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# Rahman Syndrome:

# Hypopituitarism Might Be Responsible For Changing Height Pattern

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## INTRODUCTION

Histones have important structural and regulatory roles mediating the dynamic packaging of DNA. The dysregulation of histone modification leads to overgrowth syndromes, such as Sotos and Weaver syndrome. Recently heterozygous variants in HIST1H1E, which encodes linker histone H 1.4 has been associated with Rahman Syndrome, which is characterized by a very rare complex phenotype consisting of overgrowth, dysmorphism, and intellectual disability. Growth pattern is typical and shows overgrowth in early ages decreasing over time. Here we report a new case of Rahman syndrome presenting with a novel finding of hypopituitarism.

## CASE

A $11^{7/12}$ years-old-boy was referred for hypothyroxinemia with normal TSH. He was born at 36 weeks, with a birth weight of 3660 g (+2.37 SDS) and length of 52 cm (+1.63 SDS). There was a complaint of tiredness, weight gain, hair loss, slowing of thoughts, and tendency to sleep for two months. On examination, his height, weight and target height were 158 cm (+1.46 SDS), 61 kg (+1.72 SDS) and 183.5 cm (+1.18 SDS) respectively. He had high anterior hairline, prominent forehead, sparse eyebrows, wide nasal bridge, hypertelorism, prominent cheekbones, dental erosions, simple auricles, fleshy hands and ears, pes planus, camptodactyly, kyphoscoliosis, pectus carinatum, and mild mental retardation (Fig. 1). Repeated thyroid function tests and symptoms were consistent with central hypothyroidism. Evaluation for other pituitary functions revealed central adrenal insufficiency. Levothyroxine and hydrocortisone replacements were initiated. Although the patient was growing well with IGF1 and IGFBP3 within normal limits, very low growth hormone (GH) response to clonidine and L-dopa stimulation tests (L-dopa and clonidine stimulated peak GH: 2.13 and 3.06 mcg/l respectively) were noted (Fig. 2). Pituitary MRI was normal. A whole exome analysis was performed and revealed a de-novo heterozygous 1bp duplication in *HIST1H1E* (p.Ala145Glyfs*51), which predicted a truncated protein. The duplication was located in the carboxyl-terminal domain where all previously reported variants have been located.

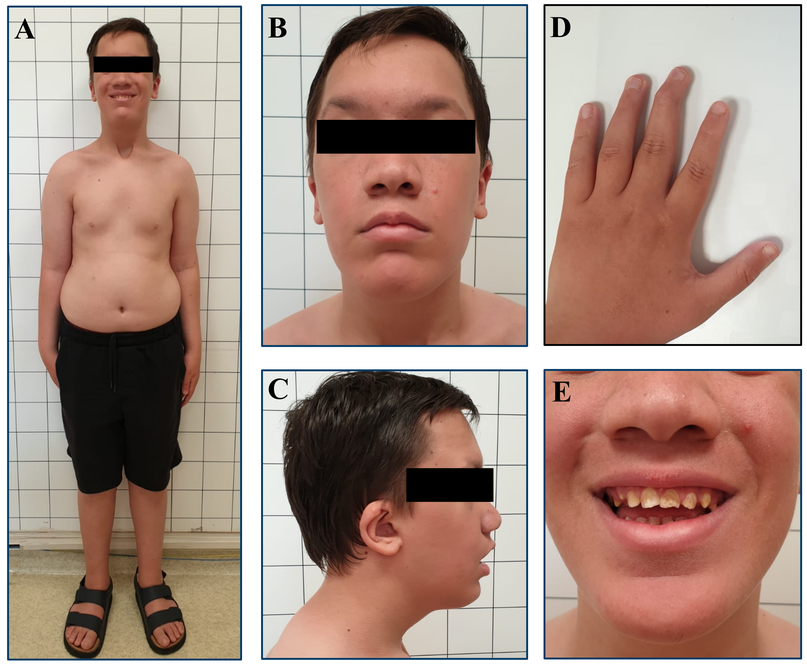


***Figure 1:*** Patient at $11^{7/12}$ years. Note the pectus deformity, (A), high anterior hairline, prominent forehead, sparse eyebrows, wide nasal bridge (B), simple auricles and kyphoscoliosis (C), fleshy hands, camptodactyly (D), and dental erosions (E).

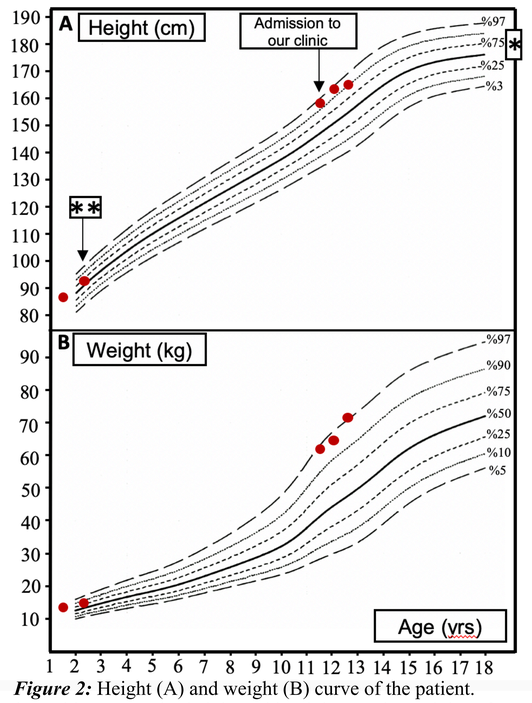


***Figure 2:*** Height (A) and weight (B) curve of the patient.
* Mid-parenteral height. **Height and weight from retrospective patient records.

## CONCLUSIONS

Our case is the first case of Rahman syndrome with complete endocrine evaluation and shows hypopituitarism as a novel manifestation of the disease. This finding might explain previously unexplained progressive decline in height percentile with age in Rahman Syndrome. Normal IGF-I and IGFBP-3 levels despite bona fide GH deficiency remains to be explained.

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