Complex Chromosomal Rearrangement der(5)ins(5;3)(q31;q25q29), t(3;12)(q24;p12.2) In A Dysmorphic Child, - A Case Report

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Complex chromosome rearrangements (CCRs) are structural aberrations or rearrangements involving three or more cytogenetics breakpoints on two or more chromosomes [1]. Balanced and unbalanced are known to have significant risk of mental retardation and phenotypic anomalies. CCRs are also associated with infertility in males and recurrent abortion in females. Here we report one case of apparently balanced CCR involving three chromosomes 3, 5 and 12 in a child with abnormal features. G banding and FISH were performed to clarify the nature of this complex abnormality.

The proband was a 3 years old Malay girl, referred for cytogenetic analysis due to abnormal features. She was very short at 5th centile, has triangular facies, strabismus, short neck and had significant delay in speech. Blood investigations including full blood count, serum amino acid, renal, liver and thyroid function tests were normal. There was no history of mental retardation, congenital malformation, or recurrent miscarriages in either family. Peripheral blood lymphocytes of the proband was cultured and chromosome preparations were made as per standard procedures. Karyotype analysis was carried out based on ISCN (2016). Fluorescence in situ hybridisation (FISH) technique was carried out using Whole Chromosome Painting Probes (WCP) for chromosome 3, 5 and 12 as per standard procedures. Cytogenetic analysis on 32 GTG banded metaphases at the resolution level of 400-550 bphs showed 46,XX,der(5)ins(5;3)(q31;q25q29),t(3;12)(q24;p12.2) complex karyotype pattern (Figure 1). This abnormal karyotype showed derivative chromosome 5 resulting from an insertion of a segment 3q25q29 from the long arm of chromosome 3 into the long arm of chromosome 5 at band 5q31. The segment is replaced by translocation of a segment 12p12.2 from the short arm of chromosome 12 to the chromosome 3 at band 3q24. This three way translocations has been confirmed by FISH using WCP for chromosome 3, 5 and 12 (Figure 2).

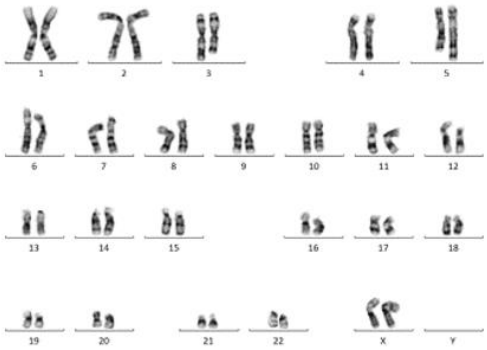

Fig. 1: Karyotye showing 46,XX,der(5)ins(5;3)(q31;q25q29),t(3;12)(q24;p12.2) complex karyotype pattern

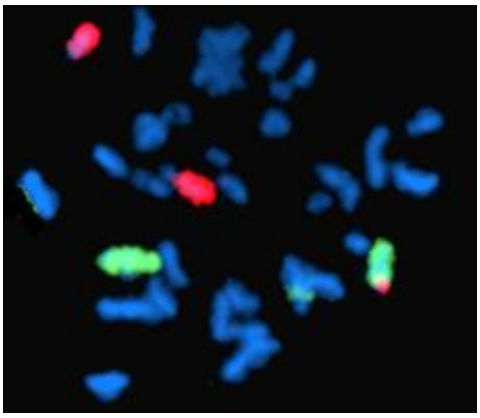

Fig. 2: FISH metaphase stained by WCP probes specific for chromosomes 3 (Green) and 12 (Red) showed the segment of chromosomes 12 distal to 12p12.2 has been translocated onto chromosome 3 at band 3q24. Part of chromosome 3 from 3q25 to 3q29 was translocated and inserted at band 5q31 of chromosome 5**.**

CCRs are very rare events in the human population that can be inherited or de novo and can be balanced or imbalanced. Balanced CCRs can lead to an unbalanced condition of gametes during meiosis. Most de novo CCRs originate from spermatogenesis and cause mental retardation in high incidence, whereas most familial CCRs are of maternal origin and usually have three to four breakpoints [2]. This proband had CCRs with 4 chromosomal breakpoints and involved three chromosomes. The abnormal features in this present case might be attributable to gene disruption, cryptic imbalances and/or from position effects of genes. Recently, FISH with specific DNA probes for whole chromosomes or for indicated specific chromosomal segments, has significantly improved the characterization of CCRs [3]. Although FISH contributes in elucidating the complexity of CCR, painting FISH is limited in detecting submicroscopic deletions or identifying changes due to gene position effect.

There are several mechanisms that leads to chromosomal rearrangements. A simultaneous double stranded DNA breaks were induced by unknown stimulus including free radiation or ionizing radiation, followed by joining of the break fragments in the wrong place due to microhomology shared by these regions [1]. The origin of the complex translocation in the present case, whether inherited or de novo, could not be established due to lack of consent of parents for the cytogenetic examination.

Keywords: Complex Chromosomal Rearrangements (CCRs)

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