Growth and Pubertal Development in Addison's Disease

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Abstract We evaluated the growth, bone age and pubertal development in a boy with Addison's disease who had been followed-up over a period of 15 years. The predicted final height was acceptable, because his bone age was retarded and delayed epiphyseal closure prolonged the period of growth. Pubertal development was delayed. Endocrinological examination revealed associated partial hypogonadotropic hypogonadism.

Key Words: Addison's disease, growth, bone age, pubertal development, partial hypogonadotropic hypogonadism

Introduction

Addison's disease is rare in children and there are few reports about growth and pubertal development in patients with this condition (1, 2). The growth and pubertal development were assessed in a patient with adequately treated Addison's disease who had been followed up over a period of 15 years.

Case Report

The patient is a boy who currently is 18 years 7 months old. His grandmother and mother had diabetes mellitus. A younger sister was healthy. Salt craving and skin pigmentation were noted at the age of 2 years, and he

was admitted at the age of 3 years 6 months for investigation of frequent vomiting and lethargy. At that time his height was 98.7 cm (+0.7 SD), weight was 14.5 kg (+0.2 SD), and bone age was consistent with his chronological age. Blood pressure was 96 mmHg in systole. Laboratory tests revealed low blood glucose (15 mg/dL), diminished serum sodium (119 mEq/L) and chloride (88 mEq/L). Endocrinological data are shown in Table 1. The plasma adrenocorticotropin (ACTH) was elevated, and cortisol, aldosterone and testosterone levels were low. The luteinizing hormone (LH)(basal: 5.5→peak: 9.1 mIU/mL; radioimmunoassay (RIA)) and follicle stimulating hormone (FSH)(1.9→2.8 mIU/mL) responses to a standard gonadotropin-releasing hormone (GnRH) test showed a prepubertal pattern. There was an abnormally low rise in plasma cortisol to the rapid ACTH test and prolonged ACTH stimulation test. No tissue autoantibody

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Table 1 Endocrinological data at diagnosis.

BLOOD		URINE	
GH	2.85ng/ml	17-KS	0.2mg/day
TSH	2.2 μ U/ml	17-OHCS	0.5mg/day
ACTH	>800pg/ml	Adrenaline	3.1 μ g/day
Testosterone	<20ng/dl	Noradrenaline	38.4 μ g/day
Aldosterone	<10pg/ml		
Cortisol	<12.5ng/ml		
DHEA-S	<200ng/ml		

was detected. Under the diagnosis of idiopathic Addison's disease, the patient was treated with hydrocortisone and fludrocortisone (3).

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His height was above average (+0.7 SD) at the time of diagnosis. Analysis of growth showed slightly reduced growth velocity and no pubertal growth spurt; the SD score of his height was -1.4 at the age of 14 years 7 months (Fig. 1). However, his height is 169.2 cm (-0.2 SD, predicted height: 165.5 cm) at present and he is still growing.

Radiographs of his left hand are shown in Fig. 2. Bone age was consistent with chronological age at diagnosis, but then gradually became retarded (Fig. 1). His bone age is 15.4 years (Tanner-Whitehouse 2 (TW2) RUS method for Japanese) at present, and epiphyseal closure has not occurred. Testicular enlargement (more than 4 mL) occurred at the age of 12 years 10 months, and pubic hair appeared at the age of 16 years. Testicular volume is 8 mL, pubic hair is Tanner stage 3, and phallus is Tanner stage 3 at present. Endocrinological data are shown in Table 2. The LH (basal: 0.9→peak: 1.9 mIU/mL; immunoradiometric assay (IRMA)) and FSH

Fig. 1 The patient's growth curves for height, bone age and growth velocities.

(3.7→4.3 mIU/mL) responses to the standard GnRH test were prepubertal.

Discussion

The predicted final height in this patient with Addison's disease was acceptable despite low growth velocities and long-term steroid replacement. Deficiency of adrenal androgen may delay pubertal development and skeletal maturation and prolong the period of growth. However, some workers have reported normal pubertal development in patients with Addison's disease (1, 2). Although this patient had the first sign of puberty (testes volume: 4 mL)

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Fig. 2 Radiographs of the left hand and wrist. A: 11 years 7 months of chronological age (CA)(bone age: 10.6 years), B: 17 years 1 month of CA (bone age: 14.9 years), C: 18 years 7 months of CA (bone age: 15.4 years).

Table 2 The course of endocrinological data.

Age	3y6m	8y8m	12y10m	17y10m	18y7m
Testosterone (ng/dl)	<20	<10	30	167	205
LH (mIU/ml)		5.5	4.3	1.5	3.2
FSH (mIU/ml)		1.9	4.7	2.9	5.3
DHEA-S (ng/ml)		<200	<200	<200	31
Sm-C (U/ml)		0.81	1.36	0.79	1.13

titers to pituitary cells is needed to elucidate the cause of adrenal insufficiency of this patient. It may be assumed that deficiency of adrenal androgen is related to the hypogonadotropic hypogonadism.

References

at the age of 12 years 10 months, there was inadequate further development. The cause of the delayed puberty was thought to be partial hypogonadotropic hypogonadism. X-linked congenital adrenal hypoplasia is known to be associated with hypogonadotropic hypogonadism (4, 5, 6, 7). At present, the diagnosis of hereditary adrenal hypoplasia can only be made if a sibling or male cousin has been found to have adrenal insufficiency, so our patient was thought not to be hereditary. Further examination for autoantibodies including antibody

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