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P1-9 | 47,XY,+del (X)(q21.31)/46,XY mosaicism in prenatal diagnosis—Case report of a rare event

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Objectives: Aneuploidies involving the sex chromosomes are the most common anomalies in humans. In many cases, these anomalies are present in mosaic and may involve either the whole chromosome or just part of it. These anomalies constitute a challenge in prenatal diagnosis because it is generally very difficult to establish a reliable genotype-phenotype correlation. Here, we report a rare event of a mosaic in which one cell line carries an additional abnormal X chromosome, with a terminal deletion at q21.31 region, and a normal XY constitution in the majority of the cells.

Methods: A healthy 36-year-old G1P1 woman was referred for prenatal diagnosis at 11 + 5 weeks of gestation for increased nuchal translucency. Chorionic villus biopsy was performed, and molecular rapid aneuploidy result indicated an anomalous situation for the X chromosome in a male fetus. As the material was not sufficient to establish a culture, an amniocentesis was performed at 17 + 3 weeks and karyotyping and microarray were performed in order to characterize the anomalous result.

Results: The results obtained indicated the presence of a mosaic involving an extra X chromosome with a terminal deletion, [47,XY, +del (Xq)/46,XY.arr [GRCh37] Xp22.33q21.31(169921_89283237) x1~2], which is compatible with a Klinefelter syndrome variant.

Conclusions: Pregnancies affected by X chromosome aneuploidies diagnosed prenatally are at an increased risk of adverse fetal and neonatal outcomes. High quality information is critical for informed decision-making in pregnancy following a prenatal diagnosis of sex chromosome aneuploidy.

P1-11 | High resolution chromosomal microarrays in the general prenatal population: Pathogenic CNVs and VOUS in a 2016 state-wide cohort

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Objectives: Since the publication of a landmark study by Wapner et al[1] showing the advantages of a targeted chromosomal microarray (CMA) over karyotype for prenatal diagnosis, CMA utilization has expanded rapidly. The yield of CMA and rates of variants of uncertain/unknown significance (VOUS) vary according to the CMA platform and indications for testing. This study aimed to analyse the diagnostic yield of whole genome high resolution SNP CMA in a state-wide cohort and compare this to the yield reported in the 2012 study.

[1] Wapner R, et al. Chromosomal microarray versus karyotyping for prenatal diagnosis. N Engl J Med 2012;367:2175–84.

Methods: Data on all amniocenteses and CVS done in 2016 in the state of Victoria, Australia, were analysed. G-banded karyotype or CMA analysis with Affymetrix Cytoscan 750K (0.2 Mb resolution) was performed according to request by the clinical referrer. Results were analysed according to indication for testing and type of abnormality, specifically pathogenic copy number variant (pCNV), abnormality detectable by karyotyping, or VOUS. The major indications for prenatal diagnosis were ultrasound abnormalities, first trimester combined screening (FTC), non-invasive prenatal testing (NIPT), history of chromosome abnormality, single gene testing, and advanced maternal age (AMA). Statistics were performed in STATAv14.

Results: Of the 1468 samples in 2016, 83.2% (n = 1221) were analysed by CMA and 16.8% by karyotype. The results of the CMA group included 29 (2.4%) pCNVs, 68 (5.6%) VOUS, and 190 (15.6%) other major abnormalities detectable by karyotype (aneuploidies and large deletions). The highest rate of pCNVs occurred in those tested for ultrasound abnormality (3.2%), which was not significantly different to that reported by Wapner (2.8%). Rates of pCNVs by other indications were 1.2%, 0.8%, and 1.9% for FTC, NIPT, and other combined indications, respectively. The upward trend in annual total chromosome abnormalities in our population continued in 2016 (n = 363).

Conclusions: Our overall rate of pCNVs was significantly higher than the 0.9% previously reported, though the yield for ultrasound-indicated diagnosis was not significantly different. Likely factors contributing this difference include more specific indications for testing in our population, such as fewer for AMA alone and different CMA platforms. Also, as time progresses, a previously assigned VOUS may become a pCNV (or benign variant) when linked to a phenotype. The expansion of CMA to our general population has maintained high detection rates at a time of declining procedures. Our rates of VOUS are relatively high, posing challenges for the genetic counselling workforce.

P1-12 | ATAD3A deletions: A challenge in prenatal diagnosis

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Objectives: The *ATAD3* gene cluster is part of the ATPase family AAA-domain containing proteins consisting of three paralogs, *ATAD3A*, *ATAD3B*, and *ATAD3C* located in tandem on chromosome 1p36.33. The *ATAD3* genes encode mitochondrial membrane proteins that contribute to the stabilization of large-mitochondrial protein complexes. Recently, deletions in the *ATAD3* gene cluster