50% and 75% admixture of trisomic DNA to total DNA.

DNA from amniotic cells was extracted using QIAamp DNA Blood Mini Kit samples. D concentrations were measured by a spectrophotometer Lambda Bio Plus and in all cases normalized.

The level of detection differs between particular trisomies; in trisomy 21, this method regularly detects trisomy whether the concentration of trisomic DNA is 30% (in some but not all cases in 25% and rarely in 12.5%). In trisomies 13 and 18, the borderline of detection is higher and in both stays at the level of 50%.

10.P40

Prenatal diagnosis of a complex rearrangement involving three inversions and two duplications on chromosome 17

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A chromosomal inversion involves chromosome breaks at two different sites, followed by a 180° rotation and reunion of the intrachromosomal segment. Inversions have an incidence of 0.13/10,00 liveborns. Phenotypic manifestations occur when a critical gene is disrupted.

The short arm of chromosome 17 is a recognized region of genomic instability. Genomic rearrangements at 17p13.3 include interstitial deletions and duplications. Array comparative genomic hybridization (aCGH) has allowed the identification of a growing number of new microdeletion and microduplication syndromes that cause mental retardation. Submicroscopic duplications are now being reported for almost all microdeletions syndromes and have a distinct behavioral and phenotypic expression.

A prenatal diagnosis performed at the 17th week gestation, because of advanced maternal age, revealed by GTG banding the presence of a de novo abnormal chromosome 17. Fluorescence in situ hybridization techniques were performed using WCP, p53, subtelomeric 17p, Miller-Dieker, Smith-Magenis and Her2/neu probes. These hybridizations showed that only several breakpoints.

To determine whether there was any microdeletion or microduplication, aCGH analysis was performed with a Microarray Agilent 180k, showing that there were two microduplications: one of 558 kb on 17p13.2–p13.3 and another of 76 kb on 17q12, in two of the breakpoints established, with no disequilibrium of the subtelomeric region. Anatomophatological studies revealed no alterations in the fetus.

Our report describes an abnormal chromosome 17 with at least three inversions, two paracentric (in the short arm) and one pericentric. Genomic duplications in the terminal end of the short arm of chromosome 17 are of particular interest because many of them have been shown to be related to neurologic disorders.

This is the first report of a prenatal diagnosis with an intrachromosomic rearrangement in chromosome 17, involving at least three breakpoints, with two microduplications detected by aCGH.

Keywords: Prenatal diagnosis, array-CGH, Complex rearrangement

10.P41

Prenatal diagnosis of terminal 11q deletion

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The majority of 11q deletion cases described may be included in the "distal 11q deletion syndrome", or Jacobsen syndrome. This is a rare but clinically recognizable condition with an incidence of 1/100,000 births. The most common clinical features are psychomotor delay, characteristic facial dysmorphism and malformations of the heart, kidney, genitalia, central nervous system and skeleton. Patients usually have visible deletions of chromosomal bands 11q23, 11q24, and/or 11q25. Approximately

85% of the cases are de novo deletions, and only a few prenatal cases have been reported.

We report the clinical case of a 30-year-old pregnant woman who was referred to our laboratory with a positive first trimester prenatal screening for Down syndrome.

The cytogenetic analysis revealed a terminal deletion on the distal 11q chromosome. Fluorescence in situ hybridization using a whole-chromosome painting probe and subtelomeric probes confirmed the terminal deletion and excluded other material involvement. Parental karyotypes were normal. Second trimester ultrasound revealed clinodactyly and a cardiac defect described as a subvalvular and intraventricular communication. The couple opted for medical termination of pregnancy.

The postmortem examination of the 22-week fetus showed facial dysmorphism, cardiac defects and uterus bicornis.

There are few reports of prenatally diagnosed 11q−, and there seems to be a phenotypic variability. Some cases had a positive prenatal screening for Down syndrome and/or abnormal prenatal ultrasound with olygohydramnios, nuchal thickening, heart malformations and kidney anomalies. Other reports mention no structural fetal abnormalities.

The present case, similar to others, had a positive first trimester screening. The fetus presented abnormal fingers, cardiac defects and malformations of genital tract, identified at the second trimester, which is consistent with the del11q− phenotype. This case reinforces the phenotypic variability associated with partial monosomy of distal 11q in the fetus and the difficulty of establishing genotype–phenotype correlations.

Keywords: Deletion 11q, Prenatal diagnosis, Clinical features, Positive first trimester screening

10.P42

Prenatally diagnosed de novo balanced chromosomal rearrangements: high risk of late-onset neurodevelopmental and -psychiatric disorders and improved genetic counseling by next-generation sequence mapping

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Carriers of de novo balanced reciprocal translocations or inversions are believed to have 6–9% risk of congenital malformations and/or developmental delay. However, systematic data regarding late-onset disorders are lacking. A cohort (N=41) of unselected carriers of de novo balanced reciprocal translocations or inversions detected prenatally in the period 1970–2008 was identified in the Danish Cytogenetic Central Register. Using information obtained in national medical registries, we compared morbidity in the cohort to that of a 5:1 matched control group (N=205). Carriers were offered clinical reexamination, analysis with Affymetrix SNP 6.0 Array, and breakpoint mapping by next-generation sequencing (NGS) mate-pair analysis.

We observed no serious congenital malformations in the unselected cohort. However, the risk of neurodevelopmental and/or psychiatric disorders, including mental retardation, learning disabilities, severe attention and/or behavioral disorders, autism spectrum disorders, and severe mood disorders, was significantly elevated (19.5% vs. 8.3% among the controls, p=0.04). Analysis for copy number variants >100 kb did not provide prognostic information about late-onset disorders. By mate-pair analysis of the first nine affected and ten unaffected carriers, we could detect the breakpoints involved in ~90% of the cases. Although genes were truncated in both groups, truncated genes known to be associated with related phenotypes (e.g. NPAS3) were