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Case Report

Genetics Section

A Case of Partial Trisomy of 10q and Partial Monosomy of 6p Resulting from Maternal t(6;10) (p23;q24)

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ABSTRACT

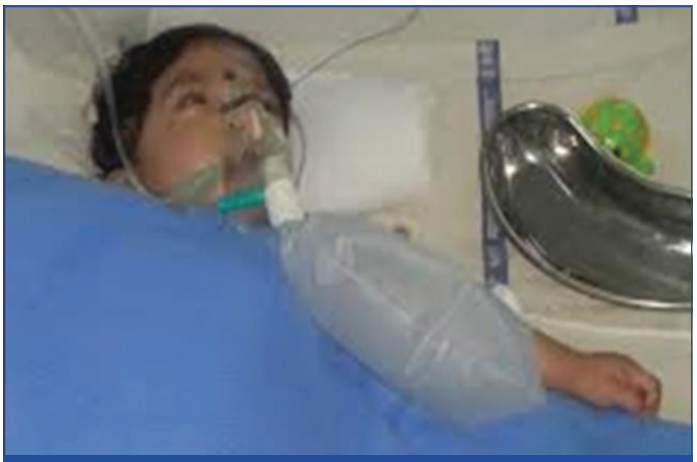
Chromosomal analysis is practiced routinely since long time in congenital malformations to find out structural and or numerical chromosomal aberrations. Translocation is one of the structural chromosomal aberrations where exchange of genetic material between the chromosomes is seen because of two breakpoints. On the basis of involvement of type of chromosome, two different types of translocation are defined. A case of two-year-old girl child with the history of developmental delay, generalised hypotonia and recurrent infections was reported whose cytogenetic analysis showed additional genetic material on 'p' arm of one chromosome 6. To find out the additional genetic material, parental chromosomal study was done which revealed balanced translocation between 'q' arm of chromosome 10 and 'p' arm of chromosome 6 and normal chromosomal pattern in father. Balanced translocation in mother gave rise to formation of derivative chromosome 6 which was transmitted to daughter causing partial trisomy of 10q and partial monosomy of 6p. This gain and loss of genetic material could be the cause of phenotypic features. In the current case, karyotyping was an investigation of choice and offering genetic counselling regarding prenatal diagnosis in future pregnancy was a thoughtful step.

Keywords: Autosomal balanced translocation, Chromosomal analysis, Developmental delay, Karyotyping

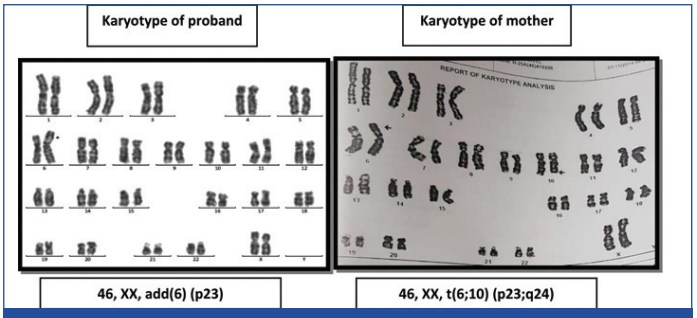
CASE REPORT

A two-year-old girl child was referred to Paediatric Department of a tertiary care Hospital for lower respiratory tract infection. Parents gave history of recurrent respiratory infection for which either they used to go to general practitioner or give home remedies like warm water, honey. They were not able to explain the details of medicines given by general practitioner. The parents were phenotypically normal and there was no history of consanguineous marriage. Parents gave history of abortion at four months because of presence of microcephaly and congenital anomalies of kidney. They could not furnish more details of reports of congenital anomalies. Two years after the abortion the girl child was born at term and gave history of cry immediately after birth. She had microcephaly, round and flat face, depressed nasal bridge [Table/Fig-1]. She had generalised hypotonia and parents gave history of developmental delay. Parents did not visit any hospital after her birth for developmental delay. There was no eye to eye contact. To find out the cause of developmental delay, the blood sample was sent to cytogenetic laboratory of Department of Anatomy. Chromosomal analysis was conducted by a) taking a culture of peripheral blood by using Phytohemagglutinin M Form (PHA) Gibco®, Roswell Park Memorial Institute (RPMI) 1640 media and Foetal Bovine Serum (FBS) (Gibco®) at 37°C for 72 hours; b) harvesting by using colchicine solution, Potassium chloride (KCl) and fixative; c) staining and banding by using Giemsa and trypsin solution; d) analysis by using Metasystem software and current guidelines from International System for Human Cytogenomic Nomenclature (ISCN) [1].

Chromosomal analysis revealed that there is extra genetic material on 'p' arm of chromosome 6 [Table/Fig-2]. To trace the origin of extra genetic material parental chromosomal study was advised. It showed normal male chromosomal pattern for father but mother showed balanced translocation between 'p' arm of 6 and 'q' arm of chromosome 10. The mother's karyotype was 46, XX, t (6;10) (p23;q24) and girls karyotype was 46, XX, add (6) (p23) [Table/Fig-2]. Balanced translocation in mother gave rise to formation of derivative chromosome 6 which was transmitted to daughter causing partial trisomy of 10q and partial monosomy of 6p. Unfortunately, the girl child died because of respiratory distress and so other details could not be found and molecular techniques could not be applied.



[Table/Fig-1]: Photograph showing phenotypic features of proband.



[Table/Fig-2]: Karyotype of proband and mother.

DISCUSSION

Translocation is a chromosomal aberration where changing location of part of or whole chromosome, joining other chromosome and resulting in formation or not formation of new chromosome with or without genetic loss occurs. Robertsonian and reciprocal are

the two types of translocations where break points are seen in homologous or non homologous acrocentric chromosomes and non homologous chromosomes with at least one of them being a non acrocentric chromosomes and interchange of chromosomal fragments between them respectively [2,3]. Unless one or both of the chromosomal breakpoints involve an important functional gene, these balanced chromosomal re-arrangements would not produce a significant phenotypic effect either [4]. All the chromosomes in human body are prone to break and join with other chromosomes leading to translocation and this activity is unplanned [4]. Person will be phenotypically normal where there is no loss of genetic material. Breaking and joining of part of chromosome results into formation of two derivative chromosomes with no gain or loss of genetic material.

Balanced reciprocal translocations usually get diagnosed when couples present with infertility, recurrent abortions and or history of child with congenital anomalies. Recognition of carrier status in balanced translocation is crucial to know as formation of possibility of defective gametes in the translocation carrier rises which may be responsible for recurrent abortions or congenital anomalies [5]. Formation of trisomy or monosomy of part of chromosome may lead to congenital malformations and abnormal phenotypic features. Chromosomal translocations are among the most common genetic abnormalities in humans [6]. The incidence of balanced translocation is 0.29% [7], 0.6% in infertile couples, 9.2% in patients with recurrent abortions [5] and 0.08-0.3% in general population [8]. Individuals carrying balanced translocation may have offspring with unbalanced karyotype. This may result in symptoms ranging from mild to severe mental retardation with multiple congenital defects depending on the chromosomes involved [9].

Presence of partial trisomy of chromosome 10 and partial monosomy of chromosome 6 together is rare. In the present case additional genetic material on 'p' arm of one chromosome 6 in two years old girl child with the history of developmental delay, generalised hypotonia and recurrent infections is discussed. This chromosomal aberration is resulted from maternal t (6;10) (p23;q24) which generated partial trisomy 10(q24qter) and partial monosomy 6(p23pter) in the child. There may be no loss or gain of gene so mother did not show any clinical features and or motor involvement, but at least one breakage in the chromosome must have occurred in the process of translocation which may have resulted into loss of some nucleotides causing alteration in normal gene. Some change at the functional level of gene is expected as mother gives history of first abortion. It is observed that faulty oocyte with abnormal genetic makeup may be resulted in case of female carriers of chromosomal translocation due to progression in the process of oogenesis which is devoid of an arrest in meiosis and this may lead to aneuploidies in the conceptus [10]. There may be higher chance of formation of unbalanced gametes which may end up in abortion or child with developmental delay. Production of normal or faulty gametes depends upon chromosome and breakpoint of chromosome involved [11]. In the present case, the child had inherited derivative chromosome 6 and normal chromosome 10 from mother. The derivative chromosome 6 was formed by fusing 6p and 10q. This fusion occurs at chromosome 6 at 6 (p23) positions which results in partial monosomy of 6 (p23pter) and partial trisomy of 10(q24qter). Combined effect of the excess amount of gene of 10(q24qter) (distal trisomy of 10q) and deletion of gene of 6 (p23) may be responsible for child's developmental delay and other phenotypic features.

Partial monosomy of 6p is also rare to see. Partial trisomy of long arm of chromosome 10 was first described in 1965 [12]. Monosomy and or trisomy observed may be because of translocation of chromosome of 10, 6 and other autosomes [13]. It is a rare condition which is associated with variety of clinical features. In the current case it is formed because of inheritance of derivative chromosome 6 from maternal balanced translocation t (6;10). During reciprocal translocation between p arm of chromosome 6 and q arm of chromosome 10 being formed, the re-arrangement may get generated in terminal part of 6p and deletion of 6p23 may occur which may lead to monosomy of 6p23 as one set of 6p23 is now present on the other normal chromosome 6.

Location of breakpoint in chromosome and alteration in the gene content during reciprocal translocation decides the clinical features. It is observed that deletions of 6(p23pter) is associated with microcephaly, genital anomalies, language impairment, and delayed motor development [14], dysmorphic features like presence of epicanthic fold, low set ear, deformed ear, high arched palate, flat occiput [15] hypotonia, developmental delay, eye abnormalities, defects in heart and kidney [16]. Plenty of genes are located on chromosome band 10q24 which are seen linked to developmental and neurological disorders, tumourigenesis and hormone metabolism [17]. Developmental delay to varying degree is present and most cases also display somatic growth delay. Patients with trisomy 10(q24qter) tend to have more severe clinical features such as heart or renal abnormalities [14]. In the current case, the child showed similar features of developmental delay, hypotonia and dysmorphic features like round and flat face, depressed nasal bridge. The presence of clinical features is combined effect of partial trisomy of chromosome 10 and partial monosomy of chromosome 6. Similar to the present case, balanced translocation between 6p23 and 10q24 was documented in mother and an unbalanced rearrangement, der(6) t(6:10) (p23;q24) mat, in the 30-day-old male child. The child has inherited a derivative chromosome 6 with partial deletion of 6(p23pter) and partial trisomy 10(q24qter), which has resulted in fusion of genes of two different chromosomes. Clinical features like depressed nasal bridge, high forehead, agenesis of left ear, atrial septal defect, craniosynostosis and growth retardation were observed in deletion of 'p' arm of chromosome 6 [15]. In most of the cases where trisomy 10q is seen because of translocation of 10q is derived from father. It is observed that life is more compatible with syndromes where paternal reciprocal translocation is seen and this may be because of withdrawal of imprinting effect [18]. In the present case, the inheritance is from maternal side and early death of patient may follow the imprinting effect which shows non compatible with life.

Molecular karyotype of the patient is useful to identify involvement of exact gene and co-relate with phenotypic features. In the current case, molecular study was not possible because of early death of the patient. Parents with autosomal balanced translocation should be advised to take genetic counseling and importance of prenatal diagnosis should be explained in detail to reduce further incidence in the family.

CONCLUSION(S)

It is essential to conjecture that the clinical expression of the child was because of extragenetic material from trisomy of 10q and monosomy of 6p, which was resulted from balanced translocation in mother. Felicitous genetic counselling regarding prenatal diagnosis in future pregnancy to prevent recurrence should be emphasised.

REFERENCES

[1] McGowan Jordan J, Simons A, Michael S. An International System for Human Cytogenomic Nomenclature, structural chromosomal arrangements, translocation, Kargar publication, 2016, pp 75.
[2] Lubs HA, Ruddle FH. Chromosomal abnormalities in the human population: Estimation of rates based on new haven newborn study. Science. 1970;169(3944):495-97.
[3] Kim SR, Shaffer LG. Robertsonian translocations: Mechanism of formation, aneuploidy and uniparental disomy and diagnostic considerations. Genet Test. 2002;6:163-68.
[4] Paththinige CS, Sirisena ND, Kariyawasam UGIU, Dissanayake VHW. The frequency and spectrum of chromosome translocations in a cohort of Sri Lankans. Biomed Research International. 2019;2019:9797104. https://doi.org/10.1155/2019/9797104.
[5] Tilak P. Effect of reciprocal translocation on phenotypic abnormalities. International Journal of Human Genetics. 2010;10:113-19. https://doi.org/10.1080/09723757.2010.11886094.

[6] Stern C. Chromosome translocations in couples with in-vitro fertilization implantation failure. Hum Reprod. 1999;14:2097-101.
[7] Vasileuska M. The incidence and type of chromosomal translocation from prenatal diagnosis of 3800 patients with Republic of Macedonia. Balkan J Med Genet. 2013;16(2):23-28.
[8] Kochhar PK. Reproductive outcome of couples with recurrent miscarriage and balanced chromosomal abnormalities. J Obstet Gynaecol Res. 2013;39(1):113-20.
[9] Kukolich MK, Estabrooks LL, Martin SL. Chromosome abnormalities due to maternal translocations not detected with routine amniocentesis. Genetics in Medicine. 1999;1:46.
[10] Hunt PA, Hassold TJ. Sex matters in meiosis. Science. 2002;296(5576):2181-83.
[11] Burns JP. Analysis of meiotic segregation in a man heterozygous for two reciprocal translocations using the hamster in vitro penetration system. Am J Hum Genet. 1986;38:945-64.
[12] De Grouchy J. Translocation 6-12, 13-15 et trisomy partielle 6-12 (probablement10). Ann Genet. 1965;8:16-20.
[13] Davis J. 10q trisomy syndrome with unusual cardiac and pulmonary abnormalities. J Med Genet. 1998;35(1):72-74.
[14] Liu HY, Huang J, Li T, Wu D, Wang HD, Wang Y, et al. Clinical and molecular cytogenetic analyses of four patients with imbalanced translocations. Mol Cytogenet. 2016;9:31.
[15] Klein OD. Case report: Y; 6 translocation with deletion of 6p. Clinical Dysmorphology. 2005;14(2):93-96.
[16] Ganguli B. Clinical expression of an inherited unbalanced translocation in chromosome 6. Case Reports in Genetics. 2011;1-4.
[17] Davies AF. Delineation of two distinct 6p deletion syndrome. Hum Genet. 1999;104(1):64-72.
[18] Hou JW. Chromosomal 10q26 Trisomy resulting from paternal t(9;10) (pter;q26.1). J Formos Med Assoc. 2003;102:887-92.

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