A Man with Klinefelter's Syndrome having Normal Stature

Introduction

Klinefelter's syndrome (KS) describes the phenotype of one of the most common sex chromosome abnormalities in humans—with an incidence of one in every 500–600 newborn males.[1,2] The typical presentations are tall stature, narrow shoulders, broad hips, and features of primary hypogonadism—loss of libido, erectile dysfunction, infertility, loss of body hair, bilateral atrophied testes, bilateral gynecomastia, azoospermia or oligospermia, low testosterone, elevated luteinizing hormone (LH), follicular stimulating hormone (FSH), etc.[3,4] Unfortunately, most of the Klinefelter patients are diagnosed during adolescence because of gynecomastia or in adulthood following infertility. We describe a case of Klinefelter patient who did not feature the typical tall phenotype of KS.

Case

A 38 years old man came with the complaint of infertility for the last 9 years. He has been married for the same duration and his wife has never conceived. Over the years, his wife has consulted with various physicians for infertility and was treated for polycystic ovarian syndrome (PCOS) but he refused to consult with any physician for himself. He has also complained of a lack of libido and underwhelming sexual performance for the same duration.

He has no history of smelling problem, jaundice, any chronic illness, significant injury, surgery, chemotherapy, or any kind of radiation exposure. He does not smoke and has no history of substance abuse.

He is a product of non-consanguineous marriage with a normal childhood. His puberty started around 12 years of age and his teenage period was uneventful too. His height was the same as his other siblings [Figure 1].

On examination, his height was 160 cm, upper segment, and lower segment ratio 1:1, wide arm length 162 cm, and weight 70 kg. His both breasts were enlarged but non-tender. Decreased body hair and pubic hair were at stage 4, which had been regressing over the last few years—according to his statement. His stretched penile length (SPL) was 12 cm. There was no scar mark or abnormal pigmentation around his genitalia. His both testes were firm, non-tender, and atrophied (right testis volume—4 cm^3, left testis volume—3 cm^3). His other systemic examinations revealed no abnormality.

His laboratory reports showed: semen analysis—azoospermia, LH—30.75 mIU/ml (1.9–9.3 mIU/ml), testosterone—2.9 nmol/L (5.72–26.2 nmol/L), thyroid stimulating hormone (TSH)—0.93 µIU/ml (0.3–5.5 µIU/ml), free thyroxin (F.T4)—0.94 ng/dl (0.7–1.8 ng/dl), and Prolactin—7.22 ng/ml (2.1–17.7 ng/ml). After hormonal evaluation and karyotyping, he was diagnosed with a case of primary hypogonadism due to Klinefelter syndrome (47, XXY) [Figure 2]. Other investigations reports were within normal limits.

He was thoroughly counseled about his condition and associated risks. Regarding the fertility issue, he was counseled that he can be benefited from assisted reproductive techniques, such as intracytoplasmic sperm injection (ICSI) preceded by testicular sperm aspiration. He was prescribed testosterone replacement therapy (250 mg) once fortnightly to improve his quality of life with a plan to make it weekly if necessary.

Discussion

KS was first described by Harry F. Klinefelter in 1942.[5] About 80% of KS patients show a 47, XXY karyotype, 20% have other numeric sex chromosome abnormalities (48, XXXY, 48, XXYY, 49, XXXXY), 46, XY/47, XXY mosaicism, or structurally abnormal sex chromosomes.[6]

The typical features of prototypic KS case are tall body habitus (feminized in some cases) characterized by long legs, narrow shoulders, decreased facial and pubic hair, gynecomastia, small and firm testes.[3,4,6] Affected patients present with seminiferous tubules dysgenesis, azoospermia or oligospermia, features of hypergonadotropic hypogonadism—testosterone deficiency, elevated levels of FSH and LH.[7] A variable degree of mental retardation may also be present.[4]

In rare scenario, KS cases can be present with short to normal body habitus as well as other features of KS. The presence of an additional isochromosome Xq with the prevalence of 0.3–0.9% in males with KS is responsible for this unique feature.[3] To our knowledge, only 25 cases with 47, X, i (Xq), Y KS have been reported so far.[2]

Zang *et al*. described that the origin of an additional isochromosome Xq as an unusual event, because it would require a double error during meiosis.[8] Arps *et al*. proposed that the most probable origin of an additional isochromosome Xq is a misdivision of the centromere or a sister-chromatid exchange of one X chromosome.[3]

According to previous literatures, the absence of a diploid Xp arm in 47, X, i (Xq), Y Klinefelter patients correlates to a mild phenotype as genes of the Xp arm are relevant for the clinical manifestations of the KS.[9-11]

The only clinical difference between the 47, XXY and 47, X, i (Xq), Y KS patients which has been reported is normal-to-short stature in the latter patients.[9] It is well documented that 47, XXY males show a mean increase in height of about 6.5 cm in comparison with their male relatives. Height can exceed the average, presumably because of delayed epiphyseal plate

Figure 1: Patient with his sibling (with the permission of the patient and his sibling)

closure and the extra copy of short stature homeobox (SHOX) gene on Xp.[12-14]

Unfortunately, most of Klinefelter patients are diagnosed late, whereas an early clinical treatment of the hypergonadotropism during puberty could have attenuated seminiferous tubules hyalinization. For future fertility semen can be preserved in sperm banks though this facility is available only in a few countries. Otherwise, KS patients can be benefited from assisted reproductive techniques, such as ICSI only if sperm is found after testicular aspiration. Similar cases have been reported earlier by Ron-El *et al*. and Bergere *et al*.[15,16]

Patients are commonly prescribed with testosterone replacement therapy. However, these patients require regular monitoring as KS is often associated with multiple co-morbidities.[17]

We could not confirm the presence of Xq isochromosome due to a lack of resources. The patient came for follow-up regularly. His quality of life improved significantly after testosterone replacement therapy (250 mg/week). However, the patient did not pursue the assistance of ART.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

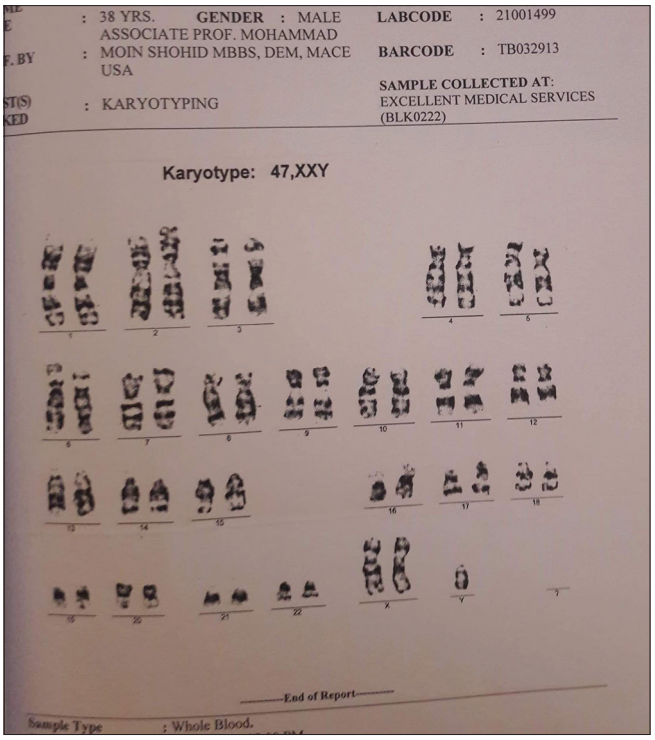

Figure 2: Karyotype of the patient

Acknowledgment

None.

Author contributions

Dr Mohammad Moin Shahid: Planning and writing the article. Dr. Sharmin Ferdousi: Writing the article.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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Submitted: 25-Jan-2023 **Revised:** 16-May-2023
Accepted: 23-May-2023 **Published:** 28-Aug-2024

Access this article online

Quick Response Code:

Website: https://journals.lww.com/indjem/

DOI: 10.4103/ijem.ijem_33_23

How to cite this article: Shahid MM, Ferdousi S. A man with Klinefelter's syndrome having normal stature. Indian J Endocr Metab 2024;28:429-31.