Serum cortisol and cortisone as potential biomarkers of partial 11β-hydroxysteroid dehydrogenase type 2 deficiency

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Abstract

BACKGROUND

Pathogenic variations in HSD11B2 gene triggers the apparent mineralocorticoid excess syndrome (AME). There is scarce information regarding the phenotypes of subjects carrying heterozygous pathogenic variants in HSD11B2 gene. We investigated if serum cortisol/cortisone (F/E) ratio and cortisone are useful for identifying partial 11βHSD2 deficiency in those heterozygous subjects.

METHODS

We studied two patients diagnosed with AME and their families carrying either D223N or R213C mutation. We also evaluated 32 healthy control subjects (13 children and 19 adults) to obtain normal references ranges for all measured variables. Case 1: A boy carrying D223N mutation in HSD11B2 gene and Case 2: A girl carrying R213C mutation. We assessed serum F/E ratio and cortisone by HPLC-MS/MS, aldosterone, plasma-renin-activity(PRA), electrolytes, and HSD11B2 genetic analyses.

RESULTS

The normal values (median [interquartile range]) in children for serum F/E and cortisone (μg/dl) were 2.56 [2.21–3.69] and 2.54 [2.35–2.88], and in adults were 4.42 [3.70–4.90] and 2.23 [1.92–2.57], respectively. Case 1 showed a very high serum F/E 28.8 and low cortisone 0.46 μg/dl. His mother and sister were normotensives and heterozygous for D223N mutation with high F/E (13.2 and 6.0, respectively) and low cortisone (2.0 and 2.2, respectively). Case 2 showed a very high serum F/E 175 and suppressed cortisone 0.11 μg/dl. Her parents and sister were heterozygous for the R213C mutation with normal phenotype, but high F/E and low cortisone. Heterozygous subjects showed normal aldosterone, PRA, but lower fractional excretion of sodium and urinary Na/K ratio than controls.

CONCLUSION

Serum F/E ratio and cortisone allow to identify partial 11βHSD2 deficiencies, as occurs in heterozygous subjects, who would be susceptible to develop arterial hypertension.

Keywords

11βHSD2 deficiency, AME síndrome, Blood pressure, Cortisol, Cortisone, HSD11B2 mutation, Hypertension