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A CASE OF HYPOGONADOTROPIC HYPOGONADISM IN ASSOCIATION WITH INTERHEMISPHERIC LIPOMA AND HYPOPLASIA OF THE CORPUS CALLOSUM

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Abstract: *Isolated hypogonadotropic hypogonadism is characterized by impaired gonadotropin release in the context of normal anatomical and functional anterior pituitary function. The conditions usually responsible for hypogonadotropic hypogonadism are: pituitary adenoma, neoplastic metastasis, granulomatous processes, lymphocitary hypophysitis, histiocytosis X, hemochromatosis, vascular pathologies. We present a case of isolated hypogonadotropic hypogonadism associated with interhemispheric lipoma and hypoplasia of corpus callosum.*

Key words: *hypogonadotropic hypogonadism, interhemispheric lipoma, hypoplasia of corpus callosum, Kallmann's syndrome.*

1. Introduction

Hypogonadotropic hypogonadism (HH) or secondary hypogonadism is defined as a clinical syndrome that results from gonadal failure due to abnormal pituitary gonadotropin level, which results from either absent or inadequate hypothalamic gonadotropin-releasing hormone (GnRH) secretion or failure of pituitary gonadotropin secretion. We present a case of isolated HH associated with interhemispheric lipoma and hypoplasia of corpus callosum (CC).

2. Case report

A 20-years old man was referred to the endocrinological unit for evaluation of delayed puberty and micropenis. On physical examination the patient's height and weight were 182 cm and 78 kg respectively (BMI 23.6 kg/m2). On genital examination, his testis had 3 ml in volume and descended into the scrotum. The stretched penile length was 5 cm and his pubic hair was Tanner stage 2.

The patient appeared of normal intelligence, a normal sense of smell on olfactometry, and no other dysmorphic

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features. There was no family history of anosmia, delayed puberty or hypogonadism. No history of cryptorchidism, head trauma, pathological episodes, or drug consumption was reported. The patient did not report eating disorders or vigorous physical activity.

The results of routine laboratory were within the normal range: complete blood count, glucose, ALT, AST, cholesterol, triglycerides, urea and creatinine, electrolytes (table 1).

Table 1

Laboratory findings in presented patient

Parameter	Patient's values	Normal values
Hemoglobin (g/dL)	13.6	13-18
Hematocrit (%)	39.4	40-52
White blood cell (µL)	10480	4100-10900
Red blood cell (mil./µL)	4.67	4.5-6.5
Platelet (µL)	277000	150000-400000
Fasting serum glucose (mg/dL)	102.7	70-105
ALT (UI/L)	14	41
AST (UI/L)	14.6	37
Blood urea nitrogen (mg/dL)	32.36	10-50
Creatinine (mg/dL)	0.87	0.7-1.2
Uric acid (mg/dL)	3.9	7
Calcium (mg/dL)	9.8	9,2-11
Sodium (mol/L)	141	135-145
Potassium (mol/L)	4	3.5-5.3
Chloride (mol/L)	108	98-106
Testosteron (nmol/L)	1.16	9.9-27.8
FSH (UI/L)	0.46	1.5-12.4
LH (UI/L)	0.17	1.7-8.6
PRL (ng/mL)	10.64	5-20
Cortisol (nmol/L)	520	AM: 101-530 PM: 79-470
TSH (µU/mL)	4.8	0.27-4.2
FT4 (pmol/L)	20.83	10-23

The endocrine functions of gonads, pituitary, thyroid, adrenals were evaluated in basal concentration and after stimulation with specific releasing hormones. Morning (AM 8:00) endocrine examinations including serum cortisol, thyroid stimulating hormone (TSH), free triiodothyronine (FT3), free thyroxin (FT4), insulin-like growth factor-1 (IGF-1), prolactin (PRL) were within normal ranges. On the other hand, serum concentration of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) were undetectable in the context of low testosterone level suggested the diagnosis of HH (Table 1).

In order to assess gonadotropin pituitary function a GnRH test (100 µg IV) was carried out. Blood samples for testosterone, LH and FSH determination was collected at basal level, 24 and respectively 48 hour after GnRH administration (Table 2).

Table 2

Stimulation test with GnRH analogue

	Basal	24 h	48 h
Testosteron (nmol/L)	1.11	1.76	2.96
FSH (UI/L)	0.4	1.66	2.64
LH (UI/L)	0.1	2.52	1.29

The patient underwent radiological examination of the pituitary gland by Magnetic Resonance Imaging (MRI). MRI showed an interhemispheric mass of 2.5/1.8/1.0 cm in size, and hypoplasia of CC (fig. 1 and 2). Lipomas have typical fat density (-50 to -100 Hounsfield Units) on computed tomography (CT). On MRI lipoma appears hyperintense signal on T1 weighted image, intermediate signal on T2 weighted image and suppressed on fat-suppressed image.

Based on clinical, endocrinological data, as well as imagistic evaluation a diagnosis of adult idiopathic hypogonadotropic hypogonadism was made, caused by

isolated gonadotropin deficiency associated with interhemispheric lipoma and hypoplasia of CC.

Therefore, the patient began substitutive treatment with testosterone undecanoate 1000 mg IM initially administered at 6 weeks and then every 3 months. Under testosterone therapy, his penile length increased to 8 cm, pubic hair advanced to Tanner stage 4, and patient experienced a feeling of improvement in well-being.

In the context of interhemispheric lipoma the patient will be assessed only by imagistic evaluation without indication of surgery.

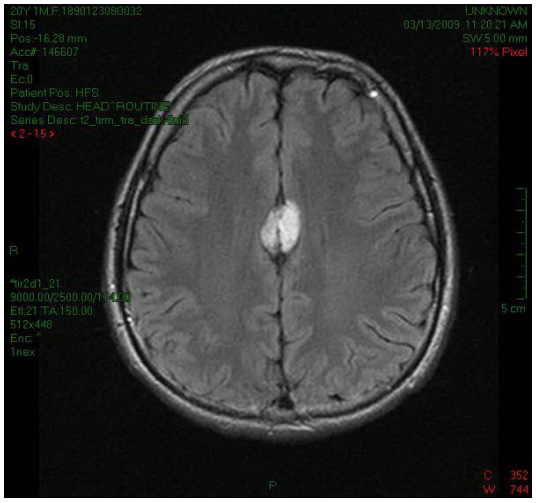

Fig. 1. *Interhemispheric lipoma on MRI transversal section (T2)*

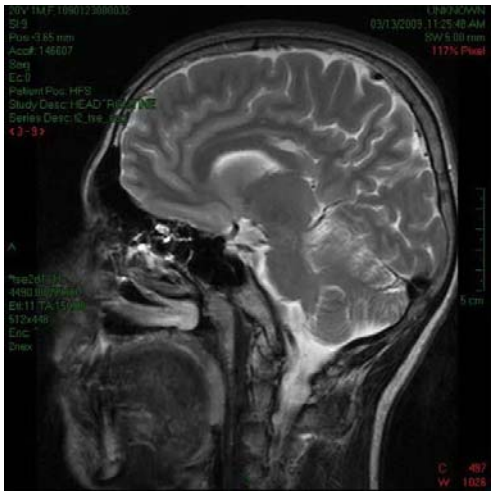

Fig. 2. *Interhemispheric lipoma and hypoplasia of corpus callosum on MRI sagittal section (T2)*

3. Discussion

Isolated HH is characterized by impaired gonadotropin release in the context of normal anatomical and functional anterior pituitary function. Serum concentrations for LH, FSH, and sex hormones are inappropriately decreased in the patient with hypogonadism. The conditions usually responsible for HH are pituitary adenoma, neoplastic metastasis, granulomatous processes, lymphocitary hypophysitis, histiocytosis X, hemochromatosis, vascular pathologies [13]. Traumas, acute diseases, alterations in nutritional status with significant decreases of weight could be responsible for the alteration in gonadotropins production and release, but through a thorough history these etiologies can be excluded. The underlying cause may be also due to developmental defects of GnRH neurons, impairment of functional activity in GnRH neurons, abnormal interaction between the GnRH ligand and its receptor, or the release of intact gonadotropins [9].

When aplasia of GnRH neurons is associated with defects in development of the olfactory bulb (Kallmann's syndrome), anosmia is the clinical symptom that indicates this type of GnRH deficiency [5], [6]. Kallmann's syndrome represents 50-52% of cases of isolated HH, while normosmic isolated HH is found in 48-50% of cases [9], [11].

In our case the patient had a normal sense of smell on olfactometry but unfortunately because we were not able to perform genetic testing, based on the data we concluded that the diagnoses is idiopathic HH.

Our patient presents with inter-hemispheric lipoma and hypoplasia of CC on imagistic evaluations. Intracranial lipoma is a congenital malformation that develops by abnormal differentiation of normally present tissues [1]. Inter-hemispheric lipoma is the most frequent intracranial lipoma, and is often associated with agenesis of CC. Lipomas represents approximately 0.34% of all intracranial tumors. Intrahemispheric lipomas accounts for 47% of intracranial lipoma and have frequency of 1/2500 to 1/25000 as reported in a necropsy study [4]. Intracranial lipomas are malformations not neoplasia, and thereby lipoma cells do not multiply but hypertrophy like any normal adipose cells. Because they are usually asymptomatic, intracranial lipomas are incidentally discovered. Interhemispheric lipoma is commonly associated with more severe congenital anomalies, and may present with headache, seizures and behavioral abnormalities. Surgery is not usually performed for interemispheric lipoma due to the associated high morbidity. In this case reported our patient was asymptomatic and surgery was not indicated for interhemispheric lipoma.

Dysgenesis of the CC may be complete or partial and represents a developmental anomaly that occurs *in utero*. Agenesis and hypoplasia of CC designates a group of malformations that range in severity from minor degrees of deficiency of the splenium to total failure of formation of the telencephalic commissunes [7].

The cause of agenesis of CC is usually not known, it can be inherited as either an autosomal recessive feature or an X-linked dominant feature. Maternal alcohol consumption during pregnancy has also been recognized as a risk factor. Seems to

be a male predilection (M/F=2/1). In some cases may result in mental retardation but intelligence may be only mild impaired and subtle psychosocial symptoms may be present [8].

The presence of lipoma may secondarily disturb the development of CC, resulting in hypoplasia or agenesis. Interhemispheric lipoma is often associated with partial agenesis of the CC [12].

Currently there is no specific medical treatment for callosal disorders, but individuals with agenesis of the CC and other callosal disorders may benefit from a wide range of developmental therapies and educational support [10].

In isolated HH during adulthood testosterone replacement is indicated to be continuously administered either long-acting testosterone undecanoate intramuscularly every 3 months [2] or daily oral or transdermal application of testosterone gel. Fertility therapy usually requires gonadotropin treatment with hCG and FSH [3].

In conclusion we presented the case of a rare associated between isolated HH associated with interhemispheric lipoma and hypoplasia of corpus callosum.

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