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Klinefelter Syndrome and Short Stature: An Atypical Presentation

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Abstract: ***Klinefelter síndrome (KS) patients classically have tall stature and hyperegonadotropic Hypogonadism (HH). Short stature generally is not recognized as associated feature of the syndrome. We present a severe short stature patient with KS and its response to the use of growth hormone recombinant (GHr) treatment.***

Keywords: Klinefelter syndrome; hypergonadotropic hypogonadism; Growth hormone recombinant

1. Introduction

KS is the most common sex chromosome disorder, characterized by HH and infertility. Children with KS have three mainclinical characteristics: tall stature; small testes (for Tanner Pubertal Stage) and mental retardation and/or learning difficulties. There are few KS reports onthe literature associated with short stature and this presentation represents a difficult diagnosis. In this article, an unusual case of KS is described.

2. Case Report

A 12.3 years - old male patient consulted to a pediatric endocrinologist because of short stature. His medical history reported a controlled pregnancy, born at 39 weeks of gestational age. Birth weight: 2000 gr (- 3.4 Standard Deviation [SD]), birth length: 46 cm (- 2.8 SD). He underwent a cardiac surgery due to a Tetralogy of Fallot. Father Stature: 163.5cm. Mother Stature: 150 cm. His physical exam revealed: stature 122.5 cm (- 4SD); weight 21.5 kg (- 3.0 SD). He also had a high palate and a 4 cc testicular volume. Additional exams showed mild cognitive deficit (IQ 64) and the following hormonal analysis: IGF - I: 199 ng/ml (RV 113 - 261), IGFBP - 3: 3.6 µg/ml (RV 2.1 - 4.2), f - T4: 1.5 ng/dl, TSH: 0.69 µIU/ml, and cortisol: 79 ng/ml. Clonidine Growth Hormone (GH) Stimulation Test: basal GH 0.11 ng/ml; at 30': 0.79 ng/ml; at 60': 14.0 ng/ml and at 90': 6.3 ng/ml. Bone - age (BE) was reported as being 8 years - old. Aninitial 25 - metaphases karyotype and a second 50 - metaphases karyotype were performed: 47 XXY. With these results, the following hormonal studies to evaluate hypogonadism were practiced: Inhibin B: 12.2 pg/ml, LH 4.3 mIU/ml (RV: 0.02 to 0.3), basal FSH: 27.6 mIU/ml (RV: 0.26 to 3). Testicular ultrasound showed: Both testes diminished in size with a bilateral 0.6 cc volume; the right testicle had smooth contours with increased echogenicity and calcified images. Genetics suggests performinga comparative genomic hybridization (NIM genetics), and this KS pattern was obtained: arr (X) x2, (Y). For his severe short stature, treatment with GHr was initiated at a45µg/kg/day - dose with a favorable response (Fig 1). At 15 years - old, his testes remained in 4cc. Bone densitometry (BD) was performed showing low bone density at lumbar Spine (- 2.1 SD). Hormone replacement therapy with testosterone - enantate was then initiated.

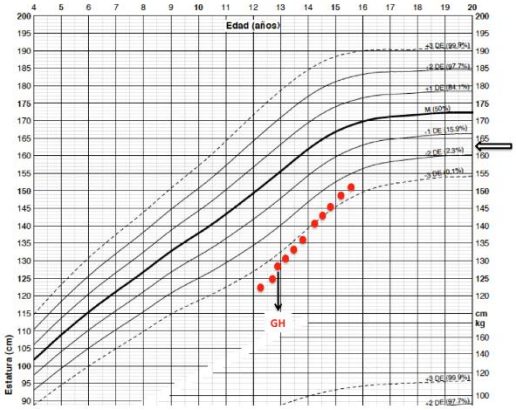

Figure 2: Colombian Growth Chart. KS patient with GHr treatment (black thin arrow). White arrow: Target Size.

3. Discussion

KS is the most frequent cause of HH in male patients [1, 2]. 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 48XXXY), and KS with a structurally abnormal X chromosome (e. g.47, iXq, Y) [2, 3]. High stature and hypogonadism are the most repetitive clinicalKS manifestations [1, 2, 4]. The diagnosis is usually performed in a high - stature - adolescence with a lack of pubertal development (usually micropenis and/or testicular hypo/atrophy) [1, 2]. However, there are few studies that show association of KS and short stature [5]. Many of these short statures – KS patients, have been treated with GHr once GH deficit is demonstrated, with a yet - unknown underlying mechanism. [6 - 9]. One karyotype varianthas been associated with normal or short stature: Xqisochromosome [10, 11]. Therefore it is suggested to perform a karyotype to all children or adolescents with severe short stature associated with no progression of testicular volume and / or cognitive disabilities [6, 9]

Ourpatient had a 47XXY karyotype, mild cognitive deficit and severe short stature (without GH deficiency). Its GHr treatment was started and indicated due to his SGA record

[12, 13]. At the beginning of the GHr treatment, his stature was at - 4.0 SD and currently it is at - 2.4 SD. Also GHr therapy has been used in patients with several genetic syndromes [14 - 16], with better treatment response if GHr is started at an early age. Sanz M, et al. Published a patient with KS without GHD, with good response to GHr treatment [17]. Being there only few reports on the literature of KS patients treated withGHr [5, 6, 9 - 11], the final height of this patient would be interesting.

4. Conclusion

The presence of short stature does not exclude the possibility of KS; it is important to consider performing a karyo type if short stature is associated with a lack of pubertal development and a cognitive disability.

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