Intragenic CASK Deletion Found in Mosaicism in a Female Patient

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Background

CASK gene encodes for calcium/calmodulin-dependent serine protein kinase, essential for normal brain development. Disruption of CASK gene is associated with Mental Retardation and Microcephaly with Pontine and Cerebellar Hypoplasia (MICPCH, MIM 300749), where patients present a remarkably consistent phenotype, including severe intellectual disability/developmental delay, severe postnatal microcephaly and a distinctive facial phenotype.

Case Report

We report a 2-year-old female infant with a 109 Kbp intragenic deletion in CASK gene found in mosaicism, within approximately 25% of the cells. To the best of our knowledge, this is the first case to report mosaicism in a female carrier of intragenic CASK deletion.

Patient’s clinical report included postnatal microcephaly and reasonable psychomotor development, but slow in the motor area. Neurological examination results were normal.

Methodology

Array CGH was performed on an Affymetrix platform, Cytoscan 750K. Data analysis was performed on ChAS Software, Affymetrix (reference NCBI_hg19). MLPA was performed on peripheral blood following standard protocols.

Results

Array CGH revealed a genomic profile with a 109 Kbp deletion at Xp11.4 (41,480,031 - 41,589,514), involving CASK, GPR34 and GPR826 genes.

MLPA analysis confirmed a CASK intragenic deletion encompassing exons 4 to 12. Additionally, MLPA also detected a mosaic state of the deletion, in about 25% of the cells, which was not possible to identify on aCGH (Figure 1).

Conclusion

The present report describes a 2yo infant with postnatal microcephaly, but reasonable psychomotor development. For the first time, an intragenic CASK deletion is reported in a mosaic state, in about 25% of the cells. Parents were later studied with normal outcome and, therefore, the variant was established as de novo. These results, with high probability, explain the subtle phenotype of moderately slow motor development found the infant.