Adrenocortical carcinoma producing 11-deoxycorticosterone: A rare cause of mineralocorticoid hypertension

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Abstract. A 37-yr-old man presented with the classic signs of mineralocorticoid excess hypertension and hypokalemia. The cause was not aldosterone excess, but elevation of plasma 11-deoxycorticosterone (DOC). Computed tomography (CT) scans showed a large right adrenal mass without signs of metastatic disease. The tumor was removed by open laparotomy, and histology revealed an adrenocortical carcinoma.

INTRODUCTION

The combination of hypertension, hypokalemia, metabolic alkalosis, and low plasma renin activity characterises mineralocorticoid hypertension (1). Hypokalemic hypertension, caused by mineralocorticoids other than aldosterone, is rare (2). We here present a patient with an adrenocortical carcinoma producing 11-deoxycorticosterone (DOC) leading to hypokalemic hypertension. DOC is an aldosterone precursor and is itself a potent mineralocorticoid (3).

MATERIALS AND METHODS

Serum and urinary aldosterone levels were determined using a commercial radioimmunoassay (RIA) kit (Diagnostic Systems Laboratories, Inc., Webster, Texas, USA). Intra-assay coefficients of variation (CVs) and inter-assay CVs were <8 and <10%, respectively. Plasma renin activity was measured with a commercial RIA kit (Biochem Immunosystems, Freiburg, Germany). Intra-assay CVs and inter-assay CVs were ≤6%.

CASE REPORT

Two yr after diagnosis, the patient is in good general condition and there is no sign of recurrence or metastatic disease, despite the large tumor size. DOC producing adrenocortical carcinomas causing mineralocorticoid hypertension are very rare, so far only 10 cases have been described in the literature.

STERIODS MENTIONED IN TABLE 2 WERE DETERMINED IN THE STEROID LABORATORY OF THE DEPARTMENT OF PHARMACOLOGY, UNIVERSITY OF HEIDELBERG. ALL STEROIDS ANALYZED WERE MEASURED BY SPECIFIC RIA, USING TRITIATED STEROIDS (AMERSHAM BIOSCIENCES, FREIBURG, GERMANY) AND SPECIFIC ANTIBODIES, RAISED AND CHARACTERIZED IN THE STEROID LABORATORY, AS DESCRIBED ELSEWHERE (4). PRIOR TO RIAS, STEROIDS WERE EXTRACTED FROM PLASMA OR URINE (PRE-TREATED WITH β-D-GALACTOSIDASE) WITH ORGANIC SOLVENTS AND CHROMATOGRAPHICALLY PURIFIED USING CELITE COLUMNS (CELITE 545 AW; SIGMA ALDRICH, TAUFKIRCHEN, GERMANY). INTRA-ASSAY CVs AND INTER-ASSAY CVs WERE 10 AND <15%, RESPECTIVELY.

A 37-yr-old male was referred to our Department for work-up of suspected pheochromocytoma in December 2001.

Steroids mentioned in Table 2 were determined in the steroid laboratory of the Department of Pharmacology, University of Heidelberg. All steroids analyzed were measured by specific RIA, using tritiated steroids (Amersham Biosciences, Freiburg, Germany) and specific antibodies, raised and characterised in the steroid laboratory, as described elsewhere (4). Prior to RIAs, steroids were extracted from plasma or urine (pre-treated with β-glucuronidase) with organic solvents and chromatographically purified using Celite columns (Celite 545 AW; Sigma Aldrich, Taufkirchen, Germany). Intra-assay CVs and inter-assay CVs were 10 and <15%, respectively.

Arterial hypertension had been discovered some weeks previously by chance, when the patient had performed a blood pressure self measurement. Ultrasonography of the abdomen had revealed a large tumor in the right epigastrium. Computed tomography (CT) had been performed on a Somatom AR. Star scanner (Siemens, Forchheim, Germany). Scan parameters had been: 5 mm slice thickness and 5 mm feed/rotation resulting in a pitch of 1. On unenhanced images, a right suprarenal mass with a size of 8.8x10.5 cm had been found. It had revealed a non-homogenous density, with values

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Adrenal carcinoma producing DOC

Since urine epinephrine concentration had been found to be slightly elevated, the attending physician postulated pheochromocytoma.

On admission to our Department, the patient reported an unremarkable past medical history. In particular, hints at endocrine disorders were missing. The patient was unmedicated and free of symptoms or signs. Specifically, on questioning, palpitations, unmotivated sweating or intermittent facial pallor were denied. Clinical examination showed an adult male of normal body composition (179 cm, 70 kg) and good general condition. Blood pressure and 24-h ambulatory systolic and diastolic blood pressure were slightly raised (Table 1), the pulse rate was normal. The liver and spleen were not enlarged. Routine hematological and biochemical findings were normal except for slight hypokalemia (Table 1). TSH, free T\(_4\) and free T\(_3\) levels were within the normal range. An ECG was normal without signs of hypertrophy and arrhythmias.

Since urinary catecholamine excretion was within the normal range and iodine\(^{131}\)-meta-iodobenzylguanidine (MIBG) scintigraphy was negative, a catecholamine producing tumor was unlikely. There were no clinical signs of hypercortisolism. Basal hormone levels of cortisol (19.3 µg/dl, normal range 5-23) and ACTH (6.8 pmol/l, normal range 2-11) and diurnal rhythms were within the normal range. Plasma levels of the androgens androstenedione (210 ng/dl, normal range 30-310), testosterone (385 ng/dl, normal range 240-830), and dehydroepiandrosterone sulfate (363 µg/dl, normal range 109-666) were within the normal range.

As the combination of an adrenal mass, hypokalemia and hypertension raise the suspicion of a mineralocorticoid-producing tumor, and since primary aldosteronism is the most common cause of mineralocorticoid induced hypertension, renin activity and aldosterone concentration were measured. Serum aldosterone concentration was found to be normal, urinary

Table 1 - Major clinical, biochemical, and hormonal findings on admission to our Department.

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Normal range</th>
</tr>
</thead>
<tbody>
<tr>
<td>BP</td>
<td>160/100</td>
</tr>
<tr>
<td>24-h ambulatory BP</td>
<td>Mean value 147/104</td>
</tr>
<tr>
<td>Serum potassium</td>
<td>3.4</td>
</tr>
<tr>
<td>Serum aldosterone</td>
<td>43</td>
</tr>
<tr>
<td>Urinary aldosterone</td>
<td>1.62</td>
</tr>
<tr>
<td>Plasma renin activity</td>
<td>0.2</td>
</tr>
<tr>
<td></td>
<td>0.12-1.59 ng Ang/l/ml/h</td>
</tr>
</tbody>
</table>

BP: blood pressure.

between 20 and 110 Hounsfield U which was due presumably to recent hemorrhage (Fig. 1A). Forty sec after IV contrast material administration, the tumor had showed intense peripheral enhancement with large central hypointensity due to necrosis (Fig. 1B). A slow wash-out phenomenon had been verified in the portal-venous phase.

Fig. 1 - Computed tomography (CT) of the abdomen reveals a suprarenal mass appearing non homogenous on unenhanced images (A) and showing central necrosis on contrast-enhanced images (B).