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CASE REPORT

Klinefelter Syndrome: a diagnosis in adolescence - case report

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Abstract

Klinefelter syndrome (KS) has been described in 1940 and is characterized by a chromosomal anomaly that affects males with an estimated prevalence of 1 in every 600 live births. It is a common genetic disorder, however, misdiagnosed due to high phenotypic variability in childhood. The diagnosis is made clinically and confirmed with chromosomal evaluation. The main clinical findings are small testicles, gynecomastia, azoospermia and increased gonadotropins wich characterizes hypogonadism. Treatment consists of hormone replacement therapy and multidisciplinary monitoring, early diagnosis and treatment are important, ideally during puberty, contributing to an improved quality of life for patients with this syndrome. It is a case report conducted at a child care unit in a inner city of São Paulo. The study respects the principles of resolution No. 510/2016, of the National Health Commission. It refers to a 16-year-old teenager with unilateral gynecomastia,pubescent testicles and difficulty in talking about his sexuality. The presence of signs and symptoms of androgen deficiency combined with karyotype 47, XXY led to the diagnosis of Klinefelter Syndrome. This study aims to warn about the most common signs and symptoms of the individuals with Klinefelter syndrome and also tests to elucidate diagnosis.

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INTRODUCTION

Klinefelter syndrome (KS) was described in 1940 and is characterized by a chromosomal anomaly that affects males, with an estimated prevalence of 1 in every 600 live births. This chromosomal disorder occurs due to genetic nondisjunction in meiosis or mitosis during gametogenesis or through post-zygotic nondisjunction during the early embryonic period, leading to aneuploidy of the sex chromosome, presenting as a cytogenetic characteristic, in the vast majority (90%), an extra X chromosome (47, XXY); and in the minority (10%), mosaicism (46 XY/47XXY), other rare and more severe aneuploidies (48 XXXY/49 XXXXY) and abnormal chromosomal structures[1-4]. This chromosomal alteration may be associated with advancing maternal or paternal age[5].

The common signs and symptoms of this syndrome are consequences of the expression of extra genes on the X chromosome that can disrupt many aspects of development, such as sexual development before birth and during puberty and changes in brain structures[6].

This syndrome is associated with testicular dysfunction, often associated with hypogonadism and/or infertility as a consequence of androgen failure. The main clinical findings are reduced testicular volume (maximum of 10 ml), azoospermia and increased gonadotropins. It can also occur with gynecomastia, delayed puberty, decreased hair growth, micropenis, tall stature, increased wingspan in relation to height, learning and speech difficulties, obesity, psychiatric illnesses associated with the image, metabolic syndrome, autoimmune diseases and cancer[1-3].

In the presence of hypogonadism associated with low testosterone levels, hormone replacement therapy remains the medical treatment of choice and its dose is individualized. This treatment does not change the already established body patterns or neurological development deficits, but it does improve well-being, attention and mood[4,5].

Although the phenotypic characteristics of the syndrome are well established, it is estimated that only 25 to 35% of male individuals with KS are diagnosed throughout their lives due to variability in clinical presentation. Given the low percentage of diagnosis in childhood and adolescence, the study aims to highlight the importance of investigating testicular changes associated or not with other signs of hypogonadism for diagnosis and treatment before adulthood.

The study is descriptive in nature, carried out in a children's care unit in a city in the interior of São Paulo; the study complies with the principles of resolution no. 510/2016, of the National Health Commission and was approved by the ethics and research committee of the University of Taubaté under number CAAE: 37218120.0.0000.5501.

CASE REPORT

JPAL, 16 years old, male, single, student, accompanied by his aunt, was referred to the Hebiatrics consultation for monitoring and guidance on sexuality.

The patient reported unilateral gynecomastia on the left for 2 years and small testicles, the latter information had not been reported to the guardian. Adolescent cared for by his aunt, had a history of pneumonia at age 7 and kidney stones at age 14, with no allergies or previous surgeries. Young man already scheduled for surgical correction of gynecomastia.

A shy individual, but with good social interaction, eating behavior and lifestyle habits compatible with the period of adolescence, denied using medications and/or legal and illegal drugs, with no family history of genetic and/or cardiovascular diseases. On physical examination, he presented a eunuchoid body type (longilinear with predominance of the lower segment), with a height of 177 cm (z-score between 0 and +1), wingspan of 180.5 cm, weight of 67.5 kg, BMI 21.54 kg/m² (z-score between 0 and +1). The genitourinary system had male hair distribution, prepubescent testicles, Marshall & Tanner criterion for sexual maturation G1 P4, with evidence of grade two gynecomastia unilateral on the left. The examination of the other devices showed no changes, except for the blood pressure measured at the time of the consultation of 136 x 90 mmHg, compatible with stage 1 hypertension.

An ultrasound of the testicular sac was performed, which showed testicles with reduced dimensions, both with a volume of 1.7 cm³, homogeneous textures, epididymis of normal shape, echogenicity and thickness, with no evidence of focal solid and/or cystic lesions in the testicles and epididymis. Spermatic cords of normal appearance (figure 1).

Laboratory tests revealed increased follicle stimulating hormone (FSH) and luteinizing hormone (LH) levels, and reduced androstenedione (Table 1). The G-band karyotype test revealed 47, XXY, confirming the diagnostic hypothesis of Klinefelter syndrome.

The adolescent was given guidance regarding sexuality and possible repercussions of the syndrome presented, as well as referral to pediatric psychology and endocrinology with new requests for laboratory tests to assess the need for hormone replacement therapy.

CASE DISCUSSION

KS is a common genetic disorder that presents with endocrine insufficiency, presenting variations in serum testosterone concentrations and phenotypic variability, which causes it to be underdiagnosed.

Possible clinical characteristics in adolescents with KS described in the literature are: small and solid testicles, decreased virilization, gynecomastia, abdominal fat, sexual dysfunction, body image problems and depressed mood. In addition to these signs and symptoms, late onset of puberty,

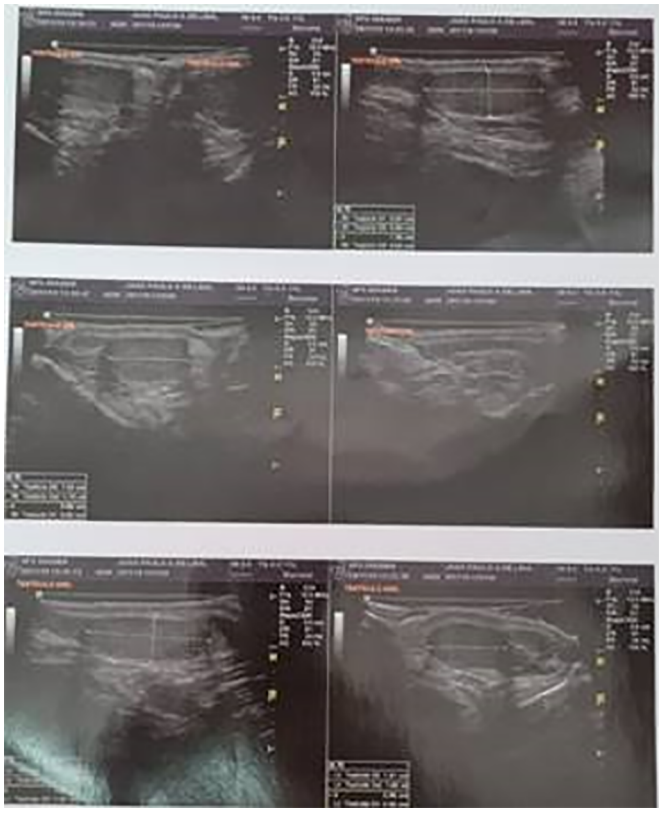


Figure 1. Ultrasound of the testicular sac.

tall stature and increased fat content[5] can be found. In the case in question, the adolescent presented gynecomastia, small and firm testicles, tall stature, hypertension and body image disturbance, compatible with the literature.

In an article published by "Hovnik et al[7]", the case of a patient who was referred to the service due to gynecomastia was reported and, during clinical evaluation, an asthenic constitution, small and topical testicles, previous history of surgical correction of hypospadias and orchiopexy were evidenced. Laboratory investigation demonstrated hypogonadism associated with decreased testosterone and karyotype 47 XXY/46XX, confirming mosaicism for KS. In the present case report, the reason for referral was similar and the findings of the physical examination guided the diagnosis, which was corroborated by the karyotype.

It is important to emphasize that the gynecomastia found in the reported case had evolved for more than 18 months, with no signs of spontaneous regression, associated with changes in the gonads, which does not characterize physiological gynecomastia.

The experience of adolescence is permeated by significant changes in body composition, development of maturity and sexual identity, which can have psychosocial consequences if such changes are not within the adolescent's expectations, which was the case with the patient in this case. As described in the literature, psychological support is useful to improve these experiences and provide opportunities to develop strategies to recognize, process and express feelings and thoughts. Boys with KS are at greater risk of impaired social cognition and less accurate perceptions of socio-emotional cues. The concept of probable fertility disorders should be discussed together with regular reviews of puberty and sexual function in adolescents[8], as was done in this case. The importance of correct and early diagnosis is precisely to be able to act in the prevention and/or treatment of its consequences immediately, such as micropenis and small testicles, learning difficulties, delayed puberty, infertility, tall stature, eunuchoid skeleton, gynecomastia, osteoporosis and other metabolic disorders, improving the individual's quality of life.

CONCLUSION

In this study, we present a case of KS diagnosed during puberty. Despite being a common genetic disorder, it is still rarely diagnosed before adulthood and, therefore, it needs to be identified by pediatricians and pediatricians for early diagnosis, preferably in the prepubertal phase, providing multidisciplinary monitoring and interventions, when necessary, in childhood and puberty. Recognition can be made through simple screening through palpation and estimation of

Table 1. Laboratory tests performed by the patient with respective reference values.

LABORATORY EXAM (10/30/2020)	VALUE	REFERENCE VALUE	
Free Testosterone	7.1	No defined value up to 17 years	
Bioavailable testosterone	166.38	No defined value up to 17 years	
Estradiol	18	Prepubescent: less than 43	
Estriol	< 0.15	Men: less than 0.15	
DHEA	61.7	Tanner IV / 15 years: 29 to 412	
Estrone	18.6	13 - 150	
17 - alpha - hydroxyprogesterone	98.7	Men > 14 years: 50 - 210	
Androstenedione- andro	0.38	Men: 0.5 - 4.8	↓
LH	43.1	Prepubescent: less than 0.3	↑
FSH	71.6	Prepubescent: less than 0.9	↑

testicular volume in routine consultations of all prepubescent and pubescent boys.

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