DISCRETE VIRILIZATION IN GIRLS WITH THE CLASSIC FORM OF CAH: THE IMPORTANCE OF A DETAILED GENITAL EXAMINATION AT BIRTH

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Introduction

FOETAL SERUM ANDROGEN CONCENTRATION ➔ EXTERNAL GENITALIA
CONGENITAL ADRENAL HYPERPLASIA CLASSIC FORMS (21OHD) ➔ FEMALE GENITAL AMBIGUITY MOST FREQUENT CAUSE
CLASSIC FORMS VIRILIZATION: SALT LOSER (SL) OR SIMPLE VIRILIZING (SV) & NONCLASSIC FORMS (NC)
VIRILIZATION (PHENOTYPE) ➔ ENZYMATIC DEFICIENCY

• OBJECTIVE: TO DESCRIBE 21OHD FEMALES WITH LATE DIAGNOSIS DUE TO DISCRETE VIRILIZATION

Methods

RETROSPECTIVE DATA: AGE AT DIAGNOSIS, 17OHPROGESTENONE, BONE AGE
GENITAL AMBIGUITY ➔ PRADER CRITERIA
MOLECULAR STUDY ➔ PREDICTED PHENOTYPE

Cases report

Case 1 ➔ first consultation 44m: precocious pubarche (2y) and clitoromegaly (without labial fusion)
Case 2 ➔ first consultation 31m; case 1 sister’s; precocious pubarche (1y) and clitoromegaly (without labial fusion)
Case 3 ➔ first consultation 7m; CAH NSL sister’s; labial fusion since birth
Case 4 ➔ first consultation 19m; precocious pubarche (3m), clitoromegaly and labial fusion since birth
Case 5 ➔ first consultation 23m; clitoromegaly and labial fusion since birth (surgically corrected)
Case 6 ➔ first consultation 27m; clitoromegaly since birth (without labial fusion)

The molecular study showed that all children carried a salt-wasting and a simple virilising mutation in either allele (Allele-SW and Allele-SV), being, therefore, the predicted phenotype SV.

<table>
<thead>
<tr>
<th>Age</th>
<th>Height</th>
<th>Prader</th>
<th>17OHP</th>
<th>BA/CA</th>
<th>Phenytype</th>
<th>Allele SW</th>
<th>AlleleSV</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>44</td>
<td>2</td>
<td>79.5</td>
<td>5.2/3.8</td>
<td>SV</td>
<td>c.-315C&gt;T;c.290-13A/C&gt;G</td>
<td>c.-103A&gt;G; p.Ile172Asn</td>
</tr>
<tr>
<td>2</td>
<td>31</td>
<td>0.09</td>
<td>158.8</td>
<td>5.6/2.9</td>
<td>SV</td>
<td>c.-315C&gt;T;c.290-13A/C&gt;G</td>
<td>c.-103A&gt;G; p.Ile172Asn</td>
</tr>
<tr>
<td>3</td>
<td>7</td>
<td>0.45</td>
<td>82.0</td>
<td>-</td>
<td>Large gene conversion</td>
<td>p.Ile172Asn</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>19</td>
<td>1.15</td>
<td>224.4</td>
<td>3.8/1.9</td>
<td>SV</td>
<td>p.Arg356Trp</td>
<td>p.Ile172Asn</td>
</tr>
<tr>
<td>5</td>
<td>23</td>
<td>2.65</td>
<td>206.8</td>
<td>5.1/2.4</td>
<td>SV</td>
<td>p.[Leu308Phefs<em>6;Gln318</em>;Arg356Trp]</td>
<td>p.Ile172Asn</td>
</tr>
<tr>
<td>6</td>
<td>27</td>
<td>0.79</td>
<td>&gt;50.0</td>
<td>5.3/2.2</td>
<td>SV</td>
<td>p.[Gln318*; Arg356Trp]</td>
<td>p.Ile172Asn</td>
</tr>
</tbody>
</table>

Comments

• We report six cases of CAH due to 21OHD, all with the classic, simple virilising form confirmed by molecular study, whose discrete genital virilisation was not identified at birth by the paediatrician.
• According to the relatives, all of them had clitoromegaly and in 3 cases there was also labial fusion at birth.
• Through this presentation, we would like to draw attention to the importance of a careful examination of the external genitalia at birth, in order to identify small alterations and obtain early 21OHD diagnosis.