CASE REPORT

Adrenocortical carcinoma, an unusual cause of secondary hypertension

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Accepted 21 November 2016

SUMMARY

We present the case of a female patient aged 39 years who was admitted to our hospital due to hypertension, severe hypokalaemia and metabolic alkalosis; physical examination was remarkable for plethoric moon face, centripetal obesity and bilateral lower extremity oedema. She was admitted for intravenous potassium replacement and further assessment of hypertension and associated clinical findings. Laboratory testing showed increased levels of aldosterone, renin, cortisol, testosterone and androstenedione. An abdominal CT revealed a large mass in the right adrenal gland with hepatic involvement. The patient was started on antihypertensive medications and underwent laparoscopic surgery for mass and liver biopsy. The pathological diagnosis was adrenocortical carcinoma with liver metastasis. Hyperaldosteronism is a cause of secondary hypertension and its diagnosis is usually benign. Adrenocortical carcinoma is a rare condition and aldosterone secreting tumours are even rarer; associated hypertension usually improves after tumour resection, but with the presence of metastasis, blood pressure control is difficult.

BACKGROUND

Essential hypertension (also referred to as primary hypertension) is one of the most prevalent diseases worldwide and it is the most common condition in patients that present to the emergency department with elevated blood pressure readings. There is a variety of common and uncommon medical conditions that can cause secondary hypertension; these conditions can coexist with primary hypertension and impair blood pressure control. In some cases, these underlying conditions can be the sole precipitator of hypertension; diagnosing and treating these other causes can potentially normalise blood pressure.

CASE PRESENTATION

A woman aged 39 years presented to our emergency department due to a history of hypertension, facial and lower extremity oedema as well as polyuria, polydipsia, irregular menses and malaise. Her medical history was resolved peritoneal tuberculosis. At the time of presentation at our hospital, her blood pressure was 170/98 mm Hg. On physical examination, she had plethoric moon face, buffalo hump, central obesity and bilateral lower extremity oedema.

INVESTIGATIONS

Laboratory tests drawn at the emergency room showed hypokalaemia (1.23 mmol/L) and glucose levels of 162 mg/dL. EKG revealed changes associated with hypokalaemia (figure 1). A central venous catheter was placed for intravenous potassium replacement and was admitted for evaluation and management. Further testing revealed hypercholesterolaemia (253 mg/dL), hypertriglyceridaemia (349 mg/dL), increased LDH (443 IU/L) and glycated haemoglobin of 8.7%. Arterial blood gases showed: PaO₂, 70 mm Hg; PaCO₂, 30 mm Hg; pH, 7.51; HCO₃⁻, 32 mEq/L; lactate 1.5 mmol/L. Chest X-ray, urinalysis and rest of initial work up were unremarkable.

DIFFERENTIAL DIAGNOSIS

Owing to the presence of hypokalaemia, hypertension, metabolic alkalosis and physical examination abnormalities, a hormonal cause was presumed, most likely suprarenal aetiology. Blood and urine samples were taken for hormonal status evaluation. Several abnormalities were found in the hormonal panel: elevated testosterone, 23.2 pg/mL (normal range 0–4.1 pg/mL), elevated androstenedione, 4.67 ng/mL (normal range 0.3–3.5 ng/mL), elevated aldosterone, 187.2 pg/mL (normal range 20–180 pg/mL), elevated renin, 89.4 µIU/mL (normal range 2.8–39.9 µIU/mL), elevated urinary cortisol, 3951 µg/24 hours (normal range 58–403 µg/24 hours) as well as elevated serum cortisol levels, 51.3 g/dL (normal range 8.7–22.4 g/dL). Serum catecholamines (epinephrine, norepinephrine and dopamine) and urine metanephrines were within normal range, ruling out pheochromocytoma. Other hormones such as adrenocorticotrophic hormone, dehydroepiandrosterone, follicle-stimulating hormone, oestradiol, luteinising hormone and thyroid hormones were normal. Owing to hormonal evaluation abnormalities, a contrast-enhanced CT of the abdomen was performed to evaluate the presence of a possible suprarenal mass. The CT revealed a 13 cm mass with hypervascularity arising from the right suprarenal gland that partially compressed the inferior vena cava; there were liver metastatic lesions as well as lymph node enlargements in mesentery and retroperitoneal space (figure 2A–C). Echocardiogram showed no evidence of cardiac abnormality. Laparoscopic biopsies of the mass and liver were obtained. Histopathological and immunohistochemistry diagnosis was adrenocortical

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To cite: Veron Esquivel D, Batiz F, Farias Vega A, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2016-217918

Figure 1 Twelve-lead EKG showing typical ST hypokalaemia segment deviation changes, more evident in precordial leads.

carcinoma. Liver biopsy showed metastatic adrenocortical carcinoma.

TREATMENT

During her hospitalisation, normal levels of serum potassium were reached with normalisation of EKG. After histopathological diagnosis, a right adrenalectomy and partial hepatectomy was performed without complications. Even after surgery, blood pressure control was difficult; oral antihypertensive treatment was added progressively until all the following medications were used simultaneously: lisinopril 20 mg PO once a day, amlodipine 5 mg PO two times a day, metoprolol 95 mg PO once a day, spironolactone 100 mg PO once a day and prazosin 1 mg PO three times a day. Blood pressure oscillated around 140/80 mm Hg.

OUTCOME AND FOLLOW-UP

Antihypertensive medication was unsuccessfully weaned off and the patient continues with the same treatment. She is currently under oncological treatment, but prognosis is poor.

DISCUSSION

Secondary hypertension screening is usually performed in patients with resistant hypertension (patients who are unable to achieve blood pressure goals with three drugs including a diuretic);¹ however, abnormal clinical and laboratory data should alert the clinician to seek underlying causes of hypertension, especially because these conditions are often treatable, leading to normalisation of blood pressure.

Aside from renovascular disease, hormonal imbalances are the most common cause of secondary hypertension;² the most common of them is primary aldosteronism and it is more prevalent than it was previously reported.³ The most frequent clinical presentation is as a unilateral aldosterone-producing adenoma; less common presentations include aldosterone producing malignant tumours and familial hyperaldosteronism.

Regardless of the source of aldosterone production, there are three key points to suspect the diagnosis: hypertension, hypokalaemia and metabolic alkalosis;⁴ these findings should encourage the decision to screen patients with plasma aldosterone concentration (PAC) as well as levels of plasma renin activity (PRA) (or plasma renin concentration); an elevated PAC, a diminished PRA and a PRA/PAC ratio >20 suggests primary hyperaldosteronism but increased concentrations in both (PRA and PAC) and a PRA/PAC ratio <10 suggests a secondary hyperaldosteronism, like a malignant secreting tumour.⁵ These findings require an abdominal CT or MRI to rule out a hormone-producing tumour.

Adrenocortical carcinoma is uncommon; its incidence is 1–2 per million per year. Approximately only 60–70% secrete hormones and its usual presentation is Cushing's syndrome.^{6–7} Only <10% of secreting tumours produce aldosterone;⁸ accordingly, this case is an uncommon presentation of this rare tumour. After adrenalectomy, blood pressure usually drops but occasionally antihypertensive drugs are needed. ACE inhibitors or angiotensin receptor blockers are recommended in combination with spironolactone rather than thiazides.⁹ Cortisol level elevation in this patient might have contributed to poor

Figure 2 (A) Axial CT of the abdomen showing right suprarenal mass (black arrow) and node enlargement in the retroperitoneal space (white arrow), (B) abdominal mass showing heterogeneous densities with contrast enhancement (black arrow) and hepatic involvement (white arrows), (C) coronal view showing large suprarenal mass (black arrow).

hypertensive control. Although ketoconazole use is controversial in Cushing's disease,¹⁰ it might have been a useful additional treatment for this patient.

Learning points

- ▶ Secondary causes of hypertension must be sought in resistant hypertension and/or in patients with clinical findings that suggest an underlying cause of hypertension.
- ▶ Hypertension, hypokalaemia and metabolic alkalosis are highly suggestive of hyperaldosteronism.
- ▶ Plasma renin activity (or plasma renin concentration), plasma aldosterone concentration and a contrast-enhanced abdominal CT are essential to determine the cause of hyperaldosteronism.
- ▶ Adrenocortical carcinomas are rare, they usually present as Cushing's syndrome and they only secrete aldosterone in 10% of cases.

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Contributors All four authors were actively responsible for the decisions taken in the patient's care. DVE and FB were responsible for data collection and conception of the case report. AFV and PACG helped with the critical revision of the article as well of the final approval of the version to be sent.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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