Abstract

Supernumerary marker chromosomes (sSMCs) are a relatively rare cytogenetic phenomenon. Their laboratory examination is often difficult, and the clinical interpretation is even more challenging. The main reason is that most sSMC carriers have no clinical manifestations. The chromosome origin and exact range of the aberration are very important, as well as the fact that sSMCs are often found in mosaics that can strongly influence both the phenotype and the interpretation of result. Prenatal sSMC finding is one of the most challenging situations in both clinical and laboratory genetics.

This work deals with the investigation process of sSMC carriers using molecular cytogenetic techniques, especially fluorescence in situ hybridization (FISH). We investigated a total of 67 families collected both prospectively and retrospectively, and we found 70 unique sSMCs in a total of 74 individuals. Six cases were familial and in three cases two sSMCs were found in one individual. According to the initial karyotype finding, the cases were divided into two groups, sSMCs supernumerary to a normal karyotype (group A) and $sSMC^{T}$s supernumerary to the Turner karyotype (group B).

The chromosomal origin was successfully determined in 88,6 % sSMCs. In group A the most common findings were sSMCs derived from chromosome 15, and those derived from other acrocentrics. Clinical evaluation of the effect of the sSMC on phenotype of the patient was concluded in 79,6 % of sSMCs, of which 53,5 % were evaluated as probably pathogenic for at least some abnormalities of the patient. The most common indications for examination in this group were the presence of congenital malformations and/or developmental delay and/or intellectual disability, and reproductive disorders. In these individuals sSMCs are generally found several times more frequently than in the general population. In group B, all sSMCs were, in accord with theoretical expectations, derived from gonosomes, and caused Turner syndrome features and gonadal dysgenesis in their carriers.

The work contributes to the genotype-phenotype correlation in sSMC carriers, provides guidance to interpretation of similar findings in future patients, and points out atypical cases. Particular attention was paid to the specifics of prenatal diagnosis. In pathogenic sSMCs, mechanisms and genes have been studied which can contribute to the abnormal phenotype. We have also confirmed the importance of FISH in the diagnostic scheme, and we have modified the investigation algorithm, especially for prenatal diagnostics.