

# Mosaicism Triple X Syndrome in a Young Woman Presenting as Primary Amenorrhea with Short Stature

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## Abstract

**Background:** Primary ovarian failure (POF) as a presentation of Triple X syndrome constitutes only 3.8% of cases in the literature. POF may be the presenting symptom in up to 10% of cases of primary amenorrhea. There is no consensus guideline on their management.

**Case Report:** A 24-year-old woman was referred to our institute for the evaluation of primary amenorrhea. She was short stature with poor development of secondary sexual characters. The cytogenetic evaluation revealed mosaicism of 46,XX/47,XXX. Her luteinizing hormone (LH) was (51.84 mIU/mL) and follicle-stimulating hormone (FSH) was (119.58 mIU/mL) suggesting premature ovarian insufficiency. Most of the subjects presented in the literature were having normal stature. Our case was different from the other being short stature with mosaicism of 46,XX/47,XXX with normal scholastic performance. **Conclusion:** This case can stress upon the utility of chromosomal karyotype in women presenting with primary amenorrhea with POF.

**Keywords:** Amenorrhea, Cytogenetic Analysis, Karyotype, Mosaicism Triple X syndrome, Trisomy.

## Introduction

Triple X syndrome is also called trisomy X or 47,XXX; sex chromosome anomaly characterized by the presence of an extra X chromosome in a female. Triple X syndrome is first described by Jacob *et al.* [1]. An extra copy of X chromosome is generally associated with tall stature, relatively underweight for their height, learning problems, menstrual abnormalities and sometimes with adult premature ovarian failure [2].

## Case Report

A 24-year-old woman, born to non-consanguineous parents, was referred to our institute for the evaluation of primary amenorrhea. She was the third born child in her family, with normal developmental milestones and having body weight of 48 kg and height 146 cm. No stigma of Turner

syndrome was noticed. She had bilateral short 4<sup>th</sup> and 5<sup>th</sup> toes. Axillary and pubic hairs were absent indicating possible androgen insensitivity. Breast development was Tanner stage-II. Her intelligence quotient was within the normal range. A preliminary diagnosis of primary amenorrhea was made.

Ultrasound of pelvic region showed small uterus of 51×21×13 mm size. Endometrium was 1.2 mm thick. Her both ovaries were rudimentary measuring 12×5 mm and 13×6 mm respectively. However, the vagina was well visualized. Her luteinizing hormone (LH) was (51.84 mIU/mL) and follicle stimulating hormone (FSH) was (119.58 mIU/mL) suggesting premature ovarian insufficiency. Cytogenetic analysis was carried out by GTG banding on cultured peripheral blood lymphocytes by standard technique. In the present study, 50 metaphase plates were analysed,

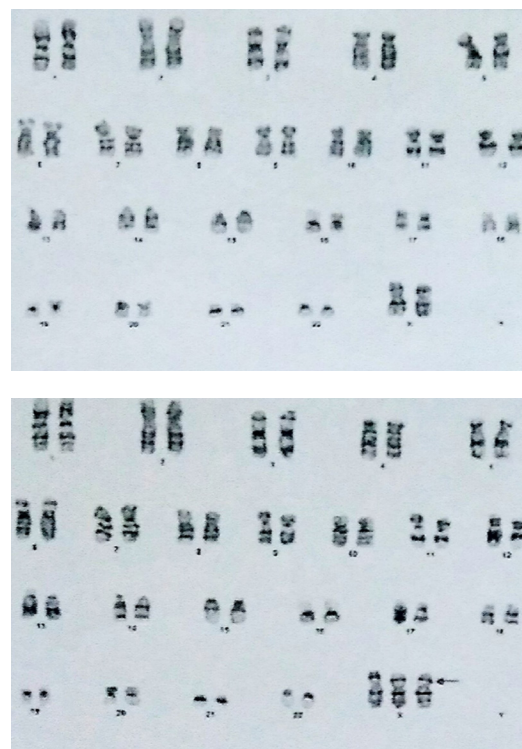
which revealed mosaicism of 46,XX/47,XXX chromosomal constitution with 90% of the cells showing 46,XX [Fig.1] and 10% of the cells exhibiting 47,XXX [Fig.2]. The index patient was having short stature. The woman was 146 cm tall considering her father and mother's height were 170 cm and 157 cm respectively with mid parenteral height was 165.5 cm. According to the Indian Academy of Paediatrics (IAP) growth charts her height is below 3<sup>rd</sup> centile [3].

In summary based upon the clinical features, hormonal assay and cytogenetics, a formal diagnosis of primary ovarian failure (POF) with mosaic triple X syndrome was made. The first association of triple X syndrome with POF is described by Jacobs *et al.* in 1959 [1]. Although non-mosaic 47,XXX karyotypes are the most frequent; mosaicism occurs in approximately 10% of cases with many combinations such as 46,XX, 47,XXX, or 48,XXXX [4].

## Discussion

POF may be the presenting symptom in up to 10% of cases of primary amenorrhea [5]. Primary ovarian failure as a presentation of Triple X syndrome constitutes only 3.8% of cases in literature [6]. Genetic cause constitutes 33% of the POF which involves mostly the X chromosome [7]. Considering the poor breast development (Tanner II) and amenorrhea, she was started initially with ethinyl-oestradiol 10 µg daily. It was planned to start with low dose estrogens and progesterone oral contraceptive pills; till she starts regular menstruation or she attained proper Tanner breast staging. Future plan for management of this case was to get her counselled by a qualified psychologist about the permanent infertility that she will have and plan for adoption if she wishes to marry in future. **Table 1** depicts 47,XXX-triple X syndrome patients with premature ovarian failure reported in the literature.

Most of the subjects presented in literature were having normal stature along with no



**Fig.1,2:** Karyotype showing 46,XX and 46,XXX.

mental abnormality. Our case was different from the other being short stature with mosaicism of 46,XX/47,XXX with normal scholastic performance. She presented with primary amenorrhea with poor secondary sexual character and was managed appropriately with low dose oral contraceptive pills.

## Conclusion

Our case is unique being presented as short stature. It also stresses upon the utility of chromosomal karyotype in women presenting with primary amenorrhea with premature ovarian failure for diagnosis and appropriate management. A multidisciplinary approach is needed for proper treatment.

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**Table 1:** Reported cases of 47,XXX-triple X syndrome.

S.No.	Year of publication/ Author	No of cases/Age	Presenting complaints	Treatment given	Outcome
1	2003, Chandana C [8]	n=1; Age= 21 yrs, height 161 cm.	Secondary amenorrhea followed by POF.	She was given conjugated equine estrogen (0.525 mg/day) from day 1 to 21 and medroxyprogesterone acetate (10 mg/day) from day 21 to 25.	Had cyclic bleeding.
2	2011, Kodandapani S [9]	n=1; 29 yrs, 168 cm.	Married for 2 yrs. Evaluated for primary infertility and diagnosed subsequently POF.	Treated with ovulation induction by gonadotrophins.	Not available.
3	2003, Goswami R [6]	n=2; Case 1: 19 yrs, height=175 cm; Case-2: 27 yrs, height =157 cm.	Both presented as secondary amenorrhea <i>Case 1</i> at age 16 yrs, height of 175 cm (90th percentile). <i>Case 2:</i> She had two pregnancies, first pregnancy had premature birth with idiopathic thrombocytopenia, neonatal death at 21 days and second pregnancy was terminated due to occipital encephalocele.	Prescribed conjugated equine estrogen and progesterone sequentially; during this therapy, she was given conjugated equine estrogen (0.625 mg/d) from day 1 to 21 and medroxyprogesterone acetate (10 mg/d) from day 21 to 25.	Had cyclical bleeding every month.
4	1983 Villanueva, Alell L. [10]	n=2; 27 yrs and 37 yrs.	<i>Case 1:</i> Premature ovarian failure, height 162.6 cm. <i>Case 2:</i> Secondary amenorrhea at age of 36, height 163.6 cm.	<i>Case 1</i> Clomiphene citrate for ovulation induction. <i>Case 2</i> was placed with cyclic estrogen and progesterone pills.	<i>Case 1</i> did not resume menstrual cycles. <i>Case 2</i> had menstrual bleed sporadically however hot flushes diminished.

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