Growth, pubertal course and long-term outcome of 46,XY boys born with atypical genitalia and low birthweight

On behalf of the I-DSD consortium*


KEY MESSAGES
- 1/3 SGA boys show incomplete catch-up growth
- No difference in urological outcome between AGA and SGA cases
- SGA boys have higher LH levels during minipuberty, and lower peak testosterone levels post HCG stimulation in childhood

INTRODUCTION
Boys born small for gestational age (SGA) often have undermasculinized genitalia. Little is known about the pubertal development and gonadal function in a longer-term in this specific group of males.

AIMS
To determine the (pubertal) development and long-term urological and endocrine outcome of undermasculinized boys born SGA compared to undervirilized boys born appropriate for gestational age (AGA).

RESULTS

Patient characteristics

<table>
<thead>
<tr>
<th></th>
<th>SGA (n=115)</th>
<th>AGA (n=64)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>EMS first presentation</td>
<td>6.5 (4)</td>
<td>7.25 (3.0)</td>
<td>0.311</td>
</tr>
<tr>
<td>EMS last assessment</td>
<td>12 (1.0)</td>
<td>12 (1.1)</td>
<td>0.531</td>
</tr>
<tr>
<td>GA: ≤37 weeks</td>
<td>71/115</td>
<td>18/64</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GA: &gt;37 weeks</td>
<td>28/115</td>
<td>9/64</td>
<td>(28.1%)</td>
</tr>
<tr>
<td>Delayed neuromotor development</td>
<td>20/102 (19.6%)</td>
<td>1/53 (1.9%)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Growth

At 2 years of age:
- 31/104 SGA boys (29.8%) had incomplete or absent catch-up growth

Growth hormone therapy:
- Only 8 cases
- Mean effect: +1.5 SD length & weight

At last assessment:
- Lower SD-scores for height and weight in SGA boys (both p<0.001) at a median age of 8.0 (SGA) and 7.7 years (AGA)

Urological

Hypospadias repair:
- The number of reinterventions was similar in both groups (1 (2); p=0.836)

EMS:
- At last assessment, nearly all boys had an external masculinization score of 12/12
- Residual hypospadias was the most frequent cause of lower scores in both SGA and AGA boys

Endocrine

Stimulation of penile growth:
- Postnatal or childhood treatment had a good clinical effect in 38/42 (90.5%) SGA and 14/15 (93.3%) AGA boys

Minipuberty/stimulation test:
- Figure: LH levels during minipuberty were higher in SGA boys (p=0.037)

Puberty:
- Majority of boys: spontaneous onset and uneventful course of puberty
- At the end of puberty: no difference in sex hormone levels was observed between SGA and AGA boys

CONCLUSION
About one-third of boys with non-specific XY DSD who have SGA show insufficient catch-up growth. The urological outcome and effect of treatments to increase penile size was similar between SGA and AGA cases. Our data suggest a dysfunction of infantile Leydig cells in SGA boys, which does not seem to persist in adult-type Leydig cells. Alternatively, alteration of the hypothalamic-pituitary-gonadal axis during infancy may underlie the hormonal changes found in SGA boys.

FUNDING
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