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Kallman's Syndrome in a Nigerian Boy: A Case Report

JBE Elusiyan[1,2], TE Babalola[2]*, OE Olorunmoteni[2,3] and AJ Kareem[2]

[1] *Endocrine and Metabolic Unit, Department of Paediatric and Child Health, Obafemi Awolowo University, Ile-Ife, Nigeria*

[2] *Department of Pediatrics, Obafemi Awolowo University Teaching Hospital Complex, Ile-Ife, Nigeria*

[3] *Department of Pediatrics and Child health, Obafemi Awolowo University, Ile-Ife, Nigeria*

**Corresponding e-mail: tolugifty@gmail.com*

ABSTRACT

Background: *Kallmann syndrome is a rare genetic hormonal condition of hypogonadotropic hypogonadism with a prevalence of 1 in 4000-10000 live born. It is often associated with anosmia or hyposmia. To the best of the author's knowledge, it has not been reported in Nigerian literature.* ***Methodology:*** *The patient had been presented at the Endocrine and Metabolic Unit of our hospital, and was thus managed. The patient's hospital records were reviewed and relevant data were extracted, with investigation results and clinical pictures presented. Ethical approval was obtained from the Institution Ethics review board.* ***Results:*** *We report the case of a 15-year-old boy who was presented with a small sized penis since birth, with only a slight increment since then. His developmental milestones were reportedly normal but he had the inability to smell. Examination revealed a well grown apparently healthy looking male, weighing 40 kg; with a normal height of 151.5 cm and BMI of 17.5 kg/m^2. The testes were 1 ml each in volume with a stretched penile length of 3.5 cm. Laboratory investigation revealed low testosterone, luteinizing hormone, and follicular stimulating hormone. His karyotype was 46XY. He was commenced on 200 mg monthly injection of testosterone to which he made significant improvement as his penile length increased to 8.5 cm over 8 months of therapy, pubic hair also developed to Tanner 3 but his testicular volume remained pre-pubertal. He also reported that he could now smell.* ***Conclusion:*** *Kallmann syndrome though a rarely reported condition in the Nigerian population, could be treatable, though attainment of reproductive capability might require further intervention. A high index of suspicion and early treatment may yield a better outcome.*

Keywords: Kallmann syndrome, Follicular stimulating hormone, Facial anomalies

INTRODUCTION

Kallmann syndrome is a rare genetic hormonal condition that is characterized by a failure to start or failure to complete puberty. It is also accompanied by anosmia or hyposmia, and, if left untreated, patients will almost invariably be infertile [1], thus prompt diagnosis and treatment are needed to improve fertility chances in these patients and improve their overall quality of life [2].

This congenital condition of hypogonadotropic hypogonadism is relatively rare, with a prevalence estimated between 1:4000 and 1:10000 for male cases overall. It is more commonly reported in males [1]. Genetics is poorly understood. Most cases are sporadic, and in the familial cases, X linked (KAL-1), autosomal dominant (KAL-2), and autosomal recessive (KAL 3) forms of inheritance have been described [3].

It is now called olfactogenital dysplasia to emphasize the association between the agenesis of the olfactory bulbs and hypogonadism [4]. Kallmann syndrome occurs when hypothalamic neurons that are responsible for releasing gonadotropic releasing hormone fail to migrate into the hypothalamus during embryonic development resulting in this unique combination of GnRH deficiency and anosmia, that define this clinical syndrome [5,6]. The syndrome has various phenotypic manifestations and is sometimes associated with various anomalies like renal agenesis, hearing loss, color blindness, short fourth metacarpal and facial anomalies [6].

The condition is usually characterized by low levels of serum testosterone, luteinizing hormone (LH) and follicle

stimulating hormone (FSH) hence the description of hypogonadotropic hypogonadism [7]. Other hormonal functions of anterior pituitary may also be disturbed. Diminished cortisol response to insulin-induced hypoglycemia has been reported [8]. Magnetic resonance imaging scan of the brain usually shows a hypoplastic olfactory sulcus with the absence of olfactory bulb in most of the cases [9], though it may at times not reveal any abnormality in the olfactory area, a fact which has been reported by Subramanian et al., [10].

Testosterone is given as part of replacement therapy to restore virilization and secondary sex characters, but to restore fertility; pulsatile treatment with GnRH will be needed [11]. Assisted reproductive technology may be required if medical therapy fails.

Given the relative rarity of this condition, there is a significant possibility of late diagnosis when puberty is delayed, and this might impact the outcome of management, this report documents the case of a 15-year old Nigerian boy managed with this condition, in the Paediatric Endocrinology clinic of the Obafemi Awolowo University Teaching Hospital Complex, Ile-Ife, to report our experience as well as the outcome of treatment. Also, the fact that this condition had not been previously reported from Nigeria to the best of the authors' knowledge, makes a case for this report.

Case Report

O.O is a 15-year old boy who was presented with a small sized penis since birth. He has noticed only a slight increment in the phallic size since birth but this is not commensurate with his age. He is a product of term gestation in a non-consanguineous peasant farming family. His developmental milestones were reportedly normal but he reports inability to smell. He was circumcised at age 5 due to the small size of his phallus. He was also noticed to have drooping eyelids since birth. At the time of presentation at our facility, he was a junior secondary school student with reported average academic performance (Figure 1).

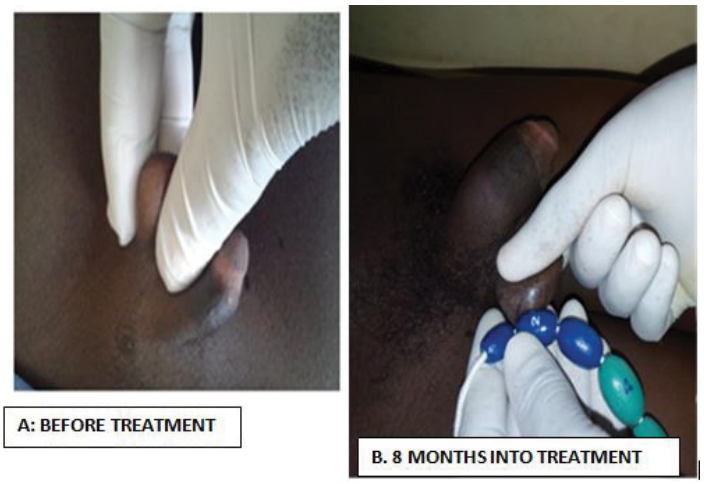

Figure 1 Genitalia before and after treatment

Physical examination showed an average-sized boy with bilateral ptosis-worse on the left, a weight of 40 kg, a normal height was 151.5 cm and a body mass index of 17.5 kg/m^2. Neurological examination revealed anosmia. Genital examination revealed bilaterally palpable pre-pubertal testis 1 ml each, normally shaped phallus of 3.5 cm stretched length and pre-pubertal pubic hair.

Examination of other systems yielded no additional abnormal finding and based on the presentation and complains, the possibility of Kallmann syndrome was considered, and a hormonal assay was done. Investigation results then showed low testosterone, low luteinizing and follicular stimulating hormones, consistent with hypogonadotropic hypogonadism. Karyotype revealed 46 XY. A magnetic resonance imaging was not done in this patient on account of affordability on the part of the parents. He was commenced on 200 mg monthly intramuscular testosterone injections. This led to a significant improvement as his penile length increased to 8.5 cm over 8-months of therapy, pubic hair also developed to tanner though his testicular volume remained pre-pubertal. The result of investigations before and after treatment is as shown in Table 1.

Table 1 Results of the investigation

Test	Norma Value	Initial Result	8 Months of Treatment
FSH	0-25 iu/ml	1.3 iu/ml	4 iu/ml
LH	0-20 iu/ml	<1 iu/ml	5 iu/ml
Testosterone	3-10 iu/ml	1.1 iu/ml	47 iu/ml
Karyotype		46 XY	
FSH: Follicle stimulating hormone; LH: Luteinizing hormone			

DISCUSSION

This report shows a male child with Kallmann's syndrome, a rare condition which has been reported in the literature to be more common in males [1]. The patient presented with classic features of hypogonadism and anosmia. There was no reported family history, and this case may well be a sporadic case, the more common pattern of presentation [1]. Bilateral ptosis was found in this patient, even though it is an infrequent association with Kallmann syndrome [12].

Hypo-gonadotrophic hypogonadism was confirmed in this patient, with significant improvement in both the clinical and laboratory features on treatment with testosterone. Although other hormonal functions of anterior pituitary may be affected, like diminished cortisol response to insulin-induced hypoglycemia [6], there was no evidence to suggest such in this patient. Magnetic resonance imaging, though desirable, was not done in this patient, based on financial constraints. This has however not significantly altered the outcome of patient care as there was a good improvement with hormonal intervention. This might thus support the practice of prioritizing investigative modalities in managing endocrine conditions especially in under challenging economic situations.

Although the patient showed a good clinical response to the replacement testosterone (induced virilization and development of secondary sex characteristics), the future fertility of the patient will also require adequate attention. This could be achieved by giving pulsatile treatment with a gonadotrophin-releasing hormone. Testosterone replacement was the preferred treatment in this patient compared to GnRH as the former has a comparatively lower cost and better availability, especially in a low-resource setting like ours. Also, though GnRH treatment has the added advantage of possible initiation of spermatogenesis, this may take several years on GnRH, and spermatogenesis might not even occur in all patients on this medication [11].

Kallmann syndrome though a rarely reported condition in the Nigerian population could be treatable, with the restoration of secondary sexual character and improved quality of life. A high index of suspicion and early treatment may produce a better outcome.

CONCLUSION

This report shows the rare but possible occurrence of Kallmann syndrome in a Nigerian population, with a good chance at diagnosis, treatment and favorable outcomes in a low-resource setting. It is treatable, with the restoration of secondary sexual characteristics and an improved quality of life. A high index of suspicion with early and appropriate treatment may produce a better outcome.

DECLARATIONS

Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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