CASE REPORTS

The Co-occurrence of Hypertension and Hyperkalaemia: Gordon's syndrome

A Case Report

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ABSTRACT

Secondary hypertension co-occurrence with hyperkalaemia is not an expected finding. Gordon's syndrome is an autosomal dominant disease which is a rare cause of secondary hypertension and hyperkalaemia is the most important feature. Normal glomerular filtration rate, hyperchloraemic metabolic acidosis, low renin, generally normal aldosterone levels and sensitivity to thiazide diuretics are the other features. A 33-year-old male patient presented with hypertension and hyperkalaemia. Due to a familial hypertension history, normal serum urea, creatinine levels and lack of drug use, we assumed that the patient had Gordon's Syndrome. Gordon's syndrome is a rare cause of hypertension and mostly reported only as case reports. Gordon's syndrome should be considered in the differential diagnosis of hyperkalaemic hypertensive patients with normal renal function.

Keywords: Gordon's syndrome, hyperkalaemia, secondary hypertension

Co-ocurrencia de la Hipertensión y la Hiperpotasemia: El Síndrome de Gordon

Un Reporte de Caso

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RESUMEN

La co-ocurrencia de la hipertensión secundaria con la hiperpotasemia no es un hallazgo esperado. El síndrome de Gordon es una enfermedad autosómica dominante y una causa rara de hipertensión secundaria, y la hiperpotasemia (o hipercalemia) es su característica más importante. Otras caracterís-ticas son: tasa de filtración glomerular normal, acidosis metabólica hiperclorémica, renina baja, niveles de aldosterona generalmente normales, y sensibilidad a diuréticos tiazídicos. Un paciente de 33 años se presentó con hipertensión e hiperpotasemia. Debido a una historia familiar de hipertensión arterial, urea sérica normal, niveles de creatinina y falta de uso de medicamentos, concluimos que el paciente tenía el síndrome de Gordon. El síndrome de Gordon es una causa rara de hipertensión, que aparece principalmente sólo como reporte de casos. El síndrome de Gordon se debe considerar en el diagnóstico diferencial de pacientes hipertensos hiperpotasémicos con función renal normal.

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Palabras claves: Síndrome de Gordon, hiperpotasemia, hipertensión secundaria

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INTRODUCTION

Secondary hypertension accounts for 5–10% of the hypertensive population. The exact prevalence of secondary hypertension is unknown and diagnosis in the majority of these patients probably is overlooked (1). Suggested findings of secondary hypertension are, hypertension that occurs before the age of 35 years, uncontrolled high blood pressure with use at least triple antihypertensive medications with one of them a diuretic, abdominal bruit, hypokalaemia, central obesity, striae, flushing, bradycardia or tachycardia (2, 3). Hyperkalaemia co-occurrence with hypertension is not an expected finding.

Gordon and colleagues identified in the 1980s that Gordon's syndrome is an autosomal dominant hereditary disease (4). Hypertension and hyperkalaemia are the main characteristic, hyporeninaemia, variable aldosterone levels, normal renal function are other features of the syndrome (4, 5). Gordon's syndrome is a very rare cause of secondary hypertension. In this case report, we present clinical and laboratory findings that fit Gordon's syndrome.

CASE REPORT

A 33-year-old male patient was admitted to the Nephrology outpatient clinic in an external facility with a headache. An initial examination recorded blood pressure of 200/100 mmHg, urea 30 mg/dL, creatinine 0.91 mg/dL and serum potassium 7 mmol/L. The patient was hospitalized for blood pressure regulation and was treated for hyperkalaemia. The patient was prescribed therapy involving lercanidipine 10 mg/day and polystyrene sulfonate 13.2 g three times a day per oral. In the three-day follow-up period, the patient's blood pressure had dropped to 140/90 mmHg although potassium levels remained above 5.5 mmol/L.

The patient was then referred to our clinic for an investigation of the aetiology of hypertension and hyperkalaemia. The patient had been diagnosed with hypertension approximately one-year earlier, during which his blood pressure had been measured as 200/110–190/100 mmHg. Subsequently, he had not taken medication for hypertension for the last one-year. The patient's father had also been diagnosed with hypertension and underwent haemodialysis for three years and had died at the age of 42 years. In addition, the patient had three aunts with hypertension, two of whom had also died (Figure).

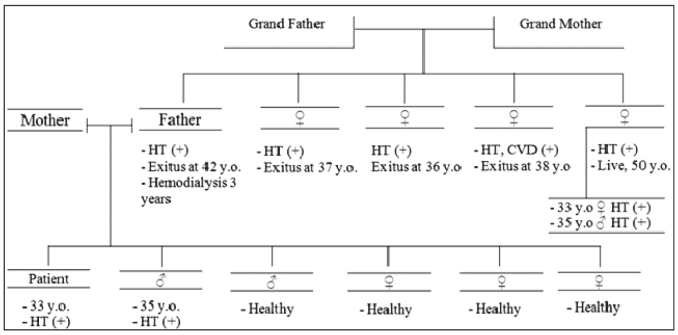

Figure: Patient family chart.

Figure: Patient family chart.
Abbrevations; HT: Hypertension, CVD: cerebrovascular disease, y.o: years old

Upon a physical examination, blood pressure was 150/100 mmHg, height was 170 cm, weight was 70 kg and body mass index was 24.2 kg/m^2. The patient displayed no pretibial oedema. The laboratory findings were as follows: urea: 36 mg/dL, creatinine: 1.12 mg/dL and serum potassium: 5.7 mmol/L. He was prescribed amlodipine at 10 mg/day and polystyrene sulfonate at 13.2 g twice daily. Tests for secondary hypertension, including cortisol levels, parathyroid hormone, thyroid hormone levels, renin activity, aldosterone levels, metanephrine levels in a 24-hour urine sample and renal artery doppler ultrasonography revealed no abnormal findings.

During a follow-up period of 10 days, the blood pressure remained between 140/80 mm Hg and 150/90 mmHg and serum potassium levels remained above 5 mmol/L (Table).

Gordon's syndrome was suspected due to the co-occurrence of hypertension and hyperkalaemia, leading to the addition of indapamide 2.5 mg once daily to the therapy. During a follow-up visit, the patient's blood pressure was 140/80 mmHg, serum potassium was 5.8 mmol/L and creatinine was 0.88 mg/dL, at the second month after discharge.

DISCUSSION

The co-occurrence of hypertension and hyperkalaemia was reported by Paver *et al* in 1964 (6) and Gordon *et al* in 1970 (7) in patients with normal kidney functions.

Table: Hospitalization and policlinic laboratory results

Parameter	External Hospital	Our Hospital 1st day	5th day	7th day	1st month	Normal values
Blood pressure (mmHg)	200/100	150/100	130/90	130/80	130/80	120/80 mmHg
Serum potassium	7.0	5.7	5.7	5.4	5.1	3.5–5.0 mmol/L
Serum sodium	140	135	132	136	138	136–145 mmol/L
Serum calcium		9.5	8.8	9.1	9.5	8.4–10.2 mg/dL
Serum urea	30	36	42	32	31	13–43 mg/dL
Serum creatinine	0.91	1.12	0.89	0.91	1.02	0.7–1.2 mg/dL
Serum glucose	88	94	91	108	97	70–105 mg/dL
Haemoglobin	14.4	15.1			13.1	13.6–17.2 g/dL
Blood Ph		7.39	7.33		7.36	7.35–7.45
$PaCO_2$		36.8	38.7		43.8	35–45 mmHg
HCO_3		21.9	20.8		24.9	22–26 mEq/L
Urine spesific gravity	1020	1019		1014		1001–1030
Urine Ph	5.5	5.5		5.0		4.6–8
Serum PTH			37.5			8–51 pg/mL
Serum TSH			1.69			0.35–4.94 µIU/mL
Serum cortizol			7.8			5–15 µg/dL
Serum aldosteron			237			70–300 pg/mL
Plasma renin activity			18.43			7.79–49.72 µIU/mL
24-hour urine potasium			42.2		17.42	25–125 mmol/day
24-hour urine sodium			44		58.5	40–220 mmol/day
24-hour urine protein			74.8		93.6	10–140 mg/day
24-hour urine metanephrine			10.24			52–541 µg/day
Urine volume			2200		1300	400–3000 mL/day
Renal doppler ultrasonography		Velocity and spectral pattern changes supporting to renal artery stenosis was not detected.				
		Right renal arterial resistive index (RI); 0.55				RI < 0.70
		Left renal arterial resistive index (RI); 0.53				

$PaCO_2$: carbon dioxide; HCO_3: bicarbonate; Urine Ph: potential of hydrogen; Serum PTH: parathyroid hormone; Serum TSH: thyroid-stimulating hormone; RI: resistive index

Gordon *et al* (7) reported that these patients had accompanying metabolic acidosis, low renin and aldosterone levels and reported that hypertension and hyperkalaemia could be controlled through sodium restriction. These findings are mirror image of Bartter's syndrome (4, 7).

In 1980, the condition was termed as Type 2 pseudohypoaldosteronism due to the low serum aldosterone levels and increase chloride absorption in the distal nephron was implicated in the pathogenesis (7, 8). In a study that reviewed the general features of 28 patients with hyperkalaemic hypertension, family history was found to be significant in 17 patients, with familial inheritance down to the third generation and with no gender preference and the condition was termed Gordon's syndrome (4). The Type 2 phenotype of pseudohypoaldosteronism is far different to other familial hypertension syndromes with normal or low serum potassium (5, 9).

Gordon's syndrome is an autosomal dominant tubular disorder affecting the distal tubules, and four subtypes have been described, depending on the chromosomal mutations involved. The mutation sites include: 1q31-42, 17p11-q21, 12p13, and an unknown locus (11–13), and these mutations have been associated with with-no-lysine kinases (WNK) 1 and WNK 4 in the family of serine-threonine-kinases. No-lysine kinases 4 decreases the activity of the thiazide-sensitive Na^+-CI^- co-transporter in the distal convoluted tubule; a mutation deactivates WNK4 and causes an increase in the activity of the thiazide-sensitive Na^+-CI^- co-transporter in the distal convoluted tubule. In contrast, WNK1 increases the activity of the thiazide-sensitive Na-CI co-transporter by inhibiting WNK4; and a mutation in WNK1 causes an increased expression of WNK1, which results in a higher inhibition of WNK4 (5, 9, 10).

In addition, in 2012 and 2013, genetic defects in Kelch-Like 3 (KLHL3) or Cullin 3 (CUL 3) were reported to cause Type 2 pseudohypoaldosteronism (14, 15). Cullin 3 protein forms a complex with KLHL 3 protein, and the interaction of KLHL3 with CUL3 and WKN4 induces WNK4 ubiquitination, resulting in a decrease in WNK4 protein levels. The interaction between KLHL3 and WNK4 has been reported to result in a decrease in WNK4 protein levels (16–18). The mutations in WNK1 or WNK4 are associated with increased activity of the Na^+-Cl^- co-transporter, which causes excessive chloride and sodium reabsorption in the distal tubules and volume expansion. Hypertension resulting by sodium retention suppresses renin secretion.

Sodium presentation to the cortical collecting tubule is a driving force for sodium reabsorption and potassium excretion through the renal outer medullary potassium channel (ROMK). Excessive sodium chloride reabsorption in the distal tubule as a result of the mutation causes a decrease in ROMK-mediated potassium excretion (Na^+-K^+ exchange in the principle cells) as a result of decreased sodium presentation in the cortical collecting tubule. The decreased excretion of potassium from the collecting tubules (as a result of electronegativity in the distal tubule) causes potassium retention and hyperkalaemia (4, 5, 9, 10).

In addition, a less negative charge of the collecting tubule lumen inhibits H^+ excretion and causes metabolic acidosis. Gordon's syndrome is characterized by normal kidney functions, low fractional sodium excretion, hyperkalaemic metabolic acidosis, low renin and aldosterone levels, hyperkalaemia and severe hypertension occurring in the third decade of life (7, 8, 10). Suggested treatment includes a low-salt diet and the use of thiazide diuretics, which inhibit the activity of the Na^+-Cl^- co-transporter and increase potassium excretion by decreasing sodium reabsorption and increasing distal sodium presentation (4, 7).

A genetic mutation analysis could not be performed in the present case due to unavailability of such a test in our hospital and the high costs abroad; however, the patient had no additional conditions that would suggest hyperkalaemia, and the correction of hypertension and hyperkalaemia through a low-salt diet and indapamide administration, and the history of hypertension on the father's side of the family and other clinical and laboratory data all pointed to Gordon's syndrome.

Gordon's syndrome is a rare cause of hypertension and very few case reports exist. It should be considered as a potential differential diagnosis in patients with hyperkalaemic hypertension and with normal kidney function.

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