Altered Sequence of Pubertal Changes and Accelerated Bone Maturation in A 10-Year-Old Japanese Boy with Nonendocrine Short Stature Treated with GH.

Seiji Sato, Makoto Anzo, Tsutomu Kamimaki, Maki Fukami and Nobutake Matsuo

Department of Pediatrics, Keio University School of Medicine, Tokyo, Japan

Abstract. A 10-year-old Japanese boy with nonendocrine short stature who was treated with GH showed discordant pubertal development and advanced skeletal maturation. GH therapy was started at 6.8 years of age at a dose of 0.5u/kg/week, when his height age was 3.3 years and bone age was 4.8 years. At 10.3 years of age his height and bone age reached 7.5 and 9.0 years, respectively, but unexpectedly he developed pubic hair (Tanner stage II, with a testicular volume of 4mL). It appears that the pharmacological dose of GH prematurely induced Leydig cell activity in this patient.

Key words: GH therapy, nonendocrine short stature, Leydig cell activation, abnormal pubertal development, accelerated bone maturation

Whether GH therapy improves the final-height in normal short children remains to be determined [1]. We report the case of a patient with nonendocrine short stature in whom bone age was unexpectedly advanced and the sequence of the appearance of secondary sex characteristics was abnormal under GH therapy.

Case Report

A boy was born as a small-for-date infant (2,060g in weight and 45cm in length) after an uncomplicated 39 week pregnancy and deliv-

ery. He was first seen in our clinic for short stature at 12 months of age when he weighed 6090g and measured 65cm (-4.3SD), and his bone age was 3 months. The endocrinological data (Table 1), bone survey, and karyotype were all normal, and the diagnosis of nonendocrine short stature was made. GH therapy (0.5U/kg/week) was introduced at the age of 6.8 years. At that time, his height Z score was -4.5, height age was 3.3 years, and his bone age was 4.8 years. At the age of 8.8 years, height Z score was -3.6, height age was 5.6 years, and bone age was 6.3 years. No secondary sex characteristics were developed. At the age of 10.3 years, his pubic hair was at Tanner stage II, each testis was 4mL in volume, and serum LH, FSH and testosterone concentration was 0.6mLU/mL, 3.8mLU/mL, and 120ng/dL, respectively. His height Z score was -2.9, height age was 7.5 years, and bone

Correspondence: Dr. Seiji Sato, Department of Pediatrics, Keio University School of Medicine, 35 Shinanomachi, Shinjuku-ku, Tokyo 160 Japan

Table 1. Endocrinological data

Insulin loading test	peak GH	45.2 ng/mL
Glucagon–propranolol loading test	peak GH	19.3 ng/mL
GH during night	mean GH	6.12 ng/mL
	peak GH	11.8 ng/mL
Urinary GH	18.2 , 13.8	ng/g Cr
Thyroid hormones		
T3	194	ng/dL
T4	11.3	μ g/dL
F-T4	1.5	ng/dL

Table 2. Clinical course

Calender age (years)	6.8	8.8	10.3
Height (cm)	96.0	110.4	120.8
Height Z score	−4.5	−3.6	−2.9
Height age (years)	3.3	5.6	7.5
Bone age (years)	4.8	6.3	9.0
Predicted adult height (cm)		160.1	153.5
Testicular volume (mL)	1.0	1.0	4.0
Pubic hair (Tanner stage)	I	I	II
Blood testosterone (ng/dL)	20	10	120

age was 9.0 years. The predicted adult height by the Bayley-Pinneau method was 160.1cm at age 8.8 years and 153.5cm at age 10.3 years, respectively (Table 2 and Figure).

Discussion

GH therapy was of questionable value in increasing the final-height of this patient since the rate of skeletal maturation exceeded that of linear growth towards the end of therapy, and his predicted final height decreased from 160.1cm(8.8 years of age) to 153.5cm (10.3 years of age). Pubic hair appeared when his testicular volume reached 4ml. In normal Japanese adolescents, pubic hair nearly always develops after the testicular volume

has reached 6-8mL [2]. We suspect that this patient's early appearance of pubic hair was caused by premature Leydig cell activation induced by GH therapy that also led to accelerated skeletal maturation. Our experience indicates that patients on pharmacological dose of GH should be carefully observed for premature Leydig cell activation.

References

1. Brook CGD. Who is for growth hormone? BMJ 1992; 304: 131-2.
2. Matsuo N. Skeletal and sexual maturation in Japanese children. Clin Pediatr Endocrinol 1993; 2 (Suppl 1): 1-4.

Abnormal Pubertal Development under GH Therapy