal adenoma and bilateral renal cell carcinoma. This case emphasises the importance of investigating secondary causes of hypertension with consideration of diagnosis of primary hyperaldosteronism particularly in patients with suboptimal control with multiple agents who may be overlooked because their blood pressure is not grossly elevated. Consideration of Conn's Syndrome is particularly important in patients presenting with hypokalaemia alongside their hypertension, although hypokalaemia, as well as metabolic alkalosis, are present in only a minority of patients with primary hyperaldosteronism (9). As outlined in this case a raised Aldosterone: Renin Ratio is indicative of primary hyperaldosteronism, however the diagnosis should be confirmed with a saline infusion test, as seen in this case, or with alternatives of fludrocortisone suppression, oral sodium loading or captopril challenge tests (9).

Primary hyperaldosteronism infers a greater cardiovascular risk than essential hypertension (9,10) with an increase seen in the frequency of myocardial infarction, atrial fibrillation and cerebrovascular injury, (10,11) and as such its detection and treatment is important and beneficial to patients. Its importance is further emphasised by the Endocrine Society's recent recognition of primary hyperaldosteronism as a major public health issue (9). Identification of hyper aldosteronism as a result of an adrenal adenoma is of particular significance due to the potential for curative resection. Meta-analysis suggests that the cure rate of unilateral adrenal ectomy in primary hyperaldosteronism is approximately 50.6% with cure defined as blood pressure sustained below 140/90 without the use of antihypertensive agents (12). In this case our patient continued therapy with a low dose Angiotensin Receptor Blocker (ARB)

Table 1:

	Before surgery	Post surgery
Blood pressure	141/88 mmHg	120/76 mmHg
Medications	Lercanidipine 20 mg OD Telmisartan 80mg OD Hydrochlorothiazide 25mg OD	Telmisartan 20 mg OD
Creatinine	82 µmol/l (65 – 107)	106 µmol/l
Urea	4.7 mmol/l (2.8 – 8.6)	7.9 mmol/l
eGFR	>60 ml/min/1.73m^2	>60
Serum Potassium	2.9 mmol/l (3.3 – 5)	4.7mmol/l
Serum Sodium	144 mmol/l (133 – 146)	137mmol/l

but this yielded excellent control of blood pressure and all other agents were ceased.

The renin angiotensin aldosterone system is an extensively studied physiologic mechanism. Changes in blood pressure influence dilatation or constriction of the afferent arteriole and renin secretion. Renin secretion results in conversion of angiotensinogen to angiotensin I and subsequently angiotensin II, mediated by Angiotensin Converting Enzyme. Angiotensin II then stimulates aldosterone release from the adrenal zona glomerulosa. The net result of this system's activation is increased renal sodium resorption and increased blood pressure (13). This pathway and its role in blood pressure maintenance is generally accepted and disruption of this system is the leading cause of secondary hypertension. A higher incidence of renal cell carcinoma is seen in patients with hyperaldosteronism compared to the general population (2-4) and some research suggests that survival and proliferation of renal cell carcinoma may be influenced by increased levels of aldosterone (14,15). Actions of aldosterone in addition to its documented renal and cardiovascular roles that are yet to be understood may represent additional value of identification and management of hyperaldosteronism.

Despite an association between primary hyperaldosteronism and renal cell carcinoma observed in the literature, we believe this is the first case report describing a case of bilateral renal cell carcinoma in a patient with Conn's syndrome in remission.

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