Six 11-Beta Hydroxylase Deficiency Patients: Identification of Two Novel Mutations

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In this study, we aimed to define the molecular spectrum of CYP11B1 gene mutations in 6 Turkish patients and to evaluate the phenotype-genotype correlation.

In patients who were considered to have 11-beta hydroxylase deficiency by Endocrinology Department and Pediatric Endocrinology Department, CYP11B1 gene sequence analysis using a next-generation sequencing platform was performed in Medical Genetics Department, Faculty of Medicine, Ege University. Mutations detected were then confirmed by Sanger sequencing method.

In this study, 7 different CYP11B1 gene mutations were detected in 6 patients who were referred to molecular analysis due to sex development disorder. Four patients carried the same mutation on both alleles, whereas 2 patients were compound heterozygous. Cardinal phenotypic features of the patients were ambiguous genitalia, hypertension, hypokalemia, and gynecomastia. Two of the 7 mutations were detected for the first time in this study. These were p.R120G and p.A199P mutations.

In cases presenting with adrenogenital syndrome, if their endocrine test results are consistent with 11-beta hydroxylase deficiency, molecular analysis should be performed.

17-Hydroxylase Deficiency: Rare Cause of Delayed Puberty

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17-hydroxylase deficiency (17OHD) is a very rare disorder characterized by glucocorticoid deficiency, hypergonadotropic hypogonadism, hypertension, and hypopotassemia. Mutations in the CYP17A1 gene cause 17OHD. Herein, we present three adolescents, one single and two cousins, with delayed puberty.

The patients were raised as girls. All of the patients were pre-pubertal. Initial clinical findings are given in the Table 1. Hydrocortisone, 17-beta estradiol, and antihypertensive treatments were initiated. First case achieved Tanner 5 breast development at 15.64 and had menarche at 15.72 years old. Alendronate was started due to osteoporosis (L-L4 BMD was -3.1). Second girl achieved Tanner 5 breast development at 15.08 and had menarche at 16.64 years old. The third patient could only been followed for six months because of advance age. A known mutation in the first patient and a novel mutation in the second patient were found in the CYP17A1 gene.

Adrenal functions as well as gonadotropins should be examined in adolescent girls with no thelarche and pubarche associated with hypertension, and 17OHD should not be forgotten.

Table 1. Initial clinical findings

<table>
<thead>
<tr>
<th>Case</th>
<th>Genomic</th>
<th>cDNA</th>
<th>Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>g.6452G&gt;A</td>
<td>c.1319G&gt;A</td>
<td>p.R440H</td>
</tr>
<tr>
<td>2</td>
<td>g.276_280delCCCTG</td>
<td>c.104_108delCCCTG</td>
<td>p.P35Rfs*15</td>
</tr>
</tbody>
</table>

Cases Genomic cDNA Protein

1 g.6452G>A c.1319G>A p.R440H
2 g.276_280delCCCTG c.104_108delCCCTG p.P35Rfs*15