

## Original

# The Long-Term Effect of Replacement Therapy in a Short Girl with Autoimmune Atrophic Thyroiditis of Prepubertal Onset

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**Abstract.** A 9 yr 11 mo old girl was admitted to our hospital because of short stature. Her growth rate gradually decreased and her height was 120 cm (-2.5 SD) on admission. The mother's and father's heights were 157 cm (-0.2 SD) and 163 cm (-1.3 SD), respectively. Her bone age was retarded (6 yr 10 mo). An MRI indicated pituitary enlargement, which mimicked adenoma. Evaluation of the pituitary-thyroid axis and thyroid function proved she had primary hypothyroidism ( $T_3$  0.5 ng/ml,  $T_4$  1.0  $\mu$ g/dl, TSH 1,030  $\mu$ U/ml). These findings, thyroid autoantibody (anti-microsome antibody 400 xs) and histopathology (moderate fibrosis and mild lymphocytic infiltration) suggested acquired hypothyroidism due to autoimmune atrophic thyroiditis of prepubertal onset. Since the evaluation, she has been treated with levothyroxine. The pituitary enlargement disappeared within 3 mo after levothyroxine replacement. The growth rate increased and her height reached 153.2 cm (-1.0 SD) during 10 yr replacement (at 19 yr 11 mo of age). An improvement in her final height was obtained by long-term thyroid hormone replacement therapy. Enough endocrinological study and repeated MRI evaluation are necessary in cases of pituitary enlargement which mimics adenoma before considering surgery.

**Key words:** autoimmune thyroiditis, primary hypothyroidism, short stature, pituitary enlargement, replacement therapy

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### Introduction

Juvenile primary hypothyroidism may result in a permanent height deficit (1). Autoimmune atrophic thyroiditis is an uncommon disease in childhood. Patients with this disorder of prepubertal onset develop juvenile acquired primary hypothyroidism which is a cause of short stature (2, 3).

We report a short girl with pituitary enlargement, which mimicked macroadenoma (pseudoadenoma) due to autoimmune atrophic thyroiditis. And we also report the long-term effect of levothyroxine replacement therapy on her final height.

### Patient Report

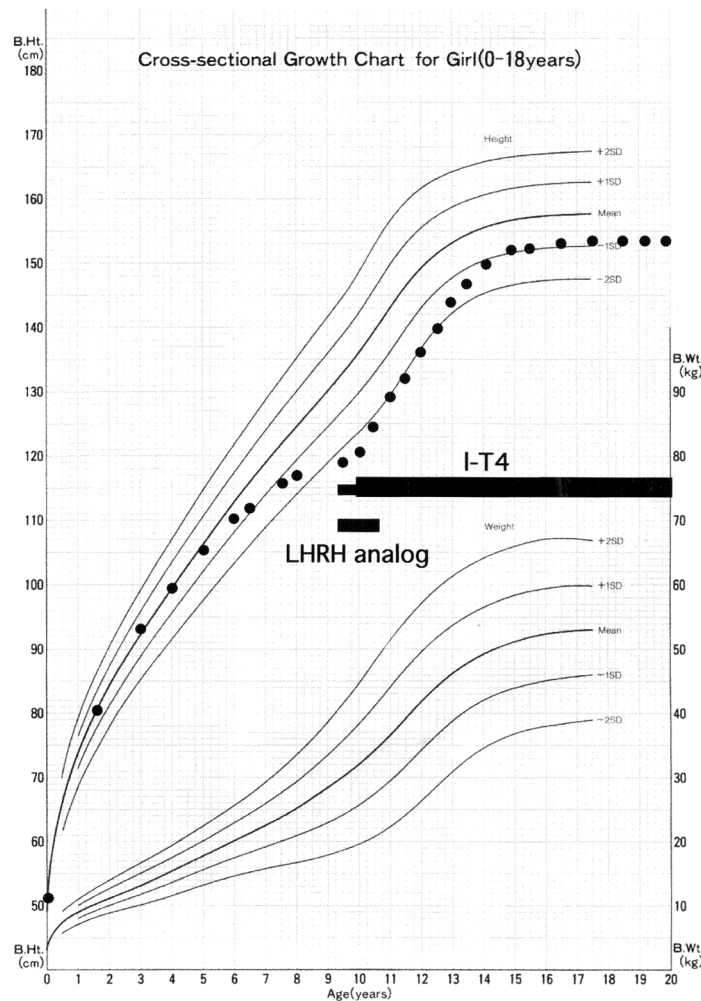
A 9 yr 11 mo old girl was admitted to our hospital because of short stature and suspicion of pituitary tumor. She was a product of 41 wk gestational age and her birth weight was 3930 g. She had been healthy, and her growth and

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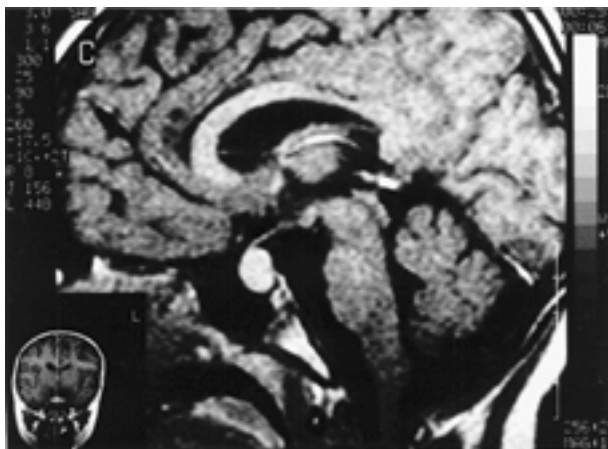
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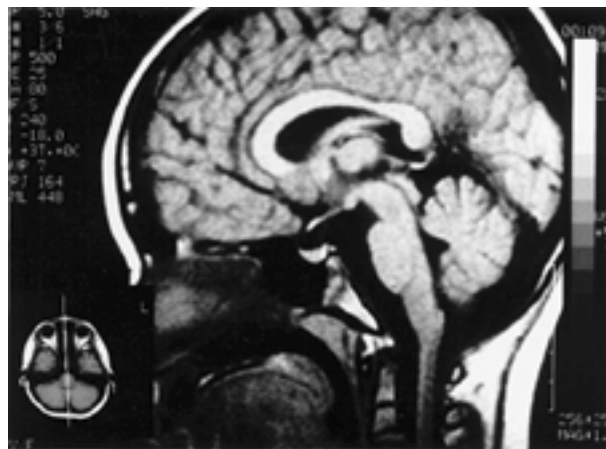
**Fig. 1** Changes in height plotted on the female standard growth curves for Japanese.

development were normal until she reached 5 yr of age. Her family history was unremarkable. Her growth rate gradually decreased after 5 yr of age and her height was 120 cm ( $-2.5$  SD) and body weight was 29 kg (degree of obesity:  $+32.6\%$ ) on admission (Fig. 1). She was a short and obese girl without goiter or webbed neck, and was in early puberty (breast development of Tanner stage II). The mother's and father's heights were 157 cm ( $-0.2$  SD) and 163cm ( $-1.3$  SD), respectively. The target height for her family was 153.5 cm. Her bone age was retarded (6 yr 10 mo). Enlargement of the

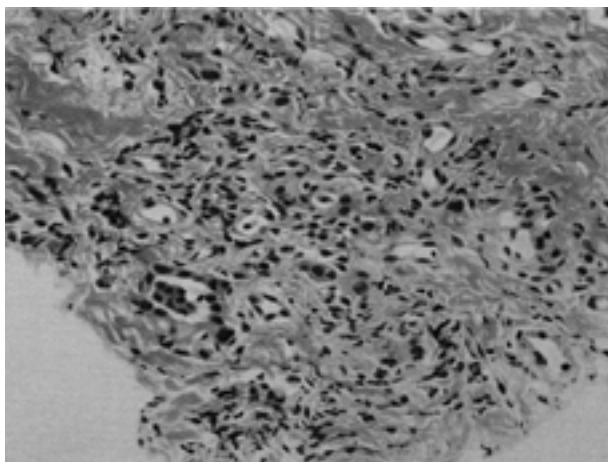
sella turcica in a plain cranial X-ray and MRI findings indicated pituitary enlargement, which mimicked macroadenoma (Fig. 2). The evaluation of the pituitary-thyroid axis (serum basal and TRH stimulated peak TSH levels were  $1,030 \mu\text{U/ml}$  and  $2,420 \mu\text{U/ml}$ , respectively) and thyroid function ( $\text{T}_3$   $0.5 \text{ ng/ml}$ ,  $\text{T}_4$   $1.0 \mu\text{g/dl}$ ) proved she had severe primary hypothyroidism. Ultrasonography of the neck proved that the thyroid gland was not enlarged but relatively small in spite of significant TSH increase. These findings, low basal metabolic rate ( $-22.3\%$ ), positive thyroid autoantibody (anti-



**Fig. 2** Pituitary mass with suprasellar expansion was proven by MRI. Gadolinium-enhanced image.



**Fig. 4** The pituitary enlargement disappeared on serial MRI after three months of thyroid hormone replacement.



**Fig. 3** Histopathology of thyroid tissue (needle biopsy). Moderate fibrosis and mild lymphocytic infiltration. Magnification,  $\times 80$ .

microsome antibody 400 xs) and the histopathology of thyroid tissue obtained by needle biopsy (Fig. 3: moderate fibrosis and mild lymphocytic infiltration) suggested juvenile acquired primary hypothyroidism due to autoimmune atrophic thyroiditis of prepubertal onset. The increase in the pituitary-gonadal axis also proved pubertal response (serum LH and FSH levels after LHRH stimulation were 29.4 mIU/ml

and 16.6 mIU/ml, respectively).

Since the evaluation, she has been treated with levothyroxine. The dose of levothyroxine was gradually increased to 100  $\mu\text{g}/\text{day}$ , and this medication was continued thereafter. The serum thyroxine concentrations were maintained in the normal range during levothyroxine replacement. The pituitary enlargement disappeared on serial MRI after three months of thyroid hormone replacement (Fig. 4). Thyroid autoantibodies have been positive (anti-microsome antibody 6400–102400 xs, anti-thyroglobulin antibody 100–400 xs) during levothyroxine replacement.

Intranasal LHRH analog (buserelin) was administered for two years (from 10 yr 0 mo to 11 yr 11 mo of age) to suppress the pubertal development, because severe juvenile hypothyroidism could cause a distinct form of isosexual precocity (4). Her pubertal development was suppressed during LHRH analog treatment. The growth rate and the maturation of bone increased after levothyroxine and LHRH analog administration, and her bone age reached 10 yr 6 mo at the end of LHRH analog therapy (11 yr 11 mo of chronological age). The onset of menarche occurred at 14 yr 2 mo of age, and she had regular

menstrual cycles thereafter. At 15 yr 7 mo of age her height and bone age reached 152.8 cm and 15 yr 0 mo, respectively. Her height at 19 yr 11 mo of age reached 153.2 cm ( $-1.0$  SD) after ten years of levothyroxine replacement (Fig. 1).

## Discussion

We reported a short girl with autoimmune atrophic thyroiditis of prepubertal onset. Her height SD score was  $-2.5$  SD at the start of levothyroxine therapy. Her final height reached 153.2 cm ( $-1.0$  SD) after ten years of levothyroxine replacement. It was comparable with her target height (153.5 cm) and 1.0 SD shorter than projected height from the height before onset of hypothyroidism (at 5 yr of age). Serious loss of the final height was prevented by long-term thyroid hormone replacement therapy. A permanent deficit in adult height has been reported in patients with autoimmune thyroiditis with long-standing hypothyroidism despite adequate treatment with levothyroxine (1). Early recognition and treatment of the disease should be achieved for a preventive care of hypothyroidism before serious short stature ( $-3$  or  $-4$  SD) results. The effect of two year LHRH analog therapy on her final height improvement was not sufficient. Her pubertal development was suppressed during LHRH analog treatment, but maturation of bone was not sufficiently suppressed by LHRH analog therapy. Her bone age was 6 yr 10 mo on admission and reached 10 yr 6 mo at the end of two years LHRH analog therapy.

Pituitary enlargement (thyrotroph hyperplasia) as a result of primary hypothyroidism is a well-recognized entity (5). Thyroid hormone therapy causes a regression of pituitary thyrotroph hyperplasia (6). After levothyroxine replacement therapy, the pituitary enlargement in our patient resolved within a few months, but sometimes it may be difficult to distinguish

between hyperplasia and adenoma, and pituitary enlargement may also have been secondary to thyroid failure. Before considering surgical procedures for patients with pituitary enlargement which mimics adenoma, a continuous effort to perform enough endocrinological studies, which include a trial of replacement therapy for thyroid hormone deficiency and repeated MRI evaluations, are suggested to exclude hypothyroid induced pituitary swelling.

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