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A Rare Cause of Hypokalemia: Aldosterone-Secreting Adrenocortical Carcinoma

Hipokaleminin Nadir Bir Nedeni: Aldosteron Salgılayan Adrenokortikal Karsinom

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Dear Editor,

Adrenocortical carcinoma (ACC) is a rare malignancy accounting for 0.05-0.2% of all cancers (1). Determinants of prognosis are the stage of disease and completeness of resection(2). Approximately 60% of ACCs are hormonally active and glucocorticoids and/or androgens are most frequently over-secreted (2). Rapid development of signs and symptoms of Cushing's syndrome is the most frequent presentation (3). Aldosterone-secreting ACC is extremely uncommon, comprising 0% to 7% of all functioning ACCs and presents with severe hypertension and profound hypokalemia (4). Here we report a case diagnosed as aldosterone producing adrenocortical carcinoma presented with severe hypokalemia and hypertension.

A 32-year-old man referred to our instution because of pain and marked weakness especially in his lower extremities for 2 months. On admission his blood pressure was 180 mmHg systolic and 110 mmHg diastolic. Laboratory investigation revealed severe hypokalemia (2.6 mmol/l (normal: 3.5-5.5 mmol/l), elevated serum aldosterone (39.0 ng/dl (normal: 0.8-13 ng/dl) with suppressed plasma renin activity (0.07 ng/ml/h). Serum sodium level was 142 mmol/l (normal: 135-146 mmol/l). Serum aldosterone level was not supressed (38.2 ng/dl) after saline infusion test. Serum dehydroepiandrosterone sulfate (DHEA-SO4) was 150 mcg/dl (normal: 80-560), Δ4-androstenedione was 1.91 ng/ml (normal: 0.5-4.8) and total testosterone was 447.3 ng/dl (normal: 229.8-799.8) (Table 1).

Suppressed renin levels, increased aldosterone levels with an aldosterone/renin ratio >30 were suggestive findings of aldosterone-producing adenoma of the adrenal gland or bilateral adrenal hyperplasia. Computed tomography demonstrated a large (4.6 cm) left-sided adrenal tumour which is heterogeneous and has lobulated margin without a contrasting pattern of adenoma (Figure 1). 24-h urinary catecholamines and low-dose dexamethasone-suppressed plasma cortisol concentrations were all normal.

At surgery, an adrenal mass (70.1 grams) was removed, which was encapsulated and lobulated. Tumour diameter was 3.5 cm. Histopathological examination showed focal necrosis. The tumour infltrated its capsule and sinusoidal invasion was present. 20 mitotic cells/10 high power fields were seen. Ki-67 proliferation index was %25. Vimentine, synaptophysin and melan-A were positive, chromogranin was focal positive and pancreatin was negative with immunohistochemical examination. The tumor met five of the criteria of Weiss used in histological diagnosis of adrenocortical carcinoma (number of mitosis, nuclear atypia, atypical mitosis, capsular invasion and sinusoidal invasion). Pathological diagnosis was adrenocortical carcinoma.

There were no sign of adrenal insufficiency during and after the surgery. He did not take any treatment after surgery. Serum potassium and aldosterone returned to normal after adrenalectomy. His symptoms such as weakness and pain were also resolved. One year after adrenalectomy, the patient is alive, normotensive, normokalemic and with no signs of recurrence of the primary adrenal tumor (Table 1).

In summary, we reported the case of a 32-year-old male who initially presented with hypertension and severe hypokalemia and was found to have an aldosterone-secreting adrenocortical carcinoma. Aldosterone-producing adrenocortical carcinom (APAC) is a rare cause of hypertension often diagnosed late. Aldosterone hypersecretion often concurs with that of other steroids, including glucocorticoids, estrogens or androgens. In most cases clinical picture reveals classical signs of Conn's syndrome; hypertension and hypokalemia. Weakness and diffuse muscular pain are common due to severe hypokalemia, but these symptoms are not useful in differentiating APAC from an aldosterone secreting adenoma or hyperplasia (5). Although there are several reports suggesting increased serum levels of

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Table 1. Potassium levels and hormone profile of the patient before and after the surgery

	Before surgery	1 month after surgery	12 months after surgery	Normal ranges
Serum potassium (mmol/l)	2.6	4.5	4.5	3.5-5.3
Plasma renin activity (PRA) (ng/ml/h)	0.07	1.76	3.33	1.5-5.7
Aldosterone (ng/dl)	39.0	8.4	16.4	0.8-13
Aldosterone/Renin ratio	557.1	4.7	4.92	
Basal serum cortisol (mcg/dl)	13.7	12.1	12.6	4.6-22.8
Plasma ACTH (pg/ml)	31.2	27.6	41.3	0-46
Serum testosterone (ng/dl)	447.3	445.3	441.0	229-799
Serum Δ4-androstendione (ng/ml)	1.9	2.0	NA	0.5-4.8
Serum DHEAs (mcg/dl)	150	163	144	80-560

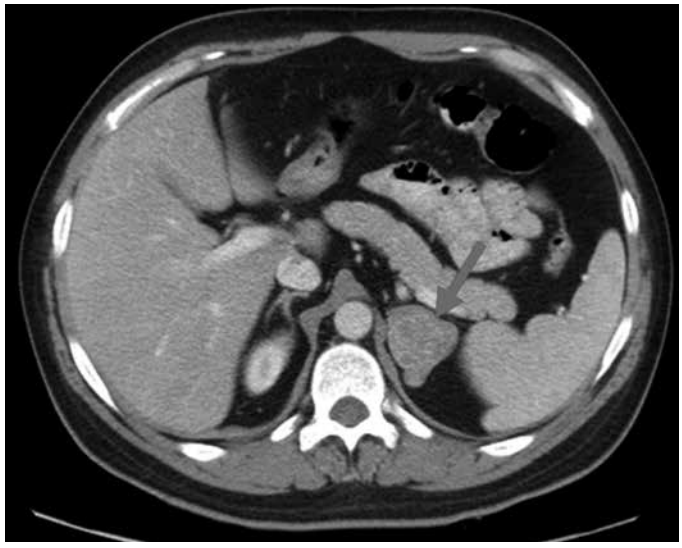

Figure 1. Appearance of left-sided adrenal tumour on computer tomography

adrenal androgens such as DHEA-S may indicate adrenocortical carcinoma (2,6), normal levels does not rule out the diagnosis as noted in our patient (7,8). The most effective treatment for ACC is complete resection, which was performed in the case of our patient (2). Pathological examination revealed adrenocortical carcinoma though focal chromogranin A expression was observed. Clinical presentation of the patient was consitent with a cortical lesion (hyperaldosteronism) and specimen was immunohistochemically positive for melan-A which is a specific marker in differantiating cortical from medullary adrenal tumors (9). It seems that neither the size at CT scan nor the histological features accurately predict clinical course and outcome in APAC (4). Although early diagnosis and surgery are cornerstones of treatment, it has been implicated that APAC may be assosicated with unique operative risks and outcomes (5). Our patient is still in good health 12 months after surgery whether he is not given any adjuvant therapy. In conclusion this patient is important to keep in mind the extremely rare cause of hypertension and hypokalemia.

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