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Delay Puberty in a 15 Years Old Boy: A Case Report

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Abstract

Kallmann syndrome is characterized by absent puberty secondary to lack of production of sexual hormones. This result in hypogonadotropic hypogonadism with micropenis and cryptorchidism in males. In females, we found lack of menstruation, although breast enlargement may be observed. Without treatment, they will be infertile. Absent of smell (anosmia) or reduce smell (hyposmia) is present in most cases. A 15 years old boy was referred to the endocrinology consultation because of absent of ejaculation during masturbation. On physical examination, we observed a normal phenotype. The neurological screening, heart and pulmonary auscultation, abdominal palpation and vital signs were all normal. Tanner classification showed pubic hair stage 2, with both testis 2 ml volume each one. With highly suspect of Kallmann syndrome with anosmia, we performed the GnRH test with the result confirming hypogonadotropic hypogonadism. The brain MRI, showed absent of olfactory bulb. The molecular study for the common genes was negative. Our case seems is a sporadic one. The patient starts testosterone injection with excellent clinical evolution.

Keywords: ***Hypogonadotropic hypogonadism; Anosmia; Kallmann syndrome***

1. Introduction

Kallmann syndrome, is characterized by absent puberty secondary to lack of production of sexual hormones. This result in hypogonadotropic hypogonadism with micropenis and cryptorchidism in males. In females, we found lack of menstruation, although breast enlargement may be observed. Without treatment, they will be infertile. Absent of smell (anosmia) or reduce smell (hyposmia) is present in most cases. Others symptoms can appear, like cleft palate, hearing lost, renal agenesis but are rare.

The incidence is 1/30000 cases in males and 1/120000 in females. The inheritance can be dominant, x-linked recessive or recessive disorder. The most common mutations are ANOS1, CHDZ, FGF8, PROK2, PROKR2 and FGFR1. Sporadic cases are more frequent [1-5].

2. Case report

A 15 years old boy was observed in the endocrinology consultation because he referred every time absent of ejaculation during the act of masturbation. His personnel and family history are unremarkable. The parents are unrelated and healthy. On physical examination we observed a normal phenotype. The neurological screening, heart and pulmonary auscultation, abdominal palpation and vital signs were all normal. Tanner classification showed pubic hair stage 2, with both testis 2 ml volume each one. His stature (165cm) and weight (60.5 kg) was in the normal range for sex and age. The body mass index (BMI) was 22.2.

The psychomotor development was normal. The history and physical examination was compatible with hypogonadotropic hypogonadism and we asked if he can smell regularly. His answer was negative. We suspect of Kallmann syndrome and we gave him alcohol soaked in cotton, but he didn't have any reaction. He confirmed that he cannot smell any alcohol odour.

With highly suspect Kallmann syndrome with anosmia, we performed the GnRH test, (TABLE 1) with the result confirming hypogonadotropic hypogonadism. In normal respond to GnRH test, depends on the stage of puberty. The prepuberal child shows a small increment in LH and FSH up to 3-4 U/l and 2-3 U/l, respectively. The magnitude of response is greater in early and mid-puberty, particularly for LH. In our case, the non-response of FSH/ LH and testosterone, is a typical GnRH test result of Kallmann syndrome.

TABLE 1. **GnLH test with determination of LH, FSH and testosterone level.**

GnLH test	LH mUI/ml	FSH mUI/ml	Testosterone ng/dl (n : 5 - 500)
0 minutes (m)	<0.1	<0.1	315
30 m	0.9	1.3	
60 m	0.8	1.6	
90 m	0.8	1.8	
120 m	0.9	2.0	223

The brain MRI showed absent olfactory bulb, which is common in this syndrome (FIG. 1). Morphological abnormalities of olfactory apparatus in Kallmann syndrome are best evaluated with MRI. Olfactory bulbs are visualized better in coronal planes. Olfactory bulbs are seen as well-defined structures along cribriform plate. Olfactory sulci are seen between Gyrus rectus and medial orbital gyrus.

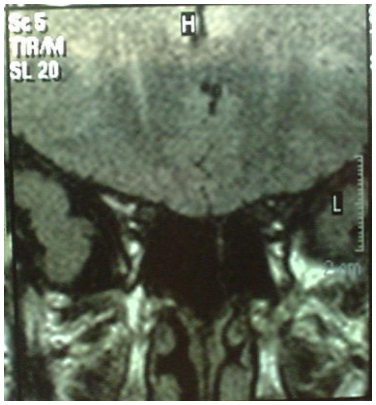

FIG. 1. **Olfactory MRI-absent of olfactory bulb in both sides.**

The molecular study for the common genes was negative. The patient starts testosterone injection with excellent clinical evolution. The starting dose was 50 mg intramuscular every month. After 3 months, he started to showed external sexual characteristics. Every 6 months we can increase 50 mg, according to the clinical evolution. The treatment continues even after puberty has been initiated to maintain secondary sex characteristics and normal levels of testosterone.

3. Discussion

This case with the clinical presentation of practically absent external sexual characteristics associated with anosmia and reduce olfactory bulb, is compatible with Kallmann syndrome [1-3]. Comparing our case with what we found in the literature, they all showed hypogonadism, but not all of them, has anosmia. Some of them showed diminished sense of smell (hyposmonia). The molecular study was negative but this can appear in many situations. The syndrome is the cause of lack of ejaculation. Our case seems sporadic [1-4].

The genes of Kallmann syndrome plays an important role in the migration of olfactory neurons to the olfactory bulbs and also the migration that synthetize GnRH at the same time to the olfactory nerves and hypothalamus.

In Kallmann syndrome, the mutations in genes disrupt this migration and for this reason, cannot stablished the olfactory via. This case showed us one more time that a detail history can be the key of a diagnosis.

The anosmia confirmation was important, because this symptom appears in the Kallmann syndrome and not in others hypogonadotropic hypogonadism cases.

The treatment is with hormone replacement therapy to induce puberty and fertility. Testosterone esters is most frequently used for puberty in male and estrogens in female patients. Pulsatile GnRH administration or exogenous gonadotropins are used to restore fertility [5].

REFERENCES

1. https://ghr.nlm.nih.gov/condition/kallmann-syndrome
2. Neil S, Richard Q. Kallmann syndrome. BMJ. 2012;345:e6971.
3. Catherine D, Jean-Pierre H. Kallmann syndrome. Eur J Hum Genet. 2009;17:139-146.
4. Shilin Z, Tao W, Jun Y, et al. A fertile male patient with Kallmann syndrome and two missense mutations in the KAL1 gene. Fertil Steril. 2011;95(5):1789.e3-6.
5. Gomez MCC, Vicente MAV, Miguel MAA, et al. Late-diagnosed Kallmann syndrome. Endocrinol Nutr. 2015;62(2):106-8.