The reason for incomplete penetrance of the large-scale chromosomal copy number variation (CNV) in human genome is still debated. One of the possible compensatory mechanisms may be related to intrinsic genetically and developmentally determined epigenetic chromatin modifications. For example skewed X-chromosome inactivation (sXCI) may have a protective effect for a woman's health by suppressing X-linked CNVs in her karyotype. However, one can suggest, that inheritance of these CNVs from maternal side by the embryo may be incompatible with its normal development. If this true, male embryos or female embryos with random X-inactivation are in the elevated risk group in families with pregnancy loss. To test this hypothesis, X-inactivation status was estimated by classical methylation-specific assay in blood lymphocytes from 203 women, heterozygous for AR locus, with a history of spontaneous abortions with normal karyotype as well as in 97 women without reproductive problem, having two or more pregnancies with successful outcome. The incidence of sXCI was significantly higher in women with pregnancy loss than in the control (21% and 7%, respectively, p=0.009). Subsequent molecular karyotyping of 9 women with reproductive losses and extreme sXCI (≥90%) using SurePrint G3 Human CGH+SNP 4×180K Microarray Kit (Agilent Technologies, USA) revealed X-linked CNVs for eight of them presented by Xp22.33, Xq28 microduplications and Xp11.23, Xq24 microdeletions. Surprisingly, enrichment analysis revealed that genes localized within CNVs are associated with intellectual disability (RAB39B, UBE2A, L1CAM, CLIC2, p=0.0043), including X-linked syndromic mental retardation, Nascimento type (MIM 300860) and Xq28 microduplication syndrome (MIM 300815). An observed link between pregnancy loss and risk for birth of a child with developmental delay or intellectual disability requires special attention for further elucidation of essential genetic and epigenetic mechanisms related to prenatal selection and accumulation of X-linked CNVs in the population. This study is supported by the Russian Foundation for Basic Research, grant 18-015-00437.

1.P24

P1070 - 9q21.13q21.31 deletion in a patient with intellectual disability severe speech delay and and dysmorphic features a newly recognized microdeletion syndrome

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The increased use of chromosomal microarray analysis has led to the identification of new microdeletion/microduplication syndromes, enabling better genotype-phenotype correlations.
Interstitial deletions involving the long arm of chromosome 9 are rare but recently a microdeletion syndrome at 9q21.13 was suggested, with mental retardation, speech delay, epilepsy, autistic behaviour and moderate facial dysmorphism as the main characteristics.
Here we present a male child with intellectual disability, severe speech delay, microcephaly and dysmorphic features carrying an interstitial deletion, detected by the Affymetrix Cytoscan HD microarray, of 6.56 Mb at 9q21.13q21.31 region encompassing 16 OMIM genes (arr[GRCh37] 9q21.13q21.31(76551542_83116342)x1).
Among the genes in the deleted region the PRUNE2, PCSK5, RORB and TRPM6 genes are expressed in the nervous system and have been describe as being candidate genes to play a role in mental retardation or neurological disorders. Although the cohort of patients identified with deletions in this region is still small our patient phenotype partially overlaps the others described in the literature.
The collection of more cases with deletion of the 9q21.13 region will help establishing a clear classification for this CNV, finding the real weight in the patient's phenotype, delineating the genetic counseling for their families, and clearly establishing this microdeletion as a syndrome.

1.P25

Rare congenital chromosomal aberration dic(X;Y)(p22.33;p11.32) in adult patient with primary myelofibrosis

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Constitutional translocations between sex chromosomes are rather rare in humans. We report the unique case of a very rare congenital translocation between chromosomes X and Y, forming dicentric chromosome dic(X;Y)(p22.33;p11.32), in an adult male with a malignant hematological disease.
Primary myelofibrosis was diagnosed in a 63-year-old man following liver transplantation after hepatocellular carcinoma. Analysis of the bone marrow sample showed a karyotype 46,X,dic(-X;Y)(p22.33;p11.32) in all mitoses; this was verified with mFISH. A cytogenetic examination of stimulated peripheral lymphocytes revealed the constitutional karyotype 46,X,dic(X;Y)(p22.33;p11.32)[20]/45,X[10]. The 45,X cell line was confirmed with FISH in 35% of interphase nuclei. The SRY locus was present on the dicentric chromosome. A CGH/SNP array (Illumina) revealed gain of 153,7 Mbp of the X chromosome and 803-kbp microdeletion (including the SHOX gene), which were also confirmed with FISH. SHOX encodes a transcriptional factor that regulates the growth of the long bones. The deletion of the SHOX gene together with the Madelung deformity of the forearm and the short stature of the proband led to a diagnosis of Léri-Weill dyschondrosteosis (LWD). The gain of almost the whole X chromosome (153,7 Mbp) was considered a variant of Klinefelter syndrome (KS). The levels of gonadotropins and testosterone were consistent with gonadal dysfunction. A malformation of the right external ear was detected.
We have reported a rare structural aberration dic(X;Y)(p22.33;p11.32) in a patient with primary myelofibrosis. The related genomic imbalance is associated with two known hereditary syndromes, LWD and a KS variant, identified in our proband at an advanced age. Because the breakpoints did not involve known cancer genes, we inferred that the hematological malignant disease suffered by the proband is unrelated to this congenital chromosomal aberration.
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1.P26

Case report of a small deletion in 1p36.11 encompassing the AHDC1 gene causative for Xia Gibbs syndrome

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Several patients with de novo mutations in the AHDC1 gene have been described since Xia et al. presented the Xia-Gibbs syndrome (OMIM #615829) in 2014. Patients exhibit common features like developmental delay, hypotonia, language delay, mild dysmorphic features, sleep apnoea, seizures, and hypoplasia of corpus callosum. The