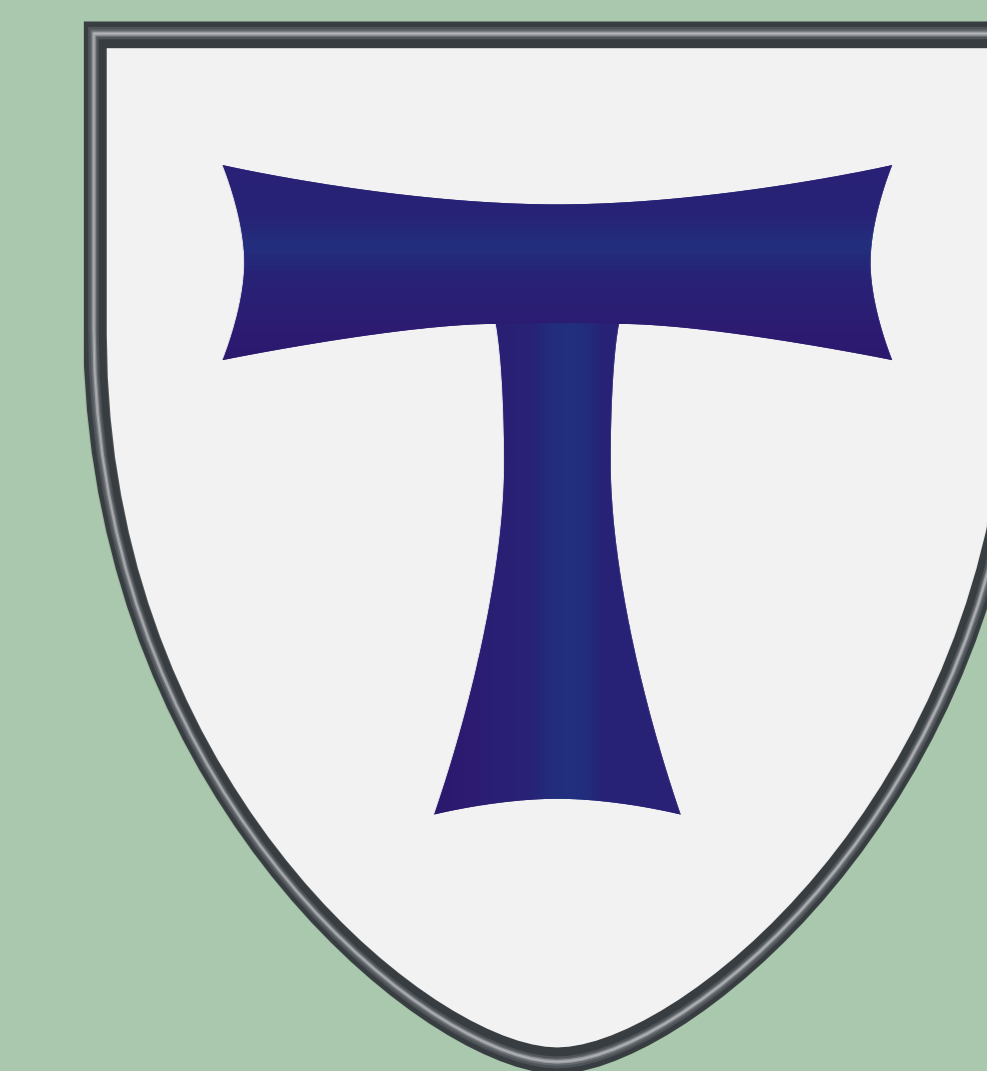


A girl with concurrent congenital adrenal hyperplasia, isolated growth hormone deficiency type II (IGHD II) and a new mutation in the GH 1 gene



N.Genthner, W. F. Blum, C.Kamrath, and S. A. Wudy

Justus Liebig University, Center of Child and Adolescent Medicine, Division of Pediatric Endocrinology and Diabetology, Giessen, Germany

INTRODUCTION

Classical salt wasting congenital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency (21OHD) is a rare disorder, as is isolated growth hormone (GH) deficiency Type II (IGHD II) due to mutation of the growth hormone gene GH1.

Here we present a highly unusual and instructive case in which both diseases occurred in parallel and a new mutation in the GH I gene was discovered.

CASE

- Early Childhood:
 - Diagnosis of classical salt wasting CAH due to 21OHD by hormonal and genetic analyses
- Adolescence:
 - Failure of growth spurt at puberty to reach family target height range.
 - At the age of 15 years height of 148.3cm (-2.8 SDS) (parental target height 155cm (-2,03 SDS))

METHOD

- Testing for growth factors IGF-I and IGF-BP3
- X-ray of the left hand (bone age)
- GH stimulation test (arginine test)
- SHOX diagnostics (biosencia Humangenetik, Ingelheim)
- Next generation sequencing gene panel (biosencia Humangenetik, Ingelheim)

RESULTS

- Growth hormones
 - IGF-I level low (84µg/L, SDS -3.39)
 - IGFBP-3 normal (2.95mg/L, -SDS 0.54)
- X-ray:
 - Unusual for a patient with CAH, bone age was delayed by 3 years
- GH stimulation test (arginine test)
 - GH increase to max. 12,6 ng/mL
- SHOX Diagnostics
 - negative
- Next generation sequencing gene panel
 - heterozygous variant c.235T>G p.(Cys79Gly) in exon 3 of the GH1 gene was detected

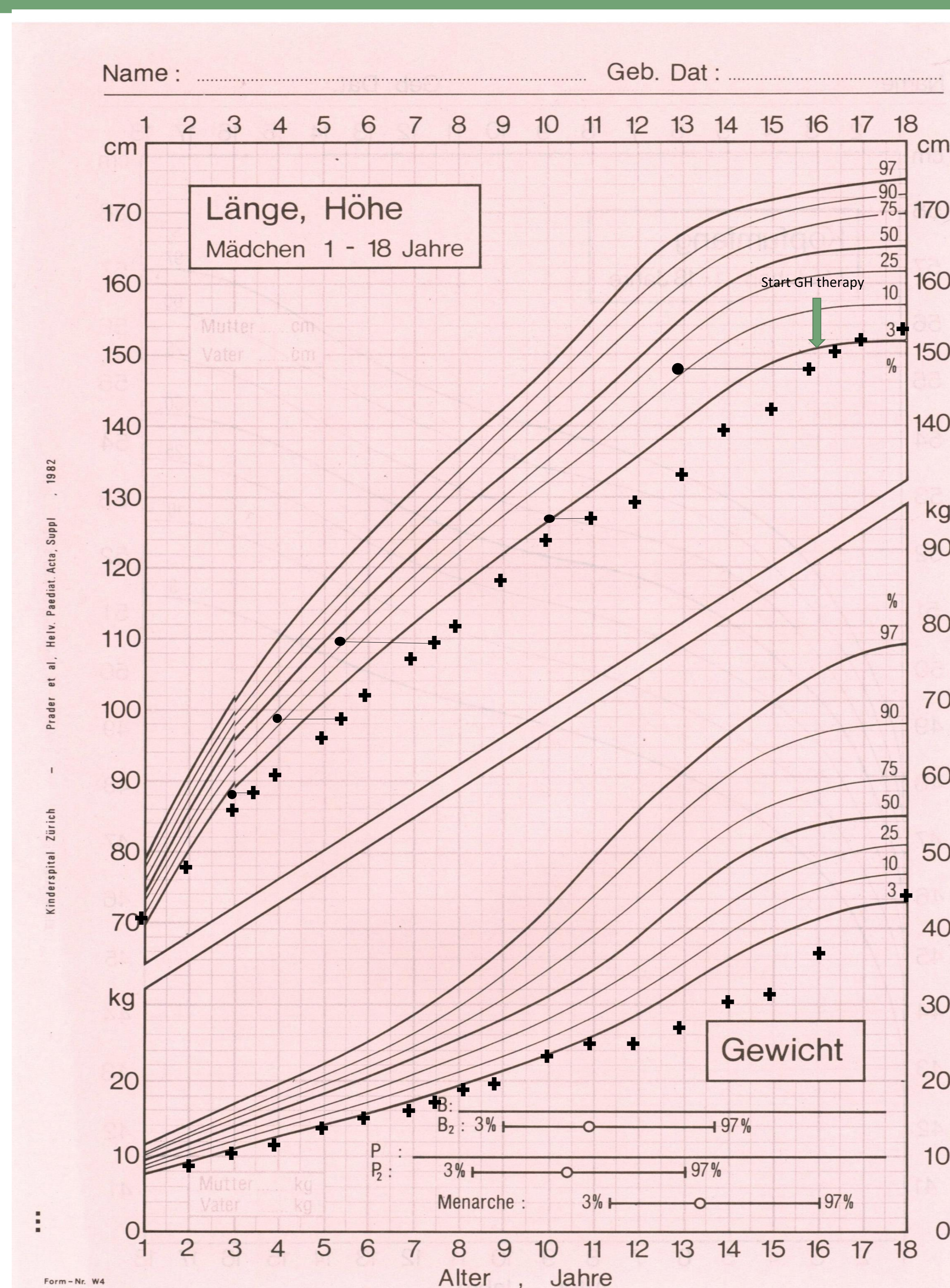


Figure 1, girls growth curve 1-18years, Prader et al

CONCLUSIONS

- GH exon 3 mutation of our patient is highly likely to cause the formation of partially bioinactive GH as has been described for the mutation Exon 3, c.236G>C by Besson et al. (1)
- This mutation (loss of cystein) interrupts the disulfide bridge at position 53 of the mature GH peptide which is important for the correct tertiary structure
- A "toxic" GH variant is formed, which interferes with the secretion of normal GH and further leads to the destruction of somatotrophic cells.
- Negative dominant effect in heterozygous : IGHD type II patients
- additional genetic analysis of both parents, detected the same heterozygous variant of the GH1 gene in the father
- paternally inherited, autosomal dominant form of IGHD type II was diagnosed
- Important: a normal GH stimulation test does not rule out growth hormone deficiency in any case!

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CONTACT INFORMATION

The authors have nothing to disclose

Nora.Genthner@paediat.med.uni-giessen.de

