*Iran J Public Health, Vol. 45, No.3, Mar 2016, pp.376-380*

**Case Report**

# Newborn with Supernumerary Marker Chromosome Derived from Chromosomes 11 And 22- A Case Report

***Mohammad Yahya VAHIDI MEHRJARDI [1, 2], Masoud DEHGHAN TEZERJANI [3], Mahmoud NORI-SHADKAM [4], Seyed Mehdi KALANTAR [2, 3], *Mohammadreza DEHGHANI [1, 3]***

1. *Medical Genetics Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran*
2. *Dept. of Medical Genetics, Shahid Sadoughi University of Medical Sciences, Yazd, Iran*
3. *Research and Clinical Center for Infertility, Shahid Sadoughi University of Medical Sciences, Yazd, Iran*
4. *Dept. of Pediatrics, Shahid Sadoughi University of Medical Sciences, Yazd, Iran*

***Corresponding Author:** Email: mrezdehghani@gmail.com

**(Received 14 Jul 2015; accepted 11 Nov 2015)**

**Abstract**

The interpretation of supernumerary chromosome is important for genetic counseling and prognosis. Here, we used SNP array and conventional karyotyping method to identify a denovo marker chromosome originated from chromosome 22 and 11 in a newborn transferred to the Neonatal Intensive Care Unit of Shahid Sadoughi Hospital in 2015. Clinical abnormalities identified in the newborn were dysmorphic face, intrauterine growth retardation, atrial septal defect (ASD), the hypoplasia of corpus callosum and septum pellucidum. These clinical abnormalities can be related to this marker, and it may help genetic counselor for predicting abnormality risk in susceptible individuals as well as prenatal diagnosis.

**Keywords:** Supernumerary marker chromosomes, Karyotype, SNP array, Partial trisomy 22, Partial trisomy 11

## Introduction

A supernumerary marker chromosome (SMC) is a chromosomal fragment or a marker that originates from other chromosomes and found in addition to the 46 normal chromosomes. Because SMCs are so small, their origin cannot be determined by conventional cytogenetic technique, and new molecular cytogenetic techniques are necessary for their identification (1-3). SMCs are found in 0.4-1.5/1,000 of prenatal diagnosis and 0.66/1,000 in newborns. They are more prevalent in mentally delayed populations with the frequency of 3.27/1,000 (4). Although SMCs are associated with phenotypic heterogeneity such as congenital abnormalities, abnormal sexual development, and mental impairment (5), they can also be found in the individuals with a normal phenotype. Hence, determining of the risk of an abnormal phenotype associated with SMCs is difficult, especially when they happen as denovo cases (6). The clinical variability is related to SMCs depends on their size, euchromatic pattern, mosaicism and uniparental disomy. Therefore, characterization of their structure is necessary for predicting clinical feature and prognosis (7, 8).

Here, we report a new born with SMC confirmed to be dup (22) (q11.1 - q11.21), dup (11) (q23.3 - q25) by SNP array. To our knowledge, this case with SMC is the first one with combination of partial trisomy 22q and trisomy 11q.

## Case Report

The patient, a twenty-d-old baby girl, was born by vaginal delivery at 37-week gestation because of second pregnancy. The first child was a 5-yr-old boy and he had no sign of clinical abnormality. The mother (27 yr old) and the father (30 yr old) were healthy and nonconsanguineous couple. The patient birth weight was 2.300 g, length 49 cm, and head circumference 33 cm. Because of difficulties in breathing after delivery, she was transferred to the Neonatal Intensive Care Unit of Shahid Sadoughi Hospital, Yazd, Iran, 2015. The baby died after one day because of respiratory arrest.

Clinical examination showed that the child had a variety of abnormal clinical features including intrauterine growth retardation, frontal bossing, broad nasal bridge, low set and dysplastic ears with a skin tag, cleft palate, premature sutures and bottom feet (Fig. 1). Echocardiogram showed atrial septal defect (ASD) and systolic ejection of the left ventricle. Brain sonography revealed the hypoplasia of the corpus callosum and septum pellucidum. Peripapillary atrophy was remarkable according to ophthalmologic examination. Laboratory result for metabolic screening and congenital infections were normal. Sonography indicated that genital tract and kidneys were normal.

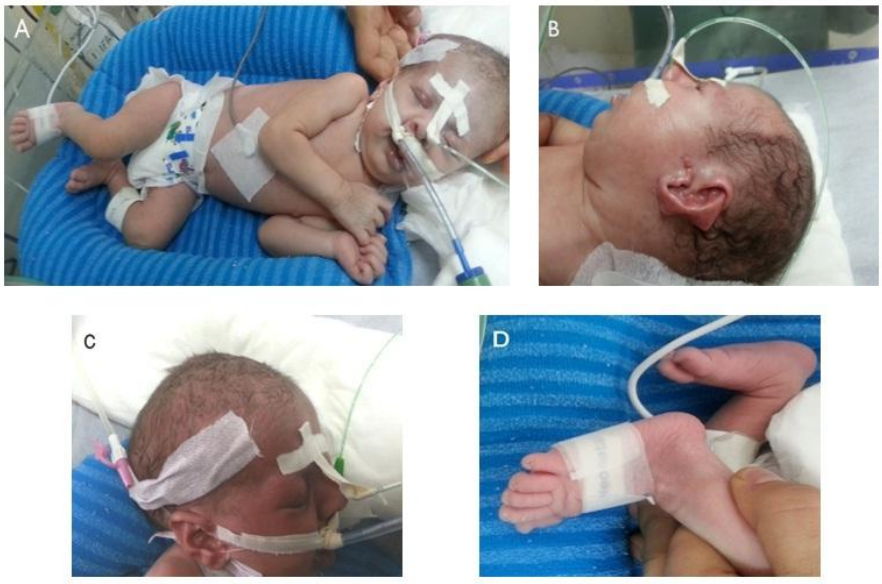


**Fig. 1:** Clinical features of the case A: dysmorphic features B: auricular tags C: frontal bossing D: Rocker bottom feet

The study was approved by the local Ethics Committee of Shahid Sadoughi University of Medical Sciences and written informed consent was obtained from patient's parents.

Cytogenetic analyses were performed using peripheral blood of the patient and her parents according to standard phytohemagglutinin-stimulated lymphocyte and G-banding. The initial evaluation of the newborn karyotype revealed 47, XX,+mar (Fig. 2). For identification of the marker chromosome structure and origin, Single Nucleotide Polymorphism (SNP) array was performed using Illumina Human CytoSNP-12 V2.1 beadchip array. Then Illumina KaryoStudio 1.3 and Genome Studio V2010.2 were used for analyzing of generated data. The SNP array profile indicated the marker chromosome had originated from duplication of chromosome 11 and 22 (47, XX, +mar,arr dup (22) (q11.1 - q11.21), dup(11) ( q23.3 - q25) (Fig. 3). ). After this marker chro-

mosome was identified in the newborn by SNP array, we guessed this marker could be originated form balanced translocation in her parents. However, high-resolution G banding revealed maternal and paternal karyotype was normal. The appearance of marker chromosome indicates denovo chromosome abnormality. The duplicated region of chromosome 22-covered 4626534 bp (over 50 coding genes) and the duplicated region of chromosome 11 covered 18,215,729 bp (over 200 coding genes).

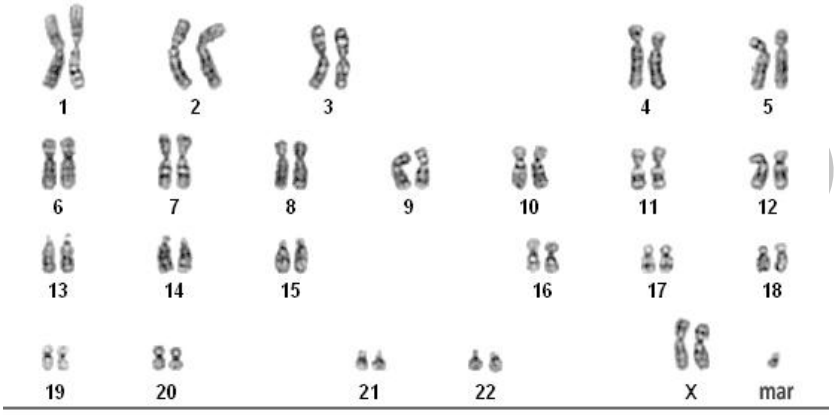


**Fig. 2**: The representative karyotype showing 47,XX,+mar

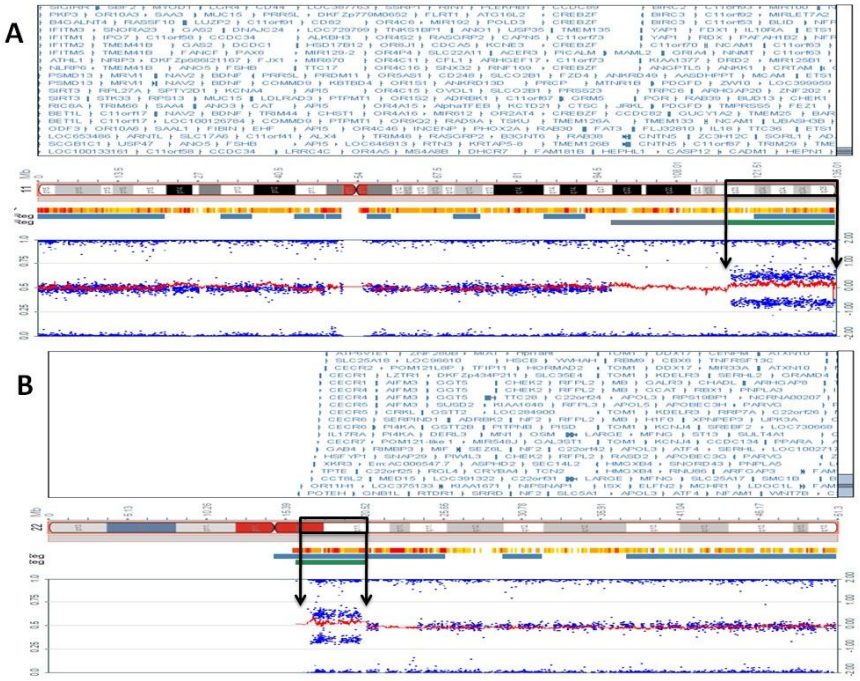


**Fig. 3**: SNP array profile of the case. The image shows **A:** duplication of 11q23.3-q25; 18,215,729 bp 116728277-134944006, **B:** duplication of 22q11.1-q11.21;4626534 bp 16114244-20740778

## Discussion

In order to diagnose a genetic condition, especially chromosomal abnormalities, new molecular techniques such as SNP array need to support conventional cytogenetic study. The SNP array helps genetic counselor for the determining of clinical abnormalities risk and prognosis of affected individuals for future pregnancy by detecting exact range of chromosome aberration and copy number alterations (CNAs) (9). The marker chromosome originated from the duplication of 11q and 22q is a rare constitutional chromosomal abnormality, and according to our knowledge, it has not been reported yet. The interpretation of clinical abnormalities associated with supernumerary chromosomes is difficult, especially when these marker chromosomes diagnosed at the prenatal stage. Denovo marker chromosomes are more likely to cause abnormalities in comparison with inherited chromosomes marker.

The duplication of 22q11.2 region may be clinically significant, since there are several syndromes related to this region such as Cat eye syndrome (CES), a trisomy or tetrasomy of 22q11), DiGeorge syndrome (a microdeletion) and supernumerary der (22) t (11;22) syndrome (10, 11). Previous studies reported duplication of the distal part of 11q as partial trisomy 11q syndrome" or "duplication 11 (q21/q23 →qter) syndromes. The duplicated region 11q23-qter approximately contains two hundred genes with their multiple transcripts. The respiratory problem of our case may be related to ROBO (Roundabout, axon guidance receptor) gene family, located at 11q24.2, which encodes the receptors for the midline repellent slits and play a role in axon guidance. These genes have an important role in regulating of axon guidance across the midline in the brain (12). One of the most important member of this family is ROBO4 (roundabout, axon guidance receptor, homolog 4 [OMIM 607528]) expressed under hypoxic condition at the sites of active angiogenesis (13). Zhao et al. reported four patients with duplication of 11q21–q23.2 region who suffer upper airway anomalies (14). Therefore, the respiratory problem of our case that led to her death can be attributed to the duplication of this region.

## Conclusion

SMC originated from partial trisomy of chromosome 22q and 11q can present dysmorphic face, intrauterine growth retardation, respiratory problem, atrial septal defect (ASD) and the hypoplasia of corpus callosum and septum pellucidum. SNP array technique beside conventional karyotyping method is helpful for identification of copy number variation especially in prenatal diagnosis.

## Ethical considerations

Ethical issues (including plagiarism, obtaining informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

## Acknowledgements

Our research group would like to thank the family of patient for their kind cooperation. The authors declare that there is no conflict of interests.

## References

1. Trifonov V, Fluri S, Binkert F, Nandini A, Anderson J, Rodriguez L, Gross M, Kosyakova N, Mkrtchyan H, Ewers E, Reich D, Weise A, Liehr T (2008). Complex rearranged small supernumerary marker chromosomes (sSMC), three new cases; evidence for an underestimated entity? *Mol Cytogenet*, 1:6.
2. Feenstra I, Koolen DA, Van der Pas J, Hamel BC, Mieloo H, Smeets DF, Van Ravenswaaij CM (2006). Cryptic duplication of the distal segment of 22q due to a translocation (21;22): three case reports and a review of the literature. *Eur J Med Genet*, 49(5):384-395.
3. Ma R, Peng Y, Zhang Y, Xia Y, Tang G, Chang J, Guo R, Gui B, Huang Y, Chen C, Liang D, Wu L (2015). Partial trisomy 2q33.3-q37.3 in a

patient with an inverted duplicated neocentric marker chromosome. *Mol Cytogenet*, 8:10.
4. Viersbach R, Engels H, Schwanitz G (1997). Identification of supernumerary der(20) chromosomes by FISH in three patients. *Am J Med Genet*, 70(3):278-283.
5. Buckton KE, Spowart G, Newton MS, Evans HJ (1985). Forty four probands with an additional "marker" chromosome. *Hum Genet*, 69(4):353-370.
6. Douet-Guilbert N, Marical H, Pinson L, Herry A, Le Bris MJ, Morel F, De Braekeleer M (2007). Characterisation of supernumerary chromosomal markers: a study of 13 cases. *Cytogenet Genome Res*, 116(1-2):18-23.
7. Liehr T, Mrasek K, Weise A et al. (2006). Small supernumerary marker chromosomes--progress towards a genotype-phenotype correlation. *Cytogenet Genome Res*, 112(1-2):23-34.
8. Starke H, Nietzel A, Weise A et al. (2003). Small supernumerary marker chromosomes (SMCs): genotype-phenotype correlation and classification. *Hum Genet*, 114(1):51-67.
9. Szuhai I (2012). *Microarrays in Diagnostics and Biomarker Development* (springer, France).
10. Crolla JA, Howard P, Mitchell C, Long FL, Dennis NR (1997). A molecular and FISH approach to determining karyotype and phenotype correlations in six patients with supernumerary marker(22) chromosomes. *Am J Med Genet*, 72(4):440-447.
11. Jedraszak G, Receveur A, Andrieux J, Mathieu-Dramard M, Copin H, Morin G (2015). Severe psychomotor delay in a severe presentation of cat-eye syndrome. *Case Rep Genet*, 2015:943905.
12. Sabatier C, Plump AS, Le M, Brose K, Tamada A, Murakami F, Lee EY, Tessier-Lavigne M (2004). The divergent Robo family protein rig-1/Robo3 is a negative regulator of slit responsiveness required for midline crossing by commissural axons. *Cell*, 117(2):157-169.
13. Huminiecki L, Gorn M, Suchting S, Poulsom R, Bicknell R (2002). Magic roundabout is a new member of the roundabout receptor family that is endothelial specific and expressed at sites of active angiogenesis. *Genomics*, 79(4):547-552.
14. Zhao HQ, Rope AF, Saal HM, Blough-Pfau RI, Hopkin RJ (2003). Upper airway malformation associated with partial trisomy 11q. *Am J Med Genet A*, 120A(3):331-337.