World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(CASE REPORT)

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Rare association of Kallman Morsier syndrome with a non-functioning pituitary microadenoma

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World Journal of Advanced Research and Reviews, 2023, 18(01), 217–219

Publication history: Received on 25 February 2023; revised on 04 April 2023; accepted on 07 April 2023

Article DOI: https://doi.org/10.30574/wjarr.2023.18.1.0556

Abstract

Kallmann's syndrome (KS) is a form of hypogonadotropic hypogonadism associated with a defect in the sense of smell, due to abnormal migration of gonadotropin-releasing hormone-producing neurons. We report the case of a patient aged 16 years and 6 months who presented a micropenis with poor development of secondary sexual characteristics and anosmia. Plasma levels of luteinizing hormone, follicle stimulating hormone and testosterone were very low, while chromosomal analysis showed a 46XY karyotype. Hypothalamic-pituitary MRI showed bilateral agenesis of the olfactory bulbs associated with a 4 mm pituitary microadenoma. The patient was put on hormone replacement therapy with a good response.

Keywords: Hypogonadotropic hypogonadism; Kallmann's syndrome; Micropenis; Anosmia

1. Introduction

Morsier-Kallmann syndrome is a genetic disease characterized by the association of hypogonadotrophic hypogonadism by gonadotropin deficiency and anosmia or hyposmia related to hypoplasia of the olfactory bulbs, rare (estimated at 1/10,000), its prevalence is 4 times less frequent in girls compared to boys [1].

SK was first described in 1944 by Franz Josef Kallmann, in most cases it is discovered during the investigation of delayed puberty, more rarely the disease is suspected when a young boy has micropenis and/or cryptorchidism associated with anosmia [2].

2. Case report

Patient aged 16 years and 6 months presented to the department of endocrinology and metabolic diseases CHU Mohamed VI for a micropenis, he has as history an orchidopexy performed at the age of 3 years, infertility in the maternal uncle. On examination, a growth retardation was noted since childhood, anosmia since the age of 7.

Clinical examination revealed a body of eunuch proportions, he had a body weight of 62 kg, a height of 159 cm, a body mass index of 24.52kg/m^2. He had bilateral gynecomastia without galactorrhea. His secondary sexual characteristics were deficient (Tanner stage G1P2). He had a micropenis (stretched phallus with a length of 3.5 cm). The scrotal contents were barely palpable on both sides. Scrotal ultrasound revealed prepubertal testes (0.1 and 0.2 cc). The neurological examination was unremarkable except for a decreased sense of smell.

Hormone assays identified a hypogonadotropic hypogonadism profile with total testosterone of 0.58 ng/mL, luteinizing hormone of 0.1 IU/mL and follicle-stimulating hormone of 1 IU/mL. The exploration of the other hypothalamic-pituitary

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axes was without particularity: prolactin and cortisol blood level are within the normal limits, he had a normal thyroid function. The karyotype showed a 46XY pattern.

Radiologically, hypothalamohypophyseal MRI showed bilateral hypoplasia of the olfactory bulbs associated with a 4 mm pituitary microadenoma, making the diagnosis of Kallmann syndrome. The patient was put on synthetic androgens to induce virilization. He received intramuscular injections of testosterone (80 mg every 3 weeks) with a gradual increase in dose to 250 mg per month. Evaluation after 1 year of regular quarterly follow-up showed masculinization of the voice and the appearance of coarse pubic hair. Morning erections were reported, testicles and penis increased in size respectively (testicles = 2 cc, phallus = 6 cm).

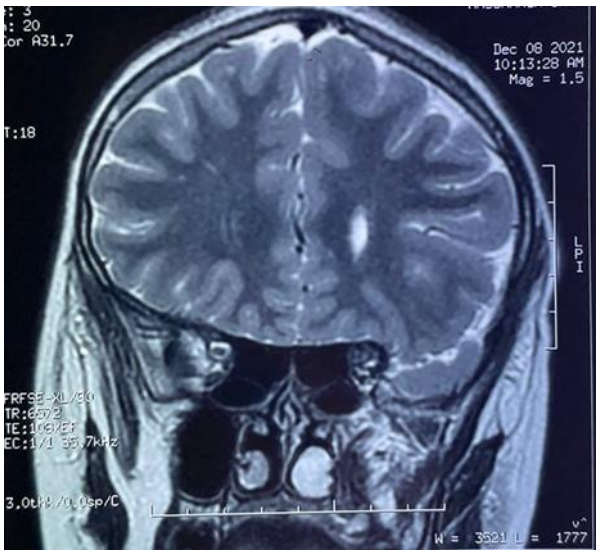

Figure 1 Coronal section showing agenesis of the olfactory bulbs

3. Discussion

We report a case of rare association of KS with a non-functioning pituitary microadenoma. This association was previously reported by Bolu et al [3] in their MRI evaluation of 120 male patients with idiopathic hypogonadotropic hypogonadism. Patients with hypogonadotropic hypogonadism were diagnosed with microadenomas and contrast-irregular pituitary in 18.2% and 10.7% of cases, respectively.

KS is an isolated form of hypogonadotropic hypogonadism associated with a defect in the sense of smell. It is due to defects in olfactory structures and impaired migration of GnRH-secreting neurons in the preoptic and hypothalamic regions [4].

The clinical presentation of the patient seems to be consistent in the literature, with the classic association of hypogonadotropic hypogonadism and anosmia [5]. The diagnosis is suspected in the absence of pubertal development after the age of 14 years. In girls, KS is revealed by primary amenorrhea in more than 90% of cases, breast development is very variable, often present and sometimes almost normal [6], syncinesia (mirror movements), visual attention anomaly, ocular motor anomaly, ptosis, cerebellar syndrome, deafness, hollow feet, hollow palate, cleft lip and/or palate, dental agenesis, renal agenesis [7].

When there is a strong clinical suspicion of KS, a blood test is required, which will reveal hypogonadotropic hypogonadism (testosteronemia <3.5nmol/l in boys and low serum estradiol concentrations in girls, sometimes below the limit of detection), with low or paradoxically normal plasma LH and FSH levels [8]. The evaluation of the anteropituitary functions is imperative in order to assess the whole pituitary functions; this precaution allows not to ignore other insufficiencies.

MRI has rapidly become the examination of choice to confirm the diagnosis of Kallmann de Morsier syndrome, by analyzing the olfactory tracts, located above the sieve blade of the ethmoid. All sequences allow to determine the absence or not of olfactory bulbs and the thickness of the section should not exceed 3mm showing agenesis or hypoplasia of the olfactory bulbs [9].

The treatment of hypogonadism in KS is aimed at triggering pubertal development with testosterone injections in males and estrogen-progestin in females and then ensuring the maintenance of secondary sexual characteristics, as well as the development of fertility, using gonadotropins or pulsatile GnRH to obtain testicular growth and spermatogenesis in males or ovulation in females, which allows for the restoration of fertility in a large majority of cases.

4. Conclusion

KS is a rare genetic pathology whose diagnosis is based on clinical evidence of arrested or incomplete sexual maturation associated with anosmia or hyposomia and is confirmed by hormone dosage and hypothalamic-pituitary MRI focused on the olfactory bulbs however genetic study is not always conclusive. Early diagnosis has allowed for optimal management, the objective of which is to maintain secondary sexual characteristics and to induce fertility in the event of a planned pregnancy.

Compliance with ethical standards

Acknowledgments

We would like to thank the teams of endocrinology, radiology and biology departments of Mohammed VI university hospital of Marrakech.

Disclosure of conflict of interest

The authors declare that there are no conflicts of interest that could be perceived as prejudicial to the impartiality of the reported research.

Statement of ethical approval

The present research work does not contain any studies performed on animals/humans subjects by any of the authors.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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