BILATERAL TESTICULAR REGRESSION
ETIOLOGY AND OUTCOME IN A LARGE BELGIAN SERIES

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KEY MESSAGES
➢ Prenatal or obstetric complications in 50%
➢ 3/33 (9.1%) had (likely) pathogenic DHX37 variants
➢ More severe phenotype indicating early bilateral testicular regression
➢ Little penile growth after childhood IM testosterone
➢ Testosterone replacement therapy resulted in satisfactory pubertal height gain

INTRODUCTION
The etiology of bilateral testicular regression (BTR) remains unexplained in the majority of cases. Evidence supporting both a vascular and genetic origin have been reported. However, whether different etiologies result in different clinical subgroups is unclear. Furthermore, long-term outcome data of individuals with BTR regarding statural and penile growth are very scarce.

AIMS
To assess the underlying factors associated with the development of BTR (i.e. pregnancy, neonatal and genetic factors) and explore long-term growth and pubertal outcomes

METHODS
Participants: Individuals born with BTR (n=33) recruited in five Belgian centers at an age of 14.2 ± 5.3 years
Cross-sectional study: Clinical and genital exam
Retrospective data: Initial presentation and management
Genetic analysis: Exome-based testing of genes (n=241) involved in gonadal development and spermatogenesis

RESULTS

Management and puberty

Testosterone treatment during childhood:
• 9/32 (28.1%); Median age: 6.0 (IQR: 10.3)
• IM Sustanon® 25mg/4weeks: 3-months
• Little to no effect in 2/6 (33.3%)

At study visit:
• Age: 14.2 ± 5.3 years
• Prepubertal: 15/33 (45.5%)
• Testosterone replacement therapy: 21/32 (65.6%)

Median dose: 100mg/2weeks (Range: 16-186)

Growth:
• Adult height: 176.5 ± 5.6 cm
• Peak height velocity: 9.4 ± 1.6 cm/year
• Growth puberty: 24.0 ± 6.7 cm

Stretched penile length:
• 9.6 ± 3.1 cm (<7cm: n=3)

Genetics

Clinical information:
• Case 1 & 3: little to no penile growth after IM testosterone treatment
• Case 2: female gender of rearing

CONCLUSIONS

➢ Pregnancy and obstetric complications were found in over half of cases
➢ No new genes were identified
➢ DHX37 variants were identified in three cases:
  ➢ All had micropenis/small phalic structure at birth
  ➢ Two cases were treated with (dihydro)testosterone during infancy and showed little to no penile growth
➢ Pubertal height gain is satisfactory