Novel treatment (new drug/intervention; established drug/procedure in new situation)

Medical intervention in a constitutionally tall child

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Summary

Constitutionally tall stature (CTS) in children is a normal variant of growth within populations. Based mainly on psychological factors, sex steroids have been prescribed since the 1950s to induce puberty, as a mean to reduce final adult height. Controversy remains in the treatment of CTS, as well as lack of established criteria for initiating treatment. We report a constitutionally tall Saudi boy who was treated with sex steroids and was successful in reducing his final adult height.

BACKGROUND

There are large differences in the mean height between populations across the world due to variations in both environmental and genetic influences.¹ It is estimated that 50–90% of height variation is accounted for by genetic factors where the rest are due to environmental factors.²

Constitutionally, tall children (CTS) represent a normal variant of extreme growth among healthy individuals occurring in about 3% of a normally distributed population.³ Numbers and figures vary substantially among various populations, the Scandinavians and the Dutch among the tallest people in the world.²

CTS is defined as a child with a height above the 97th percentile of the growth curve, or as height 2 SDs above the mean for age, sex and population group.² Birth length is usually at the 75th percentile, and tall stature becomes evident at 3–5 years of age as growth starts to accelerate and crosses percentiles till it slows down and follows the smooth curve of the 97th percentile.²

Diagnosis is usually made from family history and examination, which should show no apparent abnormalities excluding other excessive growth syndromes.^{2–4} Children with CTS presenting to medical care report concerns that include feeling different, being teased, have difficulty in purchasing clothes and carry predicted difficulties in finding future partners.⁵

Hormonal therapy to reduce adult height has been practiced in boys and girls since the 1950s.² In 1956, Goldzieher published the first formal clinical study about the use of oestrogen in treatment of tall girls.^{6–7}

Treatment for CTS remains very controversial, especially in the indication for treatment, accuracy of height predictions, long-term side effects of therapy and ethical problems related to tampering with normal growth.⁸

We report a constitutionally tall Saudi boy who came to medical attention with concern of his excessive growth.

CASE PRESENTATION

A Saudi boy who presented with his parents to the endocrine clinic at the age of 3 years and 4 months with the concern of excessive growth. His growth centiles for

weight and height were 24 kg and 115 cm, respectively, which both were above the 97th percentile. His medical and surgical history was free from any complains and he had attained normal developmental milestones. Birth weight was 4.7 kg. Birth length 53 cm. Paternal height measured 182 cm, maternal height 170 cm, maternal grandfather's height was 194 cm, who is the tallest family member.

His parents noticed that he was growing very fast, and needed new clothes and shoes frequently. Despite the presence of tall family members, his excessive growth started to be a matter of concern to them. Clinical examination revealed a well and healthy boy. He was prepubertal and his systemic examination was normal.

Within the context of the history and physical examination, it was clear that he was a constitutionally tall child. In his early school age years, he started having problems coping with his peers. He was frequently being teased and bullied, to the extent that family sought psychiatric advice to support and help their child.

He had frequent visits to the endocrine clinic. During his visits, family was told about the available mode of therapy to induce puberty in attempt to reduce final adult height. Family was also advised that the best time to start this therapy would be at the age of 10–12 years. The parents had some reservations about inducing puberty at an early age due to social reasons.

INVESTIGATIONS

- ▶ TSH: normal
- ▶ Morning growth hormone: normal
- ▶ Morning IGF-1: normal
- ▶ At the age of 3 years and 4 months his bone age was corresponding to 5 years
- ▶ At the age of 12.1 years his bone age was corresponding to 13.6 years
- ▶ Pituitary MRI: normal

DIFFERENTIAL DIAGNOSIS

1. Familial tall stature
2. Acromegaly
3. Thyrotoxicosis

4. Marfan syndrome
5. Homocystinuria

The diagnoses 2–5 excluded by clinical ground and investigations.

TREATMENT

At the age of 12.1 years, with a height of 185 cm, the family decided to start the hormonal therapy. By this time he had already showed signs of puberty (pubic hair tanner 4, testicular volume 8–10 ml bilaterally). He also had facial and axillary hair. His bone age was corresponding to 13.6 years and predicted adult height was 204 cm.

Testosterone was initiated at a dose of 250 mg on a weekly basis and continued for a total of 14 months.

OUTCOME AND FOLLOW-UP

During this time he was seen at 4 months intervals. Height, growth velocity and puberty were assessed at each visit. Fourteen months after starting therapy he had grown a total of 7 cm and showed no attained height over two consecutive visits. Bone age at the time of termination of treatment corresponded to 17 years and the height recorded was 192 cm. One year from termination of treatment, final adult height was 194 cm, recording a post-treatment growth of 2 cm.

Prediction of adult height in this case was based on the Bayley and Pinneau's tables, revised for use with Greulich-Pyle x-ray hand standards.

The child was compliant to medication and the side effects experienced were very mild, mainly in the form of facial acne.

DISCUSSION

This constitutionally tall child whose parents concerned about his excessive growth, worried about his final adult height and social acceptance. In spite of induction of puberty was initiated at an advanced bone age, a total reduction of 10 cm was achieved compared with the predicted adult height prior to therapy.

The published predicted adult heights used as an indication for treatment vary between 175 cm in Swiss girls and 185 cm in German or Dutch girls. In boys the reported heights are as low as 195 cm and as high as 205 cm.^{4 8}

The lower limit for possible intervention is 9–9.5 years and 9.5–10 years in girls and boys, respectively.⁴

A successful reduction in final adult height may be broadly affected by the following: bone age, duration of therapy and the dose given for treatment.

Height reduction is clearly more pronounced when starting therapy at a younger bone age.² It amounts to 21.3 or 16.6 cm in the youngest and to 2.8 or 2.9 cm in the oldest bone age groups in boys and girls, respectively.⁹

Starting therapy at a bone age of 14 or older for both girls and boys results in a final height that significantly exceeds height prognosis at the time of start of treatment, suggesting that treatment had resulted in induction rather than reduction of growth.²

For boys, the doses of long-acting testosterone esters recommended in most studies are about 500 mg/m²/month, which correspond to roughly four times the normal testosterone production rate of adult men or to

about 8–10 times that of early adolescence.² In clinical practice, 2 weekly intramuscular injections of 500 or 250 mg once a week are used.^{4 9}

Treatment should continue up to a bone age of 17 years, when 99% of the adult height is reached according to the Bayley-Pinneau prediction model. Therapy in boys usually continues with an average of 14 months.⁹ Therapy should not be stopped at an earlier bone age to avoid post-treatment growth, which might cause significant reduction of height limiting effect ranging from 1 to 2 cm in girls and 2 to 3 cm in boys.

The mean height reductions vary from 4.8 to 12.7 cm in boys and from 3.6 to 5.3 cm in girls.⁹

Most adverse events experienced during therapy are mild. In boys, aggravation of acne is the most common side effect reported.^{4 8} Others include weight gain, oedema, gynaecomastia and reversible decrease in testicular volume.⁴

To date, no evidence of long-term side effects of high doses of sex steroids have been demonstrated.²

Comparing our results with the literature, we were successfully able to reduce the final adult height by a total of 10 cm within a short period of time, despite a relatively late presentation, but still within the accepted limits to initiate therapy. Our patient experienced only acne. His therapy was terminated at the recommended bone age.

Learning points

- Constitutional tall stature can be a psychosocial concern in boys.
- In spite of late testosterone therapy, a reduction of height may be achieved in constitutional tall stature.
- In a short-term observation, testosterone of 250 mg weekly for a year therapy for a child with tall stature was observed as a safe treatment.

Competing interests None.

Patient consent Obtained.

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