Two brothers with late onset apparent mineralocorticoid excess

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Introduction

Apparent mineralocorticoid excess (AME) is a rare congenital autosomal recessive disorder resulting from mutations in the HSD11B2 gene, which encodes the kidney isozyme of 11-ß-hydroxysteroid dehydrogenase type 2, inactivating circulating cortisol to the less-active metabolite cortisone. Less than 100 cases have been reported in the literature so far.
In affected individuals cortisol can cross-react and activate the mineralocorticoid receptor, leading to aldosterone-like effects in the kidney. AME is usually diagnosed within the first years of life in children presenting with failure to thrive, severe hypertension (HT), low renin and aldosterone levels, profound hypokalemia and hypernatremia, but it can also present later in life, in apparent healthy children or adolescents. Measurement of urinary free tetrahydrocortisol and tetrahydrocortisone ratio (allo-THF+THF)/THE is important in the diagnosis.

Case report

We describe the case of two brothers, aged 14 and 7 years, which were diagnosed during a routine visit as suffering from HT (repeated pressure values above the 95th percentile for gender and age, 160/110 in the first brother and 150/110 in the second one). They were in good general conditions and their clinical examination was normal. At echocardiography, the oldest one had a moderate left ventricular hypertrophy. As they had no risk factors for primary HT, we performed laboratory and instrumental exams to detect a secondary form of HT. We found hypokalemia just in the older brother (2.66 mmmol/L), with low levels of aldosterone (undosable in both) and renin leves in the low range of normality both in orto and in clinostatism. The urinary steroid profile revealed a marked increase (allo-THF+THF)/THE ratio (value of 6,41; normal value < 1,5). So we have initiated to treat both with spironolactone, blocking the mineralocorticoid receptor and obtaining a good control of their pressure. In the first we have also began the potassium supplementation

	14-YEARS OLD BROTHER	7-YEARS OLD BROTHER
ACTH (pg/ml) (NV 7.2-63.3)	87.1	-
Cortisol ore 8.00 (ug/dl) (NV 4.0-25.0)	17,7	14.8
Active Renine (uU/ml) - IN ORTO (NV 3.3-41.0) - IN CLINO (NV 2.4-29.00)	 - 5,4 - 2	 - 4.1 - not available
Aldosterone (pg/ml): - ORTO (NV 35.0-300.0) - CLINO (NV 7.5-150.0)	 - NOT DETECTABLE - NOT DETECTABLE	 - NOT DETECTABLE - NOT DETECTABLE
Plasmatic Na (mmol/L)	145	142
Plasmatic K (mmol/L)	2.66	3.14
THF+alloTHF/THE (N< 1.5).	**8.91**	**6.41**

Discussion

Our cases suggest that it is important to think about AME also in apparent healthy children or adolescents, because the disease can remain unrecognized until late childhood or adolescence. An early diagnosis and a prompt treatment of AME are important to prevent end-organ damage, sudden stroke, cardiac and renal insufficiency.