GONADAL OUTCOME IN 17BETA-HSD AND 5ALPHA-REDUCTASE DEFICIENCY

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INTRODUCTION
5α-reductase type 2 deficiency (5a-RD) and 17β-HSD type 3 deficiency (17B-HSDSD) are rare differences/disorders of sex development (DSD) in which impaired function of steroidogenic enzymes causes undervirilisation in individuals with a 46,XY genotype.

AIM
We aim to increase knowledge on long-term gonadal function and gonadal pathology in these conditions.

METHOD
Eligible individuals were identified using the International DSD (I-DSD) Registry.
Inclusion-criteria:
• Current age ≥16 years
• Genetically confirmed diagnosis
• Data available on gonadal outcome
Data collection:
• Information on laboratory results, pathology results, hormone treatment and surgeries
• Representative block(s), slides or images of gonadal tissue were requested to allow a uniform analysis of the gonadal tissue.

RESULTS
A total of 36 subjects from 10 different centres were included in this study. Their characteristics are shown in Table 1.

<table>
<thead>
<tr>
<th>5α-RD</th>
<th>17B-HSD</th>
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<tbody>
<tr>
<td>Subjects, n</td>
<td>18</td>
</tr>
<tr>
<td>Age first presentation, y (IQR)</td>
<td>6.5 (4.8-15.5)</td>
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<tr>
<td>Age diagnosis, y (IQR)</td>
<td>11.8 (5.0 – 16.3)</td>
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<tr>
<td>EGS first presentation, (range)</td>
<td>7.0 (2.5 – 11.0)</td>
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<tr>
<td>Female gender of rearing, n</td>
<td>11 (61%)</td>
</tr>
<tr>
<td>Gender change, n</td>
<td>4 (22%) FtM</td>
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<td>Hormone therapy, n</td>
<td>1 (6%) GnRHa</td>
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<tr>
<td></td>
<td>8 (43%) Estrogen</td>
</tr>
<tr>
<td>Gonadectomy, n</td>
<td>6 (33%)</td>
</tr>
<tr>
<td>Age gonadectomy, y (IQR)</td>
<td>10.0 (6.0 – 18.3)</td>
</tr>
</tbody>
</table>

Table 1. Characteristics of both groups. Data are presented as median (interquartile range) unless otherwise stated.

Endocrine gonadal function
Pubertal/postpubertal individuals without treatment and/or gonadectomy had testosterone levels within the low-normal range, see figure 1A. However, elevated gonadotrophins were common, especially in 17B-HSDSD. LH levels are shown in figure 1B. Median FSH levels were 29 (range 2 – 75) and 8 U/L (2 – 61) in 17B-HSD and 5a-RD, respectively.

Gonadal pathology
No (pre)malignancies were reported.

CONCLUSIONS
• A significant percentage (22%) of individuals with 5α-reductase type 2 deficiency and 17B-HSD changed gender, mostly in late adolescence/early adulthood.
• To prevent virilisation before making a definitive decision about gonadectomy, treatment with GnRHa is being used.
• When gonads are left in situ, testosterone levels are in the low-normal range in postpubertal individuals.
• Germ cell (pre)malignancies seem uncommon in these patients, but central reassessment of gonadal material is ongoing to confirm this finding.

Together, these data support a conservative approach towards definitive sex assignment, genital surgery and gonadectomy early in life in these conditions.

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