Pituitary hyperplasia as a complication of severe hypothyroidism due to Hashimoto's thyroiditis could impair pituitary function.

Domenico Corica[1], Francesca Granata[2], Karol Galletta[2], Malgorzata Wasniewska[1]

[1] *Department of Human Pathology of Adulthood and Childhood, Unit of Pediatrics, University of Messina, Messina, Italy*

[2]*Department of Biomedical, Dental, Morphological and Functional Imaging Sciences, Unit of Radiology, University of Messina, Messina, Italy.*

Poster N°
P3-209

Introduction

Long-standing primary hypothyroidism is an unusual cause of pituitary hyperplasia (PH) in children, sometimes difficult to distinguish on CT or MRI from primary pituitary tumors. Loss of thyroxine feedback determines overproduction of thyrotropin releasing hormone (TRH), followed by TSH-releasing cells hyperplasia in the anterior pituitary and a consequent pituitary enlargement. Levothyroxine replacement therapy has been shown to usually determine regression of PH. We report the case of 11-years-old girl with PH in which growth arrest was the only symptom of a severe primary hypothyroidism due to Hashimoto's thyroiditis (HT).

Case report

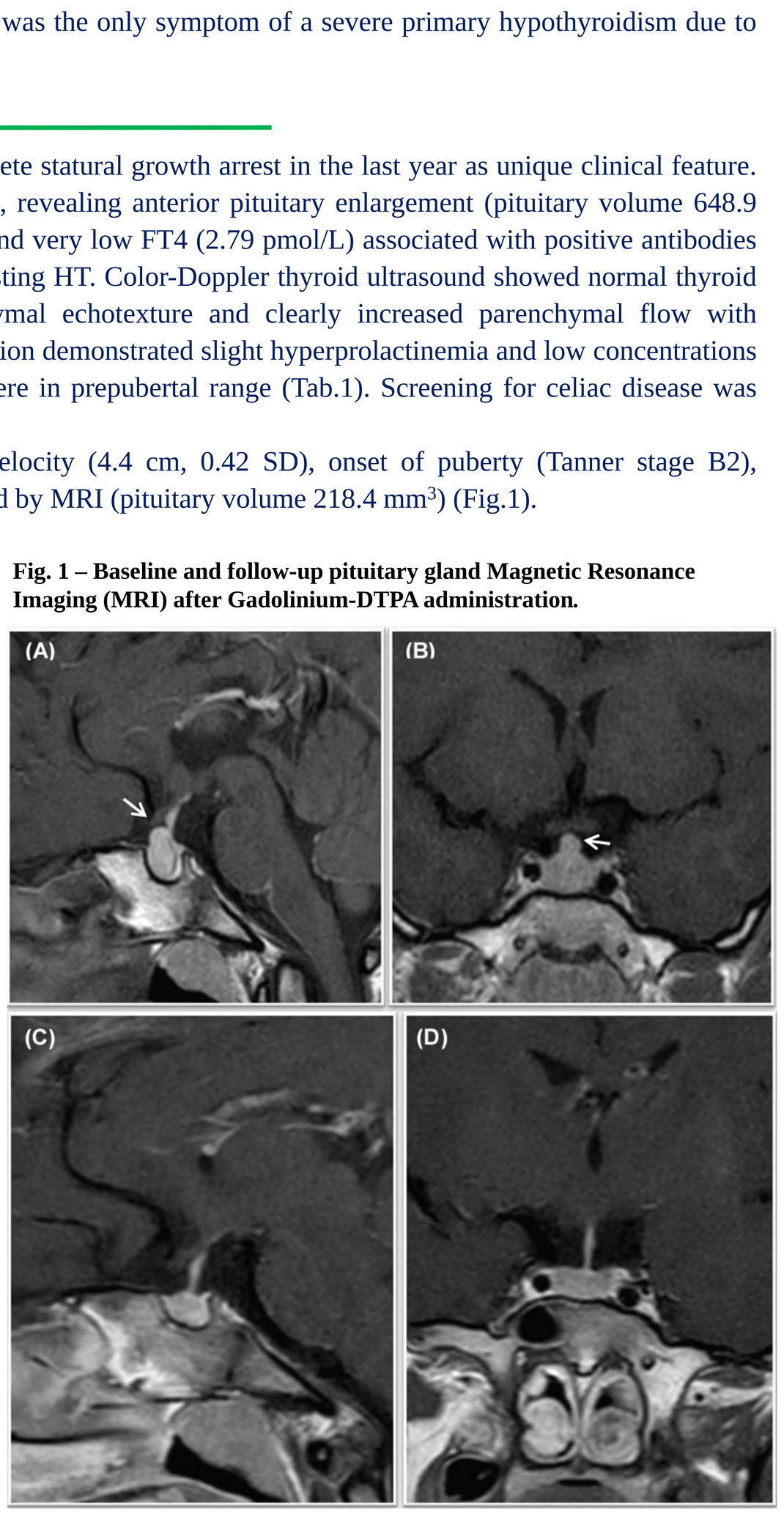
A 11-years-old, Caucasian, prepubertal girl referred to Outpatient Clinic because of complete statural growth arrest in the last year as unique clinical feature. To exclude the intracranial expansive pathology, brain MRI was immediately performed, revealing anterior pituitary enlargement (pituitary volume 648.9 mm^3) (Fig. 1). Hormonal evaluation documented: markedly elevated TSH (319 µUI/ml) and very low FT4 (2.79 pmol/L) associated with positive antibodies to thyroglobulin and thyroid peroxidase (289 UI/ml and 4580 UI/ml, respectively), suggesting HT. Color-Doppler thyroid ultrasound showed normal thyroid volume associated with diffusely hypoechogenic, coarse and heterogeneous parenchymal echotexture and clearly increased parenchymal flow with homogenous distribution, consistent with chronic thyroiditis. Other basal hormonal evaluation demonstrated slight hyperprolactinemia and low concentrations of cortisol, IGF-1 with subnormal GH secretion (Tab.1). Gonadotropins and estradiol were in prepubertal range (Tab.1). Screening for celiac disease was negative. Levothyroxine treatment (2 mcg/kg/day) was immediately started.

Six month after the beginning of levothyroxine, patient presented increased growth velocity (4.4 cm, 0.42 SD), onset of puberty (Tanner stage B2), normalization of thyroid and pituitary function (Tab.1). PH regression was also documented by MRI (pituitary volume 218.4 mm^3) (Fig.1).

Tab.1- Auxological data and hormonal pattern at diagnosis and during follow-up.

	Diagnosis	One-month follow-up	Six-months follow-up	Normal values
Stature (cm)	130	131.6	134.4	
Weight (kg)	34.5	32.4	31.4	
TSH (µUI/ml)	319	7.21	0.6	0.27 - 4.2
FT4 (pmol/L)	2.79	11.7	18.7	12 - 22
FT3 (pg/ml)	1.2	4.58	5.36	2.0 - 4.4
Antibody to TG (UI/ml)	289	---	291	0 - 115
Antibody to TPO (UI/ml)	4580	---	1755	0 - 34
IGF-1 (ng/ml)	88.5	148.3	182.8	146 - 462
GH peak to clonidine (ng/ml)	6	---	10.52	≥ 8
GH peak to glucagon (ng/ml)	7	---	---	≥ 8
Cortisol (ug/dl)	5.30	7.68	11.87	7.3 - 32
ACTH (pg/ml)	11.3	14.64	13.93	0 - 50
Estradiol (pg/ml)	< 5	136	42.3	12.5 - 166
FSH (mUI/ml)	2.15	4.59	4.01	< 11.1
LH (mUI/ml)	< 0.3	0.74	0.88	< 11.9
PRL (µUI/ml)	497	91.1	88.6	102 - 496

Fig. 1 – Baseline and follow-up pituitary gland Magnetic Resonance Imaging (MRI) after Gadolinium-DTPA administration.



Baseline *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).*

Six months after levothyroxine's beginning*, Sagittal (C) and Coronal T1-weighted (D) images revealed a decrease in size of the pituitary gland and regression of the mass effect.*

Conclusions

PH due to primary hypothyroidism should be considered in the differential diagnosis of statural growth arrest. PH may cause a temporary deficit of the pituitary hormones secretion and, in particular, a GH secretion impairment due, at least partially, to TRH-induced transdifferentiation of somatotroph into thyrotroph cells. In patients with pituitary enlargement, thyroid function tests are important to recognize PH secondary to PHT to avoid unnecessary surgery.

Radiana S, et al. Somatotroph to thyrotroph cell trans differentiation during experimental hypothyroidism- a light and electron-microscopy study. Journal of Cellular and Molecular Medicine 2003 7 297-306
Vidal S, et al. Transdifferentiation of somatotrophs to thyrotrophs in the pituitary of patients with protracted primary hypothyroidism. Virchows Archiv 2000 436 43-51.