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Case Report

Triple X syndrome: a rare case entity with premature ovarian failure, recurrent abortion and secondary infertility

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ABSTRACT

Triple X syndrome is a sex chromosome abnormality characterised by extra X chromosome, occurring in 1 in 1000 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 presented with premature ovarian failure, recurrent abortion and secondary infertility. This case emphasizes the need for chromosomal analysis in women presenting with premature ovarian failure leading to recurrent abortion and secondary infertility.

Keywords: Triple X syndrome, Premature ovarian failure, Recurrent abortion, Secondary infertility, Karyotyping

INTRODUCTION

X chromosome mosaicism is usually associated with abnormal sexual development and reproductive performance, such as recurrent spontaneous abortion, primary or secondary amenorrhea, infertility and premature ovarian failure. Our preliminary data suggests that chromosomal analysis should be done routinely in every couple with recurrent spontaneous abortion and in women with premature ovarian failure. The reproductive performance of X chromosome mosaicism is highly variable and difficult to define. Triple X syndrome is a sex chromosome abnormality characterized by extra X chromosome, occurring in 1 in 1000 female births.¹ Triple x syndrome (47xxx) is not extremely rare, although one might think so, as the majority of cases go undiagnosed.² The sex chromosome have aneuploid count in SCA; e.g. 47xyy, 47xxy, 47xo etc. SCA may be mosaic.³

CASE REPORT

A 31 year old female came with inability to conceive since 13 years of her marriage and secondary amenorrhea

with recurrent abortions. She attained her menarche at 14 years of age and her early developmental milestones were normal. She menstruated normally till the age of 25 year and then menstruated irregularly at the interval of 2-3 months. She had 2 abortions at 6-7 week of pregnancy, then she came in our OPD and underwent all investigations of infertility and premature ovarian failure. She underwent diagnostic laprohysteroscopy and 5 times IUI before this.

On examination

Her height was 162 cm, weight 58 kg and BMI was 21.64. She had a female phenotype with normal secondary sexual characteristic. A gynaecological examination revealed normal genitalia. In her investigation USG showed ET-4mm, uterus- normal sized and both ovaries showing AFC-2. Hormonal assay was done showing FSH-35 IU/L and serum estradiol 30pg/ml. AMH-0.4 ng/ml, serum thyroid and prolactin was normal. Karyotyping revealed trisomy XXX so she was diagnosed to have premature ovarian failure, recurrent abortion and secondary infertility. HSA were normal. She was planned for OD IVF. Before this she undergone

diagnostic hysteroscopy and laparoscopy and oocyte donation and IVF done and failed so next time she again planned for OD with ICSI along with endometrial preparation. We started with inj. triptorelin 0.05mg from day 25 of previous cycle for 5 days., tab estradiol valerate 1 B.D from day 20 - day 2, 1 T.D.S. from day 2 - day 7, 2 T.D.S from day 7 up to day of ovum pick up, 17B estradiol 1.5% once daily local application, tab sildenafil 25 mg B.D per vaginal, tab aspirin 75 mg once daily, 1 - arginine sachet once daily. OD with ICSI done and ET done she became pregnant with positive BHCG after 14 days.

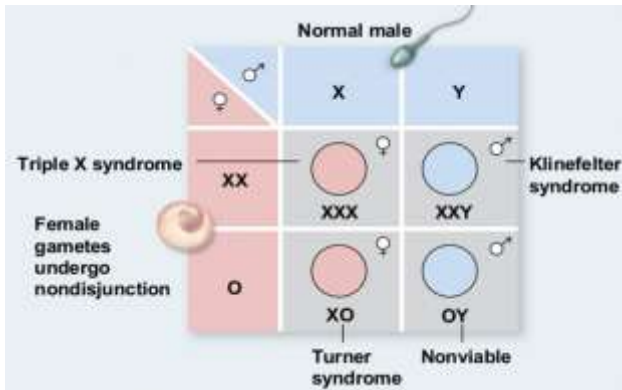


Figure 1: Genetic basis of triple X syndrome.

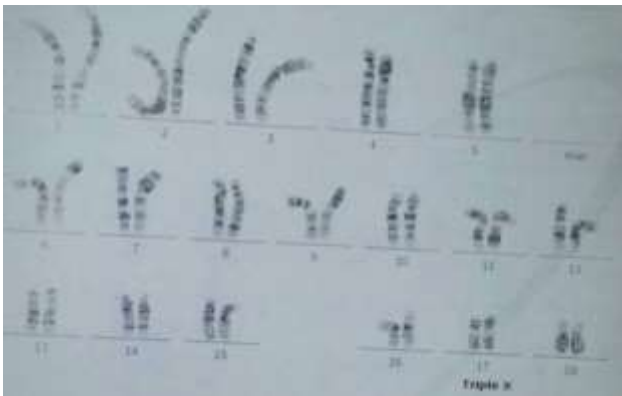


Figure 2: Karyotype report of patient.

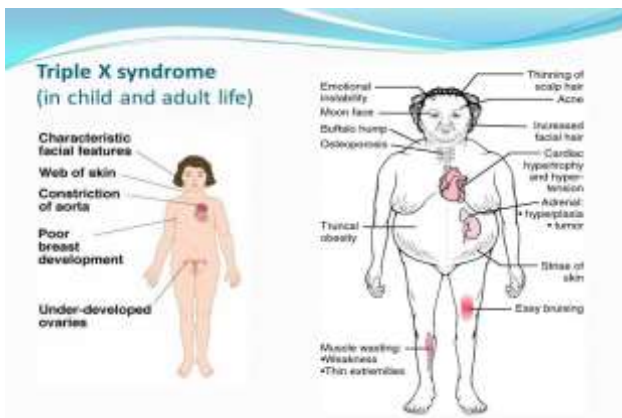


Figure 3: Clinical presentation of triple X syndrome.

DISCUSSION

Triple X syndrome was first described by Jacobs in 1959 as super female is a sex chromosomal aneuploidy with female phenotype.⁴

Premature ovarian failure is defined as cessation of ovarian function before the age of 40 and associated with elevated gonadotropin, serum level of FSH >40 IU/L and it occurs in 4 to 18% in those with secondary amenorrhea. Women with POF suffer from infertility, amenorrhea and sex steroid deficiency. POF affect 1to 3% of reproductive age group.⁵ Genetic factor responsible for 1/3rd cases of POF. Triple X syndrome (Trisomy X) is a genetic condition that only affects females. Girls and women with triple X syndrome have an extra X chromosome. Females usually have two X chromosomes and are described as 46, XX. Females with triple X syndrome have an extra X chromosome, so three in all. Triple X syndrome is sometimes called 47, XXX; Mosaic Triple X syndrome. Most women and girls with triple X syndrome have one extra X chromosome in the cells of their body. But quite a few girls and women have some cells with three X chromosomes and some with a different number of X chromosomes. This is known as mosaicism. Mosaicism can change the effects of triple X syndrome.

What causes Triple X syndrome? In most cases it's not known what causes triple X syndrome. Girls usually inherit one X chromosome from their father and one from their mother. Girls with triple X syndrome can inherit their extra X chromosome from either parent but it's more common from their mother. This type of mistake is known as non-dysjunction. Fertilised by a single X-carrying sperm, the egg will then develop into a baby with three X chromosomes. In around one fifth of all cases, a mistake occurs just after fertilisation during the copying of the early cells that will become an embryo, then a fetus and then a baby.⁶ It seems that most women with triple X syndrome have no problem in becoming pregnant and can expect to have healthy children, although no direct studies of fertility in triple X syndrome have been carried out. The extra X chromosome is not usually passed on to their children. A high prevalence of cardiac and neural defect and sex chromosomal abnormalities have been reported in off springs.⁷ Triple X syndrome affects individual girls and women differently. Some are scarcely affected, if at all, while others can have obvious and significant problems.

These are the most typical features:

Speech delay, Need for some extra learning support, Rapid growth at 4-13 years, with especially long legs, Vulnerability to difficulties in making friends at school age, normalising in adolescence, increased vulnerability to behavioural and social stress, mild delay in physical development.

When this occurs, a woman in her 20s, 30s or early 40s starts having irregular periods and may miss them

altogether for a few months. The supply of eggs to the ovaries stops before the expected age for menopause and the ovaries stop functioning normally. The reason why this might happen in some women with triple X syndrome isn't known for certain but it's theoretically possible that since half the eggs of a woman with triple X syndrome would be expected to have an extra X chromosome they are perhaps side-lined. The only proven mean of achieving pregnancy in infertile woman with triple XXX is ART with donor oocyte.

CONCLUSION

If a case of premature ovarian failure and recurrent abortion and secondary infertility should be investigated with karyotyping and to get pregnancy with endometrial preparation and ART (OD). Prematurian ovarian failure should be treated with HRT. Its eye opener that each and every patient with normal phenotype presenting with recurrent abortion, premature ovarian failure and infertility should be investigated with karyotyping along with all investigation. Patient should be referred to research organizations to receive individual and family support. The prognosis is variable, depending on the severity of the manifestations and on the quality and timing of treatment.

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