Interesting case report ECARUCA (2015-04)

Interstitial 16p13.3 microduplication: Case report and critical review of genotype-phenotype correlation

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Abstract:
We report on a patient with a recognizable phenotype of intellectual disability, multiple congenital anomalies, musculoskeletal anomalies and craniofacial dysmorphisms, carrying a de novo 0.4 Mb duplication of chromosome region 16p13.3 detected by SNP-array analysis. In addition, myopia, microcephaly and growth retardation were observed. The causal 16p13.3 duplication is one of the smallest reported so far, and includes the CREB binding protein gene (CREBBP, MIM 600140), whose haploinsufficiency is responsible for the RubinsteineTaybi syndrome, and the adenylate cyclase 9 gene (ADCY9, MIM 603302). By comparing the clinical manifestations of our patient with those of patients carrying similar rearrangements, we confirmed that 16p13.3 microduplications of the RubinsteineTaybi region result in a recognizable clinical condition that likely represents a single gene disorder. In addition, our case allowed us to define with more precision the smallest region of overlap (SRO) in all patients reported so far, encompassing only the CREBBP gene, and is useful to confirm and further define the phenotypic characteristics due to duplication of the CREBBP gene, being the first case of interstitial duplication with microcephaly and growth defects reported to date.

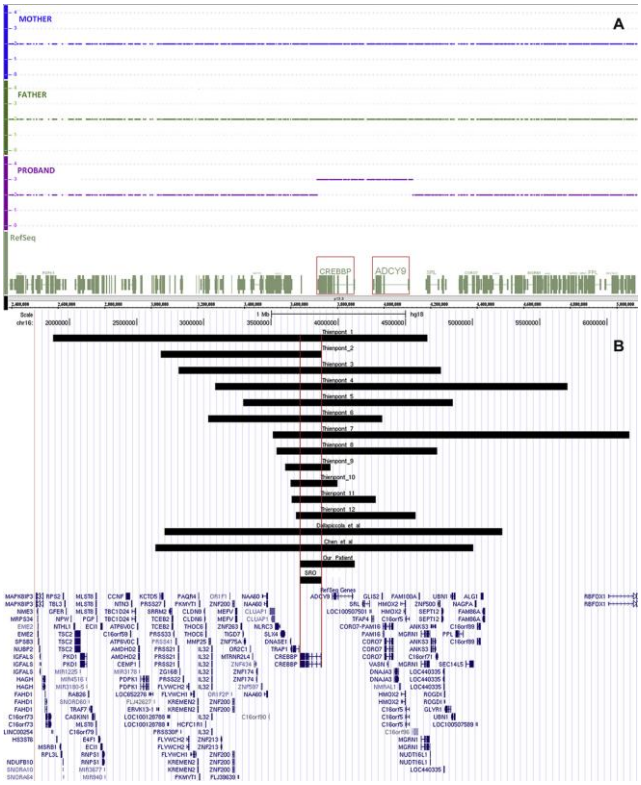

Fig. 1. A: Results of genome-wide human SNP 6.0 array. Copy number state of each probe is drawn along chromosome 16 from 2,400,000 bp to 5,000,000 bp (USCS Genome Browser build March 2006, hg 18) and visualized using the Genome Browser tool in Affymetrix Genotyping Console software v. 4.1. The upper panel represents the copy number state of the mother, the middle panel of the father and the lower panel of the proband. Values of Y-axis indicate the inferred copy number according to probe intensities. Also, genes affected by the duplication are shown. B: A view in the UCSC Genome browser (NCBI build 36, March 2006) of the

duplicated region in our patient and patients reported in mentioned studies. The last black bar represents the smallest region of overlap (SRO) encompassing only the CREBBP gene.

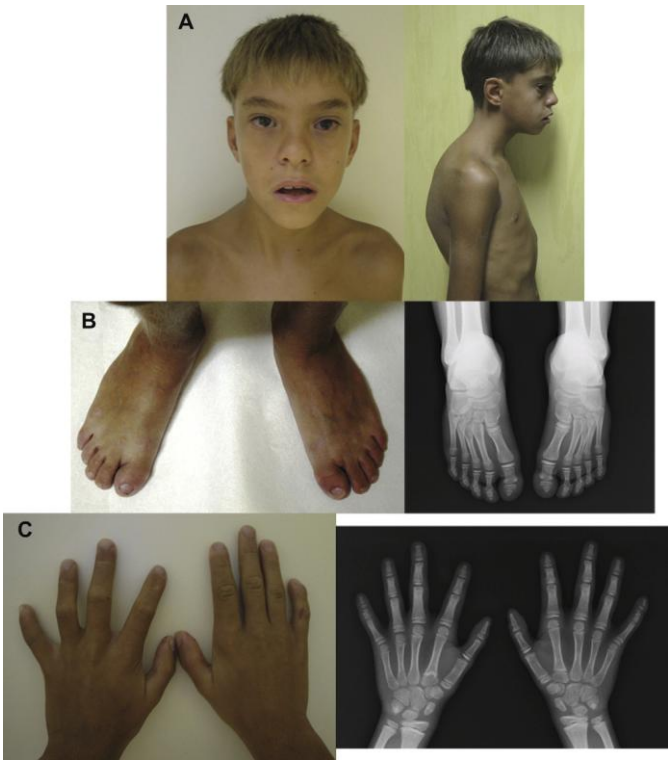

Fig. 2. A: Face with upward slant of palpebral features, narrow palpebral fissures, palpebral ptosis and epicanthus, dysmorphic ears, thoracic deformity; B: Feet with short and stubby first toes, X-rays showing short first metatarsal bones and cone shaped distal phalanges of the 1st toes; C: Hands with low set thumbs, mild skin syndactyly, 5th finger clinodactyly, camptodactyly of the 1st, 3rd, 4th and 5th fingers of the left hand, and 2nd, 4th and 5th fingers of the right hand, X-rays showing cone shaped third phalanges of the 1st and 2nd fingers.