Mosaic Turner Syndrome - A Case Report

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ABSTRACT

Mosaic Turner Syndrome is a chromosomal disorder characterized by the presence of two or more different cell lines, typically involving a mixture of normal (46,XX) and abnormal (45,X) karyotypes. This condition affects approximately 1 in 2,500 live female births worldwide. Unlike the classic form of TS, which presents with a uniform 45, X karyotype, Mosaic Turner Syndrome exhibits a mosaic pattern that can result in a wide spectrum of clinical manifestations. Fetus with Mosaic Turner Syndrome may exhibit a range of phenotypic features, including cystic hygroma, congenital heart defects, and growth disorders. The variability in clinical presentation underscores the importance of comprehensive prenatal evaluation and monitoring. Early detection and intervention can significantly improve outcomes and provide valuable insights into the natural history and progression of the syndrome. The objective of the present study was to study a rare mutation associated with sex chromosome aneuploidy and mosaicism of Y chromosome. By examining case study and current research, we seek to enhance our understanding of this complex condition and contribute to the development of effective prenatal management strategies.

Keywords: Mosaicism; Turner syndrome; Mosaic turner syndrome; Karyotype; Chromosome; Aneuploidy

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INTRODUCTION

TS (TS) is the most common sex chromosome abnormality in females in approximately 1 in 2500 live births [1]. Although about 50% of the cases have classical karyotype 45X, another half of them may present with chromosomal abnormalities containing karyotypes with an X-isochromosome or ring X, or mosaicisms. 45XO mosaicism is a rare mutation that is associated with sex chromosome aneuploidy and mosaicism of the Y chromosome. Mosaic Turner Syndrome (MTS) happens when the sex chromosomes do not divide properly during early fetal development [2]. One common type is 45,X/46,XX, which means some cells have only one X chromosome (45,X) and others have the usual two (46,XX). People with this mosaic pattern often have milder symptoms compared to those with only one X chromosome. There are also other rare mosaic patterns like 45,X/47,XXX, 45,X/47,XXY, and 45,X/48,XXXX. These involve additional chromosomal changes beyond the typical 45,X pattern, leading to a variety of symptoms and challenges in diagnosis

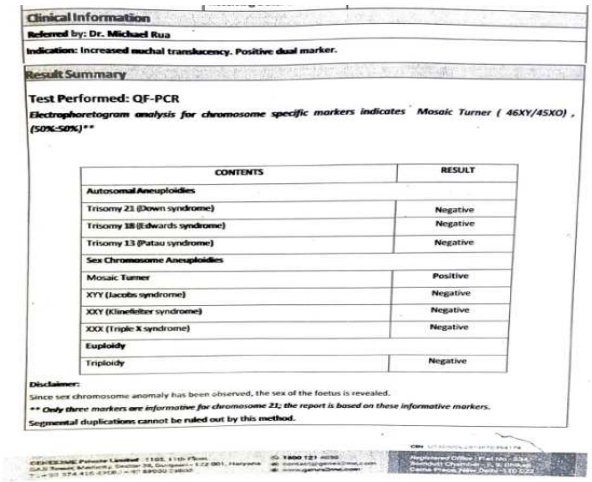
and treatment [3]. The clinical manifestations may range from partial virilization and ambiguous genitalia at birth to patients with a completely male or female phenotype [2]. The objective of the study was to study a rare mutation associated with sex chromosome aneuploidy and mosaicism of Y chromosome.

CASE REPORT

An autopsy was performed on 13^{+5} weeks male fetus in the department of Anatomy, GMCH, 32, Chandigarh after obtaining informed consent from parents. The fetus was obtained from the Department of Obstetrics and Gynaecology, GMCH-32, Chandigarh after medical termination of pregnancy. The mother was 25 years old with G_3A_2 obstetrical history. The maternal and family history indicated no chromosomal abnormality or any drug exposure. The mother was fully vaccinated for tetanus toxoid and had folic acid intake during the first trimester. There was no history of alcohol intake or smoking in both parents. The fetus was examined externally and photographs were taken. The internal examination was done according to autopsy protocol.

The ultrasound scans indicated maternal cervix length 3.6CMs, internal os closed and no fluid seen in the cervical canal. The fetal anatomy on ultrasound showed thickened nuchal translucency measuring approximately 3.9 mm and reversal of A wave in ductus venosus.

QF-PCR Report: Electrophoretogram analysis for chromosome specific markers indicated negative results for autosomal aneuploidies but positive for MTS (Figure 1). CMA test confirmed the pathogenic interpretation of the MTS (Figure 2) with karyogram showing 45 XO (Figure 3).



Clinical Information

Referred by: Dr. Michael Rua

Indication: Increased nuchal translucency. Positive dual marker.

Result Summary

Test Performed: QF-PCR

Electrophoretogram analysis for chromosome specific markers indicates Mosaic Turner (46XY/45XO) , (50%:50%)**

CONTENTS	RESULT
Autosomal Aneuploidies	
Trisomy 21 (Down syndrome)	Negative
Trisomy 18 (Edwards syndrome)	Negative
Trisomy 13 (Patau syndrome)	Negative
Sex Chromosome Aneuploidies	
Mosaic Turner	Positive
XYY (Jacobs syndrome)	Negative
XXY (Klinefelter syndrome)	Negative
XXX (Triple X syndrome)	Negative
Euploidy	
Triploidy	Negative

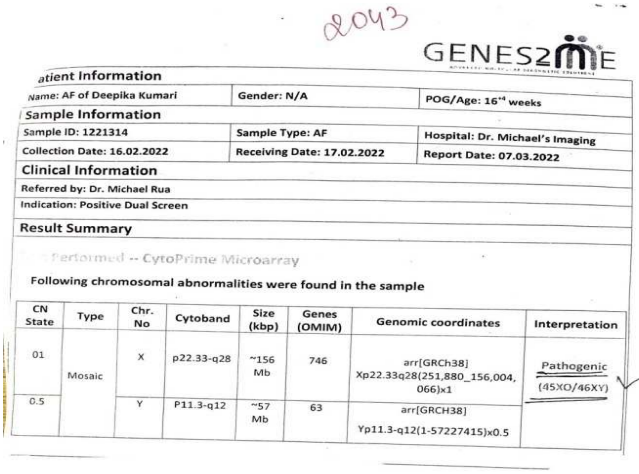
Disclaimer:

Since sex chromosome anomaly has been observed, the sex of the foetus is revealed.

***** Only three markers are informative for chromosome 21; the report is based on these informative markers.***

Segmental duplication cannot be ruled out by this method.

Figure 1: Electrophoretogram analysis for chromosome specific markers indicating positive result for Turner Mosaic.



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GENES2ME

Patient Information

Name: AF of Deepika Kumari	Gender: N/A	POG/Age: 16^{+4} weeks

Sample Information

Sample ID: 1221314	Sample Type: AF	Hospital: Dr. Michael's Imaging
Collection Date: 16.02.2022	Receiving Date: 17.02.2022	Report Date: 07.03.2022

Clinical Information

Referred by: Dr. Michael Rua

Indication: Positive Dual Screen

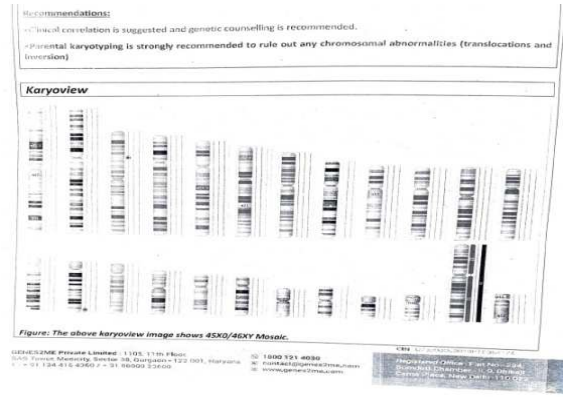
Result Summary

Performed -- CytoPrime Microarray

Following chromosomal abnormalities were found in the sample

CN State	Type	Chr. No	Cytoband	Size (kbp)	Genes (OMIM)	Genomic coordinates	Interpretation
01	Mosaic	X	p22.33-q28	~156 Mb	746	arr[GRCh38] Xp22.33q28(251,880_156,004,066)x1	Pathogenic (45XO/46XY)
0.5		Y	P11.3-q12	~57 Mb	63	arr[GRCH38] Yp11.3-q12(1-57227415)x0.5	

Figure 2: CMA test confirming the pathogenic interpretation of the Mosaic Turner.



Recommendations:

•Clinical correlation is suggested and genetic counselling is recommended.

•Parental karyotyping is strongly recommended to rule out any chromosomal abnormalities (translocations and inversion)

Karyoview

Figure: The above karyoview image shows 45XO/46XY Mosaic.

Figure 3: karyogram showing Mosaic Turner45 XO.

RESULTS

The external examination of the fetus revealed enlarged genital tubercle (Figure 4). The internal examination of the genitourinary system showed absence of right kidney with ureter and testis (Figure 5). There was no evidence of another associated anomaly in other systems.

Figure 4: Enlarged genital tubercle.

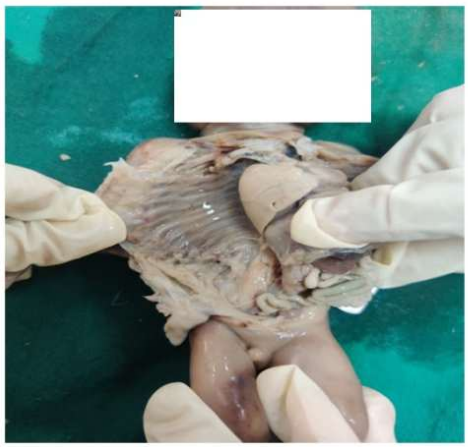


Figure 5: Absence of right kidney, ureter and testis.

DISCUSSION

TS is a condition where one of the X chromosomes is missing or has a structural anomaly. It is characterized by short stature, delayed puberty, primary amenorrhea (absence of menstruation), a webbed neck, and an outward bend of the arms at the elbows (cubitus valgus). The main causes of TS are errors during cell division, such as nondisjunction (failure of chromosomes to separate) and chromosomal lag or loss [4]. The incidence of 45, X in spontaneous abortions is high. In about 70% of cases, the single X chromosome is inherited from the mother, meaning the error usually occurs in the paternal chromosome [5]. The reason for the high frequency of X or Y chromosome loss is unknown. It is also unclear why the 45, X karyotype is often lethal before birth but can be compatible with life after birth. The genes responsible for TS are likely located on the X and Y chromosomes and may escape X inactivation [5]. Isochromosome formation, where a chromosome has two identical arms, can occur through two mechanisms: division through the centromere during meiosis II or exchange involving one arm of a chromosome and its homolog. The Xq isochromosome is linked to autoimmune disorders but not congenital abnormalities [6,7]. The clinical presentation of TS varies widely. The phenotype (observable traits) is not always predicted by the genotype (genetic makeup), especially in cases of mosaicism. In mosaicism, the severity of symptoms depends on the ratio and distribution of different cell populations in various tissues and organs [8]. The Congenital malformation of the renal/urinary system is found in approximately 30-40% of TS cases as reported by Abulatan et al. [3] The author reported multicystic dysplastic kidney whereas in our case report the right kidney was absent with ureter. Once a case of TS is diagnosed prenatally, it is essential to do post diagnostic evaluation. The patients diagnosed with TS should undergo an echocardiogram with views of the aortic arch, cytogenetic studies to check for Y chromosome material that could increase the risk of gonadoblastoma, a kidney ultrasound, and be referred to an endocrinologist for future sex hormone replacement and growth hormone therapy.

Furthermore, TS mosaicism with a Y chromosome has been shown to have an increased risk of germ cell tumors like gonadoblastoma and dysgerminoma. In a cohort study that examined cancer incidence in women with TS, it was discovered that the Y-chromosome lineage developed gonadoblastoma of the ovary by 25 years in the group with a cumulative risk of 7.9% [9].

CONCLUSION

The fetus was diagnosed with Mosaic Turner Syndrome (45, XO/46, XY) using Cytoprime Microarray. This diagnosis was confirmed by a fetal autopsy, which supported the genetic analysis findings. The prenatal diagnosis of TS is important to find out the exact genetic defect which is important for genetic counselling.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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