Childhood Growth of Boys with Congenital Hypogonadotropic Hypogonadism

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Introduction

Congenital hypogonadotropic hypogonadism (CHH), a rare genetic disorder characterized by low gonadotropin and sex steroid levels, provides a model to study the impact of sex steroid deficiency on childhood growth. We characterized growth patterns in male CHH patients with special emphasis on genotype-phenotype correlation and growth during the minipuberty of infancy.

Design and participants

Growth charts of 36 Finnish and Danish males with CHH were evaluated; the most recent national growth reference data were used for comparisons (1,2). Fifteen patients (42%) had a genetically verified diagnosis of CHH (*KAL1, FGFR1, GNRHR* or *PROK2*). Patient characteristics are detailed in table 1.

Results

In CHH patients, the mean (±SD) length standard deviation score (SDS) at birth (0.2 [1.6] SDS) decreased significantly during the first 3 (to -0.9 [1.2] SDS, $P<0.01$) and 6 months of life (to -0.7 [1.3] SDS, $P<0.05$) (**Fig. 1A**). The respective mean length SDSs were lower than the mean mid-parental target height (MPH) SDS ($P<0.05$). We further tested the postnatal growth deflection by including only growth data of CHH patients with birth length within the normal range (±2 SD). Even within this subgroup (n=11), the average length SDS decreased significantly from birth (-0.3 [1.3] SDS) to 3 months (to -1.0 [1.3] SDS, $P<0.01$). During the first 6 mo of life, CHH patients grew thinner (mean change in weight-for-height, -6.7 [11] %, $P<0.05$). Between 2 and 3 years, the mean height SDS (-0.2 [1.3] SDS) did not differ from MPH SDS (P=NS). Thereafter, childhood growth remained constant. At an average age of 15.8 (0.8) years, height SDS reached its nadir (-1.8 [1.4] SDS), reflecting pubertal failure. Their final height (FH) SDS, however, did not differ from MPH SDSs (P=NS) (**Fig.2**). No clear genotype-growth associations emerged.

Characteristics	Patients with CHH
Number of subjects	36
Age, yrs	30.7 (12)
Age at induction of puberty, yrs	16.1 (2.1)
Birth weight, g	3560 (460)
Birth length, cm	51.3 (2.9)
Mid-parental target height, SDS	-0.2 (0.7)
Kallmann syndrome	26 (72%)
Patients with molecular genetic diagnosis	15 (42%)
Mutation(s) in	
KAL1	7 (19%)
FGFR1	5 (14%)
GNRHR	2 (6%)
PROK2	1 (3%)
History of micropenis and/or cryptorchidism	18 (50%)
Testosterone treatment for micropenis	2(6%)
Non-reproductive features of CHH	
Dental agenesis	2 (6%)
Cleft lip/palate	2 (6%)

Table 1. Characteristics of males with CHH.

Conclusions

Moderate postnatal length deflection is a novel feature of CHH, and may reflect early androgen deficiency. Childhood growth patterns are not of clinical value in targeting molecular genetic studies of CHH.

Disclosure statement

The authors have nothing to disclose

References

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2. Tinggaard et al., Acta Paediatr. 2014 Feb;103(2):214-24.

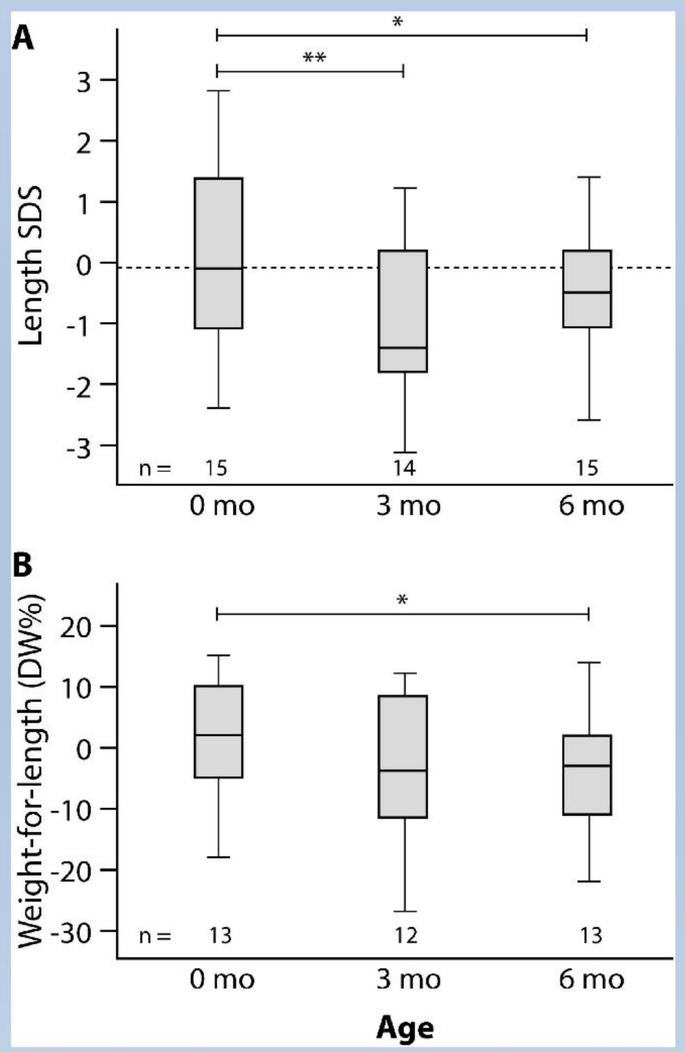

Figure 1. A, Length SDS of patients with CHH during the first six months of life. B, Weight-for-length in patients (DW%) with CHH. *P < 0.05 and **P < 0.01.

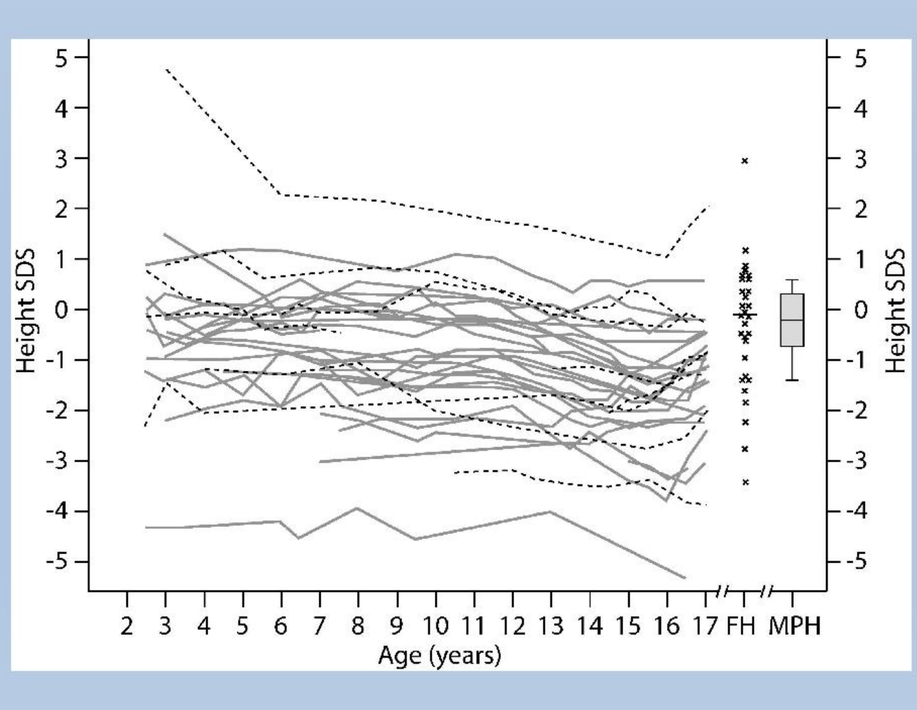

Figure 2. Height SDSs of 27 Finnish (grey line) and 9 Danish (dashed line) males with CHH. Final heights (FH) (crosses, n=31) and MPH (box plot, n=22) are shown. Horizontal line in the FH plot indicates the median.

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