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PRIMARY ALDOSTERONISM IN A PATIENT WITH AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE ASSOCIATED WITH POLYCYSTIC LIVER DISEASE

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ABSTRACT

Polycystic kidney disease is an autosomal dominant genetic disorder (ADPKD) associated with arterial hypertension, as a common and early manifestation. However, the combination of hypertension and hypokalemia is very rare in these patients and may have another cause. We present a case of a 45 years old man with ADPKD associated with primary hyperaldosteronism. Unilateral suprarenal macroadenoma on abdominal CT scan, severe hypokalemia and low activity of plasmatic renin led to diagnosis.

Keywords: polycystic kidney disease, activity of plasmatic renin, hypokalemia, primary aldosteronism

Introduction

Autosomal polycystic kidney disease (ADPKD) has a hereditary transmission and affects almost 12.5 million people worldwide, with an european prevalence less than 5 patients to 10000 people, and about 4000 cases in Romania (1). This disorder is caused by mutations in either of two genes: PKD-1 (polycystin-1) on chromosome 16, or PKD-2 (polycystin-2) on chromosome 4, and have various extrarenal manifestation as: hepatic cysts, intracranial aneurysms and arterial hypertension (2,3). Hypertension occurs early in ADPKD, usually before renal failure. Up regulation of the renin-angiotensin-aldosteron system is the major key in pathogenesis of hypertension, possibly caused by renal vascular compression due to cyst expansion (4,5). However, association with hypokalemia is very rare in these patients and is necessary to exclude other causes.

We report the case of a 45-year-old man hospitalized in Nephrology Department of Emergency County Hospital Constanta for severe sinus bradycardia (Figure 1) due to severe hypokalemia (1.6mmol/L). Main symptoms on presentation were: severe weakness, peripheral paresthesia and dizziness, progressively installed 1 week before. No history of vomiting, diarrhea or loop diuretic therapy was reported in the recent

antecedents. The patient was diagnosed with hypertension secondary to ADPKD, associated with PLD (polycystic liver disease) 3 years ago and received treatment with betablockers, calcium blockers, thiazides and angiotensin converting enzyme inhibitor. Patient's medical history included two hemorrhagic strokes in left lenticular area. There is no family history of hypertension or ADPKD.

Physical examination revealed high blood pressure (155/90 mmHg), sinus bradycardia (32 bpm) and diminished tendon reflexes at the inferior limbs. Other laboratory test showed hypernatremia (157mmol/L, normal range between 136 – 145 mmol/L), metabolic alkalosis (bicarbonates= 35mEq/L), normal plasma calcium level (9.3 mmol/L), normal serum creatinine (1.16 mg/dL), normal blood urea nitrogen (35 mg/dL), normal ESR, mild hepatic cytolysis (ASAT=41UI/L, ALAT=39 UI/L), urinalysis with hypostenuria, microalbuminuria and hyaline casts.

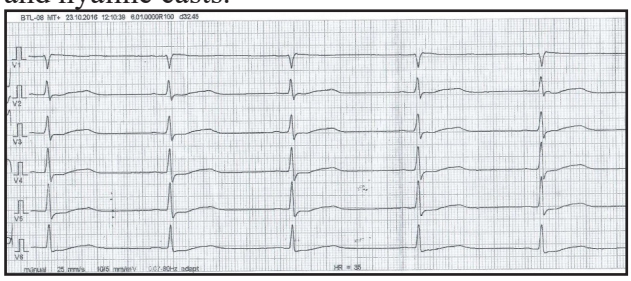
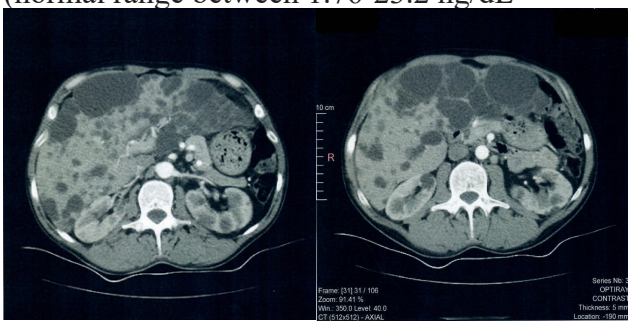


Figure 1. ECG at admission

Checking the previous laboratory test we found a moderate hypokalemia one year before, with serum potassium level 2.4 mmol/L.

Abdominal computer tomography (CT) (Figure 2) revealed a hypodense tumor in the left adrenal gland of 27/12 mm (Figure 1). A low plasma renin activity determined by chemiluminescence techniques (2.2 ng/mL/h) with normal salt diet for 5 days was found. A spot of urine potassium level was 11 mEq/L and the aldosterone serum level was 145.3ng/dL (normal range between 1.76-23.2 ng/dL



A B

Figure 2. Abdominal CT scan showing multiple hepato-renal cysts (A) and macroadenoma in left adrenal gland (B)

After treatment with iv potassium chloride, kalemia progressively increased (initial 60 ml/day, then 120 ml/day) and, associated with antialdosteronic diuretic (spironolactone 150 mg/day) and oral potassium supplements, the serum potassium level reached normal value (Table 1).

Tabel 1. Serum Potassium level evolution after treatment

Day of hospitalization	1	2	3	4	5	6	7	8	9	10
Serum potassium (mmol/L)	1.6	1.8	2.1	2.3	2.5	2.4	3.2	3.2	3.5	4.2
Serum natrium (mmol/L)	156	157	149	144		147		142		136
Alkaline reserves (mEq/lCO2)	35	35		34		35	33		31	30
BP (mmHg)	162/95	136/78	110/70	150/90	130/60	140/90	130/70	130/90	130/70	140/80
VA (bpm)	35	40	44	64	74	68	62	58	64	70
Plasma renin activity (ng/mL/h)				2.2						
Treatment	234 mg K oral + 5.86 g KCL iv	234 mg K oral + 5.86 g KCL iv	234 mg K oral + 6 g KCL iv	234 mg K oral + 8.8 g KCL iv + S 100 mg	234 mg K oral + 8.8 g KCL iv + S 100 mg	234 mg K oral + 8.8 g KCL iv + S 200 mg	234 mg K oral + 5.9 g KCL iv + S 200 mg	234 mg K oral + 3 g KCL iv + S 200 mg	234 mg K oral + 1.5 g KCL iv + S 200 mg	S 200 mg

S=spironolactone, BP=blood pressure, VA=ventricular allure, K=potassium

The surgical excision of the adenoma was considered but it was excluded due to the extremely difficult surgical approach. However, the serum potassium level was maintained within normal values only with anti-aldosterone treatment (spironolactone) at the dose of 100 mg/ day.

Discussion

Primary hyperaldosteronism (PA) occurs as a result of autonomous hypersecretion of aldosterone with suppressed serum renin level being responsible of 5% to 12% of all secondary hypertension (6-8), 8.75% reported in a romanian study (9). Most frequent etiology is unilateral or bilateral adrenal tumor and the hallmark of the disease is hypokalemia resulting from persistent potassium secretion mediated by aldosterone activity in the renal collecting tubule. Positive screening for primary hyperaldosteronism is ratio of aldosterone plasma concentration (ng/dL)/ direct renin plasma concentration (ng/L) higher than 7.7 or ratio between aldosterone plasma concentration (ng/dL) and plasma renin activity (ng/mL/h) over 40.

However, hypokalemia occurs rarely also in ADPKD making differential diagnosis more difficult. By now, a total of 13 patients (3 men and 10 women) with ADPKD associated with Conn disease (primary aldosteronism) have been reported in the literature (10-15). The mean age at diagnosis of primary aldosteronism was 40 years old (age range between 23 to 57 years) and all the patients presented plasma hypokalemia (mean K= 2.6 ± 0.8 mEq/L) and low plasma renin activity (average of 0.31 ± 0.22 ng/mL/h) at the time of diagnosis. Only in 4 cases anti-aldosterone medication was administered, in all the other patients adrenalectomy was performed.

Some studies have shown that persistent hypokalemia has a role in kidney cysts formation in patients with PA and ADPKD (16, 17) and may lead to kidney failure. In addition to worsening of hypertension, hyperaldosteronism may contribute to the increase in size of renal cysts and the appearance of renal fibrosis due to the occurrence of inflammatory processes in the target organs. In addition to the vascular effect due to renin angiotensin aldosterone system (RAAS) activity, aldosterone excess contributes to the development of metabolic syndrome associated with hypertension, endothelial dysfunction and insulin resistance (18).

On the other hand, hypertension in patients with ADPKD occurs mainly as a result of RAAS activation, possibly by compression of the renal vascular system as a result of the enlargement of the cyst, leading to bilateral renal ischemia. In some studies, it was observed that plasma renin activity and aldosterone plasma concentration in hypertensive patients with ADPKD were significantly higher than in patients with essential hypertension (19). Other studies support the major role of intrarenal RAAS activity in the occurrence of secondary hypertension in patients with ADPKD. Activation of RAAS may increase the formation and augmentation of the renal cysts through its mitogenic effects (20). The other causes involved in the pathogenesis of hypertension in ADPKD are increased sympathetic nervous system activity and arterial stiffness endothelial dysfunction, increased endothelin-1 secretion.

Also, there are reported 3 cases of hypokalemia associated with hypertension due to secondary hyperaldosteronism in patient with ADPKD (21-23). Therefore, imaging by abdominal CT or MRI, are recommended for the correct diagnosis.

The sensitivity of CT imaging to differentiate solitary adenoma from adrenal hyperplasia has been reported at 85% (24) or higher (25). In our case, the abdominal CT scan showed a well-defined hypodense mass in the left adrenal gland and normal aspect of the right (Figure 1).

The particularity of our case is the presence of liver cysts and the history of repeated cerebral hemorrhage, as a result of cerebral aneurysmal dilatations. Also, the initial value of serum potassium was lower compared to the reported cases. Low plasma renin activity and abdominal computer tomography have established the diagnosis. After literature review, it seems to be the second reported case of PA-associated with autosomal dominant polycystic kidney and liver disease, but the first with other complications of ADPKD, such as cerebral aneurysmal dilatation.

Renal cysts also have been reported to

develop in patients with primary or secondary hyperaldosteronism where hypokalemia was present. Although these studies do not demonstrate causality, the relationship between PA and ADPKD requires further investigation. After treatment of PA and normalization of potassium levels it is necessary to monitoring the change in cyst size and number. The cyst evolution may help explain the interaction between PA and ADPKD; in addition, further studies are needed to determine whether adrenalectomy may lead to worsening of renal function and progression of ADPKD.

Conclusion

In ADPKD patients associated with resistant hypertension and hypokalemia, other cause of hypertension should be considered, like primary aldosteronism.

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