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INTRODUCTION

• Gene SHOX defect are the most prevalent cause of genetic short stature.

• Gene SHOX haploinsufficiency due to deletions or mutations in heterozygosis causes a wide spectrum of phenotypes ranging from very severe disharmonic short stature (S. Léri-Weil, S. Turner) to very mild forms with the appearance of idiopathic short stature (IST) of difficult clinical recognition.

• Auxological study directed at evaluating body disproportions such as the sitting height/height (SH/H) ratio in patients with IST has been postulated as useful for orienting the study of the SHOX gene.

AIMS

• To establish the prevalence of SHOX gene defects in children with disharmonic short stature evaluated by the (SH/H) ratio regardless of the presence of dysmorphic features and radiological anomalies.

PATIENTS & METHODS

• Prospective study of 37 consecutive patients with height < -2 SD and (SH/H) ratio > +2SD.
• All patients initially underwent Genetic Study using:
  - MPLA (P018, MRC Holland) or CGH array (Desing ISCA 8x60, Agilent).
  - Sequencing of all exons of the SHOX gene and flanking intronic regions was carried out in patients without SHOX gene deletion or its regulating regions.
• Normal Growth Reference Patterns:
  - Height (Spanish Growth Study 2010).

RESULTS

<table>
<thead>
<tr>
<th>SHOX Gene defects</th>
<th>n = 11</th>
<th>Age (x ± SD)</th>
<th>Height (x ± SD)</th>
<th>X-ray</th>
<th>Disharmonic ratio ( cms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SHOX Gene defects</td>
<td>8</td>
<td>9.9 ± 3.3</td>
<td>-2.7 ± 0.9</td>
<td>m−6</td>
<td>6/8</td>
</tr>
<tr>
<td>Turner syndrome</td>
<td>3</td>
<td>9.3 ± 3.3</td>
<td>-3.0 ± 0.9</td>
<td>m=2</td>
<td>0/3</td>
</tr>
</tbody>
</table>

FREQUENCY GEN SHOX DEFECTS (n = 11): 29.7%

| PATIENTS WITHOUT SHOX GENE DEFECTS IN CHILDREN WITH DISHARMONIC SHORT STATURE |
|-----------------------------|-------------------|-----------------|-------|-------------------------|
| n = 26                      | Age (x ± SD)      | Height (x ± SD) | X-ray | Disharmonic ratio ( cms) |
| Disharmonic                 | 24 (14M, 10 V)    | 10.2 ± 1.1      | -2.5 ± 1.1 | m done     |
| Harmanaric                  | 2 (1M, 1 V)       | 9.3 ± 3.3       | -2.7 ± 0.1 | m done     |

CONCLUSIONS

1. The frequency of SHOX gene defects in our cohort with disharmonic IST evaluated by the (SH/H) ratio was 29.7%.
2. The (SH/H) ratio is a highly useful parameter for identifying patients with disharmonic IST and orienting SHOX gene study.
3. A significant proportion of patients with disharmonic IST remain undiagnosed, which renders this an open field for clinical research.