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Distal deletion at 22q11.2 in a patient with Oculo-auriculo-vertebral Spectrum

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Abstract/Resumo

Oculo-auriculo-vertebral Spectrum (OAVS), also known as Craniofacial Microsomia or Goldenhar Syndrome, presents wide phenotypic and etiological heterogeneity. It affects mainly the structures originated from the first and second pharyngeal arches. In addition, other major anomalies also may be observed, including congenital heart diseases, which are the main cause of OAVS deaths. Some recent studies have been investigated genomic imbalances in patients with this condition and deletions or duplications in the 22q11.2 region represent the most frequent alterations found in OAVS. The chromosome 22 has eight low copy repeats (LCRs) named from A to H, being the proximal deletion of ~3Mb (LCR22A-LCR22D) associated with 22q11.2 deletion Syndrome. There are five cases of OAVS with distal 22q11.2 deletion described in the literature. In this study, we report a patient with OAVS and a distal deletion in the 22q11.2 regions between LCRs D and E. The proband is a girl, first child of healthy, young and non-consanguineous parents. She was referred for genetic evaluation because she presented cleft lip and palate, intestinal atresia, annular pancreas, hydronephrosis and congenital heart disease. The dysmorphologic evaluation also revealed bilateral pre-auricular tags, left auditory canal stenosis, right nasal cleft and zygomatic hypoplasia with facial asymmetry. The genomic imbalances investigation was performed by MLPA technique using P250-B2 DiGeorge (MRC-Holland MLPA®) kit, and array genomic hybridization (aGH) using the CytoScan 750K Array chip (Affymetrix®, Santa Clara, CA, USA), which revealed a distal deletion of 1.498 kb at 22q11.2 encompassing the region from LCR22-D to LCR22-E. This is the sixth case of OAVS associated of distal 22q11.2 deletions and the second encompassing the region between LCR22-D to LCR22-E (type I deletion). All share some phenotypic signs, such as pre-auricular tags, facial asymmetry, cleft lip and palate, and congenital heart diseases. Some candidate genes in this region have been studied by having an important role in pharyngeal arches development and in congenital heart diseases, such as YPEL1, HIC2 e MAPK1/ERK2. This case contributes to genotype-phenotype correlation and reinforces that candidate genes for OAVS, in the 22q11.2 region, may be located between LCRs D and E.

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Keyword/Palavras-chave: Oculo-auriculo-vertebral Spectrum; Goldenhar Syndrome; Craniofacial Microsomia; 22q11.2 distal deletion

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