MKRN3 Gene Mutation in a Case of Familial Central Precocious Puberty

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Background

Gain-of-function mutations in *KISS1* and *KISS1R* genes and loss-of-function mutations in the gene encoding *the makorin RING-finger protein 3 (MKRN3)* expressed only in the paternal allele are the most common genetic reasons of familial central precocious puberty (CPP).

Aim

We report a case of familial CPP and a pathogenetic variant in the *MKRN3* gene.

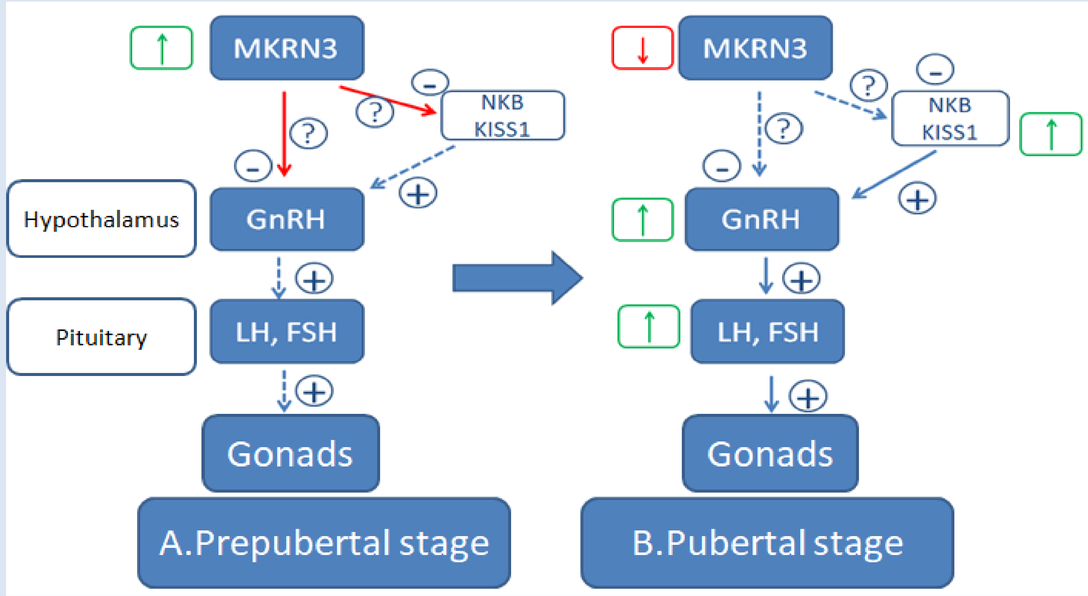

Figure 1. Initial mechanism of puberty in *MKRN3* deficiency

Case

7 years and 4 months old, girl

Complaint: Breast and pubic hair development of three months duration

Medical history: Normal

Family history: Unrelated parents, precocious puberty history in her father, paternal uncle and cousins (Figure 2).

Physical examination

- Weight: 34 kg (2.06 SDS), Height: 127 cm (0.78 SDS), BMI: 97p
- Target height 148.1 cm (-2.01 SDS)
- Predicted adult height 148.4 cm (-2.26 SDS)
- Mother's height -1.52 SDS, Father's height -3.44 SDS
- Breast Tanner stage II
- Pubic hair Tanner stage II
- Other system examinations normal

Laboratory and imaging findings : Thyroid function tests and routine biochemical examinations were normal. Other laboratory and imaging results are shown in Table 1.

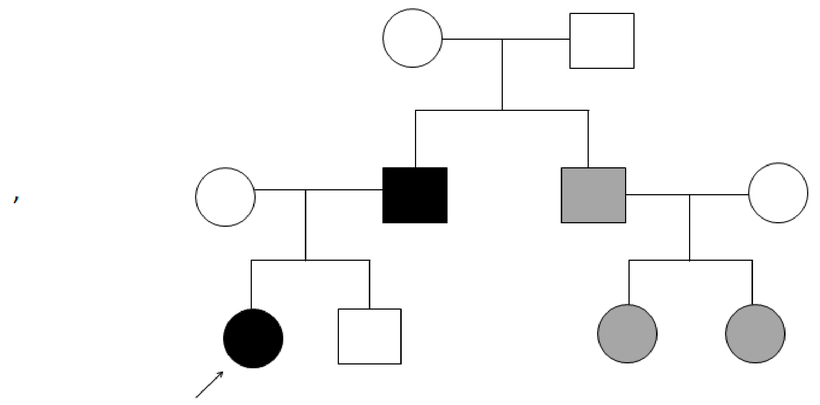

Figure 2. Pedigree

Figure 3. Electropherogram
C.482dupC heterozygous variant detected in *MKRN3* gene in the index case and her father (previously described, premature stop codon formation by frame shift)

Table 1. Laboratory and imaging findings

Basaline LH (N<0.1)	Basaline FSH (N: 0.1-4.3)	E_2 (N<12)	Peak LH after LHRH test	Peak FSH after LHRH test	Bone age (Greulich-Pyle)	Uterus length	Right ovary	Left ovary	Cranial MRI
0.8 IU/L	4.1 IU/L	17 pg/mL	18.1 IU/L	14.1 IU/L	10.5 years	50 mm	3.8 mL	3.3 mL	Normal

Clinical follow-up

- GnRH agonist treatment was started (3.75 mg leuprolide acetate every 28 days)

9 years and 3 months

- Weight 47 kg (2.25 SDS), Height 139.5 cm (0.55 SDS)
- Annual growth velocity 6.5 cm/year
- Bone age 12 years (ΔBA/ΔCA: 0.75)
- Predicted adult height 154.8 cm (-1.17 SDS)
- Breast Tanner stage III, Pubic hair Tanner stage III

Conclusion

In the evaluation of CPP cases, family history and genetic analysis are important in terms of early diagnosis and treatment with genetic counseling of the next generations.