CASE REPORT

Bilateral Aldosterone-Producing Adrenocortical Carcinoma: a Rare Entity

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Abstract Adrenal cortical carcinomas (ACC) are rare aggressive malignant neoplasms with a reported incidence of 1–2 cases per 1 million population and account for 0.05–0.2 % of all malignancies. About 60 % are functional tumors and majority, 40 % present with Cushing's syndrome. Rarely, 2.5 to 11 % present with hypertension due to increased secretion of aldosterone and are usually unilateral. Bilateral aldosterone-producing adrenocortical carcinoma (APAC) has not been reported yet. We report a case of bilateral APAC in a 22-year-old male.

Keywords Aldosterone · Carcinoma · Hypertension · Hypokalemia

Introduction

Adrenal cortical carcinomas (ACC) are unusual and aggressive malignant neoplasms with reported incidence of 1–2 cases per 1 million population and accounts for only 0.05–0.2 % of all malignancies [1]. In larger series APAC accounts

for 2.5 to 11 % of functional ACCs [1, 2]. Persistent hypertension and weakness due to unrelenting hypokalemia are the typical presenting features, and high index of suspicion is required to establish the diagnosis. Only unilateral aldosterone-producing adrenocortical carcinomas (APACs) have been reported in literature. Here, we report a rare case of a young male presenting with hypertension and persistent hypokalemia and diagnosed with bilateral APAC.

Case Report

A 22-year-old male was referred to our hospital for evaluation of generalized weakness, persistent headache, and on-and-off left flank pain. His hypertension was not being controlled even on three antihypertensive drugs. There was no history suggestive of renal failure or raised intracranial tension. General physical and systemic examination was unremarkable. All routine blood investigations were unremarkable except persistent hypokalemia (2.9 mmol/l). Ultrasound whole abdomen with renal artery Doppler to look for renal artery stenosis revealed normal bilateral renal artery flow dynamics, but to surprise there was a left heteroechoic suprarenal mass; bilateral kidneys appeared to be normal and rest of the abdominal findings were unremarkable. Contrast enhanced abdomino-pelvic computerized tomography scan of the abdomen revealed bilaterally heterogeneously enhancing suprarenal masses with calcifications of size 10.1×7.7 cm and 2.7×2 cm on the left and right side, respectively, with no evidence of distant metastasis, Fig. 1. Bilateral kidneys were grossly normal. He was initially evaluated on the lines of pheochromocytoma with 24 h urine vanillyl mandelic acid (VMA) 136 mg/24 h (normal range 1.6–7.3), metanephrine 76.5 µg/24 h (normal ≤ 374.7), adrenaline 3.83 µg/24 h (normal range 4–20), and noradrenaline 184.03 µg/24 h

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Fig. 1 Non-contrast and contrast enhanced abdomino-pelvic computerized tomography scan of the abdomen showing bilateral heterogeneously enhancing suprarenal masses of size 10.1×7.7 cm and 2.7×2 cm on the left and right side, respectively with calcifications

(normal range 20–105). There was no uptake in tumor on metaiodobenzylguanidine (MIBG) scan. Then due to persistent hypokalemia he was also evaluated for plasma aldosterone levels and plasma rennin activity. The aldosterone levels were 429 pg/ml (normal range, 10.0 to 105.0) in the supine position and 727 pg/ml in the upright position (normal range, 34.0 to 273.0). Plasma rennin activity was 0.09 nmol/l/h. After this initial work-up, he was started on spironolactone (100 mg twice daily) and oral potassium chloride. An open bilateral adrenalectomy with left radical nephrectomy was performed as mass on left side was not separable from the kidney. The left-sided tumor was grossly gray-tan solid mass measuring $11 \times 8 \times 8$ cm. Histopathology revealed a solid nest of anaplastic cells with frequent mitoses and necrosis consistent with adrenocortical neoplasm with invasion into perinephric fat and anterior surface of the kidney with renal vein thrombus, Fig. 2. On immunohistochemistry (IHC) study, tumor cells of left and right adrenal mass were focally immunopositive for inhibin and synaptophysin, respectively, and both were immunonegative for CK, EMA, PAX8, and chromogranin, Fig. 3. His potassium level and blood pressure normalized after 2 weeks. He was started on steroid replacement therapy in consultation with an endocrinology team. The patient is doing fine at 3 months of follow-up.

Discussion

Approximately, 60 % of patients with ACC presents with clinical features of adrenal hormone excess [3]. ACCs are

bilateral in only 2 to 10 % of cases [4]. ACC with an exclusive oversecretion of mineralocorticoids, i.e., aldosterone and presenting with hypertension are exceedingly rare [2]. In less than 1 % of patients with Conn's syndrome with primary hyperaldosteronism, a unilateral APAC can be identified [5]. Bilateral aldosterone-producing ACC have not been reported yet. ACC has a bimodal distribution by age, with cases clustering in children under 5, and in adults 30–40 years old. Excess aldosterone secretion leads to hypokalemia and hypertension. A few specific symptoms such as muscle weakness and cramping, palpitations, headache, polydipsia, polyuria, and nocturia, or a combination of these symptoms, may be present in cases of marked hypokalemia [6]. Our patient reported with similar complaints of generalized weakness and headache with persistent hypertension. Patients with suspected primary hyperaldosteronism, in the morning ambulatory paired random plasma aldosterone concentration and plasma renin activity can be done as screening test, and can be confirmed by an oral sodium loading test, an intravenous saline infusion test, or a fludrocortisone suppression test [2]. Management includes local and distant staging and investigations to determine the functional status and type of adrenal tumor. After exclusion of metastasis and preoperative preparation, surgery is the mainstay of treatment, even in bilateral adrenocortical carcinoma. Adjuvant mitotane treatment may be utilized to potentially improve cure rates and increase survival. But, a robust clinical literature has not been consistent. A higher rate of recurrence-free survival with mitotane was provided by Terzolo et al. in 2007 [6]. Mitotane concentrations ≥ 14 mg/l predict response to adjuvant treatment and is

Fig. 2 Histopathologically, the aldosterone-producing adrenocortical carcinoma shows solid nests of bland to anaplastic cells, with frequent mitoses and necrosis (H&E, $\times 400$)

Fig. 3 Immunohistochemistry of left (a) and right (b) adrenal tumor focally positive for synaptophysin (a) and inhibin (b)

associated with a prolonged RFS. A monitored adjuvant mitotane treatment may benefit patients after complete surgical excision of ACC [7]. The patient reported has also been started on mitotane therapy. Rarely, genetic association as in multiple endocrine neoplasia type 2, Von Hippel-Lindau syndrome has to be looked for, especially in cases of bilateral disease [8, 9]. The significance of keeping the possibility of APAC in a patient with persistent hypertension and hypokalemia, is well presented in this case report.

Conclusion

This case report highlights that, while rare, aldosterone-producing adrenocortical carcinomas (APACs) do occur and high index of suspicion should be kept in a patient presenting with uncontrolled hypertension. Bilateral aldosterone-producing adrenocortical carcinoma reported here is probably the first, reported in literature.

Acknowledgments Bombay Hospital

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

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