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Case Report

ADHD-like behavior in a patient with hypothalamic hamartoma

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Abstract

We report a male patient with hypothalamic hamartoma (HH) who manifested central precocious puberty (CPP) at 4 years of age. Gonadotropin-releasing hormone (GnRH) analogue treatment was started at 6 years of age and his pubertal signs were suppressed. At 9 years of age, the patient was emotionally unstable, aggressive, and antisocial. He had severe attention deficit hyperactivity disorder (ADHD)-like behavior and conduct disorder. No seizure activity was observed. GnRH analogue treatment was discontinued for 8 months from 9 years and 4 months of age due to his mother's illness. During this period sexual urges were observed. Treatment with daily methylphenidate markedly improved his behavioral problems. However, his sexual urges were not suppressed until 3 months after the GnRH analogue treatment was restarted. The present case is unique because the patient's behavioral problems were observed despite the parahypothalamic type of HH and absence of seizures. This case is also rare because behavioral problems were observed without seizures, and no ADHD cases with hamartoma have been reported previously. Recently, clinical studies have described an association between psychiatric morbidity, including ADHD, and hyperandrogenism disorders. Our patient's ADHD-like symptoms might be due to hyperandrogenism. In such cases, GnRH analogue with methylphenidate could be effective for improving ADHD-like symptoms.

Keywords: Attention deficit hyperactivity disorder; Central precocious puberty; Hypothalamic hamartoma; Conduct disorder; Gonadotropin-releasing hormone analogue

1. Introduction

Hypothalamic hamartoma (HH) is a rare congenital malformation of the hypothalamus with a prevalence estimated at 1 in 50,000 to 100,000 [1]. Most HH patients present with central precocious puberty (CPP) and/or gelastic seizures, which are associated with cognitive deterioration and behavioral disturbance. HH is classified into two types, namely, parahypothalamic and intrahypothalamic [2]. In general, the former includes CPP only and the latter includes CPP as well as other neurological and psychological impairment such as seizures, mental retardation, and behavioral disorders.

We report a male patient with a rare combination of the parahypothalamic type HH, CPP, and ADHD-like behavior, successfully treated with GnRH analogue and methylphenidate (MPH).

Abbreviations: ADHD, attention deficit hyperactivity disorder; CPP, central precocious puberty; HH, hypothalamic hamartoma; GnRH, gonadotropin-releasing hormone

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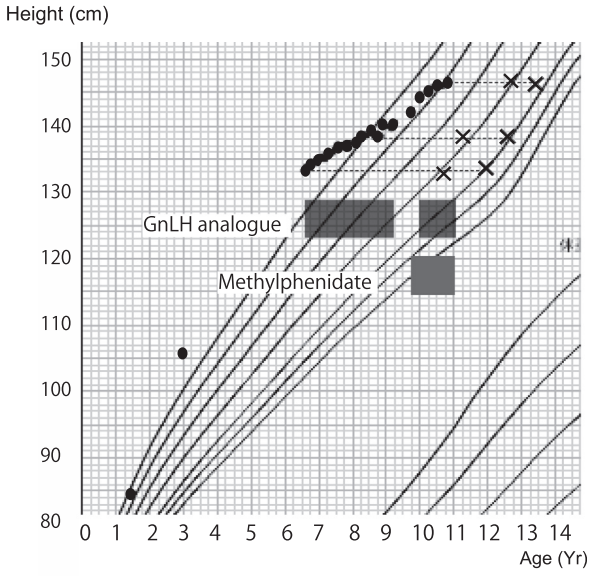

Fig. 1. Patient's growth curve. The upper curve shows height, and the lower curve shows body weight. Bone age is indicated by XXX. The patient displayed tall stature since 4 years of age. He was treated with GnRH analogue at 6 and 9 years of age, and was treated with methylphenidate at 9 years of age. After GnRH therapy started, his growth rate pubertal signs were suppressed.

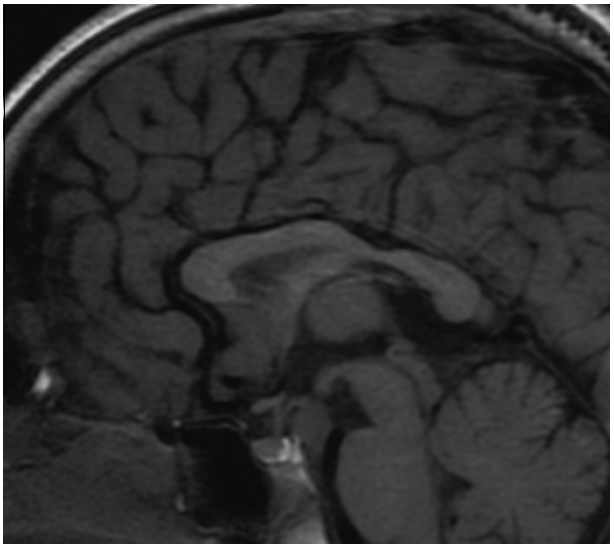

Fig. 2. Magnetic resonance imaging of the brain. A hypothalamic hamartoma was detected as an isointense hypothalamic mass of 0.9 cm × 1.1 cm × 1.2 cm in the tuber cinereum. The tumor was classified as peduncular and parahypothalamic, and the third ventricle was not distored.

2. Case report

The patient was born at 40 weeks with a birth weight of 3.064 g after a non-problematic gestation period. He had tall stature at 4 years of age, and pubic hair and deepening of his voice were observed at 5 years of age. Around the same time (3–4 years of age), the patient's mother noticed he exhibited hyperactivity, and thieving behavior. At the time he was referred to our hospital at 6 years and 9 months of age, his height was 133.3 cm (+3.2 SD) and his weight was 31.5 kg (+2.5 SD) (Fig. 1). The patient had enlarged testes (15 ml), Tanner stage III pubic hair, elevated serum testosterone (6.96 ng/ml), and bone age of 12 years. Serum luteinizing hormone (LH) and follicle-stimulating hormone (FSH) levels were in the pubertal range both before and after the GnRH loading test (Table 1). Magnetic resonance imaging of the brain showed an isointense hypothalamic mass of the tuber cinereum (Fig. 1). The tumor had a peduncular structure and was characterized as parahypothalamic without distortion of the third ventricle (Fig. 2). He was diagnosed with CPP and was treated with a GnRH analogue (30 mcg/kg) every 4 weeks for 3 months. After 3 months of treatment, his gonadotropin and testosterone levels were suppressed (Table 2), and his pubertal signs also showed gradual suppression. In the lower grades of elementary school, he had been emotionally unstable, aggressive towards friends and authoritative figures, and antisocial. GnRH analogue treatment was discontinued for 8 months from 9 years and 4 months of age due to his mother's illness. During this period, and sexual urges were observed. He had severe attention deficit hyperactivity disorder (ADHD)-like behavior and conduct disorder. His ADHD rating scale score-IV [3], as evaluated by his elementary teacher, was 40 (inattention 17, hyperactivity–impulsivity 23), and his intelligence quotient (IQ), as estimated using the Wechsler Intelligence Scale for Children (Third edition) was 88 (verbal IQ 95, performance IQ 82). At 9 years and 9 months of age, long-acting MPH (18 mg/day) was started and increased to 27 mg/day. One month after starting methylphenidate, his behavioral problems markedly decreased and his ADHD rating scale score-IV improved to 28 (inattention 13, hyperactiv ity–impulsivity 15). However, his sexual urges were not

Table 1
Laboratory findings for a male patient aged 6 years, 9 months with a hypothalamic hamartoma. Testosterone 6.96 ng/ml (<0.05). IGF-1 451 ng/ml (50–290). GnRH loading test.

Parameter	Baseline	After 30 min	After 60 min	After 90 min	After 120 min
LH (mIU/ml) (normal range)	2.0 (0.02–0.44)	32.8	25.3	19.1	16.0
FSH (mIU/ml) (normal range)	4.0 (0.18–2.58)	10.1	10.5	9.7	9.4

LH, luteinizing hormone; FSH, follicle-stimulating hormone.