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Pitfalls in the diagnostics of aldosterone-producing adrenocortical carcinoma

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A 50-year-old male with a hypertensive crisis with deep hypokalaemia, metabolic alkalosis, and symptoms of muscle weakness and numbness was admitted to the hospital two years after the initial diagnosis of hypertension. Serum aldosterone level was elevated, and plasma renin activity was lowered (Fig. 1A). Aldosterone-to-renin ratio exceeded 100 ng/dL/ng/mL/h [cut-off value > 20–40 (1)]. Computed tomography (CT) of the abdomen revealed a tumour in the right adrenal gland, size 32 × 26 × 31 mm (Fig. 1B). The radiological description was as follows: "the unenhanced attenuation of 29 HU (Hounsfield Units), 74 HU one minute after contrast infusion and 48 HU in the late phase, resulting in the absolute percentage wash-out value of 57%". Consequently, lipid poor adenoma was recognised. The diagnosis of primary hyperaldosteronism was confirmed in saline infusion test, and adrenal venous sampling showed lateralisation of aldosterone secretion to the right adrenal gland. The patient underwent laparoscopic adrenalectomy. Histopathology revealed a 4 cm fragmented tumour with unexpected features of atypical mitosis, mitotic rate 6/50 high-power fields, sinusoids invasion, and < 5% of clear cells. Ki67 index proliferation was high (7–8%), and the tumour met criteria of adrenocortical carcinoma. After adrenalectomy, both hypertension and hypokalaemia resolved. The patient was referred to our Department, where mitotane treatment was introduced. Due to significant liver enzyme elevation the therapy was withdrawn after only five months. To date, 67 months after surgery, the patient is free of recurrence as well as biochemical and clinical features of hyperaldosteronism.

Hypertension is regarded as one of the most frequent cardiac disorders. About 10–20% of hypertensives have secondary hypertension. Primary aldosteronism (PA) is the commonest form, with approximately 10% of unselected hypertensives affected [1]. PA is almost always caused by benign lesions. In exceptional cases, adrenocortical carcinoma (ACC), an orphan malignancy with heterogenous clinical phenotype, can be a source of autonomous aldosterone production [2]. The typical presentation of ACC is Cushing's syndrome and/or hyperandrogenism. Although the co-secretion of several adrenal hormones including aldosterone is also a hallmark of ACC, pure aldosteronism is atypical and extremely rare (approx. 2.5% of all functional ACC cases [3]).

Careful evaluation of every adrenal tumour, even with univocal primary aldosteronism phenotype, can help to avoid pitfalls in non-routine situations. Abnormal cortisol after 1 mg dexamethasone suppression as well as elevated androgens levels could have been indicative for adrenal malignancy in the reported case; however, they were not performed. What is more, all patients with PA should undergo abdominal CT and/or magnetic resonance. As the described case shows, the cessation of the diagnostic process with only spironolactone therapy in patients with clinical suspicion of PA can have dramatic consequences and should not be practiced. According to Endocrine Society guidelines [1], excluding masses that may represent malignancy is the first diagnostic goal in every patient with hyperaldosteronism. Typically, large masses are at greater risk of malignancy; however, small ACCs and aldosterone-producing ACCs (APACs) have also been reported [2, 4]. Tumours with density ≤ 10 HU in non-contrast CT generally do not need further radiological evaluation. All other lesions should be treated with caution. Although unenhanced attenuation values subtly exceeding 10 HU are typical for lipid

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Parameters	Results	Normal range
Plasma aldosterone (ng/dl): recumbent supine after saline infusion	 12,3 80,6 48	 1,76-23,2 2,52-39,2 <10
Plasma renin activity (ng/ml/h)	0,12	>1
Aldosterone-to-renin ratio (ng/dl/ng/ml/h)	671,6	<30
Morning plasma cortisol (µg/dl)	12,5	6,2-19,4
Urine metoxycatecholamines (µg/24h)	231/240	<1000
Plasma potassium (mmol/l)	2,1	3,5-5,5
Potassium urine excretion (mmol/24h)	114,7	25-125

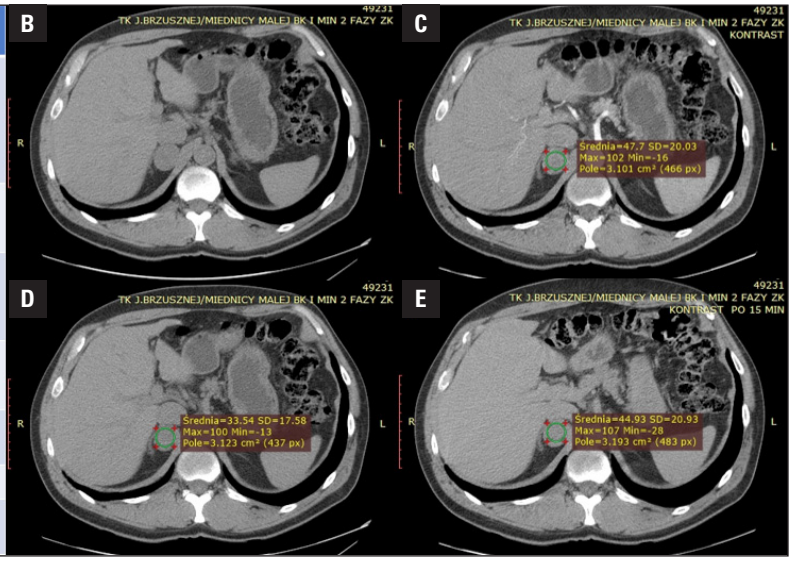

Figure 1. *A. Hormonal test results. B. Computed tomography (CT) of the abdomen showing the tumour in the right adrenal gland. C.–E. Re-evaluation of CT images showing suspicious attenuation values before, 1, and 15 minutes after contrast administration, respectively*

poor adenomas, one should consider values close to 30 HU suspicious, regardless of hormonal status. Absolute percentage wash-out (APW) values characteristic for lipid poor adenomas are more than 50% and 60% 10 and 15 minutes after contrast administration, respectively. Surprisingly, in the case discussed above, the re-evaluation of CT images showed slightly different attenuation values than previously noted: 34 HU, 48 HU, and 45 HU before, 1 minute, and 15 minutes after contrast infusion (Fig. 1C–E). In consequence, APW was only 21%. However, even the previously calculated APW of 57% was incorrect for the 15th minute of wash-out and corresponded to suspicious imaging phenotype.

In the case described, the time gap from first CT to adrenalectomy was as long as a year because of the misleading radiological description suggesting lipid-poor adenoma. Fortunately, the course of the disease was favourable with no distant metastases. Adrenocortical carcinoma is considered an aggressive tumour of rapid clinical course and poor prognosis with unexpected, even late recurrences [5]. However, less dynamic courses of the disease have also been reported for APACs [2]. However, close monitoring of each ACC patient after surgery is necessary. One should also note that the change of hormonal profile of a recurrent tumour may rarely occur due to dedifferentiation of cells with altered steroidogenic enzymes profile.

To conclude, precaution in the approach to every adrenal mass is of great importance in order not to miss atypical ACC cases.

Author's statement

Agnieszka Ł.Sz. and K.M.N. are the first co-authors.

Conflict of interest

None declared.

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