

CHARACTERIZATION OF SMALL SUPERNUMERARY CHROMOSOME BY ARRAY-CGH IN PRENATAL DIAGNOSIS

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INTRODUCTION

Supernumerary marker chromosomes (SMC) are centric chromosomal segments, relatively common in prenatal diagnosis, that, by definition, cannot be characterized unambiguously by conventional chromosome banding.

Marker chromosomes are of particular interest in clinical cytogenetic because they are nearly 10 times more frequent in individuals with mental retardation (0.426%) than in the normal population (0.043%), and are present in 0.077% of prenatal diagnosis. The genotype-phenotype correlation for SMCs will be very important for genetic counseling because the clinical outcomes vary greatly.

We employed a 60K targeted oligo-array CGH to identify and characterize a marker chromosome in a prenatal diagnosis like a duplication of 5,2 Mb in 22q11.2 chromosome, (OMIM 608363). Conventional Cytogenetic Techniques like Karyotype and FISH were not able to characterize exactly the size and the genetic material of this SMC.

CASE REPORT

- A prenatal diagnosis for advanced maternal age was done to a pregnant woman in the 17+5 week.
- The cytogenetic analysis with G-banding revealed female karyotype with presence of supernumerary marker chromosome in all analyzed cells, 47,XX,+mar (Fig. 1). Parental karyotype was normal, confirming the novo origin of SMC in the fetus.
- With FISH techniques, we could conclude that the SMC was a derivative of chromosome 14/22 centromeric region (Fig. 2).

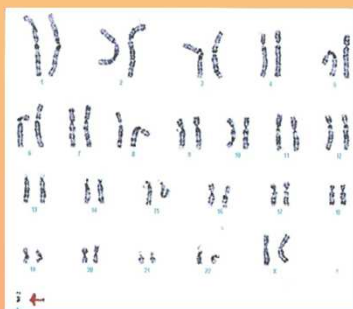


Figure 1: Karyotype in amniotic fluid.

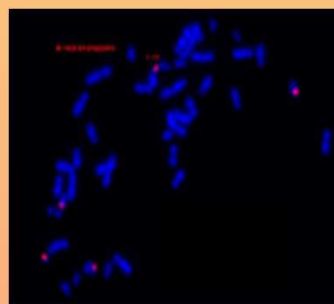


Figure 2: FISH CEP 14/22.

- SMC was characterized with a 60K targeted Oligo Array-CGH (Karyonim), build 37, hg19, showing a 5.2 Mb duplication (170007540-22210530) from 22q11.21 to 22q11.23, containing the region for Duplication Syndrome 22q11 (OMIM 608363) (Fig 3).
- We have done FISH techniques for DiGeorge region (DGCR2) confirming the result found in array-CGH (Fig 4).

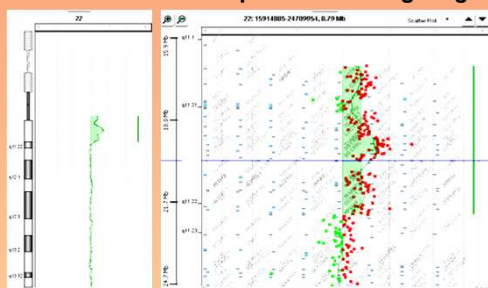


Figure 3: 60 K Oligoarray (KaryoNim) of fetus, showing the duplication 22q11.21-q11.23 responsible for 22q11 duplication syndrome.

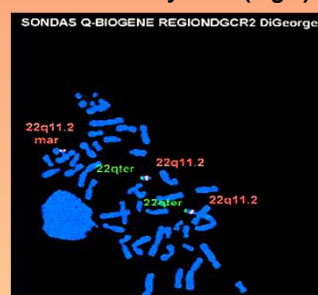


Figure 4: FISH for the SMC with a signal for 22q11.2 DGCR2 showing.

The 22q11.2 duplication phenotype appears to be generally mild and highly variable findings, even among members of the same family, range from apparently normal to intellectual disability, learning disability, delayed psychomotor development, growth retardation, and/or hypotonia.

CONCLUSIONS

1. Our case demonstrates the superiority of array-CGH technique over conventional techniques regarding the identification and characterization of SMC including material, size and genes involved.
2. The accuracy of array-CGH in SMC/phenotype correlation makes it suitable for a better genetic counseling in prenatal diagnosis.
3. Microarray study should be performed when a SMC is found in post and pre-natal cases.