1.P72

Three new cases of interstitial microdeletion 4p16.3 contributing to a genotype phenotype correlation of WHS critical region of deletion

Laura Bernardini [1], Maria Cristina Digilio [2], Francesca Clementina Radio [2], Fabio Acquaviva [3], Cristina Gorgone [4], Diana Postorivo [5], Barbara Torres [1], Viola Alesi [2], Anna Maria Nardone [5], Teresa Mattina [4], Gioacchino Scarano [3], Antonio Novelli [2], Bruno Dallapiccola [2]

[1]Casa Sollievo Della Sofferenza Foundation, Mendel Laboratory, San Giovanni Rotondo (fg), Italy; [2]Bambino Gesù Children's Hospital, Medical Genetics Unit, Rome, Italy; [3]A.o.r.n, Gaetano Rummo, U.o.s.d. Medical Genetics, Benevento, Italy; [4]Catania University, Medical Genetics, Department of Pediatrics, Catania, Italy; [5]Policlinico Tor Vergata, U.o.c. Medical Genetics Laboratory, Rome, Italy

Correspondence: Laura Bernardini

Molecular Cytogenetics 2017, **10(Suppl 1):**1.P72

Wolf–Hirschhorn syndrome (WHS) is a well-known contiguous gene syndrome due to 4p16.3 deletion. The phenotype is characterized by typical facial features ('Greek warrior helmet'), intellectual disability, pre- and postnatal growth retardation, seizures and additional findings such as skeletal anomalies, congenital heart defects, midline defects, ocular and renal anomalies. These malformations are more frequent in the patients with larger deletions, involving a large portion of 4p16 chromosome region.

In the last several years, the characterization of patients with microarray platforms allowed to elucidate the role of some genes mapping to 4p16. WHSC1 is responsible for different WHS clinical features, whereas LETM1 is the candidate gene for seizures.

We report on three new patients with small interstitial deletions mapping to 4p16.3: two (P1 and P2) with deletions very similar for localization and extent and both presenting with mild intellectual disability, growth retardation, microcephaly and dysmorphic features, the other (P3) with a deletion just partially overlapping to the others and showing intellectual disability, growth retardation, microcephaly, partial atrioventricular canal and the typical WHS facial features. All deletions involved WHSC1 gene, but in Patient 3 the deletion also encompassed the more proximal genes NELFA, POLN and miRNA943. Interestingly, among the three affected children herein reported, this patient presented with a more severe malformative phenotype including a congenital heart defect.

These three new cases of interstitial deletions 4p16.3 highlight that WHSC1 is not sufficient per se to generate the full clinical spectrum, in particular the facial gestalt, of WHS. Moreover, it confirms that a more proximal region of deletion, mapping approximately to 2 Mb from the subtelomeric region is causative of congenital malformations, such as heart defects, shown by WHS patients with larger deletions.

1.P73

A novel insertion from chromosome 18 to chromosome 15 with a 183Kb 18q deletion

Rosário Pinto Leite [1], Marta Souto [1], Pedro Botelho [1], Fernanda Pereira [2], Bárbara Marques [3], Hildeberto Correia [3], Osvaldo Moutinho [4], Márcia Martins [5]

[1]Centro Hospitalar De Trás-Os-Montes E Alto Douro, Cytogenetic Laboratory, Vila Real, Portugal; [2]Centro Hospitalar Do Nordeste, Pediatric Service, Mirandela, Portugal; [3]Instituto Nacional Doutor Ricardo Jorge, Cytogenetic Unit, Human Genetic Department, Lisboa, Portugal; [4]Centro Hospitalar De Trás-Os-Montes E Alto Douro, Gynecology / Obstetrics Service, Vila Real, Portugal; [5]Centro Hospitalar De Trás-Os-Montes E Alto Douro, Genetic Consultation, Vila Real, Portugal

Correspondence: Rosário Pinto Leite

Molecular Cytogenetics 2017, **10(Suppl 1):**1.P73

Chromosome 18q- syndrome is a rare chromosomal disorder with an incidence of 1 in 40 000 live births. The phenotype is highly variable, depending on the amount of deleted genetic material, and is characterized by mental retardation, developmental delay, hypotonia, seizures, obesity, abnormal behavior, short stature and craniofacial dysmorphisms.

We report a patient with mental retardation, dysmorphic features, hypotonia, growth retardation, severe expressive speech delay and Duane syndrome, with an insertion of 18q in 15q causing a 183Kb deletion in18q.

Cytogenetic and SNP array analysis showed a female karyotype presenting a de novo rare chromosome rearrangement: an insertion of the 18q21q23 on the 15q22 region, with deletion 18q12.3 (chr18:42,484,980-42,667,966, [GRCh37]), involving only the MIR4319 and SETBP1 genes.

There are few reports of 18q12.3 deletion associated with mild dysmorphic features, mental retardation and impairment of expressive language. To our knowledge this is the smallest deletion described, involving two genes: SETBP1 and a microRNA (MIR4319). SETBP1 gene is associated to expressive speech delay. The authors present a literature review of 18q12.3 deletion.

1.P74

An apparently balanced complex translocation involving chromosomes 1 8 and 9 in a 3 year old infant

Rosa Lobo Valentín [1], América De León Rodríguez [1], María Talavera Yagüez [2], Patricia De La Fuente Alonso [1], Álvaro Sánchez [3], Carles Garrido Fusté [4], Esther Geán [4], Albert Torrents [4], Eva Domínguez Bernal [5], Celia Reig Del Moral [5], Guadalupe Ruiz [1]

[1]Río Hortega University Hospital, Clinical Analysis Service, Cytogenetics Unit, Valladolid, Spain; [2]Ramón Y Cajal University Hospital, Medical Genetics Department, Madrid, Spain; [3]General Hospital, Anatomical Pathology Service, Segovia, Spain; [4]Reference Laboratory, Genetics Division, Barcelona, Spain; [5]General Hospital, Pediatrics Service, Segovia, Spain

Correspondence: Rosa Lobo Valentín

Molecular Cytogenetics 2017, **10(Suppl 1):**1.P74

A 3-year-old male infant, was referred to our Cytogenetics Unit due to his short stature and phenotypic features. The child was born after a spontaneus conception and a pregnancy with no sign of abnormalities (low risk prenatal screening test and no ultrasonographic alterations), so no prenatal genetic study was carried out.

The karyotype in peripheral blood (PB) lymphocytes showed chromosome abnormalities in many regions, including in chromosomes 1,8 and 9, in a three-way balanced translocation. This finding was confirmed by the multiple FISH (M-FISH) technique.

Investigations by array-based comparative genomic hybridization (array-CGH) revealed a 6.7 Mb interstitial deletion on the short arm of chromosome 8 in the region 8p11.22 - 8p12. This de novo interstitial deletion in 8p involves 37 genes. There is no evidence of this constitutional deletion being previously described in the literature.

The karyotypes of the parents and the brother were normal. The couple was recomended to attend a genetic counselling appointment and to undergo prenatal diagnosis testing for future pregnancies, despite the low risk of recurrence.

This type of chromosomal rearrangements, involving 3 breakpoints, is a very rare occurrence in the population. Either the interstitial loss of 8p arm alone or such interstitial loss plus the triple translocation are likely to be responsible for the child's pathology.

This case has shown once again the necessary contribution of each cytogenetic technique to a comprehensive approach of any disease.

Through this work, the mechanisms that lead to the generation, the selection and the stabilisation of such complex karyotypes —within cells and human tissues— are discussed.