PROKR2 in in girls with idiopathic central precocious puberty

Anna Grandone[1] , Caterina Luongo[1], Alessandra Cassio[2], Mariacarolina Salerno[3], Gianluca Tornese[4], Adalgisa Festa[1], Emanuele Miraglia del Giudice[1], Grazia Cirillo[1]

1: Department of Child, Woman, General and Specialized Surgery, Università degli Studi della Campania “L. Vanvitelli”
2: Department of Pediatrics, University of Bologna, Bologna, Italy
3: University Federico II, Pediatrics, Naples, Italy
4: Institute for Maternal and Child Health, IRCCS Burlo Garofolo, Trieste, Italy

BACKGROUND

PROKR2 is a 384-amino acid G-protein-coupled receptors (GPCR) that regulates GnRH secretion in the hypothalamus. PROKR2 mutations have been described as cause of a certain percentage of of hypogonadotropic hypogonadism and Kallmann syndrome.

In 2017 a heterozygous frameshift gain of function mutation of PROKR2 was identified in a 3.5-year-old girl with central precocious puberty (CPP).

OBJECTIVES

The aim of our study was to perform a mutation screening of such gene in girls with “early” onset CPP (first signs of puberty occurred ≤ 6 years of age).

METHODS

We enrolled 25 girls with idiopathic CPP with pubertal basal LH level or pubertal LH response to GnRH testing (mean age at first observation 5.5 years, range 2-7; mean age at first occurrence of thelarche 5 years old, range 1-6).

RESULTS

No rare variants were identified. Five polymorphisms were found (rs6076809, rs8116897, rS3746684, rs3746682, rs3746683). All except one (i.e. rs3746682) had a minor allele frequency (MAF) similar to that reported in literature. rs3746682 presented a MAF higher than described in The Exome Aggregation Consortium (ExAC) (0.84 in our population vs 0.25 from ExAC).

SNP	Position	MAF in our cohort	MAF in ExAc
rs6076809	c.-8-40C>T	0.06	0.03
rs8116897	c.458+62G>A	0.47	0.49
rS3746684	c.465C>T	0.37	0.37
rs3746682	c.585G>C	0.84	0.25
rs3746683	c.525C>G	0.18	0.10

CONCLUSIONS

Our data suggest that mutations in PROKR2 gene are not a frequent cause of central precocious puberty in girls, even in subjects with a very early onset CPP. As for other G-protein-coupled receptors (i.e. GPR54), gain of function mutations affecting these kind of hypothalamic regulating factors are a very rare cause of CPP in girls. The significance of the different MAF of rs3746682 polymorphism has to be investigated in larger samples of patients and controls.

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We have no conflicts of interesse to declare.

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Anna Grandone

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