

Supernumerary Marker Chromosome in a Child with Microcephaly and Mental Retardation

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A *de novo* supernumerary marker chromosome (SMC) was identified in a 13-month-old girl who presented with microcephaly and mild mental retardation. On further characterization by oligo-nucleotide array-comparative genomic hybridization [array-CGH], the SMC was confirmed to be 18p.

Key Words: Array-CGH, Constitutional disorders, Supernumerary marker chromosome, Microcephaly, Trisomy 18p.

Supernumerary marker chromosomes (SMC) form a heterogeneous group of chromosomes with an incidence of 0.044% in the general population and increases up to 7 times more frequent in mentally challenged population(1). This suggests that SMC influences the clinical manifestation and need proper characterization. Majority of the SMCs are derived from acrocentric chromosomes having satellited or bisatellited constriction and around half are derived from chromosome 15. Non-acrocentric SMCs are comparatively rare and 30% are coupled with phenotypic effects(2). Various reports describe origin of SMC to be derived from all the human chromosomes, they are parentally inherited or *de novo* and linked with vast clinical features from normal to extremely mild to severe(3). Recently it has been recognised that every SMC, though cytogenetically similar, have unique breakpoints(4). This could be one of the reasons why it is so difficult to build a correct phenotype-genotype correlation for each marker.

CASE REPORT

The proband, a 13-month-old girl, was referred for microcephaly and delayed psychomotor development. She was the first child born to the non-

consanguineous parents by cesarean section (birth weight: 2500g; head circumference: 32 cm). She had cranial microcephaly and neonatal hypotonia followed by hypertonia, jitteriness, apnea, and seizures. First sleep electroencephalogram report at 11 months showed epileptiform abnormality from occipital region. She had delayed psychomotor development first observed at four months and confirmed at 11 months. At the time of presentation, her height was 61.5 cm, head circumference 42.5cm and weight 4.2 Kg. She had torticollis with deviation of head to right side, ocular hypertelorism, pseudosquint eyes, clinodactyly and left simian crease. At the age of 16 months, she could sit on her own, stand and walk with support.

Cytogenetic study was carried out using peripheral blood lymphocyte by GTG-banding according to the standard procedure and 50 G-band metaphases were analyzed. Metaphases revealed female karyotype with presence of supernumerary marker chromosome in all analyzed cells i.e. 47,XX,+mar (**Figure 1**). No mosaicism was detected. Parental karyotype was normal, confirming *de novo* origin of SMC in the proband. SMC was further characterized with oligonucleotide array-CGH from Agilent(tm) using 44,000 probes showing 15 Mb duplication from 18pter to 18p11.21.

However, further confirmation of array-CGH results by FISH was not carried out.

DISCUSSION

SMC occurring as a pure trisomy 18p is an infrequent observation. The most common phenotypic association is of non-characteristic facial appearance and subnormal mental development, foot or hand abnormalities and craniofacial anomalies(5). Till date, 23 cases of trisomy 18p have been published with different origin like unbalanced segregation due to balanced parental translocation in 10 cases(6), direct tandem duplication in 6 cases(7), complex chromosomal anomalies in 3 cases(8) and SMC in four cases(5,9,10).

The occurrence of SMC is seven times more in subjects with developmental delay, which indicates the influence of SMC on phenotype. Majority of the SMC are acrocentric in origin with 50% from chromosome 15(9). Some are inherited and transmitted without clinical manifestations. This is because the gain or loss of p arm of acrocentric chromosome containing Nucleolar Organizing Region [NOR] region are less associated with clinically abnormal phenotypic manifestations due to less functional genes involved in that region [7% vs. 28% derived from non-acrocentric chromosome](2). In the present case, the SMC is due to trisomy 18p as revealed by array-CGH study and of *de novo* origin. The critical region for most trisomy 18 cases has been demonstrated at 18q while trisomy of chromosome 18 short arm does not have serious clinical repercussions. This duplication involves about 67 genes.

The present report demonstrates SMC as trisomy 18p of *de novo* origin. It also confirms that trisomy 18p is associated with subtle phenotypic expression in addition to mild mental retardation. Moreover, such cases could have been missed in absence of oligonucleotide micro-array assay.

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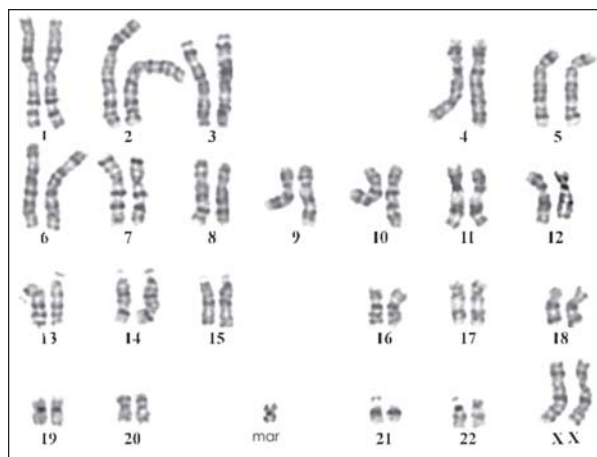


FIG.1 G-banded karyotype showing the marker chromosome.

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