CASE REPORT

Asyndromic Trisomy X Presented With Premature Ovarian Failure: A Case Report

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ABSTRACT

A 31-year-old lady with normal physical characteristics was found to have persistent high FSH and LH and was suspected possible premature ovarian failure after reported to have not normal menstrual cycle. Leucocytes were collected from patient's fresh peripheral blood sample and Giemsa banding (G-banding) was done. All metaphases were captured and analysed using Cytovision software 4.5 and the final analysis show 47,XXX.

Keywords: Triple X syndrome, 47,XXX, Premature Ovarian Failure

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INTRODUCTION

47,XXX, also known as Trisomy X or Triple X syndrome is a sex chromosome abnormality that only occur in females. Those who suffer from trisomy X have an extra copy of X chromosome when equated to the normal karyotype of 46,XX in a normal typical female. In 1959, Jacob et al., (1) conducted a screening study among newborn babies and demonstrated that the occurrence was approximately 1 in 1000 female birth with merely 10% of those cases were clinically detectable. Large majority of young girls and women with triple X syndrome never know that they have an extra X chromosome as vast majority are asymptomatic. The X chromosome is usually discovered with the standard karyotype test done based on concerned parents and health providers of affected female's unusual physical feature or development delay and in some identifiable cases, diagnosis was done by way of prenatal amniocentesis and chorionic villi sampling (CVS) of pregnant woman. Some obvious physical features include wide spaced eyes, small head circumference and hypotonia. Triple x syndrome occurs during the cell division and the there is an error called non-disjunction event which the X chromosome failed to separate properly during gametogenesis. Premature Ovarian Failure (POF) is one of the challenges faced by women with trisomy X. These patients will likely suffer irregular or skipped menstrual cycle which might be present or develop years after a pregnancy or after giving birth, or birth control pills. In general, women with POF appears to have normal fertility prior to the developments of ovarian failure (2).

CASE REPORT

Patient is 31 years old female from parent age 62 years old father and 42 years old mother with normal physical characteristics. She is the first child of four siblings from marriage of unrelated Malay parents. No history of abnormal features or investigated chromosomal disorder recorded in the family. The reasons for chromosomal analysis test were high levels of follicle stimulating hormone (FSH), luteinizing hormone (LH) and was suspected possible premature ovarian failure after reported to have not normal menstrual cycle. No other hormonal investigation was done at that time. Giemsa banding (G-banding) was done on peripheral blood lymphocytes that were collected from patient's fresh peripheral blood sample. All metaphases were captured and analysed using Cytovision software 4.5 and the final analysis showed 47,XXX in 33 metaphases examined with 400-550 ISCN bphs resolution (Figure 1).

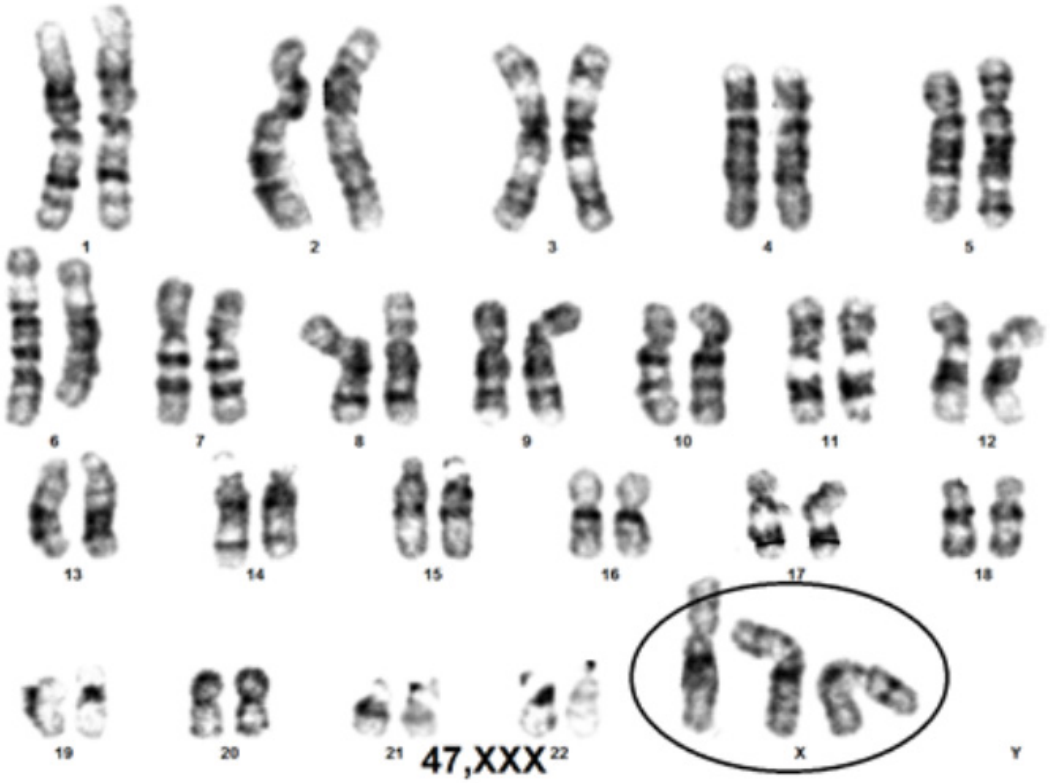

Figure 1: Karyogram of the patient's karyotype depicting 47,XXX, 400-550 ISCN bphs resolution.

DISCUSSION

This patient presented with investigative features of premature ovarian failure to physician that subsequently diagnosed as trisomy X. Goswami et. al., (3) have reported two cases of POF from a pool of 52 women with underlying trisomy X chromosomes. In these case, genetic defect was proposed to contribute to POF by increasing atresia of ovarian follicles as a result from cellular apoptosis or follicle maturation failure, and subsequently decrease the pool of primordial follicles in affected patient. In this situation, premature ovarian failure should be treated with hormone replacement therapy (HRT). Patient with normal phenotype presenting with recurrent abortion, premature ovarian failure and infertility should be investigated with karyotyping alongside with other investigation. This patient suffering from premature ovarian failure does not show any physical symptoms or dysmorphic features that can be seen after birth such as marked divergent squint eyes, beaked nose and other features in mild developmental delay in physical aspect and other hallmark of trisomy X. The syndrome is instigated by an error when cell undergoing division, a failure known as non-disjunction that ensued in yielding reproductive cells having extra chromosomes. The reproductive cells (oocyte) may acquire an additional X chromosome copy from non-disjunction. When these cells provide as the basis of genetic makeup of the foetus, an extra X chromosome will be passed down to each of her cells. Additionally, in rare instances, trisomy X may be attributed to error during cell division of early embryonic development, additionally extra X chromosome may impede gonadal potential and primary ovarian failure has been associated with X aneuploidy (4). Follicle-stimulating hormone (FSH) is responsible for the growth of ovarian follicles, and a very important hormone involve in normal cycle of reproductive system. In the ovaries, the normally functional follicles contribute to oestrogen and progesterone, and serve as pillars to the normal menstrual cycles in women. When the FSH is persistently high, some problem can happen, such as loss of ovarian function, menopause, polycystic ovarian syndrome. A study of 15 Trisomy X shown majority of patients have basal and peak LH and FSH more elevated compared to normal and may contribute to a reduced gonadal function together with other additional hormones, however more studies are necessary understand the exact mechanism in these patients (4). Suitable hormonal treatment could help prevent osteoporosis and relieve hot flashes and other symptoms of oestrogen deficiency, and especially in young women having POF, the potential benefits of hormonal therapy may outweigh the potential risks (5). As for the prognosis, patients with underlying trisomy X show variable prospect. Some of them live extremely well with negligible manifestation

of the underlying genetic error, and some others may show more substantial cognitive and psychological disturbance. Woman with underlying trisomy X must give more attention to the positive environmental factors that contribute to the support of normal psyche such as family members and having good community support, and this may help build resiliency and enhance quality of life towards normalcy of daily living.

CONCLUSION

Patient having trisomy X are usually diagnosed incidentally on genetic screening, when no remarkable features are seen. For added knowledge, this case may suggest the recommended practice of adding cytogenetics test when an adult female presenting with hormonal and fertility issues as part of the clinical investigations.

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