

An adolescent with hypertension caused by primary hyperaldosteronism due to *KCNJ5* gene mutation

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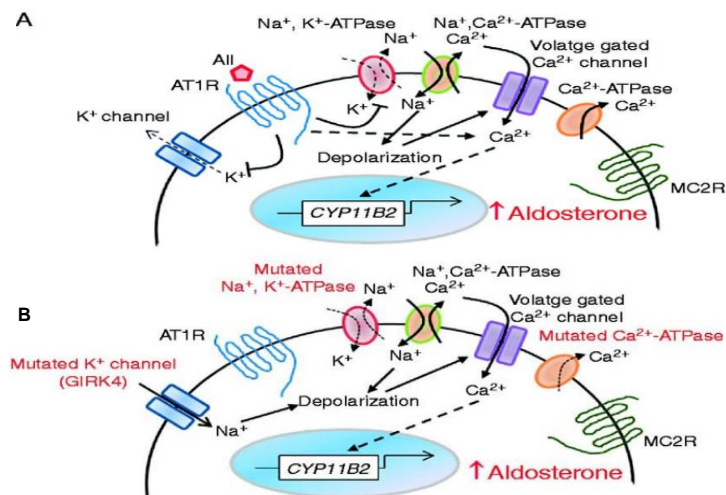
Introduction

Primary aldosteronism (PA) is a rare form of secondary hypertension. In adults PA is often caused by unilateral adrenal adenoma which can be cured by unilateral adrenalectomy. Especially in young patients hereditary causes of aldosteronism have to be considered with bilaterally affected adrenal glands. We report on an adolescent with PA due to a *KCNJ5* gene mutation.

Case Presentation

A 16-year-old boy was referred to our clinic because of hypertension. Extensive diagnostic work up revealed elevated aldosterone concentrations in serum and urine accompanied by low renin concentrations. Aldosterone was not suppressed by sodium loading which confirmed the diagnosis PA. A CT scan of the abdomen showed focal thickening of the left adrenal gland, without evidence for a clear adenoma. Adrenal venous sampling did not show lateralisation of aldosterone production. Mutation analysis was negative for the hybrid *CYP11B1/CYP11B2* gene that causes glucocorticoid-remediable aldosteronism but revealed a de novo germline missense mutation in the *KCNJ5* gene (c.452G>A (p.Gly151Glu)). This mutation has only been described in 8 families causing familial PA type III. Somatic mutations in the *KCNJ5* gene are also present in about a third of aldosterone-producing adenomas. In our patient, treatment with an aldosterone antagonist was successful for blood pressure control without surgical intervention.

Pathophysiology



Regulation of aldosterone biosynthesis. (A) normal condition. (B) genetic alterations leading to cell membrane depolarization and intracellular ionic modification. FH-III is the result of a mutation in *KCNJ5* gene, which encodes the G protein activated inward rectifier potassium channel (GIRK4) which leads to loss of ion selectivity. This increases intracellular Na⁺ and Ca²⁺ and consequently positive regulation of *CYP11B2* gene resulting in hyperaldosteronism.

Full arrows, direct activation; hatched arrows, indirect activation requiring intermediary steps.

Figure adapted from; Genetics of mineralocorticoid excess; an update for clinicians. Zennaro MC, Rickard AJ, Boulkroun S. Eur J Endocrinology (2013) 169 R15-25

Conclusion

PA is a rare cause of secondary hypertension, especially in children and adolescents. In hereditary forms of PA bilaterally elevated production of aldosterone can be expected. Therefore, for these forms of PA surgery is not the first choice treatment. We recommend mutation analysis for *CYP11B2* and *KCNJ5* gene mutation in all children and adolescents with biochemically proven PA.