LATE REFERRAL OF SIBILINGS WITH COMBINED PITUITARY HORMONE DEFICIENCY **(PROP1)**

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GENE:
PROP1

PROTEIN:
PROP1

HUMAN PHENOTYPE:
Deficiency of
- GH
- TSH
- prolactin
- gonadotropin

Evolving ACTH deficiency

Enlarged pituitary with later involution

INHERITANCE:
recessive

INTRODUCTION

PROP1 (Prophet of POUF1) mutations are the most frequent genetic cause of combined anterior pituitary hormone deficiency.
The PROP1 gene encodes a transcription factor of synthesis: somatotrophs, lactotrophs, thyreotrops and gonadothrops. These mutations are characterized by great clinical variability, including time of onset of hormonal deficiencies, hypophyseal dimensions and secretion of cortisol.

OBJECTIVE

Referral of children with growth hormone deficiency (GHD) is beside all checkpoints during childhood rather late. High genetic potential and living in countryside could be additional difficulties for GHD and additional hormone deficiencies detection.

A

METHODS

We present brother and sister addmited for tests;
boy's (age 16y 3/12) Dg: Delayed puberty
girl's (age 12 y 11/12) Dg: Short stature and Obesity.

Final height for both was according genetic potential (GP) at p90. Boy's height was on p5, BMI 28,3 (p95), volume of both testis were 1,5 ml (Prader), without secondary sexual characteristics, -5 to -7 SD delayed bone maturation, MRI scan of pituitary-enlarged.

Girl was 29 cm smaller than GP height (p 90), obese: BMI 27,2 (p95). Laboratory tests for both showed central hypothyreosis, GHD, low gonadotropins and low prolactine. Later done cortisol and ACTH were low (Synachen test) in both. Girl's bone age was -2 to -3 SD, without secondary sexual characteristics, regular size of pituitary gland with contrast opacifications.

B

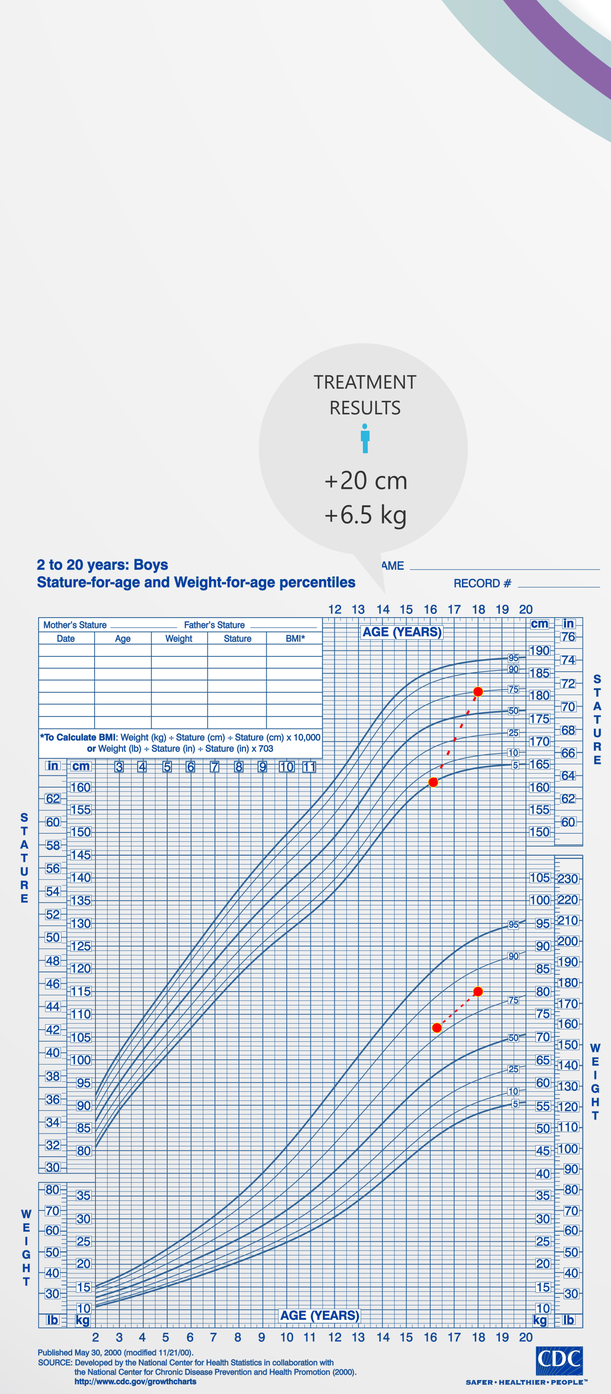
TREATMENT

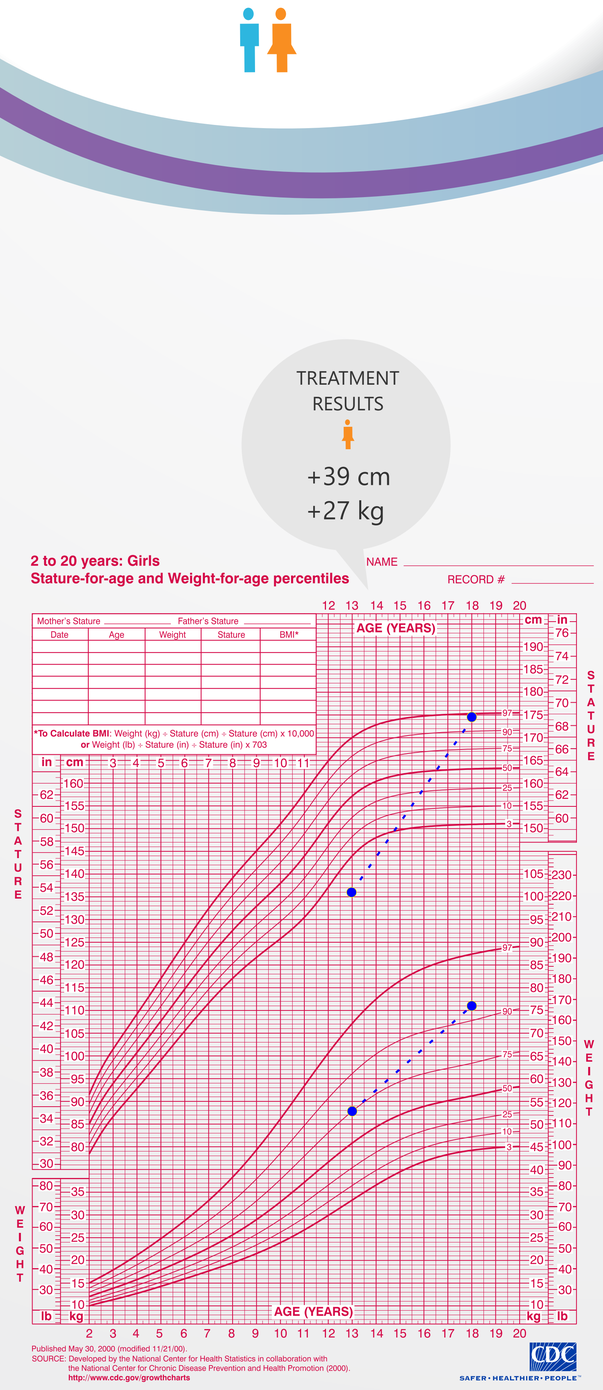
Substitution of lacking hormones:
thyroid, GH, later hydrocortisone,
depot testosterone injections monthly (boy)
- secondary sexual characteristics developed,
and in girl estrogen substitution - secondary sexual characteristics developed and later had spontaneous periods without hormone substitution.

Additional treatment for both:
Metformin (serious insulin resistance)
and supplementation with vitamin D.

TREATMENT RESULTS
+20 cm
+6.5 kg

TREATMENT RESULTS
+39 cm
+27 kg





RESULTS

The genetic study was performed by polymerase chain reaction confirmed homozygous mutation in the **PROP1** gene with a 2-bp deletion (**c.301–302delAG**). At the age of 18 years boy's height was on p75 with BMI 24,4, developed male secondary sex characteristics (monthly substitution), and girl's height was on p90, BMI 28, sexual development completed, regular periods. Both had continuous substitution with thyroid hormones, hydrocortisone, and metformin treatment.

CONCLUSION

Although first referral of brother and sister with combined pituitary hormone deficiency **(PROP 1)** was very late they gained height almost near GP, they stayed no to moderately obese and gained normal secondary sexual characteristics with continuous thyroid and suprarenal substitution.

C

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