

## Interesting case report ECARUCA (2016-01)

### An atypical 0.8 Mb inherited duplication of 22q11.2 associated with psychomotor impairment

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#### Abstract:

Microduplications 22q11.2 have been recently characterized as a new genomic duplication syndrome showing an extremely variable phenotype ranging from normal or mild learning disability to multiple congenital defects and sharing some overlapping features with DiGeorge/velocardiofacial syndrome (DGS/VCFS), including heart defects, urogenital abnormalities and velopharyngeal insufficiency. We present an atypical and inherited 0.8-Mb duplication at 22q11.2, in the distal segment of the DGS/VCFS syndrome typically deleted region (TDR), in a 3-year-old boy with motor delay, language disorders and mild facial phenotype. This 22q11.2 microduplication was identified by MLPA, designed to detect recurrent microdeletions and microduplications of chromosomal regions frequently involved in mental retardation syndromes and was further characterized by aCGH. The duplicated region encompasses 14 genes, excluding TBX1 but including CRKL, ZNF74, PIK4CA, SNAP29 and PCQAP known to contribute to several aspects of the DGS/VCFS phenotype. To the best of our knowledge, only one case of an isolated duplication in the distal segment of the TDR between chromosome 22-specific low-copy repeats B (LCR22-B) and D (LCR22-D) has been published, but the present report is the first one with a detailed description of physical and developmental features in a patient carrying this kind of atypical 22q11.2 duplication. This case illustrates the importance of reporting unusual 22q11.2 duplications to further evaluate the incidence of these rearrangements in the general population and to improve genotype-phenotype correlations and genetic counseling.

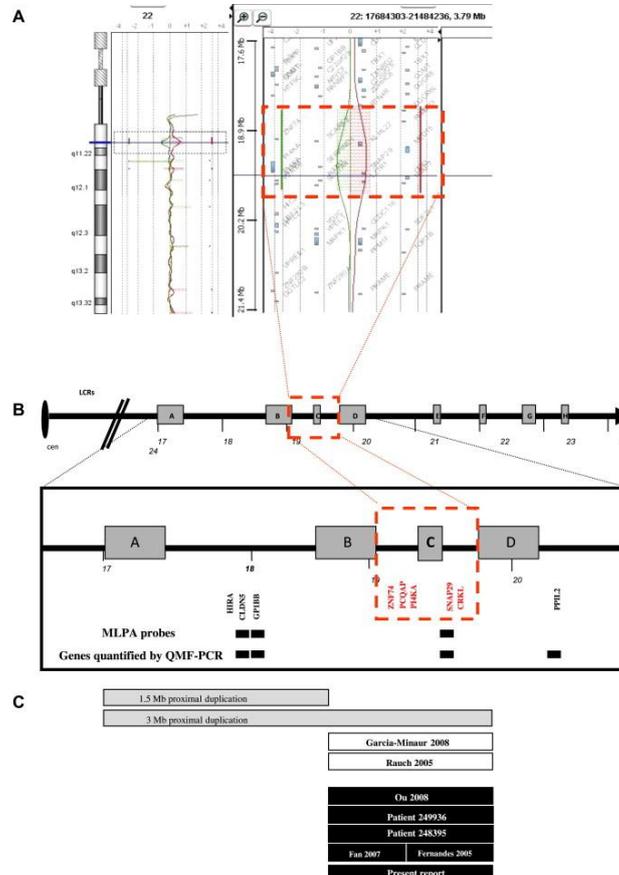


Fig. 1. Mapping of a chromosome 22 duplication in a 2.5-year-old male with motor delay, language disorders and mild facial phenotype. (A) Array-CGH genotyping of patient. Whole genome array-based CGH showed a 0.8-Mb duplication stretching from oligonucleotide P13962822 to oligonucleotide P03603078 (19.0–19.8 Mb). (B) Schematic representation of the 22q11.2 duplicated region. Numbers below the schematic represent distance (million base units) from the 22p telomere according NCBI build 36 (hg18). Gray boxes indicate LCR22s. Note that due to space limitations, only genes mentioned in the present report are listed. (C) Boxes below the map the different duplications and deletions involving region between LCR22-B and LCR22-D described in previous reports and in the patient reported in this study. White boxes indicate deletions and black boxes indicate duplications. Gray boxes indicate 1.5 Mb duplication consistent with reciprocal microduplication of the proximal nested DGS/VCFS deletion, corresponding to the DiGeorge Critical Region (DGCR) and 3 Mb duplication that is the reciprocal event of the common Typically Deleted Region (TDR). Cen: centromere; tel: telomere.

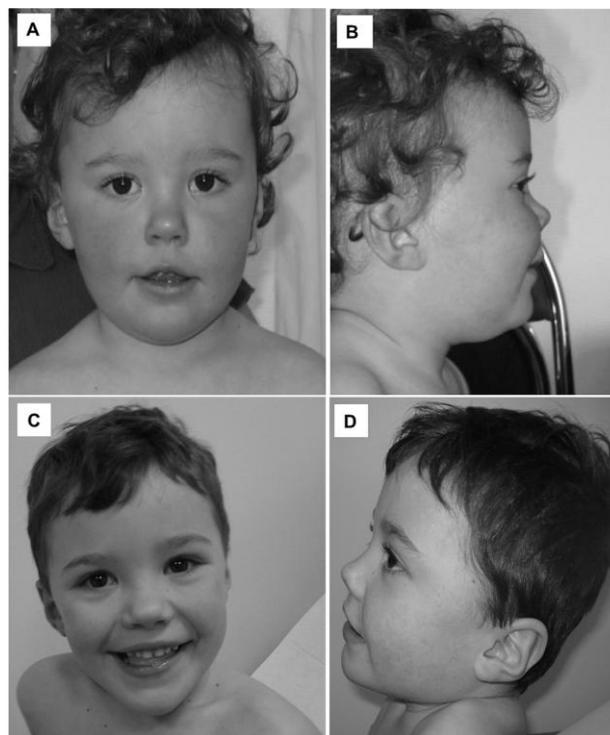


Fig. 2. Facial front (A and C) and side view of the patient (B and D) respectively at the age of 18 months and 3 years. Note prominent forehead, bilateral epicanthus, long eyelashes, anteverted nostrils, small and down-turned mouth, long filtrum, bilateral preauricular pits and high hairline.