GROWTH HORMONE DEFICIENCY DUE TO WHOLE-GENE DELETION OF *GHRHR*

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Introduction

- Various type of mutations in *GHRHR* cause isolated growth hormone deficiency type 1B. Herein, we report the clinical features associated with deletion of whole *GHRHR* gene for the first time.

4-$^{9/12}$-year-old ♀

- History: She was admitted due to severe short stature. She was born at term with birthweight of 3750 gr. Her height velocity slowed down after 2 years of age. The mother (157.8 cm, -0.82 SDS) and father (162 cm, -1.99 SDS) were second-degree cousins.
- Physical Examination: Her weight was 11.8 kg (-3.54 SDS) and height 91 cm (-3.38 SDS). Infantile facial appearance and prominent forehead were noted.
- Laboratory: Biochemistry, blood count, and thyroid function tests were normal and bone age was compatible with 2.5 years. IGF-1 (<25 ng/mL) and IGFBP-3 (610 ng/mL) levels were low. The peak GH levels following L-Dopa and ITT were 0.280 ng/mL and 0.420 ng/mL, respectively.
- Imaging: Magnetic resonance imaging revealed anterior pituitary hypoplasia.
- Treatment: Somatropin (25 mcg/kg/day) treatment was commenced.

Follow-up

- Following growth hormone treatment, annual height velocity ranged from 8 to 12 cm / year and no complications were observed. At the most recent follow-up when she was 13-year and 9-month-old, her height was 153.9cm (-0.97 SDS), BMI 19,2 (-0.49 SDS), and pubertal development compatible with Tanner stage 3.

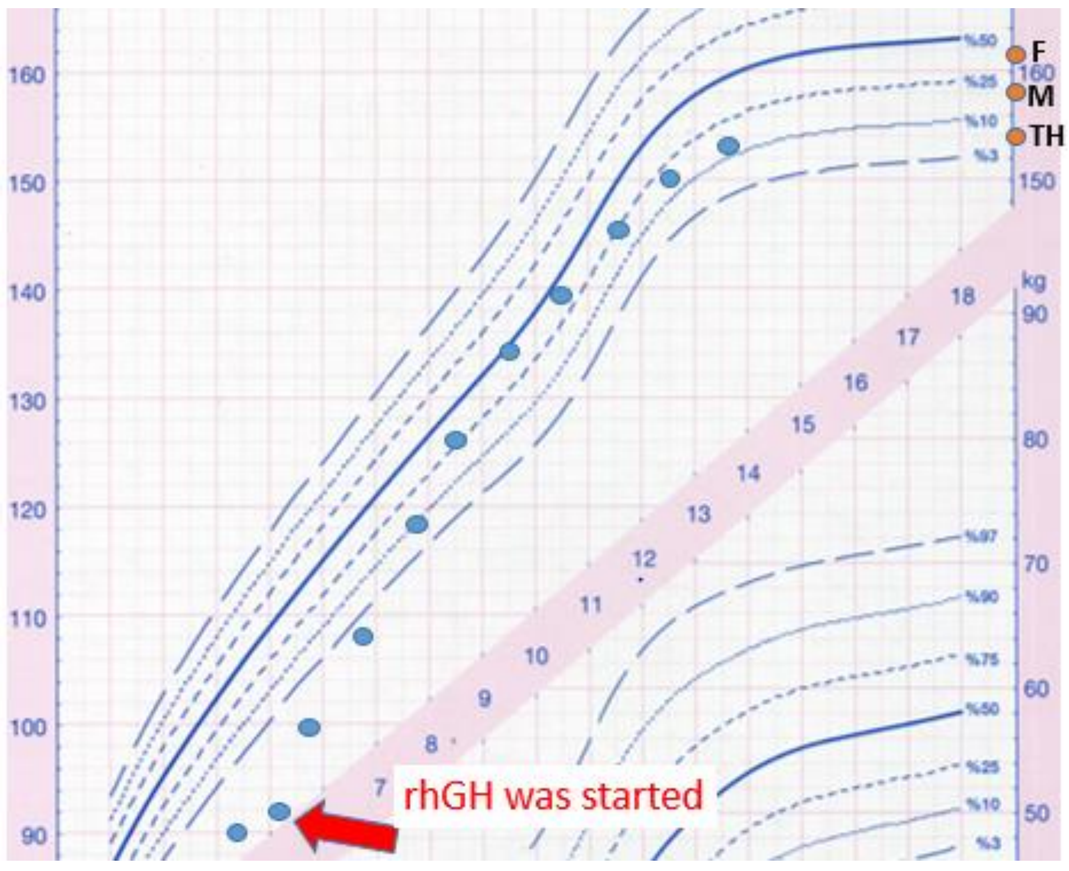

Figure: Height follow-up after rhGH therapy

Genetic Analyses and Laboratory Findings of Heterozygous Parents

- *GH1* sequencing was normal and homozygous whole-gene deletion of *GHRHR* was found.
- Both parents were heterozygous for this mutation.
- IGF-1 levels were low in the father (102 ng/mL, N:109-284) and low-normal in the mother (119 ng/mL, N:109-284). Glucagon stimulation tests revealed normal peak growth hormone responses in the mother (4.85 ng/mL) and father (10.4 ng/mL).

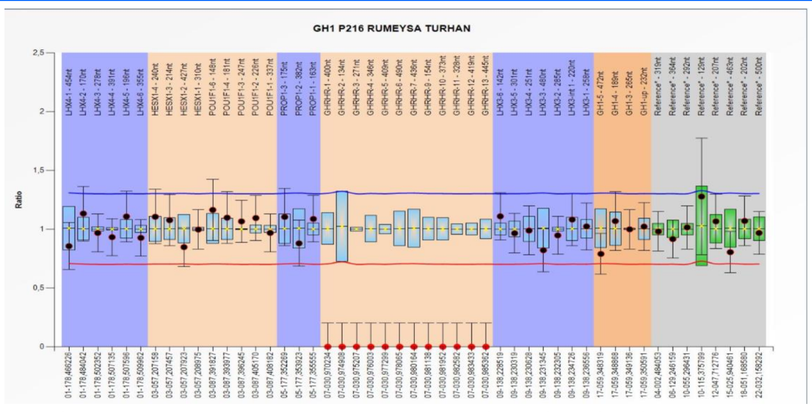

Figure: Homozygous *GNRHR* deletion in the MLPA

Conclusion

- This is the first report of homozygous whole gene deletion of *GHRHR*.
- The clinical features of homozygous whole-gene deletion of *GHRHR* are comparable with those of other types of *GHRHR* mutations.
- The carrier parents demonstrated normal growth hormone responses to the stimulation tests despite low IGF-1 levels.