International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2020): 7.803

Klinefelter's Syndrome Patient with Micropenis, Bilateral Cryptorchidism and Normal Proportionated Height, A Case Report

Karen Tous-Barrios[1], Roberto García-Bermejo[2]

[1]Physician, Sinú University. Pediatric Fellow of Sinú University. Cartagena, Colombia. E-mail id-karentousb[at]gmail.com
[2]Pediatric Endocrinologist, University of Chile. Professor of Napoleon Franco Pareja Children Hospital and Sinú University. Cartagena, Colombia. E-mail id-endocrinocartagena[at]gmail.com

Abstract: ***Klinefelter's Syndrome (KS) is the most frequent observed sex chromosomal anomaly. The classic form of KS is defined by a 47, XXY karyotype; its diagnostic rate is estimated to be only 25%, and less than 3-10% patients are diagnosed before puberty. We present a case report of a patient without previous studies, with a late diagnostic at 11 years-old with KS with micropenis, bilateral cryptorchidism and normal proportionated height. We emphasize the importance of an early diagnosis in order to offer treatment and intervention at the appropriate ages and stages of development for androgenization and minimizing potential metabolic, learning and psychosocial problems.***

Keywords: Cryptorchidism, Klinefelter syndrome, Disorders of Sex Development, 47, XXY

1.Introduction

Klinefelter's syndrome (KS) is the most common sex chromosome disorder, characterized by Hypergonadotropic Hypogonadism and infertility, with an estimated frequency of 1: 500 to 1: 1000 men. Children with KS have three main clinical characteristics: tall stature; small testes (for Tanner Pubertal Stage) and mental retardation and/or learning difficulties. A KS case report of a patient with micropenis, bilateral cryptorchisim and normal proportionated height is described.

2.Case Report

A 11.5-year-old patient consulted at first time to a pediatric endocrinologist because a "genital alteration at birth". Born at 39 weeks of gestational age, with normal weight and height at birth. In medical history was reported a bilateral cryptorchidism correction surgery, performed before having one year of life. There was no subsequent medical follow-up. Mother stature: 152 cm. Father stature: 180 cm. The mother comments that the patient has learning problems at school. His initial physical exam was height: 141 cm (-1.5 Standard Deviation [SD]); one centimeter difference between height and arm span. Weight 28 kg (-1.9 SD); with a 2.7 cm penis length (-3.0 SD).2.5 ml testicles in scrotum. Pubic Hair Tanner I. Patient hormonal analysis: FSH: 15.6 µUI/ml, LH: 3.06 µUI/ml, IGF-1: 151 ng/ml, Cortisol: 53 ng/ml. Bone age was reported as being 7.5 years. A KS pattern was obtained: Karyotype 47, XXY; Comparative Genomic Hybridization (NIM genetics): arr (X) x2, (Y) y1. Hormone replacement therapy with testosterone was initiated. Multidisciplinary management is indicated including psychology, neurology and speech therapy.

3.Discussion

KS is the most frequent observed sex chromosomal anomaly, with an estimated frequency of 1: 500 to 1: 1000 men, that has been a topic of intrigue and inquiry since the 1940s, when it was first described [1, 2]. The chromosomal aberration found in KS is due to either meiotic or mitotic non-disjunction, leading to sex-chromosomal aneuploidy; the classic form of KS, which is present in the 80–90% of the cases, is defined by a 47, XXY karyotype; the remaining 10 to 20% of the cases, are KS mosaics (e. g.46, XX/XXY), KS with higher grade aneuploidies (e. g 48, XXXY), and KS with a structurally abnormal X chromosome (e. g.47, iXq, Y) [3-5]. A KS patient is a subject of interest because of its wide spectrum of clinical manifestations, which include certain physical features, cognitive delays, and azoospermia; and, it is believed that 60% of KS patients do not know that they have this condition, being diagnosed in late-puberty or in adulthood due to infertility [4, 6]. KS physical features include: tall stature, eunuchoid habit (long limbs), cryptorchidism, gynecomastia, hypotonia, hypertelorism, clinodactyly, elbow dysplasia, pes planus, and a high arched palate [4, 7]. The diagnosis is usually performed in a tall stature adolescence with a lack of pubertal development (usually micropenis and/or testicular hypo/atrophy) [3-5].

In a previous article, it had been commented that a KS diagnosis was made in an adolescent with short stature, delayed pubertal development and cognitive disorder [5]. A prepubertal patient with bilateral *cryptorchidism* and *micropenis* (without medical follow-up) and *normal proportionated height* is currently described, demonstrating the variability of KS phenotypic expression [1, 6, 7]. Table 1.

Less than 3% to 10% of KS patients are diagnosed during the prepubertal period [8]; therefore, in the presence of a patient, as in the current case, with *micropenis* and *cryptorchidism (*mainly if is bilateral), it is suggested to perform a **karyotype** and molecular analysis (the latter for his ambiguous genitalia) [7].

There are beneficial reasons for a KS early diagnosis: despite there are only a few KS studies and the positive effect of testosterone treatment, these studies suggest that low dose of testosterone would support KS patients not only in androgenization, but also in their motor functions, academic difficulties, and social behavior [3, 9, 10]. In addition, the use of testosterone in a minipuberty-time, could also support neurodevelopment improvement [11].

On the other hand, it is known the risk of loss of bone and muscle mass, with or without a metabolic and cardiovascular compromise (including type 2 diabetes and hypertension), in hypogonadal patients without testosterone treatment [12-14]. If an early diagnosis is made, the KS patient would have an adequate and complete multidisciplinary follow-up, with a rapid access to: paediatric follow-up, endocrinology treatment, surgery, speech and language therapists, family therapists, to try to improve their quality of life [10, 15].

4.Conclusion

Even if KS is the most common chromosomal disorder in humans but patients with KS are often diagnosed late in life [1, 2]. The diagnosis rate of KS is estimated to be only 25%; and less than 10% of KS patients are diagnosed before puberty [8, 16].

Although no firm diagnosis guidelines for KS exist and extreme heterogeneity in clinical and genetic presentation is found [1, 3-7]. Knowing that less than 10% KS patients are diagnosed before puberty, is worrying because these cases will present with complex comorbidities [12, 13].

Early detection of this syndrome is recommended in order to offer treatment and intervention at the appropriate ages and stages of development, for the purpose of preventing osteopenia/osteoporosis, metabolic syndrome, other medical conditions related to hypogonadism and minimizing potential learning and psychosocial problems [4, 10-12, 17].

We must also consider mandatory the performance of additional molecular analysis in patients with KS with ambiguous genitalia to provide comprehensive genetic counseling to the family [7].

Table 1: KS Patient Phenotypic Variability. HH: Hypergonadotropic Hypogonadism.

	Age of diagnosis	**Stature**	**Body proportions**	**Testicles position**	**Penis**	**Hormonal status**	**Cognitive status**
KS Diagnostic Criteria [1, 3, 4, 7]	Usually puberty / adulthood	Frecuently too tall	Frecuently disproportionate (eunuchoid habit)	Normal or undescended	Normal or small	HH	Usually compromeated
Munera, R; et al patient [5].	Late puberty	Short	Normal	Normal	Normal	HH	Compromeated (low IQ)
Current Patient.	Prepubertal	Normal	Normal	Undescended	Small	HH	Learning problem

References

[1] Bonomi, M., et al., *Klinefelter syndrome (KS): genetics, clinical phenotype and hypogonadism.* J Endocrinol Invest, 2017.4**0** (2): p.123-134.
[2] Bojesen, A., S. Juul, and C. H. Gravholt, *Prenatal and postnatal prevalence of Klinefelter syndrome: a national registry study.* J Clin Endocrinol Metab, 2003.8**8** (2): p.622-6.
[3] Lanfranco, F., et al., *Klinefelter's syndrome.* Lancet, 2004.3**64** (9430): p.273-83.
[4] Chang, S., A. Skakkebaek, and C. H. Gravholt, *Klinefelter Syndrome and medical treatment: hypogonadism and beyond.* Hormones (Athens), 2015.1**4** (4): p.531-48.
[5] Múnera, R., M. Wilches, and R. García-Bermejo, *Klinefelter Syndrome and Short Stature: An Atypical Presentation.* IJSR, 2021.1**0** (10).
[6] Bourke, E., et al., *Klinefelter syndrome-a general practice perspective.* Aust Fam Physician, 2014.4**3** (1): p.38-41.
[7] Akcan, N., et al., *Klinefelter Syndrome in Childhood: Variability in Clinical and Molecular Findings.* J Clin Res Pediatr Endocrinol, 2018.1**0** (2): p.100-107.
[8] Abramsky, L. and J. Chapple, *47, XXY (Klinefelter syndrome) and 47, XYY: estimated rates of and indication for postnatal diagnosis with implications for prenatal counselling.* Prenat Diagn, 1997.1**7** (4): p.363-8.
[9] Gropman, A. and C. A. Samango-Sprouse, *Neurocognitive variance and neurological underpinnings of the X and Y chromosomal variations.* Am J Med Genet C Semin Med Genet, 2013.1**63C** (1): p.35-43.
[10] Ross, J. L., et al., *Androgen Treatment Effects on Motor Function, Cognition, and Behavior in Boys with Klinefelter Syndrome.* J Pediatr, 2017.1**85**: p.193-199 e4.
[11] Samango-Sprouse, C. A., et al., *Positive effects of short course androgen therapy on the neurodevelopmental outcome in boys with 47, XXY syndrome at 36 and 72 months of age.* Am J Med Genet A, 2013.1**61A** (3): p.501-8.
[12] Bhasin, S., et al., *Testosterone Therapy in Men With Hypogonadism: An Endocrine Society Clinical Practice Guideline.* J Clin Endocrinol Metab, 2018.1**03** (5): p.1715-1744.
[13] Gravholt, C. H., et al., *Body composition, metabolic syndrome and type 2 diabetes in Klinefelter syndrome.* Acta Paediatr, 2011.1**00** (6): p.871-7.

[14] Morgentaler, A., et al., *Testosterone therapy and cardiovascular risk: advances and controversies.* Mayo Clin Proc, 2015.9**0** (2): p.224-51.
[15] Bearelly, P. and R. Oates, *Recent advances in managing and understanding Klinefelter syndrome.* F1000Res, 2019.8.
[16] Aksglaede, L., et al.4*7, XXY Klinefelter syndrome: Clinical characteristics and age-specific recommendations for medical management.* in *American Journal of Medical Genetics Part C: Seminars in Medical Genetics*.2013. Wiley Online Library.
[17] Davis, S., et al., *Advances in the interdisciplinary care of children with Klinefelter syndrome.* Advances in pediatrics, 2016.6**3** (1): p.15-46.