CENTRAL HYPOTHYROIDISM WITH PITUITARY ENLARGEMENT AND NO GENE ALTERATIONS

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Introduction

Central hypothyroidism (CeH) is a characterized by defective thyroid hormone production due to failure of stimulation by thyrotropin (TSH) with a normal thyroid gland. Disorders of the pituitary gland (secondary hypothyroidism) or the hypothalamus (tertiary hypothyroidism) cause alterations of TSH secretion. CeH can be a part of multiple pituitary deficiencies or can be isolated, its clinical presentation can be moderate or severe. As in primary hypothyroidism a delayed onset of treatment can cause profound neurological defects. Low circulating free thyroxine (FT4) concentrations associated with low or normal serum TSH make the hormonal diagnosis of the CeH.

Patient report

A 9 year old boy (07 Aug. 20) was referred for **proportionate short stature** (-2.7 SD). He complained of **fatigue** and had **mild peripheral edema.**

Parameter	Values after L-T4 treatment
T4	3,1ug/dL 3,7ug/dL 4.2ug/dL 4,6ug/dL
TSH	0.09 uIU/ML 0.22uIU/ML 0,36 uIU/ML 0.5uIU/ML

Parameter	Values Before L-T4 Treatment	Reference value
T4	2.9 ug/dL 2.7 ug/dL	4.50-12,50ug/dL
TSH	0.04 Ulu/ML 0.04 Ulu/ML	0.400-4.00Ulu/ML
TRH Stimulating Test	**low TSH** <0.004 Ulu/ML **low T4** 2.70	0.400-4.00Ulu/ML 4.50-12.50 ug/dL
Prolactin	normal	
GH reserve	normal	

Ultrasound of the Thyroid gland → **NORMALIZED Homogenous thyroid**

MRI of the Sella → Enlargement ‘’tumor’’ → **NORMALIZED** after one year of sodium L Thyroxine

Discussion

CeH is usually sporadic and affects patients of all ages. The estimated prevalence is from 1: 16,000 to about 1: 100,000.

Expansive lesions, destructive processes, congenital malformations, autoimmunity, vascular accidents, haemochromatosis can also cause acquired CeH. Inheritable conditions cause of CeH in newborns and infants, or later in childhood and up to adulthood. Mutations in genes encoding transcription factors that regulate pituitary development are the major cause of heritable MPHDs. In these cases, The most frequently identified mutations associated with MPHD are in *PROP1*.

The association with multiple pituitary deficiencies and or various congenital anomalies of the pituitary, brain (absent in the reported patient) were also reason not to analyze (*HESX1*, *LHX3*, *LHX4*, *SOX3*, *OTX2*, *PROP1*, *POU1F1*).

MOST LIKELY GENES INVOLVED IN CENTRAL HYPOTHYREOIDISM WERE SEQUENCED

Genes (OMIM*)	Inheritance and phenotype (OMIM*)
TSHB (188540)	an isolated CeH of neonatal onset with low TSH, high α-GSU, normal PRL concentrations and pituitary hyperplasia reversible on L-T4 replacement
IGSF1 *(300137)*	is associated with low PRL, GH deficiency, metabolic syndrome, and postpubertal macroorchidism (+2.0 SDS)
TRHR (188545)	mutations result in CeH with normal TSH and low PRL concentrations, blunted TSH/PRL responses to TRH.
PROP1 (601538)	mutations were not tested as the child did not have combined pituitary hormone deficits (GH, PRL, LH/FSH defects, and delayed ACTH deficiency). In addition, this condition is associated with small to large pituitary volume
TBL1X (300196)	PENDING
IRS4 *(300904)*	PENDING

Cnonclusion: We present a child with central hypothyroidism which manifested an enlargement of the pituitary gland which was almost totally removed by sodium L thyroxine treatment after one year. He had a catch up growth which got him in a parental height range after 1.5 years.

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