

6q terminal deletion: a new contribution to genotype-phenotype correlation

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Deletion of chromosome 6q is a relatively rare clinical entity associated to a considerable variability of the phenotypic spectrum. Mental retardation, facial dimorphisms, seizures, and brain abnormalities are typical features of this syndrome but until recently genotype-phenotype correlations have been scarce. We report a 15-year-old boy with slight developmental delay, intellectual disability, hypotonia, bilateral eye cataracts, microcephaly, agenesis of the corpus callosum, ventriculomegaly, paroxysmal attacks, kyphoscoliosis and trigonocephaly. Cytogenetic analysis revealed a de novo karyotype 46,XY,del(6)(q25.3). Microarrays genomic analysis with Cytoscan 750K allowed the refinement of the breakpoint region to 6q26q27, spanning approximately 7.76 Mb. The variation of the features attributed to 6q deletion syndrome is due primarily to differences in size and location of the segmental aneuploidy. Several studies suggest that deletions of 6q25 region can cause more severe anomalies than those including 6q26-27. Absence of IUGR, ear anomalies, ear loss, cleft palate, cardiac defects and genital hypoplasia in our patient are compatible with studies that generally correlate those features with deletions of 6q25 region. In addition, our patient presents retinal abnormalities, which has been associated to 6q26-q27 deletion. Some new candidate genes, localized at 6qter, have recently been described as being associated with some clinical features; an example is the candidate gene DLL1 and holoprosencephaly. Analysis of the breakpoints in most cases revealed a potential common breakpoint region at 8.0-9.0Mb from the chromosome 6q terminus where a fragile site exists (FRA6E). This suggests the breakage at the FRA6E may be the mechanism behind chromosome 6q subtelomeric deletions in some of the cases. Once the genotype-phenotype correlations have been scarce until now, with this study we aim to contribute to a better knowledge of the genotype-phenotype correlation of 6q terminal deletion and help to identify critical regions for several clinical features and developmental relevant genes.