

The co-occurrence of specific chromosome abnormalities, which are responsible for recognizable syndromes create phenotypic effects that more or less reflect and combine the characteristics of each individual one. Such mixed phenotypes may be particularly difficult to clarify in newborns and infants when the particular symptoms are not yet that distinctive. We present the case of a 6-week old girl with various such ambiguous abnormalities in whom a CytoScanHD SNP-array (Affymetrix®) analysis revealed a 3,98 Mb heterozygous deletion of telomeric 4p and a 3,4 Mb duplication of telomeric 11p regions. Such abnormalities are typically encountered in Wolf-Hirschhorn (WHS) and, depending on the parental origin of the duplicated segment, in specific forms of Beckwith-Wiedemann (BWS) or Russel-Silver syndrome (RSS), respectively. To distinguish between the later two options we performed a multiplex methylation-specific PCR analysis of the promoter regions of the H19 and KCNQ1OT1 genes that enabled us to quantify the copy numbers of the methylated and unmethylated alleles. This analysis revealed that the paternal allele was duplicated, which is a known but extremely rare cause of BWS. This result also implies that the girls unbalanced deletion/duplication abnormality may have been inherited from her father who presumably carries a balanced t(4p;11p). The respective analyses to verify this notion are currently underway. Our notion is further supported by the fact that the one or the other parent of 4 from 5 cases with an analogous unbalanced translocation and a mixed WHS/BWS or WHS/RSS phenotype reported so far was a balanced translocation carrier. The sixth case with such an unbalanced t(4p;11p) reported herein suggests that such recurrent abnormalities result from nonrandom breakpoint events the underlying predisposing genomic structure of which still needs to be determined.

1.P66

Complex chromosome rearrangement involving Xp21 band in a girl with a syndromic Duchenne muscular dystrophy.

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Complex chromosome rearrangements (CCR) are rare structural chromosome aberrations involving more than

two breakpoints located on more than two chromosomes. Most of them are reported to be de novo. In such cases, CCR involve more breakpoints and more chromosomes than in familial cases. CCR can be found in phenotypically normal patients presenting, however, recurrent miscarriages or infertility. CCR can also be found in patients with phenotypic abnormalities due to a chromosome imbalance or to genes disruption at the breakpoints. Conventional karyotype generally allows their identification. However, molecular cytogenetic methods can reveal subtle rearrangements. We report, here, the identification of a de novo CCR involving chromosome X, 13 and 15 associated with a translocation between chromosome 6 and 11, in a girl presenting a delayed development and a symptomatic muscular dystrophy. FISH was performed to characterize this rearrangement, with use of probes that hybridize in DMD gene region. We found that DMD is disrupted by the breakpoint in Xp21. We also performed array-CGH that revealed no cryptic imbalance.

Duchenne muscular dystrophy usually affects males. However, females are also affected in rare instances. The majority of them have been associated with a skewed X-inactivation pattern. Of particular importance have been those in whom the manifestation of the disorder has been associated with de novo X;autosome translocations. Although these females carry two X chromosomes and therefore have two dystrophin gene loci, they manifest DMD because of a skewed X-inactivation pattern. Whereas one gene is disrupted by the translocation and lies on the active X, the other lies on the intact, inactive X chromosome. Here, our patient presented also a developmental delay probably due to the disruption of one or more other genes located in the multiple breakpoints.

1.P67

Characterization of a rare anaphoid supernumerary marker chromosome in mosaic

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Analphoid supernumerary marker chromosomes (SMCs) are a rare subclass of SMCs C-band-negative and devoid of alpha-satellite DNA. These marker chromosomes cannot be identified unambiguously by conventional banding techniques alone being necessary to apply molecular cytogenetic methods in favour of a detailed characterization.

In this work we report an alphoid SMC involving the terminal long arm of chromosome 7, in 9 years-old boy with several dysmorphic features and severe development delay.

Cytogenetic analysis revealed a mosaic karyotype with the presence of an extra SMC, *de novo*, in 20 % of lymphocytes and 73 % of fibroblast cells.

FISH analysis with alpha-satellite probes for all chromosomes, whole chromosome painting probe for chromosome 7, and D7S427 and TelVysion 7q probes, allowed establishing the origin of the SMC as an alphoid marker resulting of an invdup rearrangement of 7q36-qter region.

Affimetrix CytoScan HD microarray analysis, redefined the SMC to arr[hg19] 7q35(143696249-159119707)×2~3, which correspond to a gain of 15.42 Mb and encloses 67 OMIM genes, 16 of which are associated to disease.

This result, combined with detailed clinical description, will provide an important means for better genotype-phenotype correlation and a more suitable genetic counselling to the patient and his parents, despite the additional difficulty resulting from being a mosaic (expression varies in different tissues). Alphoid SMCs derived from chromosome 7 are very rare, with only three cases reported so far. With this case we hope contribute to a better understanding of this type of chromosome rearrangements which are difficult for genetic counselling.

1.P68

Pallister-Killian syndrome caused by mosaicism of abnormal chromosome 12 but not isochromosome 12 p

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CASE: 22 month old baby was referred to a pediatrician for lack of independent ambulation. At 27 months he could free run.

MATERIAL AND METHODS: Cytogenetic analysis on patient's peripheral blood was performed, finding an additional material of unknown origin in the telomeric region of the short arm of chromosome 12. Whole chromosome painting was made.

Array CGH technique 60 Kb was performed to identify the origin of this material and genes involved.

Karyotypes from parents and healthy sister of the patient were analyzed.

RESULTS:

Karyotype: 46,XY,add(12)(p12)[7]/46,XY[7]dn. WCP: additional material of chromosome 12.

Parents and healthy sister had normal karyotypes.

CGH array : arr[hg19] 12913.33(230.421-697.269)×1,12p13.33p11.1(835.365-34.756.209)×3 Terminal deletion of 467 Kb in short arm of chromosome 12, 12p13,33 region, and interstitial region amplification of 34 Mb in 12p13,33-12p11,1 region. Both anomalies modify the structure and / or change doses of reference genes RefSeq, involved in diseases with OMIM number.

DISCUSSION: Interstitial amplification of 34 Mb identified on the short arm of chromosome 12 is associated with Pallister-Killian syndrome (OMIM: 601803).

Clinical descriptions of patients with a triplication of 12p show the following: newborns have a high weight and a high risk of hypoglycemia. Facial anomalies consist of a short neck, flattened face, anteverted nostrils and everted lower lip. The patients have severe mental retardation involving language and learning and have sleep and behavior disorders.

It should be noted that our patient has a duplication of 12 in a mosaic form.

DECIPHER describes two patients with overlapping duplication with our case who have feeding difficulties, coloboma, prominent nasal septum, micrognathia and tricuspid regurgitation.

ISCA describes two patients with mental retardation, psychomotor retardation and short stature.

Bibliography: De novo trisomy 12p in twin girls with different levels of mosaicism, *Am J Med Gen A.* 2013 Jul; 161A(7): 1702-5.