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A nonspecific clinical picture and the course of Conn syndrome — current findings in the screening program for hypertensive patients

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Abstract

Conn syndrome (CS), next to bilateral adrenal hyperplasia, is one of the most common causes of primary hyperaldosteronism. It leads to potentially curable secondary hypertension.

The 54-year-old woman underwent an abdominal computed tomography (CT) examination for symptomatic nephrolithiasis. A focal lesion of the left adrenal gland was found with a diameter of 16 mm and a density of 34 Hounsfield units (HU). The lesion was under observation, and the next magnetic resonance imaging (MRI) scans showed a slight enlargement of the lesion to a size of 18 x 12 mm. The lesion was interpreted as an atypical adenoma of the adrenal gland. According to the course, the patient was referred to the endocrinology clinic. The patient's symptoms included hypertension and paresthesia. During two separate hospitalizations, Conn syndrome was diagnosed using a specific laboratory test. The patient was successfully treated by surgical intervention, resulting in remission of all symptoms.

This case illustrates the difficulties in diagnosing primary hyperaldosteronism. The symptoms of Conn syndrome may vary in severity or may be absent. Early diagnosis and

appropriate treatment can save many ill individuals from cardiovascular, metabolic, or renal complications. The case underscores the need for screening hypertensive patients using the aldosterone-renin ratio (ARR).
Key words: Conn syndrome; adrenalectomy; primary hyperaldosteronism; aldosterone, till-table test

Introduction

Conn syndrome (CS) is one of the most common causes of primary hyperaldosteronism, along with bilateral adrenal hyperplasia. It leads to potentially curable secondary hypertension. It also causes inhibition of renin secretion, cardiovascular and renal disease. The main symptoms of high aldosterone are polyuria, polydipsia, paresthesia and muscle cramps [1].

Case report

The 54-year-old woman underwent an abdominal computed tomography (CT) examination for symptomatic nephrolithiasis. A focal lesion of the left adrenal gland was noted, which had a diameter of 16 mm and a density of 34 Hounsfield units (HU). The lesion was under observation, and the next magnetic resonance imaging (MRI) scans showed a slight enlargement of the lesion to a size of 18 x 12 mm. The lesion was interpreted as an atypical adenoma of the adrenal gland. According to the course, the patient was referred to the endocrinology clinic. The patient's symptoms included hypertension and paresthesia.

During hospitalization, the circadian rhythm of cortisol secretion was correct, with a slight decrease in the morning cortisol level and an increase at night, with a correct adrenocorticotropic hormone (ACTH) level (Tab. 1). Secretion inhibition was not achieved in the suppression test with 1 mg dexamethasone (8.8 μg/dL). Blood pressure fluctuations and electrolyte disturbances were not observed, so tests for stimulation of renin–angiotensin–aldosterone system (RAA) activity were not performed. Diagnostic testing in hospital was not continued because of the patient's refusal.

The patient underwent hypertension diagnosis in a primary care setting and was on antihypertensive medications for 6 years. During hospitalization, the focus was on evaluating an adrenal mass, and secondary hypertension investigation was not prioritized. Multiple blood pressure measurements were taken, revealing no significant fluctuations, which excluded dysfunctions in the renin-angiotensin-aldosterone system. Therefore, ambulatory blood pressure monitoring (ABPM) was not conducted upon discharge.

The following month, the patient again visited the clinic to have a control abdominal examination CT and to complete hormonal diagnostics. This imaging revealed a nodule in the left adrenal gland — a density of 30 HU. Further laboratory testing showed elevated cortisol levels in a daily urine collection. Based on the urine parameters and imaging results, it was decided to discontinue the Liddle test. Daily blood pressure measurements were normal, and electrolyte disturbances were not noted. It was decided to perform a tilt table test, which helped to diagnose a disease — primary hyperaldosteronism (Tab. 2). The patient was qualified for adrenalectomy, after which the patient's symptoms ceased and laboratory parameters normalized.

Discussion

The prevalence of adrenal cancer is approximately 4% to 10% and increases with age, with most adrenal glands showing no hormonal activity. However, when adrenal lesion hormonal activity is detected, it usually leads to a diagnosis of Cushing's syndrome, pheochromocytoma, or Conn's syndrome [2]. In a single center study, the prevalence of Conn syndrome was reported to be 2.6% of patients in primary care [3]. Patients with CS may account for as many as half of the patients admitted to the endocrinology department due to hypokalemia [4].

Primary hyperaldosteronism (PHa) appears to be the most common endocrine cause of secondary hypertension. Although PHa may be dramatically underdiagnosed, this condition should not be downplayed [5]. The presence of PHa increases cardiovascular risk and the risk of metabolic syndrome even more than primary hypertension [6]. Similar results have been obtained in relation to renal damage in PHa patients (also compared to primary hypertension) [7]. Secondary hypertension caused by PHa is also more difficult to control by standard pharmacological means [8].

Considering the risk of serious complications and the easy misdiagnosis of PHa, a screening program for hypertensive patients is recommended in the scientific literature. A 2016 Endocrine Society guideline recommends raising suspicion CS in patients with: hypertension (BP) above 150/100 mm Hg on each of three measurements taken on different days, with high blood pressure (BP 140/90 mm Hg) resistant to three conventional antihypertensive medications (including a diuretic), or controlled BP (140/90 mm Hg) on four or more antihypertensive medications; hypertension and spontaneous or diuretic-induced hypokalemia; hypertension and adrenal incidentaloma; hypertension and sleep apnea; hypertension and a family history of early-onset hypertension or cerebrovascular accident at a

young age (40 years); and any hypertensive first-degree relatives of patients with PHa [9]. However, the more recent 2021 Japan Endocrine Society guidelines recommend PHa screening in all hypertensives, highlighting only those groups with greater clinical significance [10].

Given the low level of awareness of PHa, its plausible nonspecific course, and the need for various specialized tests for confirmation, the postulate of screening tests goes hand in hand with the idea of diagnostic simplification [11]. The screening test recommended by both the Endocrine Society and the Japan Endocrine Society is the aldosterone-renin ratio (ARR)[9,10]. ARR above 10 is classified as a 93-94% specific test for PHa in hypertensive patients, while ARR above 10 with hypokalemia increases the specificity to almost 100% [11]. In one case presented, the ratio of aldosterone to renin was elevated almost fivefold above the threshold for PHa — but hypokalemia did not occur.

The topic of the economic aspects of a screening program for PHa has been poorly explored. Currently available publications are inconclusive or advocate screening and surgical treatment rather than pharmacotherapy for undiagnosed PHa and its complications [12].
The available treatments for PHa are surgical intervention and aldosterone antagonists (e.g., spironolactone). Currently, surgical adrenalectomy is recommended for unilateral PHa unless there are contraindications and the patient consents [13], and this method was chosen in the present case. Unfortunately, appropriate treatment of PHa usually leads to regression of its complications such as secondary hypertension or renal damage [14].

In CS, not in PHa in general, the very useful diagnostic method is imaging, which concerns CT and MRI [15]. In a plausible nonspecific course of CS (as in the present case), the disease may show up as an incidentaloma when assessed over time. On the other hand, recent studies from nuclear medicine revealed a possibility of CS detection using ^{11}C-labeled metomidate in positron emission tomography (PET) [16].

Conclusion

This case illustrates the difficulties in diagnosing primary hyperaldosteronism. Symptoms of Conn syndrome may vary in severity or may be absent. Early diagnosis and appropriate treatment can save many ill individuals from cardiovascular, metabolic, or renal complications. The case underscores the need for screening hypertensive patients using the aldosterone–renin ratio (ARR).

Conflict of interests

None.

Funding

None.

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Table 1. Laboratory tests results — part 1

Parameter	1st hospitalization	2nd hospitalization	Norm range with units
Cortisol (daily urine collection)	150.0	150.0	20.9–292.3 µg/24 h
Cortisol (morning serum)	6.8	6.8	4.3–22.4 µg/dL
Cortisol (evening serum)	9.3	7.5	3.09–16.66 µg/dL
Chromogranin A	7.4	6.4	<100 µg/L
ACTH	37.55	50.59	7.2–63.6 pg/mL
Natrium	140.0	143.0	136.0–145.0 mmol/L
Potassium	4.2	4.2	3.5–5.1 mmol/L
Metanephrine (daily urine collection)	499.5	25.4	43.0–260.0 µg/24 h
Normetanephrine (daily urine collection)	160.4	92.1	128.0–484.0 µg/24 h
3-methoxytyramine	702.0	71.8	55.0–247.0 µg/24 h

ACTH — adrenocorticotropic hormone

Table 2. Laboratory tests results — part 2

	Aldosterone	Norm range with units	Renin	Norm range with units	Aldosterone-to-renin ratio
Lying	42.2	1.76–23.2 ng/L	0.9	2.8–39.9 uLU/mL	46.89
Standing	27.0	2.52–39.2 ng/L	< 0.5	4.4 - 46.1 uLU/mL	> 54