Hypothalamic Hamartoma in An Unusual Case with Delayed Puberty

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Abstract- Hypothalamic hamartoma (HH) is a rare intracranial lesion that usually presents with classic triad of central precocious puberty, gelastic epilepsy, and developmental delay. Herein, a 14-year old boy is presented in whom the diagnosis of HH was made by magnetic resonance imaging. While he did not have any complain of precocious puberty, he surprisingly suffered from delay in puberty. The definite diagnosis of HH can only be made by appropriate imaging, in a case with atypical feature of delay in puberty and in the absence of gelastic epilepsy. To our best knowledge, this is the first case of HH who is presented with delay in puberty as of first manifestation.

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Introduction

Hypothalamic hamartoma (HH) is a rare condition, presenting with classic triad of central precocious puberty (CPP), gelastic epilepsy, and developmental delay (1). HH could be due to tissue displacement during 5th and 6th week of gestation, when "the ventral aspect of the neuraxis approaches the anterior tip of the end of the notochord" (2). These patients can have endocrine and neurological symptoms, including precocious puberty, seizure, progressive behavioral, and cognitive difficulties (3).

The diagnosis of HH can be made based on a typical clinical presentation of gelastic epilepsy, CPP, developmental delay and presence of a non-calcified non-enhancing hypothalamic mass that does not enlarge over the time appearing isointense to gray matter on T1 and often hyperintense on T2 images (3). CPP due to HH usually occur significantly earlier than idiopathic CPP. In 82% of these patients, CPP occurs before age of 2 years and occasionally during their first year of life (2). In addition, rapid progression of pubertal signs and bone age are the other characteristics of CPP with HH (2). Herein, an unusual case of HH is presented who not only did not manifest with CPP, but also had a delay in puberty.

Case Report

A 14-year old boy was referred to the Children's Medical Center, Pediatrics Center of Excellence in Tehran-Iran, with chief complaint of delay in puberty. He had a history of micro-phallus in infancy that had been treated with testosterone, while no other problem has been occurred afterward. He was mentally developed well and his testis and phallus were in normal size. He had a normal sense of smelling. His height was 159 cm (25% percentile) and his weight was 65 kg (90% percentile). His maturity state was pre-pubertal. No other abnormality was detected in physical examination.

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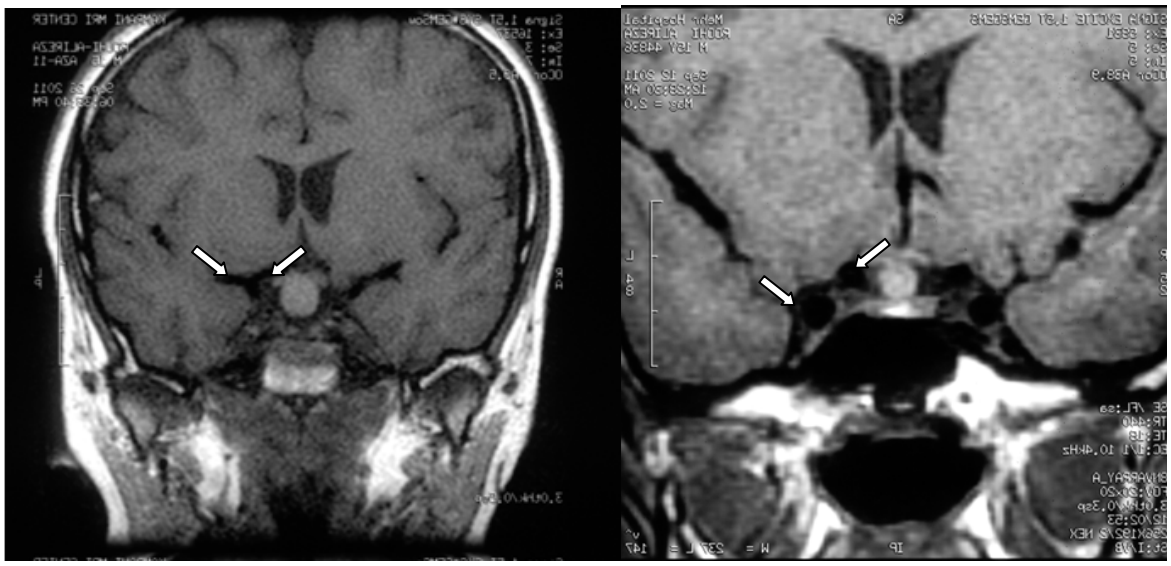

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Figure 1. A. T1 image in MRI without contrast. Well defined mass is seen at hypothalamus with lower extension along the pituitary stalk. B. T1 MRI after IV contrast. No obvious enhancement is seen.

No positive family history of a same condition and other abnormalities were mentioned. In sonography of the left wrist bones, his age was reported 13-14 years old.

Computed tomography (CT) scan showed a soft tissue density in sellar region with extension to suprasellar area. Therefore magnetic resonance imaging (MRI) was performed for the patient. T1 high and T2 intermediate signal well defined mass was seen at hypothalamus with lower extension along the pituitary stalk. After contrast injection, no obvious enhancement was seen within the lesion. Optic tracts and chiasm, cavernous sinuses and parasellar areas appeared normal (Figure 1). These findings were suggestive for HH. It should be noted that size and shape of pituitary gland was normal and stalk was displaced anteriorly. There was normal homogenous enhancement of the gland; and there was no evidence of microadenoma.

Laboratory tests showed that insulin-like growth factor 1 (IGF1) was 116 micg/l (normal range: 142-525 micg/l), luteinizing hormone (LH) was 0.5 miciu/ml (normal range: 1.7-11.2 miciu/ml) and follicle-stimulating hormone (FSH) was 1.0 miciu/ml (normal range: 2.1-18.6 miciu/ml). However, growth hormone (GH=20 ng/ml), beta human chorionic gonadotropin (beta hCG=1.0 miu/ml with negative cut point of <5 miu/ml), prolactin (6.5 ng/ml with normal range of 3.6-16.3 ng/ml) and adrenocorticotropic hormone (ACTH=10 pg/ml with normal range of 7.9-66.1 pg/ml) were normal.

Considering clinical phenotype, imaging findings and low levels of IGF1, LH, and FSH, the diagnosis of HH with delayed puberty was made for the patient.

Discussion

Hypothalamic hamartoma is a rare intracranial lesion that occurs predominantly in children (4). The triad of epilepsy, developmental delay and CPP is its main manifestations, when it attaches to the mammillary bodies (1,5). Meanwhile it has been reported that about 75% of cases of sexual precocity in children 1-3 years old were associated with HH (4).

HH could be classified to the parahypothalamic type and the intrahypothalamic type based on the MRI findings. The first one is generally associated with precocious puberty, while the second one more likely to manifest gelastic seizure (6).

This tumor can automatically release LH-RH, stimulate precocious LH-RH release from normally quiescent hypothalamic nuclei or destroy the inhibitory pathways and cause CPP (7).

Puberty is a transitional zone between childhood and adulthood, which is a period for developing sexual characteristics, make the person fertile and include somatic growth, primary sexual organ development (gonads and genitals), and the appearance of secondary sexual characteristics (breasts and pubic hair) (5,8). Early puberty defined in boys as puberty that occur before 9 years old, while delay in puberty is a clinical

condition in which the physical manifestations of puberty start late (usually more than 2.5 standard deviations later than the mean) (8,9).

In this report, a boy with HH was introduced that despite the other previous cases had a delay in puberty. The definite diagnosis of HH can only be made by appropriate imaging, in a case with atypical feature of delay in puberty and in the absence of gelastic epilepsy. To our best knowledge, this is the first case of HH who is presented with delay in puberty as of its first manifestation.

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