Disease and Diagnosis

Dis Diagn. 2021; 10(4):177-179

doi 10.34172/ddj.2021.31

Case Report

A Rare Variant of Turner Syndrome (the X Isochromosome-X Syndrome): A Case Report

Hamid Reza Samimagham[1], **Mitra Kazemi Jahromi**[2*]

[1]Clinical Research Development Center, Shahid Mohammadi Hospital, Hormozgan University of Medical Sciences, Bandar Abbas, Iran.
[2]Endocrinology and Metabolism Research Center, Hormozgan University of Medical Sciences, Bandar Abbas, Iran.

Abstract

Background: Turner syndrome occurs in nearly one in every 2000-5000 female births. This syndrome is a genetic problem in the female phenotype and the most common sex chromosome anomaly. It is diagnosed based on clinical manifestations and cytogenetic examinations. The classic syndrome (i.e., monosomy X) makes up 50% of the cases while other forms contain X chromosome variants, which do not typically manifest as the classic X phenotype.

Case Presentation: This study, presents a rare variant of Turner syndrome reported in a 20-year-old woman presenting with primary amenorrhea, hypothyroidism, and short stature who had hypergonadotropic hypogonadism with hypoplastic ovaries while without the clinical manifestations of the classic Turner syndrome. The karyotype was determined as X isochromosome-X syndrome [46 XXi (Xq)].

Conclusion: This rare syndrome occurs in approximately 7% of the cases of Turner syndrome. Rare variants of the syndrome should also be considered in female patients without the classic manifestations of Turner syndrome.

Keywords: Turner syndrome, Amenorrhea, X isochromosome-X syndrome

***Correspondence to**
Mitra Kazemi Jahromi, Endocrinology and Metabolism Research Center, Hormozgan University of Medical Sciences, Bandar Abbas, Iran.
Tel: +00989177912820,
Email: mitra.kazemijahromi@gmail.com

Received: December 14, 2020, Accepted: February 14, 2021, ePublished: December 30, 2021

Introduction

Turner syndrome is considered as a genetic problem that occurs with the complete or partial absence of the X chromosome in the female phenotype. Its classic form is 45 XO, which is found in nearly half of the patients. Mosaic forms occur in approximately 1/4th of the cases and the remaining cases include structural abnormalities that occur on the X chromosome (1).

This syndrome can present with clinical symptoms such as short stature, gonadal dysgenesis, renal heart disease, low-set ears, webbed neck, skeletal deformity, and hearing problems (2). It is usually diagnosed at birth with the observation of edema, facial dysmorphia, and severe anomalies. Nonetheless, its mild cases in variant forms can present with a delay during adulthood and may be manifested by symptoms such as delayed menarche, amenorrhea, and infertility (3). In this study, a rare variant of Turner syndrome 46 XXi (Xq) is reported in a 20-year-old woman presenting with primary amenorrhea and short stature. The drawn conclusion is that the rare variants of Turner syndrome should be clinically suspected in adult women with atypical Turner syndrome features.

Case Presentation

The patient is a 20-year-old woman presenting with primary amenorrhea, short stature, and hypothyroidism referred to the Endocrinology Clinic of Shahid Mohammadi Hospital of Bandar-Abbas, Iran. The patient was diagnosed with hypothyroidism five years ago and was taking levothyroxine (350 µg/wk) at the time of the referral. There was no positive family history of delayed menarche and short stature, and the patient was born through normal-term vaginal delivery. Her siblings had no particular health problems. In addition, the patient had no particular problems during her infancy. She had a height of 138 cm (i.e., less than the 3rd percentile) and a normal weight of 54 kg. The clinical examination revealed normal posterior hairline, a non-webbed neck with normal length, widely-spaced nipples, short toes, breasts, and axillary and pubic hair all at Tanner stage II. Her vision and hearing exam results were also normal. It is noteworthy that the patient did not consent to be photographed for the purpose of observing her problems.

Although her uterus was normal in the ultrasound (47×12 mm), her ovaries were hypoplastic. The laboratory test results were free thyroxine: 103 mmol/L (55-106), *thyroid-stimulating hormone*: 2.44 µIU/mL, *insulin-*

like growth factor-1: 172.5 mg/mL (267-471), *follicle-stimulating* hormone: 64 µIU/mL, *luteinizing* hormone: 14.5 µIU/mL, and estradiol: 59.18 pg/mL.

Her cortisol, adrenocorticotropic hormone, prolactin, testosterone, electrolyte, and *fetal bovine serum* measurement and urinalysis results, as well as her echocardiography and kidney ultrasound results were all normal. She was also evaluated for celiac disease and autoimmune hepatitis and the related results were normal. As shown in Figures 1a and 1b, her karyotype was determined as 46 XXi (Xq). Hormone replacement therapy (HRT) was started for her and levothyroxine administration continued as well.

Discussion

The current study presents a rare variant of Turner syndrome reported in a 20-year-old woman presenting without the clinical manifestations of classic Turner syndrome. Her karyotype was determined as X isochromosome-X syndrome [46 XXi (Xq)].

Turner syndrome is the most common sex chromosome anomaly in women occurring when the X chromosome is partially or completely absent (2). According to studies conducted by Christalena et al and Graham et al (4, 5), the most common karyotype for this syndrome, which makes up 50% of the cases, is 45 XO, and the remaining cases of karyotypes include various double X chromosomes such as 46 X/46 XX (20%), 46 Xr (X) or 46 X del (X, 10%), 46 XXi (Xq, 15%), and other cases (5%). The incidence of Turner syndrome is 1/2000th to 1/5000th among female births (6). The mortality rate of this syndrome is 4-5 times higher than the rate in the normal population (6). The most common manifestation of Turner syndrome includes short stature, primary amenorrhea, gonadal dysgenesis, widely-spaced nipples, a webbed neck, cardiac and renal anomalies, and a broad chest (2, 7).

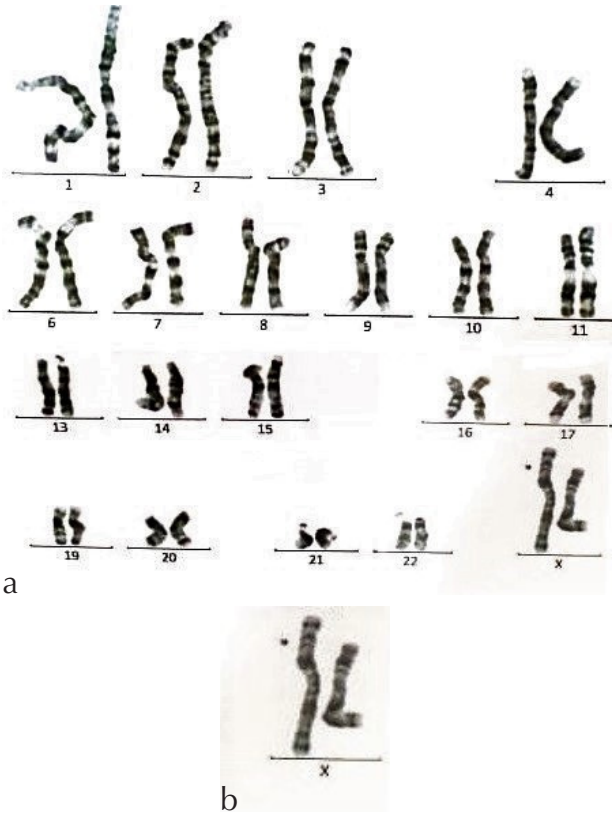

Figure 1. (a) Karyotype. (b) XXi (Xq).

The incidence of congenital heart disease in patients with Turner syndrome was 17-45% and had no relationship with phenotype and genotype (8). Sybert and McCauley (8) showed the incidence of 46 Xi (Xq, 7%), 45 X/46 Xi(Xq, 8%), 45 X/ 46 X ring (6%) + mar (1%), 45, X/46, XX/47XXX (3%), 45X/ 46XX (13%), 46, X, Xp (short arm deletion, 2%), 46X/Xq (interstitial long arm deletion, 2%), and others (6%). Renal and heart failure are less commonly observed in the variants of Turner syndrome (9). According to Sönmez et al(10), the X isochromosome-X syndrome was reported in 7%-17% of the Turner syndrome cases 46 XXi (Xq). Some studies reported similarities between the classic form of the syndrome and 46 XXi (Xq). Evidence suggests that the risk of hypothyroidism, mild intellectual disability, and partially-developed nipples increased compared to XO syndrome (11). Nonetheless, low posterior hairline, a webbed neck, and hypoplastic nails have been less reported in this population (12). Nevertheless, short stature, amenorrhea, shortening of the 4th metacarpal bone, streak gonads, and pigmented nevi are observed in both cases (11). Short stature and congenital malformations are more common in patients with a deletion of Xp. Furthermore, manifestations can be attributed to gonadal dysgenesis (10) in patients with a deletion of Xq or can present with other clinical manifestations such as cardiac and renal anomalies, intellectual disability, mental disease, and edema (12).

In this case report, isochromosome X syndrome [46 XXi (Xq)] was shown to be a milder form of the classic Turner syndrome. Rare variants of the syndrome should be considered in female patients with short stature and primary amenorrhea without the classic manifestations of Turner syndrome. The early detection and administration of growth hormones and HRT can improve the quality of life in these patients.

Conflict of Interest Disclosures

The authors have no conflict of interests.

Acknowledgements

This work was supported by the Clinical Research Development Center of Hormozgan University of Medical Sciences, Bandar-Abbas, Iran. We are sincerely thankful to Miss. Tayyebeh Zarei, the Clinical Research Development Center of Shahid Mohammadi Hospital, Hormozgan University of Medical Sciences, Bandar-Abbas, Iran.

Ethical Statement

The study approved by the Ethics Committee of Hormozgan

University of Medical Sciences (IR.HUMS.REC.1399.315).

Author's Contributions

HRS and MKJ contributed to the conception, design, and statistical analysis. Other authors contributed to data collection and manuscript drafting. MKJ supervised the study. All authors approved the final version of the manuscript.

Funding/Support

This study was financially supported by the Clinical Research Development Center of Shahid Mohammadi Hospital, Hormozgan University of Medical Sciences, Bandar-Abbas, Iran.

Informed Consent

The patient was informed and signed the informed consent form.

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