Growth impairment in children with severe autoimmune primary hypothyroidism and pituitary hyperplasia without goiter

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INTRODUCTION

Prolonged severe hypothyroidism due to Hashimoto's thyroiditis (HT) is a rare cause of pituitary hyperplasia (PH) in children. Loss of thyroxine negative feedback causes a TRH-dependent hyperplasia of pituitary thyrotroph cells resulting in adenohypophysis enlargement. A transdifferentiation of pituitary somatotroph cells into thyrotroph cells could explain growth failure in those patients.

AIM

We report a case series of patients with growth impairment diagnosed with PH due to severe acquired hypothyroidism in which evaluation of anterior pituitary function at diagnosis was performed.

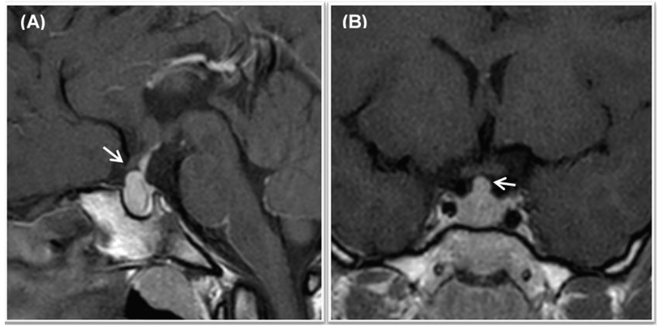
CONCLUSIONS

Since thyroid hormones promote GH biosynthesis, in severe primary hypothyroidism GH deficiency could be expected proportional to the hypothyroidism degree. However, in some hypothyroid patients IGF-1 concentration may be within normal range even though they have growth arrest. This is the largest pediatric cohort with PH due to severe HT in which growth arrest was the most evident presenting sign. Atrophic HT phenotype might be correlated with this specific clinical presentation. Prospective studies are needed to evaluate pituitary enlargement and thyroid volume in patients with extremely high TSH without goiter.

CASE SERIES

Ten Caucasian patients (6 females – 4 males) were evaluated in 4 Centers of Peadiatric Endocrinology because of **growth arrest (in 70% of patients) or growth impairment**. Median age, height and BMI at diagnosis of HT were 11 years (IQR 8 – 14.8), - 2.0 SDS (-3.58 – 0.78) and 1.12 SDS (0 – 3.1), respectively. Difference between the median values of height and target height was 1.5 SDS. Median bone age retardation was 2.5 years (0 – 5.1). No goiter was documented. **Brain MRI, performed to exclude intracranial expansive lesions, documented adenohypophysis enlargement in all of children**. Median pituitary volume was 650 mm^3 (504 - 1965). **Hypothyroidism due to HT was confirmed in the entire cohort** by biochemical evaluation (median and IQR: TSH 981 mIU/L, 236.6 – 1648; FT4 3.1 pmol/L, 0.5 - 6.2; antibodies to thyroid peroxidase 809 IU/ml, 88.8 – 4480; antibodies to thyroglobulin 352 IU/ml, 15.5 - 2040) and ultrasound evaluation [reduced (40%) or normal (60%) thyroid volume associated with diffusely hypoechogenic, coarse and heterogeneous parenchymal echotexture]. Levothyroxine treatment (2 mcg/kg/day, 1.5 - 3.5) was started. Other basal hormonal evaluation demonstrated hyperprolactinemia (60%) and low concentrations of cortisol (40%). **IGF-1 was lower than - 2 SDS in 50% of patients; those two patients underwent stimulation test growth hormone was subnormal.** Furthermore, 70% of them had high total and LDL-cholesterol levels and 50% showed high triglycerides and transaminases levels.

Fig. 1 - Pituitary gland Magnetic Resonance Imaging (MRI) after Gadolinium-DTPA administration of a patient at the time of diagnosis of pituitary hyperplasia and severe hypothyrodism



Sagittal (A) and Coronal T1-weighted (B) images showed diffuse enlargement of the pituitary gland and a homogeneous enhancement of the gland. The enlarged pars tuberalis extended into the suprasellar cystern with mild compression of the optic chiasm (arrows).

Tab. 1 – Clinical features and TSH, FT4 and IGF-1 SDS levels.

Patients	Sex	Age (years)	Height SDS	BMI SDS	Bone age retardation (years)	GA/PG	Dry and thickened skin	Hypokinetic	Apathy	Fatigue	Constipation	Sleepiness	Cold Intolerance	TSH (mUI/L)	FT4 (ng/dL)	IGF-1 SDS
Patient 1	F	13	-3.58	1.08	2.75	GA	yes	no	no	no	no	no	no	236.6	3.2	< - 2
Patient 2	F	11	-2.3	1.16	0	GA	no	yes	yes	no	yes	no	no	319	2.79	< - 2
Patient 3	F	8	-0.84	1.06	1.8	GA	yes	yes	no	yes	yes	no	no	1214	1.03	- 1.7
Patient 4	M	11.7	-1.67	2.08	3.1	GA	yes	yes	yes	yes	yes	yes	yes	962	5.5	< - 2
Patient 5	M	14.8	-2.09	0.71	2.2	GA	yes	yes	yes	yes	yes	yes	yes	1000	5.5	< - 2
Patient 6	F	8.5	-2.7	0.87	4.9	GA	yes	yes	yes	yes	yes	yes	yes	1000	1.93	- 0.5
Patient 7	F	8.5	-1.74	0.01	2.9	GA	yes	yes	yes	yes	yes	yes	yes	359.5	6.17	-1
Patient 8	M	11.1	-2.19	1.74	5.1	PG	yes	yes	yes	no	no	no	no	1648	3	-1
Patient 9	F	8.1	-0.75	2.22	0	PG	yes	yes	no	yes	no	no	yes	1113	4.3	< - 2
Patient 10	M	11.5	0.78	3.13	0	PG	no	yes	yes	yes	no	yes	no	324	0.5	0.5

Growth arrest (GA); Poor linear growth (PG)

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