

INTRAGENIC *CASK* DELETION FOUND IN MOSAICISM IN A FEMALE PATIENT

JOAQUIM SÁ^{1*}, RAQUEL LEMOS², CÍNTIA VENTURA², SOFIA M PEREIRA², JORGE PINTO-BASTO¹, PURIFICAÇÃO TAVARES¹, PAULA RENDEIRO²

1 - CGC GENETICS/CENTRO DE GENÉTICA CLÍNICA, CLINICAL DEPARTMENT – PORTO, PORTUGAL
2 - CGC GENETICS/CENTRO DE GENÉTICA CLÍNICA, CYTOGENETICS LABORATORY – PORTO, PORTUGAL

* PRESENTING AUTHOR



PORTUGAL . USA . SPAIN

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

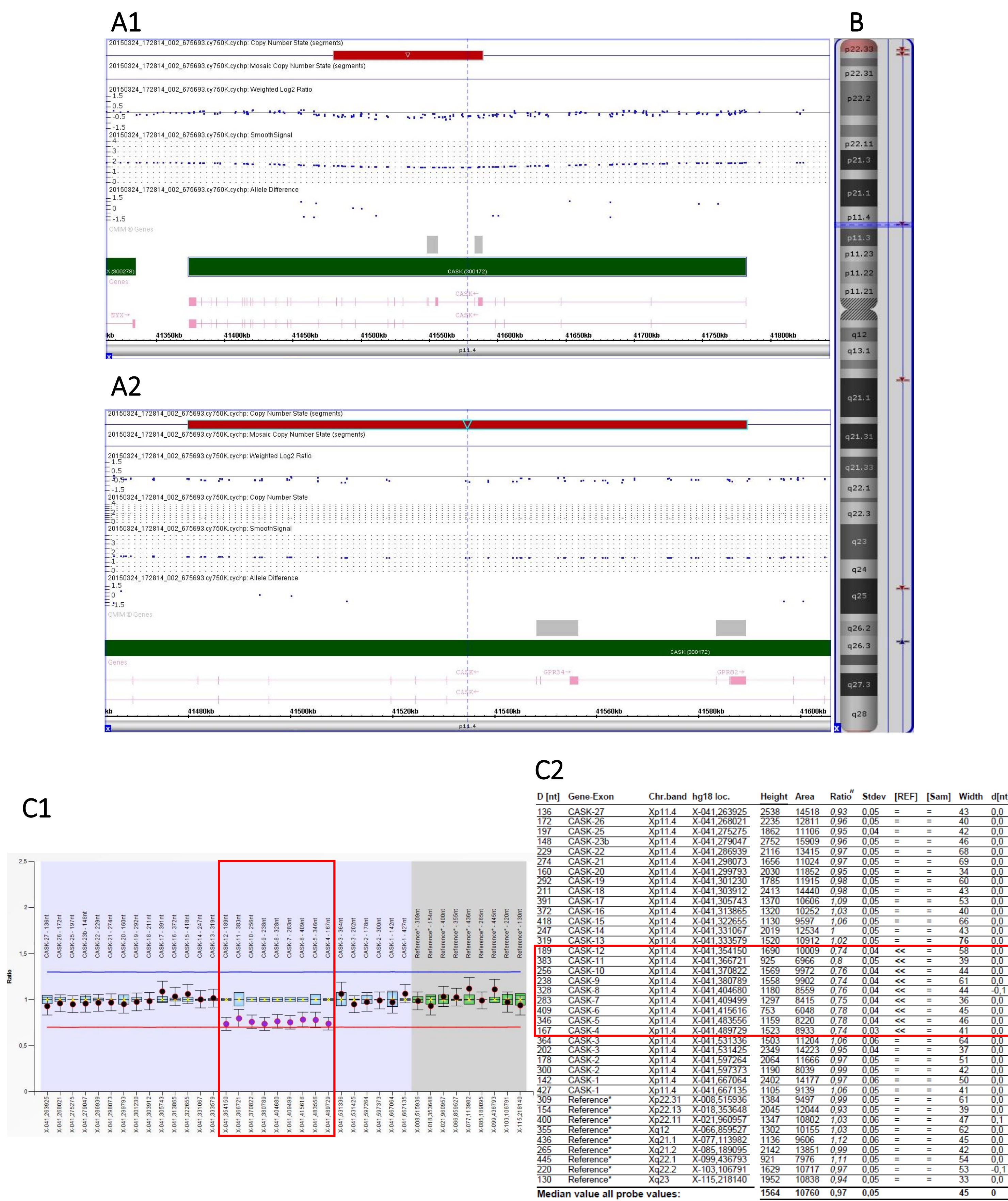
Array CGH was performed on an Affymetrix platform, Cytoscan 750K. Data analysis was performed on ChAS Software, Affymetrix (reference NCBI_hg19). MLPA was performed on peripheral blood following standard protocols.

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).

Figure 1. Array CGH results from proband with (A1) view of oligonucleotides profiles at Xp11.4, including a 109 Kbp intragenic deletion of *CASK* gene and (A2) detailed view of the *CASK* intragenic deletion, involving not only *CASK* gene, but also *GPR34* and *GPR826*. (B) View of chromosome X ideogram with focus on Xp11.4 (breakpoints: 41,480,031 - 41,589,514) deletion location. (C1) MLPA results allowed definition of *CASK* intragenic deletion, involving exons 4 to 12 and (C2) detect a mosaic state, with the deletion found in approximately 25% of the cells (inset).



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.



ABOUT THE PRESENTING AUTHOR

Joaquim Sá, Clinical Genetics Specialist at CGC Genetics

Pediatric Genetics Specialist since 2004.
Clinical Genetics Specialist at CGC Genetics since 2009.

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