CASE REPORT

Triple X Syndrome Woman Presenting as Premature Ovarian Failure

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ABSTRACT

Triple X syndrome is a sex chromosome abnormality characterized by extra X chromosome, occurring in approximately 1 in 1,000 female births. This condition often remains undiagnosed as most of them have normal phenotype, puberty and fertility. We report a case of Triple X syndrome with normal phenotype and intelligence that presented with secondary amenorrhea and diagnosed to have premature ovarian failure. This case emphasizes the need for chromosomal analysis in women presenting with premature ovarian failure leading to primary or secondary amenorrhea.

Keywords: Triple X syndrome, Premature ovarian failure, Secondary amenorrhea, Karyotyping.

INTRODUCTION

Triple X syndrome is a sex chromosome anomaly caused by the presence of an extra X chromosome in females (47, XXX instead of 46, XX). It results from nondysjunction of X-chromosome during meiotic division. This condition often remains undiagnosed as most of them have normal phenotype, puberty and fertility. It is estimated that only 10% of individuals with trisomy X are actually diagnosed. We report a case of Triple X syndrome with normal phenotype and intelligence that presented with secondary amenorrhea and diagnosed to have premature ovarian failure.

CASE REPORT

A 21-year-old girl was seen in the gynecology OPD for secondary amenorrhea. She is the first child to her parents and has one younger brother, her parents were under 30 years at the time of her birth. And her early developmental milestones were normal. She is studying in college and her academic record was good. She attained menarche at the age of 14 years and menstruated regularly till the age of 17 years, then she menstruated irregularly at the intervals of 60 to 120 days till last year. On examination, she was 160 cm tall, weight was 53 kg and BMI was 18. She had a female phenotype with breast and pubic hair Tanner stage four developments. A gynecological examination revealed normal vulva and perineum. An ultrasound of pelvis showed uterus with 52 × 50 mm, Endometrial thickness was 2 mm thick and both ovaries were atrophic. Hormonal assay was done, FSH was increased (80 mIU/ml), Serum estradiol was low (30 pg/ml). Serum prolactin, thyroid profile and serum cortisol were normal. Karyotyping was done which revealed trisomy X (Fig. 1) and was diagnosed to have premature ovarian failure due to triple X syndrome. Counseling was done to the patient and her parents. She was given conjugated equine estrogen (0.625 mg/day) from day 1 to 21 and medroxyprogesterone acetate (10 mg/day) from day 21 to 25. While taking this regimen, she had cyclical bleeding.

DISCUSSION

Premature ovarian failure (POF) is defined as cessation of ovarian function before the age of 40 years, associated with elevated gonadotropins, serum levels of FSH ≥40 IU/L and affects 1 to 3% of women of reproductive age.1 POF occurs in 10 to 28% of women with primary amenorrhea and 4 to 18% in those with secondary amenorrhea.2,3 Women with POF suffer from anovulation, hypoestrogenism. They present with primary or secondary amenorrhea, infertility, sex steroid deficiency and elevated gonadotropins.

Fig. 1: Karyotyping showing trisomy X
The etiological causes of POF are highly heterogeneous and include chromosomal, genetic, autoimmune, metabolic, infectious and iatrogenic factors. Genetic defects include 1/3rd cases of POF. Genetic defects mostly involve the X chromosome, and there may be autosomal involvement. These abnormalities range from a numerical defect like complete deletion of one X (Turner’s syndrome) and trisomy X to partial defects in form of deletions, isochromosomes and balanced X autosome translocations.4

Triple X syndrome (trisomy X) was first described by Jacobs in 1959, as super female is a sex chromosomal aneuploidy condition with female phenotype.5 Triple X syndrome is a sex chromosome anomaly caused by the presence of an extra X chromosome in females (47, XXX instead of 46, XX). It results from nondysjunction of X-chromosome during meiotic division. It is the most common female chromosomal abnormality, occurring in approximately 1 in 1,000 female births.6 As some individuals are only mildly affected or asymptomatic, it is estimated that only 10% of individuals with trisomy X are actually diagnosed. There is a considerable variation in phenotype, and some individuals mildly affected. Its symptoms vary very widely, including tall stature, hypertelorism, epicanthal folds, clinodactyly, congenital heart disease, seizures, genitourinary and some other anomalies.7

These females often have a tall stature than their female peers, not explained by parental heights.8 Affected females typically have normal intelligence but lower IQ than that of their siblings. There may be learning difficulties and they tend to have delayed acquisition of certain motor skills, language skills and impaired psychosocial adaptations.9 These girls need supportive parents and atmosphere that provides constant stimulation and love for learning and interaction. Our patient presented only with secondary amenorrhea without any other features of triple X syndrome. Pubertal onset, sexual development and fertility are usually normal in these girls. POF has been reported in approximately 1 in 1,000 female births. As some individuals are only mildly affected or asymptomatic, it is estimated that only 10% of individuals with trisomy X are actually diagnosed. There is a considerable variation in phenotype, and some individuals mildly affected. Its symptoms vary very widely, including tall stature, hypertelorism, epicanthal folds, clinodactyly, congenital heart disease, seizures, genitourinary and some other anomalies.7

Patients with triple X syndrome may have immune disturbances, as revealed by increased serum IgM levels, and associated with other autoimmune disorders.11 Early loss of ovarian function has significant psychosocial sequelae and major health implications nearly 2-fold age-specific increase in mortality rate has been reported.12 POF generates two types of consequence. One is premature hypoestrogenism, which in turn causes the premature aging of several tissues, targets of estrogen action, and thus increasing the risk of osteoporosis, cardiovascular diseases, or neurodegenerative diseases. Hypoestrogenism can nowadays be satisfactorily treated by hormone replacement therapy to be generally given until the age of physiological menopause. The second consequence is infertility. Although most patients with triple X syndrome can conceive, a high prevalence (50%) of cardiac and neural tube defects, malformations of the genitourinary tract and sex chromosomal abnormalities have been reported in their offspring, and most offspring die during early childhood.13 The only proven means of achieving pregnancy in infertile women with triple X syndrome is by assisted conception with donor oocytes.

CONCLUSION

Most of the triple X syndrome girls have normal female phenotype, pubertal development and fertility. This condition should be kept in mind in evaluating young woman with primary or secondary amenorrhea with POF. Our case emphasizes the need for chromosomal analysis in women presenting with premature ovarian failure. Management essentially involves hormone replacement and infertility treatment, the only proven means for the latter being assisted conception with donated oocytes.

REFERENCES


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