

Double Chromosomal Anomalies in Turner Syndrome: Rare Co-existence of Robertsonian Translocation with Monosomy X and Isochromosome XQ

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ABSTRACT

Background and Aim: The co-existence of a Robertsonian translocation with Turner Syndrome (TS) or variant of Turner Syndrome (isochromosome Xq) is an uncommon phenomenon. In this report we present two cases with double chromosomal anomalies. **Case Report:** In the first case, we present findings from a 19 years old female, detected to harbor classic TS combined with t(13;14) Robertsonian translocation. The second case involves a 13 years old female, with isochromosome Xq10 (a known variant of Turner Syndrome) combined with t(13;14) Robertsonian translocation. **Conclusion:** Literature around double chromosome anomalies were found to be few and our case report is one of the first few to identify structural abnormality of X chromosome (isochromosome X) along with a t(13;14) Robertsonian translocation.

Key words: Turner syndrome, Primary amenorrhea, Karyotype, Robertsonian translocation, Isochromosome XQ.

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INTRODUCTION

Turner syndrome (TS) is a genetic disorder characterized by numerical aneuploidy or structural abnormality of X chromosome that affects 1 in every 2000 live female births. The karyotype designation in round about 50% of TS patients is non-mosaic monosomy X also know as classic Turner [45,X] as observed in case one, followed in frequency by non-mosaic isochromosome Xq [46,X,i(X)(q10)], as observed in case two.^[1,2]

Robertsonian translocations have an approximate incidence rate of 1/1000 births, which makes them one of the most common structural chromosomal rearrangement seen in general population.^[3]

In this report, we discuss two cases of double chromosomal anomalies. The first case with monosomy X and the second case with isochromosome Xq10 and both associated with t(13,14) Robertsonian translocation. To our knowledge Isochromosome Xq and Robertsonian translocation t(13,14) association has not been reported previously in literature.

CASE PRESENTATION

The first case included a 19 years old female, with clinical indication of primary amenorrhea and suspected TS. The second case studied involved a 13 years old female with clinical indication of short stature. Both the patients were referred to our College of American Pathologists (CAP) and National Accreditation Board for Testing and Calibration (NABL) accredited laboratory for chromosome study by karyotyping. All patients were expected to submit a test request from with consent to use their data for research. GTG banded karyotype analysis was performed on peripheral blood lymphocytes cultured in

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RPMI 1640 (Rosewell Park Memorial Institute) medium and stimulated by phytohemagglutinin (PHA). Twenty GTG-banded metaphases were analyzed using the ASI (Applied spectral imaging) software and results were outlined as per the latest ISCN 2016 (International System for Human Cytogenomic Nomenclature) and CAP guidelines.

Case one

The karyotype analysis of the 19 years old female, with clinical indication of primary amenorrhea and suspected TS revealed monosomy X (classic TS). Presence of a Robertsonian translocation between chromosome 13 at region 'q10' and chromosome 14 at region 'q10' was also detected in all the metaphases analyzed (Figure 1). The final chromosome count was found to be 44 and the reported karyotype designation included: 44, X, rob(13;14)(q10;q10).

Case two

The karyotype analysis of the 13 years old female, with clinical indication of short stature revealed one normal X chromosome and an isochromosome on the q arm of another X chromosome at region q10. Presence of a Robertsonian translocation between chromosome 13 at region 'q10' and chromosome 14 at region 'q10' was also detected in all the metaphases analyzed (Figure 2). The final chromosome count was found to be 45 and the reported karyotype designation included: 45,X,i(X)(q10),rob(13;14)(q10;q10).

DISCUSSION

The co-occurrence of Robertsonian translocation with TS or variant of TS (isochromosome Xq) has been rarely reported in literature.^[4,5] Over the past 30 years,

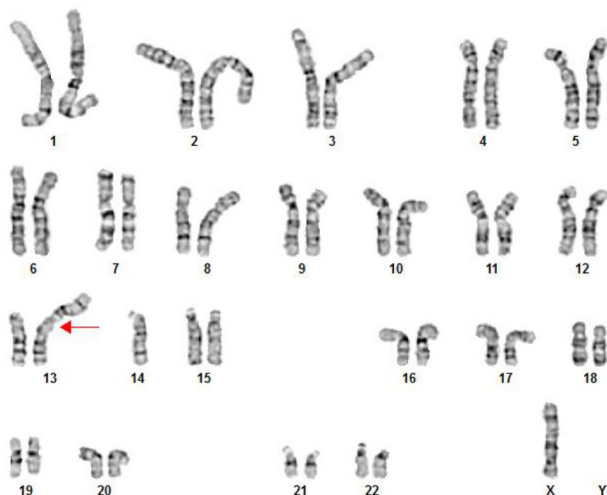


Figure 1: Case one with monosomy X and Robertsonian translocation t(13;14).

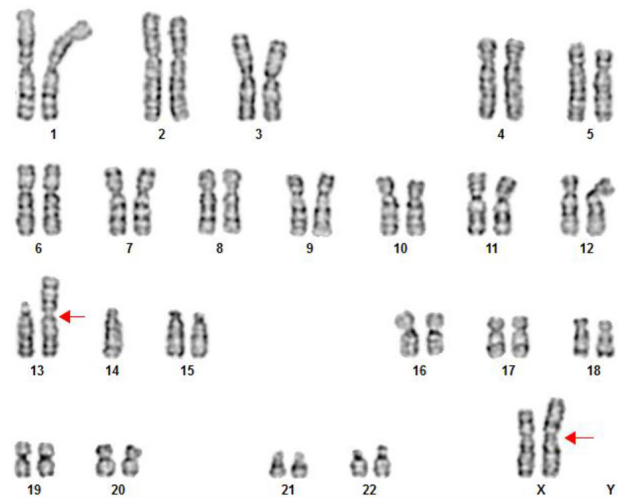


Figure 2: Case two with isochromosome Xq and Robertsonian translocation t(13;14).

cytogenetic studies have revealed, no less than 95% of all TS syndrome patients to exhibit indications of short stature or primary amenorrhea.^[2] Failure of the sex chromatids to separate during meiosis in the parental gametes or in the early embryonic division results in non-disjunction which leads to monosomy X. In majority of the monosomy X cases, the paternal X chromosome is lost and the only copy present is of the maternal origin.^[6] Normally, isochromosome Xq chromosomes are structurally dicentric consisting of proximal Xp material, formed due to chromatid breakage and reunion in proximal Xp. In some patients with Turner syndrome having structural X chromosome aberrations, the parents might also have chromosome X abnormalities in a mosaic state.^[7] Commonness of Robertsonian translocation is essentially a result of similarity in DNA sequences shared by the short arm of acrocentric chromosomes which increases susceptibility to these chromosome rearrangements. We could not obtain parental samples for both the patients for karyotype analysis and hence could not detect if the X chromosome aberration or the Robertsonian translocation were familial or de novo. Literature highlights the most frequently involved chromosomes in such cases of double chromosomal anomalies to be the sex chromosomes and the acrocentric chromosomes (similar to the two cases presented in this report).^[8]

CONCLUSION

In conclusion, double chromosomal anomalies are complex and rare events. Prenatal diagnosis can determine necessity for pregnancy termination, while early diagnosis can improve quality of life, aid in disease management and avert future issues that might transpire during adulthood, for such patients. Parental karyotype should

be encouraged in such cases which might help to rule out possibility of low level numerical/structural X chromosome abnormalities or Robertsonian translocation and also assist the couple in management of further pregnancies. Cytogenetics, thus is an efficient tool to diagnose conditions like TS, isochromosome Xq, Robertsonian translocation with certainty. The authors hope this article would add some insight and contribution to the literature available on co-existence of Robertsonian translocation with TS and its variants.

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CONFLICT OF INTEREST

The authors declare no competing interests.

AUTHOR CONTRIBUTIONS

Concept and design: Dr. Prachi

Data acquisition, analysis and interpretation: Dr. Prachi and Dr. Sandhya

Drafting of the manuscript: Dr. Sandhya

Critical revision of the manuscript: Dr. Prachi

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