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Hypothalamic Hamartoma Cause of Precocious Puberty: About Two Cases

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Abstract **Case Report**

Hypothalamic hamartoma is a rare cause of central precocious puberty in children. The use of neuroimaging in central precocious puberty in girls is essential to detect an organic cause, however exceptional, namely hypothalamic hamartoma, Although the GnRH analogs are known to be effective therapy, there are few studies of the recovery of the pituitary-gonadal axis following long-term treatment. We report 2 cases of precocious puberty revealing the presence of a hypothalamic hamartoma, collated in the endocrinology-pediatrics department at the RABAT children's hospital, to obtain a better understanding of the clinical aspects, pathogenesis, and treatment of this entity.

Keywords: Hypothalamic hamartoma, Precocious puberty, GnRH analog therapy, Neuroimaging, Pituitary-gonadal axis.

INTRODUCTION

Precocious puberty is defined as the early development of sexual characteristics before the age of 8 in girls and before the age of 9 in boys. The use of neuroimaging is essential in central precocious puberty in girls in order to detect an organic cause, however exceptional, namely hypothalamic hamartoma. We report 2 cases of precocious puberty revealing the presence of a hypothalamic hamartoma, collected in the endocrinology-pediatrics department in the RABAT children's hospital.

CASE REPORT 1:

This is a girl aged 3 years and 1 month, with no particular pathological antecedents, who presented with precocious puberty, manifested at the age of 2 and a half years by bilateral breast enlargement, sign of thelarche puberty. Clinical examination revealed a tanner stage of S3P1, with weight at +3 standard deviation and height at +1.5 standard deviation. Paraclinical examinations in favor of an advanced bone age at 5 years compared with her chronological age of 3 years, pelvic ultrasound with no abnormalities, biological tests showing elevated gonadotropin hormone levels with FSH at 8. 48 mIU/ml and LH at 3.993 mIU/ml, a LHRH test showed LH to be higher than FSH, with a high ratio LH/FSH at 2.4. The work-up was completed by a hypothalamic-pituitary MRI, which showed a hypothalamic hamartoma measuring 9*8mm. Treatment consisted of GNRH analogue injections at a dose of 3.75 mg every 26 days, with good clinical and biological progression. The child was followed in parallel by neurosurgeons, who confirmed that there was no indication for surgery.

The evolution was marked by the slowing down of the growth rate with the stagnation of puberty at unstimulated S3P1 with absence of vaginal secretion or gelastic epileptic seizure, and on the paraclinical level, the evolution was marked by the normalization of FSH and LH.

CASE REPORT 2:

She is 6 years and 9 months old, 3rd of 4 siblings, with a history of psychomotor retardation, with walking and speech at the age of 4, notion of convulsive seizures since the age of 03, she takes an antiepileptic medication, vaccinated according to the national immunization program and from a non-consanguineous marriage. The history of her illness dates back to the age of 3, with the onset of monthly menstruation, pubic and axillary hair growth, associated with headaches and seizures poorly controlled by antiepileptic drugs. Clinical examination on admission revealed a hemodynamically and respiratorily stable conscious

child, weight 30kg (+3DS) and height 132cm (+3DS), bilateral strabismus, with TANNER pubertal stage S2P2. Paraclinical workup, hypothalamic-pituitary MRI in favor of hypothalamic hamartoma. Bone age is 12 years, which is older than her chronological age of 06 years. Abdomino-pelvic ultrasound showed a pubescent uterus with a body-to-cervix ratio greater than 1. Biological hormonal tests showed FSH at 6.29 and LH at 1.96. The child was put on LH6RH analogue, 1 injection every 28 days, with a good clinical evolution. The patient was followed up in parallel in neurosurgery.

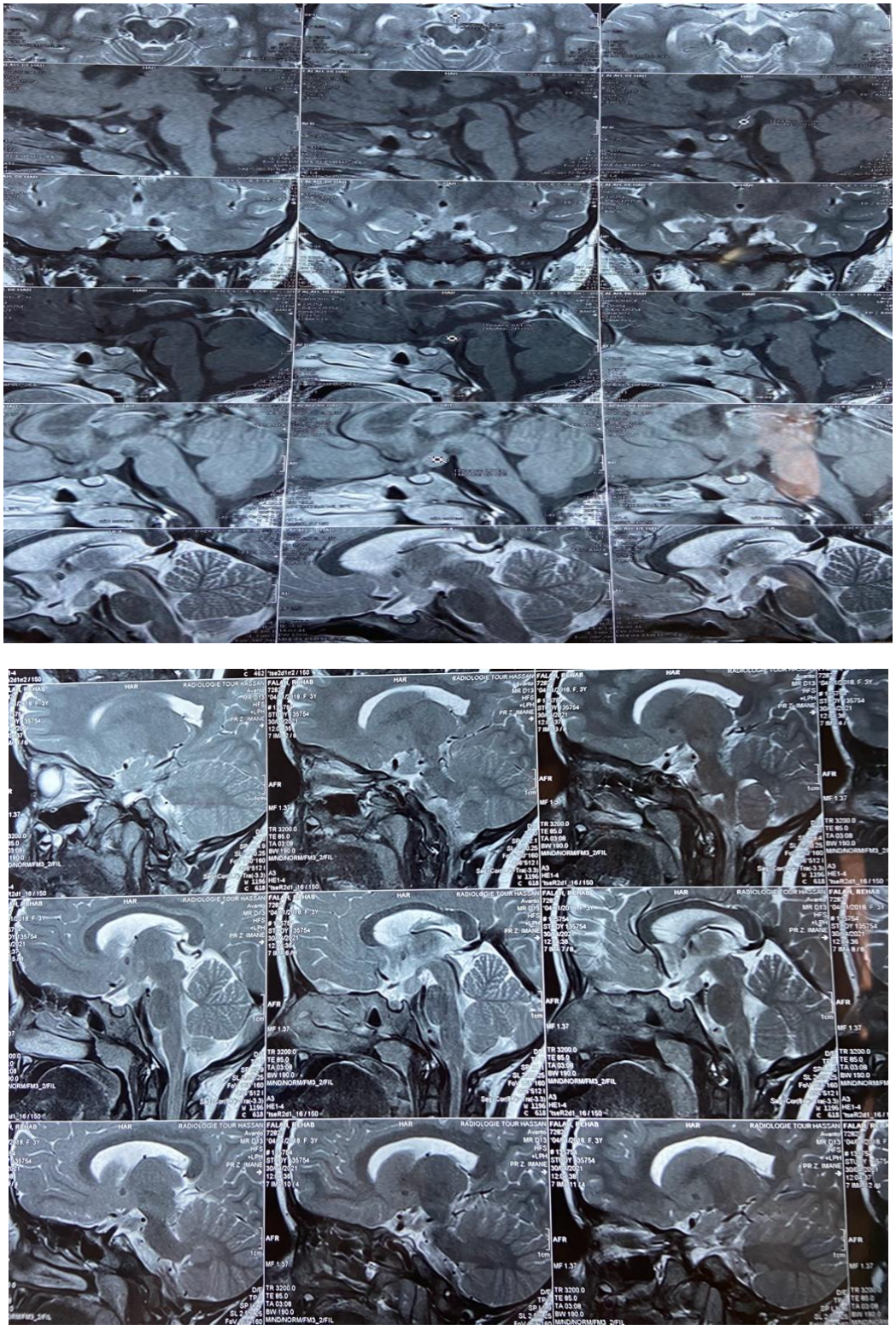

Figure 1: MRI image of hypothalamic hamartoma

DISCUSSION

Hypothalamic hamartoma is a rare disease occurring in nearly 1 to 100,000 children, with a slight predominance in boys (approximately 1.3 to 1), Nearly 95% of cases are sporadic, although 5% of cases are associated with Pallister-Hall syndrome, manifested by dysmorphology of the hands, feet (postaxial polydactyly and syndactyly), larynx (bifid epiglottis), anus and hypothalamus [5].

Hypothalamic hamartomas are non-progressive congenital lesions of the hypothalamus that occur during fetal development. Two anatomical subtypes are recognized, depending on the location of the mass lesion. The first type is the intrahypothalamic lesion, which connects to the posterior hypothalamus and the third ventricle; they appear near the mamillary bodies and are usually associated with gelastic seizures [1, 2], The second type is the parahypothalamic or pedunculated lesion located near the anterior hypothalamus, tubercle cinerreum or pituitary stalk and attaches only to the floor of the third ventricle. It is usually associated with signs of precocious puberty caused by increased release of gonadotropin-releasing hormone (GnRH) [2]. Hypothalamic hamartomas are non-neoplastic congenital malformations, made of normal brain tissue identical to adjacent hypothalamic structures but in an ectopic position. They are associated with precocious puberty, behavioral disorders and gelastic convulsions.

The mechanism is still unknown, but some authors have demonstrated by electron microscopy and immunofluorescence that the neurons of the hamathoma have a neurosecretory characteristic and contain LHRH, the hamartoma functioning as an unrestrained accessory hypothalamus [6, 7], other authors have demonstrated that there is another mechanism for LHRH hyperproduction, by compressing the posterior hypothalamus, which interferes with the physiological inhibition of gonadotropin production, and by compressing the median eminence, which stimulates gonadotropin secretion [8, 9].

Clinically, early puberty is the most frequent sign (89% of cases in Lin *et al*.,'s 1978 study) [10]. With onset around 2-3 years of age. A very early onset before the age of 1 has been described in one study, which should prompt a search for a hamartoma at all costs [11].

At present, MRI is an aid to etiological diagnosis. The tumor mass is clearly distinguishable, appended to the hypothalamus in the form of a T1-weighted isosignal and a T2-weighted hypersignal. Hamartomas are usually not gadolinium-enhanced [12].

With the use of LH-RH analogues [13], results appear to be as good in these forms as in idiopathic ones. Our study confirms this result. Treatment with LHRH analogues is merely symptomatic. The prognosis is good under regular neuroradiological control. The surgical option, according to some authors, should only be considered in cases of precocious puberty in young children and if the hamartoma is clearly pedicled on MRI.

In the cases of our patients, they are put on LHRH analogue with good clinical and biological evolution, with neuroradiological follow-up of the mass.

CONCLUSION

Precocious puberty on a hypothalamic hamartoma is a rare pathology, and resembles a congenital neuronal malformation, The long-term prognosis is preserved and the therapeutic challenge is major.

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