THREE CASES WITH FAMILIAL SHORT STATURE: LERI-WEILL SYNDROME

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Introduction

- SHOX gene is located in pseudoautosomal regions of chromosomes Xp22.33 and Yp11.32
- Loss of both SHOX alleles is defined as Langer’s mesomelic dysplasia (severe type)
- Loss of one SHOX allele is defined as Leri-Weil syndrome (moderate type)
- Heterozygous missense mutations in SHOX allele cause idiopathic short stature (mild type)
- rhGH treatment is safe and effective in improving final height in children with SHOX deficiency.

In this report, we present clinical features and responses to rhGH treatment of three cases with Leri-Weil syndrome who were being followed-up for familial short stature.

Table 1. Clinical and laboratory features of three cases diagnosed with Leri-Weil syndrome

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (Years)</th>
<th>Sex</th>
<th>Complain</th>
<th>Medical History</th>
<th>Family History</th>
<th>Height (SDS)</th>
<th>Weight (SDS)</th>
<th>BMI (SDS)</th>
<th>Sitting Height/Height (Percentile)</th>
<th>Bone Age (SDS)</th>
<th>IGF-1 (ug/L)</th>
<th>Growth velocity before treatment</th>
<th>Peak GH response (ng/ml)</th>
<th>rhGH dose</th>
<th>rhGH period</th>
<th>First Year Growth velocity after treatment</th>
<th>Genetic Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6.2</td>
<td>Male</td>
<td>Short stature</td>
<td>No Characteristics</td>
<td>Mother’s height: 143 cm</td>
<td>101 (-3.4)</td>
<td>16.4 (-2.02)</td>
<td>0.4</td>
<td>0.59 (&gt;95 p)</td>
<td>4 years 6 months</td>
<td>198 (22-208)</td>
<td>4.4 cm/year</td>
<td>6.33</td>
<td>50 mcg/kg/day</td>
<td>2 years 10 months</td>
<td>9.19 cm/year</td>
<td>Deletion of 266 Kb with 2 OMIMs in Xp22.33 region</td>
</tr>
<tr>
<td>2</td>
<td>3.6</td>
<td>Male</td>
<td>Short stature</td>
<td>Asthma</td>
<td>Mother’s height: 150.8 cm</td>
<td>89.3 (-2.85)</td>
<td>16 (-0.03)</td>
<td>2.7</td>
<td>0.61 (&gt;95 p)</td>
<td>2 years</td>
<td>79.4 (&lt;15-129)</td>
<td>4.68 cm/year</td>
<td>8.7</td>
<td>25 mcg/kg/day</td>
<td>3 years 5 months</td>
<td>10.9 cm/year</td>
<td>SHOX deletion at locus Yp11.3</td>
</tr>
<tr>
<td>3</td>
<td>1.6</td>
<td>Female</td>
<td>Short stature</td>
<td>No Characteristics</td>
<td>Mother’s height: 150.8 cm</td>
<td>75 (-2.4)</td>
<td>9.3 (-1.33)</td>
<td>0.0</td>
<td>0.58 (&gt;95 p)</td>
<td>14 months</td>
<td>83.9 (18.2-172)</td>
<td>4.96 cm/year</td>
<td></td>
<td></td>
<td></td>
<td>CNV gain with 15 OMIM genes of 1.4MB on the X chromosome</td>
<td></td>
</tr>
</tbody>
</table>

Results

Most cases with SHOX haploinsufficiency are misdiagnosed as idiopathic or familial short stature. In these cases, body disproportion and wrist radiography should be investigated carefully. SHOX deficiency should be considered especially if limb shortness and madelung deformity are present. rhGH treatment is a safe and effective option for improving final height in children with SHOX deficiency.