Clinical and molecular findings in nine new cases of tetrasomy 18p syndrome: Co-occurrence of isochromosome 18p and Copy Number Variation

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Background:

Tetrasomy 18p (T18p) (OMIM: # 614290) is a rare chromosomal abnormality that results from the presence of a supernumerary chromosome known as isochromosome 18p. It is one of the most frequent isochromosomes observed in humans with a prevalence of 1/180000 live born children. This syndrome is associated with a distinctive facial appearance, feeding difficulties in infancy, development delay and intellectual disability.

In this study, we report on the clinical and molecular cytogenetic findings of nine Tunisian cases of isochromosome 18p (I18p) in patients having in common dysmorphic features and development delay and/or intellectual disability with slightly variable phenotypes.

Patients and methods:

Karyotype

SMC

Particular
phenotype

CGH array (44K and 66K)

FISH

Results and discussion:

47,XY,+mar

Log ratio= 1
Log ratio=0,7 <1 Mosaic

Cytogenetics

Array CGH showed a gain of nearly 14Mb of the 18p arm with a log ratio equal to 1, resulting in its tetrasomy. In addition, 5 CNVs were found in 3 patients. I18p was de novo and homogeneous in 8 cases among 9.

Phenotype

Patients have in common **dysmorphic features** including a triangular face, low-set ears, a thin upper lip, horizontal palpebral fissures, epicanthus and strabismus are seen in two patient (patient number 2 and 5). In addition, microcephaly and **intellectual disabilities** and/or **development delay** with low **birth weight** were present. However two patients (patient 1 and 9) presented standard birth weight. We also observed in one patient hypospadias (patient 6), two (patient 5 and 6) had skin problems, three showed a congenital heart defect (patient 1, 5 and 6), one (patient 7) had kidney defect and ectopic testis. MRI showed a **hypoplastic corpus callosum** in one patient.

Mechanism of formation

(a): **Transverse centromeric division**
(b): Breakage distally in the centromeric region>> dicentric isochromosome and acentric fragment
(c): breakage in the proximal part of one arm producing a dicentric isochromosome with the centromeres a short distance apart

- ✓ Among 39 SMC collected since 2006 in our Laboratory, isochromosome 18p seems to be the most frequent SMC followed by derivative 15 SMC # literature
- ✓ The slight clinical variability between patients with iso18pS may be due to the different sizes of the duplicated region and genes content as well as other CNVs generated elsewhere in the genome.
- ✓ Array CGH as a first-tier test for SMCs diagnosis and characterization
- ✓ FISH is exceedingly required for characterization of SMC and definition of the chromosomal mechanics in origin of the rearrangements.
- ✓ Database: <http://ssmc-tl.com/sSMC.html>