

microcephaly, speech delay and some minor dysmorphic features were also noticed.

To investigate monogenic causes for epilepsy (presenting as epileptic encephalopathy) a next generation sequencing (NGS) of 4813 genes associated with monogenic disorders was performed using TruSight One panel (Illumina). No disease causing point mutations were detected, but the read-depth analysis of NGS alignments indicated a possible distal duplication of chromosome 14 (chr14:104,174,847-qter). To clarify the finding chromosomal microarray analysis was performed (HumanCytoSNP-12, Illumina) and two adjacent copy number variants were detected in chromosome 14: a 1.7 Mb duplication and 351 kb terminal deletion, both in the band 14q32.33. At this point r(14) was suspected, and later confirmed by routine GTG-banding. As the parents did not carry the chromosomal aberration the patient's karyotype was concluded as 46,XY,r(14)(p12q32)dn.

In conclusion, this case illustrates the necessity for integrating molecular and cytogenetic diagnostics to clarify the genetic aetiology of genetic disorders. Large structural chromosomal aberrations should be continuously included into differential diagnosis of epilepsy syndromes.

**Consent to publish:** The authors confirm that written informed consent was received by the patient for publication.

### 1.P28

#### 16p11.2 Deletion Syndrome in Prenatal Diagnosis – a rare case

Manuela Mota Freitas<sup>1</sup>, Cristina Candéias<sup>1</sup>, Sílvia Pires<sup>2</sup>, Natália Oliva-Teles<sup>1</sup>, Purificação Tavares<sup>3</sup>, Maria Do Céu Rodrigues<sup>4</sup>, Maria Da Luz Fonseca E Silva<sup>2</sup>

<sup>1</sup>Centro De Genética Médica Doutor Jacinto Magalhães, Centro Hospitalar Do Porto, Epe, Unidade De Citogenética; Unidade Multidisciplinar De Investigação Biomédica, Porto, Portugal; <sup>2</sup>Centro De Genética Médica Doutor Jacinto Magalhães, Centro Hospitalar Do Porto, Epe, Unidade De Citogenética, Porto, Portugal; <sup>3</sup>Centro De Genética Clínica, Laboratório De Citogenética, Porto, Portugal; <sup>4</sup>Centro Materno Infantil Do Norte, Centro Hospitalar Do Porto, Epe, Consulta De Diagnóstico Pré-natal, Porto, Portugal

**Correspondence:** Manuela Mota Freitas

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A microdeletion in 16p11.2 represents a rare syndrome and an even rarer occurrence in prenatal diagnosis. In individuals presenting with delayed language development and abnormal speech articulation, learning difficulties/intellectual disability, social impairments with or without a diagnosis of autism spectrum disorder (ASD), macrocephaly and vertebral anomalies, this syndrome should always be considered.

The authors describe a case with a deletion of the short arm of chromosome 16, in 16p11.2, detected at prenatal diagnosis. A woman was referred for prenatal diagnosis at 21 weeks of gestation due to fetal malformations, several hemivertebrae and single umbilical artery. Chromosome analysis was performed on GTL banded metaphases obtained from cultured amniocytes, with a resolution level of 400 bands. Molecular studies included array CGH and Multiplex ligation-dependent probe amplification (MLPA), using Salsa® MLPA® Kit P343 (MRC, Holland, The Netherlands).

The karyotype revealed an apparently normal female karyotype. Array CGH identified a 4,630 Mbp deletion on chromosome 16p11.2, which includes 138 genes. The pregnancy was terminated and the chromosome 16 microdeletion was confirmed in fetal skin by MLPA. Since parental studies were normal, this anomaly was considered “de novo”.

The clinical features of this fetus will be compared with previously reported cases with the same microdeletion. The authors enhance the importance of multidisciplinary team discussions in prenatal diagnosis cases and thorough genomic analysis, particularly when fetal malformations are detected during echography evaluations.

### 1.P29

#### RPS6KA3 duplication in a male child with severe intellectual disability

Sílvia Serafim<sup>1</sup>, Bárbara Marques<sup>1</sup>, Cristina Ferreira<sup>1</sup>, Filomena Brito<sup>1</sup>, Marisa Silva<sup>1</sup>, Laurentino Simão<sup>1</sup>, Cristina Alves<sup>1</sup>, Sónia Pedro<sup>1</sup>, Joaquim Sá<sup>2</sup>, Hildeberto Correia<sup>1</sup>

<sup>1</sup>Instituto Nacional De Saúde Doutor Ricardo Jorge, I.p., Departamento De Genética Humana, Lisboa, Portugal; <sup>2</sup>Centro Hospitalar Do Algarve, Consulta De Aconselhamento Genético, Faro, Portugal

**Correspondence:** Sílvia Serafim

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Rare inherited and de novo copy number variations (CNVs) are the cause of a variety of genetic disorders with intellectual disability (ID). Chromosomal microarray analysis (CMA) has been a rapid method to identify both large and small pathogenic genomic imbalances causing those disorders.

The identification and classification of a CNV as pathogenic is not always easy to establish. For deletions or loss of function of specific genes, the likelihood of being causal is higher, and for duplications or overexpression for the same genes, the classification is harder.

Here we present a male child with severe ID and a family history with a female sibling presenting mild ID. Affymetrix Cytoscan HD CMA identified a gain of 530 Kb on Xp22.12 (chrX:20016145\_20546410 [GRCh37]) encompassing EIF1AX and RPS6KA3 genes. Inheritance was not yet possible to assess.

Mutations in the RPS6KA3 gene causes Coffin-Lowry syndrome, a mental retardation syndrome with dysmorphic facial features and skeletal anomalies. X-linked mental retardation-19 is a nonsyndromic form of mild to moderate ID also caused by mutations in RPS6KA3. Carrier females may be mildly affected. This shows that phenotypic variability may be expected for the loss of function of this gene.

Recently both familial and isolated cases have been reported with a duplication of the entire RPS6KA3 gene associated with mild to moderate ID. These few cases suggest that increased dosage of RPS6KA3 may be the cause for ID in these patients and gives additional information on genotype-phenotype correlation of imbalances regarding this gene.

The collection of more cases with duplication of RPS6KA3, as the one described here, will help to establish a better classification for these CNVs, as well as help to better predict the phenotypic consequences and facilitate subsequent genetic counseling in the families.

### 1.P30

#### The Enigma of X Inactivation In Small Ring X Chromosomes phenotype In a XIST positive Case of a mos 46,X,r(X)/45,X

Fernanda Paula Oliveira<sup>1</sup>, Maria Do Céu Ribeiro<sup>1</sup>, Manuela Mota Freitas<sup>2</sup>, Natália Oliva-Teles<sup>2</sup>, Sílvia Álvares<sup>3</sup>, Maria Da Luz Fonseca E Silva<sup>1</sup>

<sup>1</sup>Centro De Genética Médica Doutor Jacinto Magalhães, Centro Hospitalar Do Porto, Epe, Unidade De Citogenética, Porto, Portugal; <sup>2</sup>Centro De Genética Médica Doutor Jacinto Magalhães, Centro Hospitalar Do Porto, Epe; Unidade Multidisciplinar De Investigação Biomédica, Unidade De Citogenética, Porto, Portugal; <sup>3</sup>Centro Materno-infantil Do Norte, Centro Hospitalar Do Porto, Epe; Unidade Multidisciplinar De Investigação Biomédica, Departamento Da Mulher E Da Criança, Porto, Portugal

**Correspondence:** Fernanda Paula Oliveira

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Mosaic females with a 46,X,r(X)/45,X chromosomal constitution comprise about 6-7% of cases with Turner Syndrome. A more severe phenotype is often present in individuals with small X ring chromosomes and is usually due to functional disomy. Failure of these X chromosomes to undergo inactivation is either due to lack of XIST gene or lack of its expression. The authors describe a case of a XIST-positive small ring X chromosome and the implications on the phenotype.