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Case Study

Triple X: Complication of Living with an Additional X Chromosome

Rahnuma Sarwar, Aishwarya AV Gowda and Satyajit Patra*

American International Medical University, Saint Lucia

***Corresponding Author**: Satyajit Patra, Department of Biochemistry and Genetics, American International Medical University, Saint Lucia.

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Abstract

Triple X syndrome is a genetic disorder due to Chromosomal error while forming each of the parent's germ cells or during fertilization to form the embryo that occurs only in the female newborn. Epidemiologically this affects five to ten newborns in the USA per day, which is quite a remarkable number. Though at times they may have a complete healthy asymptomatic life however we will discuss the general and common signs and symptoms it presents with, like tall stature, infertility, premature ovarian failure (POF), motor and other neurological deficits like reading, writing, auditory processing and psychological deficits like anxiety, depression and as severe as major psychotic episodes though rarely and various tremors and tic disorders. Later the manuscript will provide an overview of the diagnostic tests, how to take the approach as physician to treat them and how to prepare the parents in advance through counseling, group therapy to provide support raising a baby with triple X as they relatively look and act healthy despite the challenges they face among peers and later in getting jobs or family life. Females with triple X who want to go ahead in becoming a mother has been successful and how they can take the medical help *in vitro* or through various methods of conception and how we can promote prenatal screening through amniocentesis and Chorionic villous sampling to prevent such errors well in advance so that the parents can opt for alternatives like abortion.

Keywords: *RTriple X; Tall Stature, Infertility; Premature Ovarian Failure (POF)*

Introduction and Epidemiology

Triple X is a chromosomal abnormality that affects one in one thousand women globally. Typically, a female has two X chromosomes, one from her father and one from her mother, unlike males. According to the National Institute of Health (NIH), five to ten females are born in the USA with triple X syndrome per day. The syndrome typically develops from chromosomal nondisjunction during anaphase phase of cell division, forming an extra chromosome during the formation of the paternal sperm or the maternal oocyte. However, triple X syndrome can take place if there is an aberration in any of the successful events of the formation of the embryo once fertilization has already taken place. Triple X syndrome is also stated as deviance X, 47 XXX, Triple-X, trisomy X and XXX syndrome, super female syndrome. It is not a hereditary condition; in other words, it is not passed on from parent to child. At birth, 47, XXX females have a lower mean birth weight and smaller head circumference (HC) in the growth chart.

Toddlers with triple X syndrome may show a delay in growth and developmental milestones and slower language and speech development, abnormal motor coordination, impaired auditory processing. All the symptoms mentioned above and learning disabilities in school-age children will be detected by the child's pediatrician, primary caregivers, and teachers. The quantitative relation level is

twenty points below that of motor control and lowest in quantitative, verbal relation according to the degree of severity of the symptoms. Throughout the school, the girl struggles psychologically to cope up with peers, participating in school activities and probably needs to attend additional educational support, communication, speech, and behavioral therapy. In adults, premature endocrine gland failure or agenesis, to name a few, may appear to be causing various endocrine abnormalities. MRI's of the brain shows significant low brain volume. During the later course in life, the 47, XXX adult females most often look for or get jobs that replicate their performance skills. However, there haven't been reports of any significant intellectual disability in the majority of these cases reported. Psychotic and various psychological illness and milder version of typical affective disorders and labile temperament traits appears to be prevalent in triple X adult females. Analysis of triple X syndrome may yield additional insight into growth, brain and behavioral relations, psychopathology, auditory-processing disorders, temperament disorders, as mentioned earlier [1].

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Etiology

Although triple X syndrome is congenital, it may not always be genetic - it's because of a random genetic error. Typically, an average person has forty-six chromosomes in every cell except the reproductive cells, which has half of it 23, organized into twenty-three pairs 22 autosomes along with two sex chromosomes or allosomes. One set of chromosomes is from the mother, and the other set is from the father. These chromosomes contain genes that code everything from height to eye color.

The sex chromosomes, either XX or XY chromosome, determines a child's sex. A mother will solely pass on the X chromosome, while the father will pass on the X or Y chromosome. The child will be genetically female on receiving the X chromosome from the father. On receiving a Y chromosome from the father, the child will be genetically male. Females with triple X syndrome have a 3rd X chromosome from a random error in cell division. This error occurs before conception or early within the embryo's development, leading to one in each of these kinds of triple X syndrome nondisjunction [2].

In most cases, either the mother's ovum or the father's sperm divides arbitrarily for no apparent reason (sporadically) during meiosis, leading to an additional X chromosome. This random error is termed reduction division, and every one of the cells within the juvenile body can have the extra X chromosome. Triple X syndrome is additionally known as forty-seven, XXX syndrome as a result of the additional X chromosome.

Studies have shown that the danger of such errors will increase with advanced paternal age. In most children, the extra X chromosome comes from the mother. In approximately twenty % of children, reduction division events occur once conception within the developing vertebrate (postzygotic nondisjunction). In some affected females, solely a particular share of their cells could have 3 X chromosomes. In contrast, alternative cells have a standard body make-up (46, XX/47, XXX mosaicism). These females could have milder symptoms and fewer organic process and learning issues; however, more detailed analysis is recommended. Variants have additionally been represented during which cells contain four or 5 X chromosomes (tetra X syndrome and penta X syndrome). Such variants are usually related to a lot of severe symptoms and findings. (For more info, please see the "Related Disorders" section of this report below). Researchers believe that the signs and physical options related to chromosomal aberration X develop as a result of overexpression of the genes that escape traditional X-inactivation and bar body formation. Though females have 2 X chromosomes, one in each of the X chromosomes is "partially turned off" and a few; however, not all of the chromosomes are inactivated (X-inactivation). Researchers suspect that the presence of a 3rd X chromosome permits some genes ordinarily "turned off" to be expressed. However, the precise manner during which the additional X chromosome ultimately causes the symptoms and physical options of chromosomal aberration X isn't understood.

Signs and symptoms

The number and severity of manifestation of the symptoms related to chromosomal anomaly X vary significantly from person to person. Some females could be asymptomatic or show mild to moderate symptoms throughout their life and could completely go undetected. It's vital to notice that affected people might not have all of the symptoms mentioned below. Affected people ought to seek advice from their specialists and medical team concerning their specific case, associated symptoms, and overall prognosis [3].

Trisomy X is usually related to growth abnormalities, issues related to puberty and fertility, neurodevelopmental variations, and language-based learning disabilities. Motor tone and coordination abnormalities, tics, tremors, seizures, renal and cardiac defects, and various other mental and physical conditions. If we consider growth, most of the triple X females will have tall stature more than 75 percentile in growth chart with disproportionately long legs. Rarely a few of them may show short stature.

Puberty is delayed by six months to one year, for example, the menarche will start at 13.6 years, unlike the regular 11.5 - 12 years. The Tanner scale can measure delayed breast development. Few girls also go through precocious puberty. Premature ovarian failure (POF) or loss of ovarian function, that is, production of estrogen, progesterone, ovulation, and regular menstrual cycle is hindered and reaching menopause before the age of 40 years, or even less is one of the characteristic features of trisomy X. Amenorrhea secondary to other conditions is also presented. Various reports of women with abnormal ovaries and lack or reduced healthy oocytes were found later in life. So basically, they had a normal puberty and fertility earlier. Still, secondary to some conditions the number in healthy oocyte decreased gradually, losing their capacity to reproduce. Despite these reported cases discussed earlier, many women had relatively normal fertility and typical family and children as it's not inherited, as mentioned earlier.

IQ could also be 10 - 15 points below their relatively healthy siblings or peers, as observed by management teams if an early intervention has not begun early enough. Decreased IQ with seizure is detected in patients though the brain may have no structural abnormality. The seizure can be controlled well with medications after getting an MRI scan of the brain and Electroencephalogram (EEG) study. Motor coordination abnormalities include delayed walking, and affected women could exhibit poor limb coordination and clumsiness. Decreased muscle tone or hypotonia causing floppiness, decreased gross or fine motor disfunction less than ten percentile of the growth chart, sensory and motor integration disfunction, delayed age of walking, stiffness and contractures. Occupation and physical therapy, keyboard, and assistive therapy could be useful. Speech and language development are usually delayed and will become apparent by roughly one year to eighteen months. Women with an anomaly or chromosomal abnormality or chromosomal disorder X have a raised frequency of language-based learning disabilities as well as impaired in reading like reading comprehension deficits possibly with poor Wernicke's area development, and/or speech fluency problems probably questioning the development of their Broca's area of the brain in conjunction with different language-based disabilities. They may even have dyspraxia that affects learning in each domain. Typically, motor designing skills deficient, which affects gross and fine motor skills, speech, and language skills. Intervention ought to be initiated earlier so that the women don't experience perennial exposure to failure and criticism from peers and society.

Tics like continuous eye blinking, head twitching, motor, or vocal spasms may be observed in them, which cannot be characteristics of this condition as it can be seen in various other relatively healthy people but should be treated when impacting social development and self-esteem of the girl. Depending on the severity, this can be administered therapeutically without medications if mild, with medications just to target the tics. Before medication is prescribed, it is essential to take into consideration the drug history as these patients may be under dopamine for any secondary medical condition, which is causing the tics. Another symptom that we see in these patients is tremors like intention tremors of hands, which can impact writing for them, especially in school. For these children use of keyboards should be recommended. Medications should be prescribed if the condition is severe. Some infants with chromosomal anomaly X could have gentle facial abnormalities, and vertical skin folds called epicanthal folds, wide-spaced eyes or hypertelorism apart from the smaller head circumference. Most infants even have hypotonia of the fifth finger, which could also be abnormally bent or falcate gently.

During infancy or adolescence, women with chromosomal anomaly X typically exhibit raised height as compared to different women their age (tall stature), as already mentioned. Individuals with anomaly or chromosomal abnormality disorder X could have an elevated incidence of hysteria and attention deficit hyperactivity disorder (ADHD). In some cases, such defects improve with maturity as women reach adulthood. There aren't enough published controlled studies on activity or emotional abnormalities in chromosomal anomaly X, and therefore the incidence of such conditions is unknown. However, they're believed to occur with more significant frequency than within the general population. Early detection and treatment are useful for females with chromosomal anomaly X. In several cases, these women have few problems later in life once known early and treated symptomatically.

Less often, other abnormalities are represented in people with chromosomal anomaly X as well as excretory organ abnormalities, like the absence of an excretory organ (unilateral nephritic agenesis or atrophic kidneys) or multicystic malformation (dysplasia) of the kidneys; repeated urinary tract infections due to vesicoureteral reflux. All these can be diagnosed with renal ultrasound. Abdominal pain; constipation, flat feet (pes planus); and body part excavatum, a condition during which the os is gently depressed into the chest to have also been observed. Heart abnormalities have been additionally reported in some isolated cases.

Diagnosis

A lot of the females with triple X syndrome are healthy and show no outward signs of the condition, they will stay undetected all their lives, or maybe detected by chance while testing for another medical condition. Triple X syndrome may additionally be seen throughout prenatal testing to spot alternative genetic disorders. If triple X syndrome is suspected of supported signs and symptoms, it is often confirmed by genetic testing - body analysis employing a blood sample. Additionally, to genetic testing, counseling will assist you in gaining comprehensive info regarding triple X syndrome. Trisomy X could also be suspected primarily based upon the identification of specific neurodevelopmental, behavioral, or learning disabilities. Besides, chromosomal aberration X is more and more being diagnosed before birth (prenatally) with supported body analysis and chorionic villus sampling (CVS), amniocentesis. Throughout prenatal diagnosis, a sample of fluid that surrounds the developing fetus called amniotic fluid is removed and analyzed, known as amniocentesis. In contrast, Chorionic Villus Sampling involves the removal of tissue samples from part of the placenta. Approximately 5 - 15% of females with Turner syndrome even have a forty-seven, XXX in a mosaic pattern, possibly due to Robertsonian translocation, and this composition is found in bound white blood cells (blood lymphocytes); however, the characteristic Turner syndrome composition (45, X) is expressed phenotypically [4].

Treatment

The chromosomal error that causes triple X syndrome cannot be repaired once the baby is already born. The parents can choose for abortion within the first or second trimester if needed once detected by prenatal screening. Like all chromosomal abnormality, the syndrome itself has no cure as such. Treatment is symptomatic. If there is the delay of any physical or psychological development, learning disabilities, or physiological abnormality, hindering the daily lifestyle and the long-term development, early intervention should be provided. These services might include keeping a track on the developmental milestones by the child's physician, standard growth curve with height, weight and head circumference, activities like walking, talking, writing, physical or physiological process, menarche, kidney, and cardiac development, motor, and neurological development and medical intervention should be implemented from the beginning of the first few months of life.

Female with triple X syndrome may also be additionally liable to anxiety, mood disorders, and sensitivity to criticism. Therefore, it needs to be monitored carefully. Before the child is born, if the parents still want to carry forward with the pregnancy, then they need to be given counseling sessions to treat the children with care, love, and encouragement despite their differences and discourage behaviors

that may negatively impact learning and social functioning later in future. Assistance and support in daily operation - if the child has issues that affect day-to-day activity. Help and support facilitate activities of daily living, social opportunities, and even employment should be considered [5].

Standard therapies

Specific therapeutic methods rely on many factors as well as the age of affected individual upon diagnosing the precise symptoms, and also the overall severity of the disorder in every case. Early intervention services are suggested for infants diagnosed with chromosomal aberration X. Specialists advise biological process assessment by age four months to test the muscle tone and strength; language and speech assessment by twelve months aged to examine communicative and receptive language development; and pre-reading assessment throughout the educational institution. Genetic analysis is suggested to assess further learning disabilities and social and emotional issues. Infants with chromosomal aberration X ought to receive renal and cardiac evaluations to find abnormalities of these organs related to the disorder. Adolescents and adults who exhibit late periods (menarche), emission abnormalities, or fertility problems ought to be evaluated for primary female internal reproductive organ failure. Additional treatment ought to be targeted at infancy for physiotherapy, between twelve and fifteen months for speech delay, before grading for early signs of reading dysfunction, and by third grade for anxiety and minimal brain dysfunction. Adolescence is awkward for kids with triple X as they typically struggle once they enter secondary school years; therefore, the short-term counseling could also be necessary to assist them throughout these turbulent years. Genetic counseling is suggested for affected people and their families.

Conclusion

Triple X syndrome may be a syndrome with a high level of selection within the physical and behavioral composition. Triple X syndrome isn't rare; however, it's typically unknown. Even so, the comparatively high prevalence of triple X syndrome, there are several problems nevertheless to be studied in physical and behavioral development up to adulthood. First of all, it might be attention-grabbing to continue the follow-up of the women from the unbiased longitudinal studies and begin new cohorts of longitudinal studies. In the medical analysis, it might be attention-grabbing to check the relation between low shallowness and paranoid ideations.

Additionally, the ties between auditory-processing disorders, language development might yield insight into the event of difficulties in forming successful relationships and the way to be treated. The method of sex chromosome inactivation in chromosomal aberration X and different scientific problems needs to be studied. During this study, the pathology might yield additional insight.

Above all, any study is required to determine evidence-based treatment and support protocols in physical treatments (endocrinological treatment, fertility problems, and treatment in cases of seizures and brain abnormalities with an electroencephalogram, etc.), academic support, and psychological treatment, like psychotherapy and group psychotherapy. If this could easily be that if there aren't significant symptoms like organ failure or significant psychological issues or challenges with infertility, the female with triple X could relatively live quite a healthy life with average family and kids as it is not inherited from mother to children.

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