Differential diagnosis of low renin hypertension – pseudohypoaldosteronism type 2

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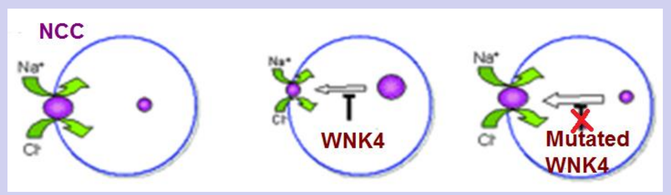
INTRODUCTION

Pseudohypoaldosteronism type 2 (PHA2), also known as Gordon syndrome is a rare inherited form of low-renin hypertension associated with hyperkalaemia and hyperchloremic metabolic acidosis in patients with a normal glomerular filtration rate (GFR). PHA2 is the result of mutations in a family of serine-threonine kinases called with-no-lysine kinases (WNK) 1 and WNK4. These enzymes regulate electron channels in the aldosterone sensitive distal nephron, resulting in disrupted electron balance. PHA2 is a genetically and phenotypically heterogeneous entity, associated with high sensitivity to thiazides.

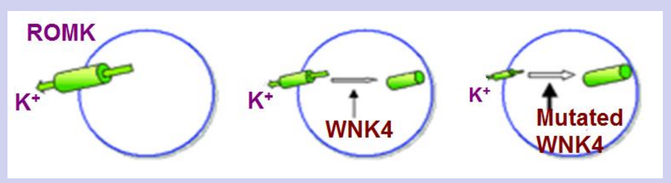
Some causes of low renin hypertension

Primary hyperaldosternosim	• Idiopathic hyperaldosteronism-Micronodular adrenal hyperplasia • Aldosternone producing adenoma • Macronodular adrenal hyperplasia • Aldosterone producing carcinoma • Familial hyperaldosteronism type I and II
Pseudohyperaldosteronism	• Deoxycoticosterone overproduction • Liddle syndrome • Apparent mineralcorticoid excess (HSD-2 deficiency) • Mineralcorticoid receptor mutation
Hyporeninemic hypoaldosternosm	• Chronic kidney disease • Pseudohypoaldosteronism type 2 s. Gordon syndrome

Mutated WNK4 is unable to retain NCC (thiazide sensitive NaCl cotranspoter) in the cytoplasm, thus increasing Na^+ reabsorbtion compared with wild type WNK4

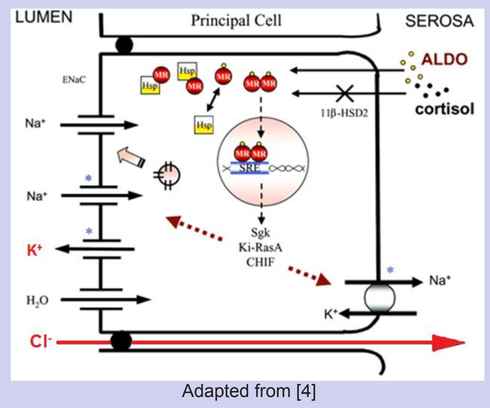


Mutated WNK4 leads to increased removal of the potassium channel ROMK of the mambrane, thus decreasing K^+ secreation



Adapted from [3]

It is hypothesized that patients with PHA2 have a chloride shunt – increased distal chloride reabsorbtion, leading to less electronegativity in the lumen, thereby decreasing the electrochemical gradient for potassium secretion



Adapted from [4]

CASE REPORT

- A 57 year old female patient with known adrenal mass – a typical adenoma found on abdominal CT 5 years ago with the diameter of 1.7 cm
- Laboratory test results excluded Cushing syndrome, but primary hyperaldosteronism was not suspected due to persisting hyperkalaemia
- She had anamnesis of treatment-naïve hypertension, cardioembolic stroke in 2011 and foramen ovale apertum enclosed with occluder in 2012
- Abdominal CT scan was repeated to evaluate the growth dynamics of the adrenal mass, revealing an enlarged left adrenal gland with a hypodense (-9 HU) vascular mass 4.1 cm in diameter
- Admitted to the hospital for left adrenalectomy

- Pre-operative testing revealed several laboratory test abnormalities

	11.04.2014.	24.09.2014.	06.01.2015.	Reference range
Sodium			142	136-145 mmol/l
Potassium	4.8	5.6	5.1	3.5-5.1 mmol/l
Calcium	2.4		2.54	2.1-2.55 mmol/l
Chloride			106	95-105 mmol/l
Creatinine	52		57	44.0-80.0 mkmol/l
GFR	95.5		100.5	
Parathormone			76.5	15.0-68.0 pg/ml
Cortisol		11.5	6.7	3.7-19.4 mkg/dl
ACTH		26.4		7.2-63.3 pg/ml
Renin		<0.5	0.5	2.8-39.9 mkU/ml
Aldosterone		95.8	81.2	25.2-392.0 pg/ml
U-Potassium			23	25-125 mmol/day
U-Sodium			119	40-220 mmol/day
Urinary pH	4.8		4.9	5.0-9.0

- Considering the findings of low renin hypertension with hyperkalaemia and normal GFR the diagnosis of PHA2 was established.
- The patient was started on antihypertensive treatment with thiazide diuretic and underwent left adrenalectomy.
- Histology conformed a hormonally inactive adrenocortical adenoma, Weiss score 2.

CONCLUSIONS

The current case demonstrates the challenges of differential diagnosis of low renin hypertension depicting the characteristic findings of PHA2. It should be noted that upon correct diagnosis this form of low renin hypertension is easily treatable with thiazide diuretics.

References

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