Magnetic Resonance Imaging of the Pituitary Gland in Patients with Central Idiopathic Precocious Puberty: The Influences of a Gonadotrophin-Releasing Hormone Agonist on Pituitary Volume

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Key words: pituitary volume, precocious puberty, gonadotrophin-releasing hormone agonist

Introduction

A progressive elevation of pituitary hormones results in enlargement of pituitary gland size (PS) which is detected by magnetic resonance imaging (MRI) in normal pubertal children (1, 2). Patients with central idiopathic precocious puberty (CIPP) have been shown to have increased PS (3, 4). However, the influence of gonadotrophin-releasing hormone (GnRH) agonist treatment and of cessation of the treatment on PS is unknown. The purpose of this study was to investigate the effect of GnRH agonist on the PS of patients with CIPP and the relationship between PS and anterior pituitary function.

Subjects and Methods

Eight girls and one boy with CIPP (chronological age (CA), girls: 2.6-9.7 years, boy: 11.4 years before the start of the treat-

ment) were enrolled in the study. Central precocious puberty is defined as gonadotrophin-dependent gonadal activation with premature onset of secondary sex characteristics before 7 years old in girls and 8 years old in boys. All the patients satisfied these criteria. Brain tumors and hamartomas were ruled out by serial assessments by cranial magnetic resonance imaging. The therapeutic GnRH agonist (leuprolide acetate depot; TAP-144-SR) was injected s.c. every 4 weeks. The dose of the agonist was 30-90 μ /kg, which has already been proved to suppress the pituitary-gonadotrophin axis (5). MRI examination of the pituitary gland was performed with a 1.5 Tesla GE Sigma System. T1 weighted images of 3-mm thickness were obtained using a spin echo pulse sequence with a repetition time (TR) of 400 ms, an echo time (TE) of 11 ms, and a field of view (FOV) of 14 cm. Strict mid-line positioning of the scan was assessed by simultaneous visualization of the anterior and posterior lobes and the stalk of the pituitary gland. The maximal height (PH) and length (PL) of the pituitary gland were measured.

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Values were compared to normal Japanese values for age which were reported by Hayakawa *K et al.*(1). MRI was performed before and every 6-12 months after start of GnRH agonist treatment.

Results

Clinical features and hormonal features of each case with CIPP are shown in Table 1. The treatment with GnRH agonist caused a decrease in the LH and FSH responses to GnRH test and plasma estradiol, which resulted in decreased urinary GH excretion, plasma IGF-I levels, and serum alkaline phosphatase (ALP) levels (Table 2). On the other hand, both the pituitary height (PH range: 6.0-9.5 mm, mean; 7.6 mm) and length (PL range: 8.0-10.7 mm, mean; 9.2 mm) in each case of CIPP before the treatment were significantly greater than those of age-matched controls revealed by

Table 1 Case 5 had low birth weight and short stature.

Clinical features of cases with CIPP

Case no.	SEX	CA (years)	BA (years)	Height (SDS)	Tanner Stage		
					Br	PH	AH
1	female	9.7	13.3	+0.3	3	3	+
2	female	3.4	5.9	+4.2	3	2	-
3	female	9.5	11.5	+2.5	4	3	-
4	female	8.1	10.3	+1.3	3	2	-
5	female	8.5	8.4	-3.2	3	1	-
6	female	2.6	3.8	+1.1	3	1	-
7	female	9.5	14	+2.3	4	3	+
8	female	9.1	13	+2.4	4	3	-
9	male	11.4	13.9	+1.5	3	+	T12cc

T: testis volume

Hormonal features of cases with CIPP before the treatment

Case no.	GnRH test LH (IU/L)	(basal/peak) FSH (IU/L)	Estradiol (pg/ml)	Testosterone (ng/dl)	IGF-I (U/ml)	GnRH agonist (μ g/kg)
1	4.0/50.9	5.8/14.9	33.0		4.9	90
2	2.8/31.9	8.2/16.5	21.0		2.5	30
3	0.7/13.0	4.8/19.3	11.0		5.8	30
4	3.7/41.2	7.8/17.4	39.0		2.6	90
5	0.7/30.6	2.5/19.9	13.2		1.7	30
6	5.2/20.1	8.3/54.5	5.0		2.7	30
7	2.7/29.3	6.4/14.6	43.4		3.9	-
8	3.6/25.4	7.1/12.5	13.2		4.1	-
9	1.2/11.9	3.9/7.4		390	4.7	30

Hayakawa *et al.* (Fig. 1-1-1-4). PH in each case during the treatment had a tendency to become lower compared with those of age-matched controls, but PL did not. Furthermore, both cases, who had finished the course of the Gn agonist treatment, showed an increase in PH after elevation of secretion of gonadotrophin. PH in case no. 8 who was not treated was significantly greater after diagnosis (Fig. 1-1).

Discussion

The pituitary gland showed linear growth except for two growth spurts. The two growth spurts of the pituitary gland were during the 1st year and during puberty (1). The second growth spurt occurs during puberty, the so-called physiologic hypertrophy of adolescence (6, 7). The pituitary spurt at puberty may be secondary to the increase in cells secreting gonadotrophins and/or those secreting GH (3). This study shows the changes of the size of anterior-pituitary gland of patients with CIPP before and after the treatment with GnRH agonist. In conclusion, gonadal suppression during GnRH agonist treatment is accompa-

Table 2 Mean $\pm$ SD peak values of LH# and FSH# after GnRH test, estradiol, urine-GH level, IGF-I, and ALP before and after 12, 24, and 48 weeks of treatment are shown. Statistically significant compared with value at beginning of study; *P<0.01; **P<0.05.

Changes of hormonal features

	0	12	24	48 weeks
LH (IU/l)#	31.3 $\pm$ 13.7	1.8 $\pm$ 1.5*	1.9 $\pm$ 1.3*	1.4 $\pm$ 1.0*
FSH (IU/l)#	23.8 $\pm$ 15.2	3.8 $\pm$ 2.8*	4.8 $\pm$ 4.6*	4.2 $\pm$ 2.8*
estradiol (pg/ml)	20.4 $\pm$ 13.3	5.0 $\pm$ 0.9*	6.8 $\pm$ 4.5*	5.0 $\pm$ 0.9*
Urine-GH (pmol/molCre)	135.6 $\pm$ 50.0	87.9 $\pm$ 48.2*	75.2 $\pm$ 54.1**	63.0 $\pm$ 38.7**
IGF-I (U/ml)	3.4 $\pm$ 1.6	2.0 $\pm$ 0.8**	1.8 $\pm$ 0.3**	2.4 $\pm$ 0.8**
ALP (IU/ml)	736 $\pm$ 380	434 $\pm$ 34*	432 $\pm$ 81*	464 $\pm$ 168*

Pituitary Size of Precocious Puberty

Fig. 1-1 Pituitary Height (female)

Fig. 1-3 Pituitary Height (male)

Fig. 1-2 Pituitary Length (female)

Fig. 1-4 Pituitary Length (male)

Fig. 1 Pituitary height (Fig. 1-1, 1-3) and length (Fig. 1-2, 1-4) in CIPP patients compared with the normal values for age. Data on normal values from Hayakawa K, et al. *Neuroradiology* 1989; 172: 171-177. Case 8 was not treated.

nied by reduction in pituitary gland size which is reversed after stopping the treatment. Especially, we consider that the height of the pituitary gland with CIPP reflects the changes in the degree of hypothalamo-pituitary-gonadotrophin activation, and MRI may be helpful in the diagnosis and treatment of CIPP.

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