Hyperreninemic Hypoaldosteronism: clinical and genetic features in pediatric patients

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INTRODUCTION AND OBJECTIVE

Isolated hyperreninemic hypoaldosteronism due to Aldosterone Synthase (AS) deficiency is a rare autosomal recessive disorder linked to aldosterone biosynthesis defect (involving *CYP11B2* gene; OMIM - *124080). Its clinical presentation varies with age: during the first weeks of life it usually presents with salt-wasting syndrome (with severe hyponatremia, hyperkalemia, metabolic acidosis, vomiting, signs of dehydration) while in misdiagnosed infants it is usually characterized by failure to thrive, anorexia, mild dehydration and electrolyte abnormalities. Growth retardation may persist throughout childhood without appropriate therapy.

We describe the clinical onset and course and the genetic evaluation of five patients with hyperreninemic hypoaldosteronism in Tuscany.

METHODS

Five patients (two males, three females) came to our attention for electrolytes disorder (hyponatriemia and hyperkaliemia, increased plasmatic renin activity, impaired aldosteron level - low/normal -) with normal cortisol and sex hormones values. Three of them presented with neonatal salt-wasting syndrome. They all have been suspected for isolated hyperreninemic hypoaldosteronism on the basis of clinical and laboratory features. Appropriate therapy with fludrocortisone was started in four of them with general improvement. All of the patients underwent genetic analysis: amplification by PCR and Sanger sequencing of 9 exons of the *CYP11B2* gene; four of them are showed in the figure below.

Ampflification of the 9 exons of the *CYP11B2* gene with flanking areas by means of PCR and subsequently sequenced directly

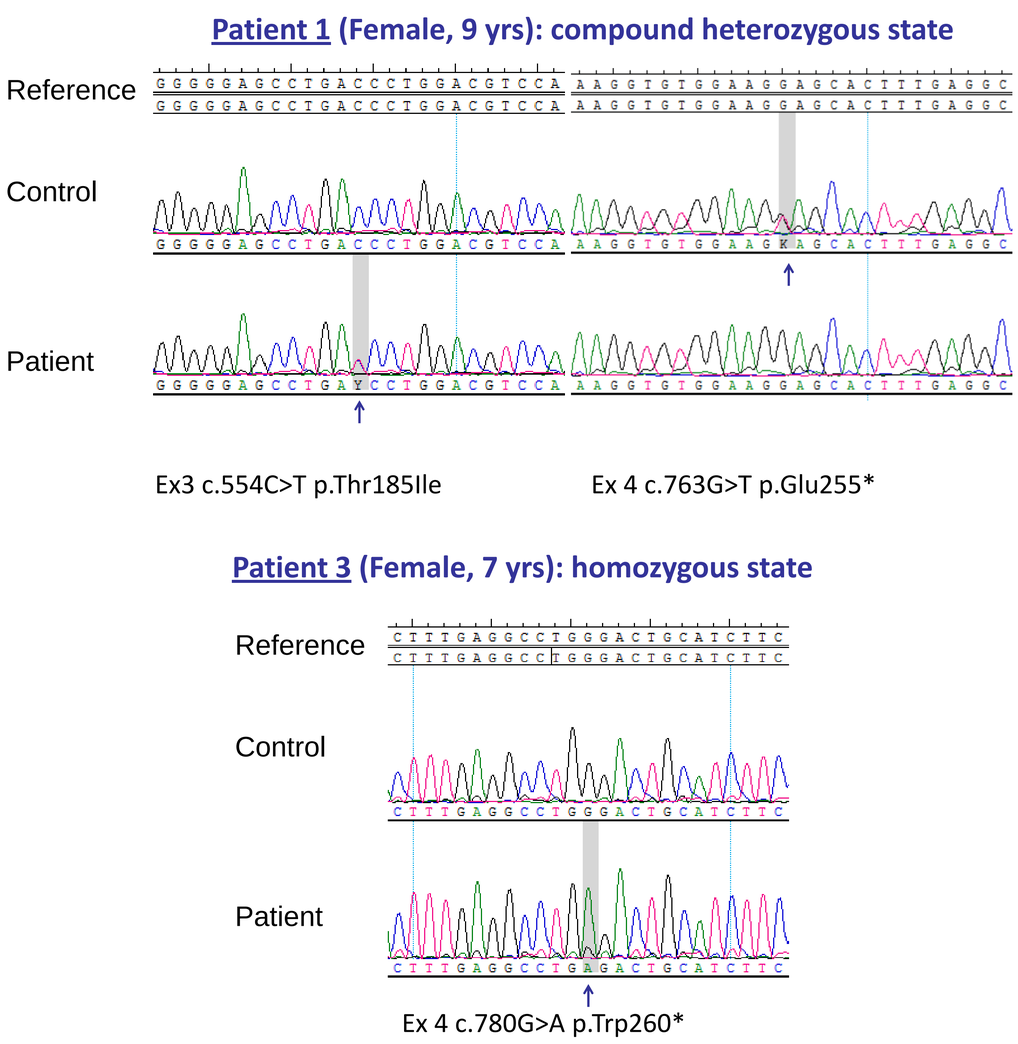

Figure: Electropherograms of segment of *CYP11B2* gene showing mutations. The mutation site is underlined and indicated by an arrow..

RESULTS AND CONCLUSIONS

Three patients showed mutations in homozygous state: c.554C>T (p.Thr185Ile) in exon 3 (Patient 2), c.780G>A (p.Trp260*) in exon 4 (Patient 3), c.1231G>C (p.Gly411Arg) in exon 8 (Patient 4). One patient showed two mutations in heterozygous state: c.554C>T (p.Thr185Ile) in exon 3 and c.763G>T (p.Glu255*) in exon 4 (Patient 1). They all supported the diagnosis of hypoaldosteronism. (*Figure*)

Clinical and laboratoristic suspect of hyperreninemic hypoaldosteronism should be supported by genetic confirmation. Therapy with fludrocortisone should be life-long administered in these patients and could be useful in order to ensure a good quality of life and may reduce long-term damage.

REFERENCES

1. P.C. White. Aldosterone synthase deficiency and related disorders. 2004 Molecular and Cellular Endocrinology 217 ;81–87.
2. K. Curnow, M.T. Luna, L. Pascoe, R. Natarajan, J. Gu, J.L.Nadler, P.C. White. The Product of the CYP11B2 Gene Is Required for Aldosterone Biosynthesis in the Human Adrenal Cortex. 1991. Molecular Endocrinology 5 (10); 1513-1522.

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