Case Report

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Pituitary Hyperplasia Secondary to Hashimoto's Thyroiditis Mimicking Macroadenoma in a Child: A Case Report

Radiology Section

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ABSTRACT

Pituitary Hyperplasia (PH), which frequently occurs secondary to hypothyroidism, can mimic pituitary adenomas, necessitating accurate differentiation to avoid unnecessary surgical intervention. The present case report outlines the diagnostic journey of a six-year-old female who presented with clinical and imaging features suggestive of a pituitary macroadenoma. Surprisingly, thyroid function testing revealed coexisting Hashimoto thyroiditis and the patient was started on thyroxine replacement therapy for two months. Upon follow-up imaging, the size of the gland was reduced, leading to a revision of the diagnosis to PH. Herein, the authors emphasise the challenges in interpreting pituitary abnormalities in children, as conditions like hyperplasia can mimic tumours on imaging.

Keywords: Nipple sign, Pituitary macroadenoma, Thyroid functions, Tumours

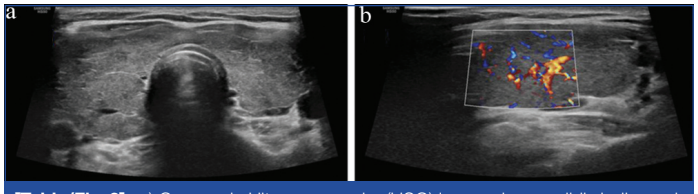
CASE REPORT

A six-year-old female with normal developmental milestones presented with frontal headache and fever for five days. On further questioning, there was a history of easy fatigability, dry skin and intolerance to cold for eight months. There were no complaints of vomiting, abdominal symptoms, rash, blurring of vision, or burning micturition. There was no family history of obesity or hypothyroidism. Three months prior, she had been diagnosed with severe pulmonary stenosis, mild pulmonary regurgitation and pericardial effusion. She underwent pericardial tapping and balloon pulmonary valvotomy for the same.

On physical examination, the patient was short-statured (height: 90 cm) and overweight (weight: 25 kg; body mass index: 27 kg/m^2). Cardiovascular, neurological and respiratory examinations were non contributory. Serum prolactin levels were raised (64 ng/mL), Thyroid Stimulating Hormone (TSH) levels were >100 µIU/mL and anti-Thyroid Peroxidase (TPO) antibodies were elevated (272.5 IU/mL) [Table/Fig-1]. A neck ultrasound revealed uneven echogenicity of both thyroid glands with significantly increased vascularity [Table/Fig-2a,b]. Based on clinical, laboratory and radiological findings, a diagnosis of Hashimoto's thyroiditis was confirmed.

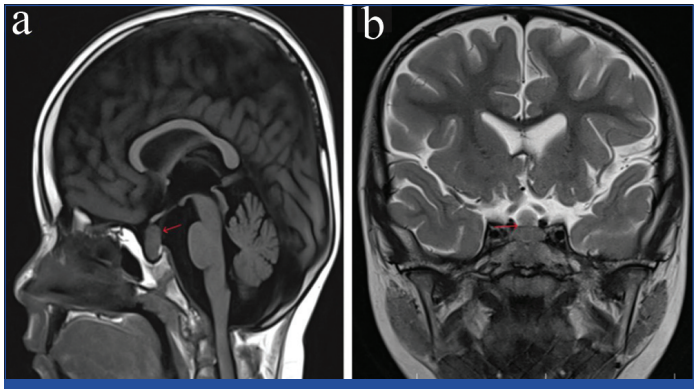
S. No.	Variables	Before treatment	After treatment	Normal values
1	TSH (µIU/mL)	>100	72.5	0.7- 6
2	Prolactin (ng/mL)	64.6	20	4- 23
3	Cortisol (µg/dL)	9.3	9	3.7-19.4
4	FSH (mIU/mL)	9.6	1.89	0.4 - 5.5
5	LH (mIU/mL)	<0.07	<0.07	0.02 - 0.3
6	Anti-TPO antibody (IU/mL)	272.5-positive	264.4 -positive	<35

[Table/Fig-1]: Hormonal pattern at diagnosis and during follow-up.
TSH: Thyroid-stimulating hormone; FSH: Follicle stimulating hormone; LH: Luteinising hormone; Anti-TPO antibody: Anti-thyroid peroxidase antibody



[Table/Fig-2]: a) Grey scale Ultrasonography (USG) image shows mildly bulky and heterogeneous echo texture of thyroid gland; b) The thyroid gland shows raised vascularity on colour doppler- suggestive of thyroiditis.

The patient's symptoms, including fever and headaches, along with elevated prolactin levels, raised concern for an underlying pituitary cause. The patient was further evaluated with an Magnetic Resonance Imaging (MRI) of the brain, which showed enlargement of the pituitary gland (15×15×9 mm) with lobulated margins and a normal sella turcica [Table/Fig-3a,b]. These findings raised suspicion of a pituitary macroadenoma and follow-up imaging was advised after two months of hormonal therapy with tablet thyroxine sodium (12.5 µg daily).

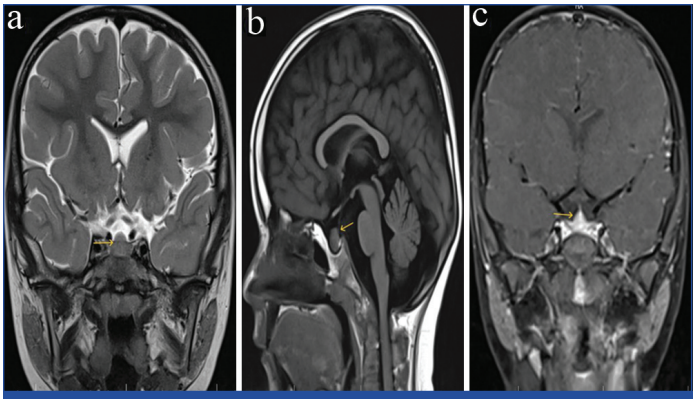


[Table/Fig-3]: MRI before thyroxine therapy: a) T1-weighted mid-sagittal image shows lobular and enlarged hypointense pituitary gland with displaced posterior pituitary bright spot (red arrow); b) T2 coronal image shows hypointense enlarged pituitary gland measuring 15×15 mm (Craniocaudal×Transverse) (red arrow).

A follow-up MRI revealed a mild reduction in the size of the pituitary gland (10.5×12×7 mm) with central protrusion and smooth contours, characteristic of the "nipple sign" typically observed in PH [Table/Fig-4a]. On T1-weighted images, the posterior pituitary bright spot was displaced and compressed [Table/Fig-4b]. No focal lesions, cysts, or haemorrhagic areas were noted. Dynamic contrast imaging showed uniform enhancement without hypoenhancing regions, with a normal pituitary stalk, optic structures and cavernous sinus [Table/Fig-4c]. Because of these findings, the diagnosis was revised to PH and hormonal therapy was continued as before.

DISCUSSION

The origins of Pituitary Hyperplasia (PH) among children can vary, necessitating an initial differentiation between physiological and pathological aetiologies. Normal life stages such as puberty, pregnancy and lactation can stimulate pituitary growth, while pathologically, it can be linked to hypothyroidism, adrenal insufficiency,



[Table/Fig-4]: MRI after two months of thyroxine therapy: a) T2-weighted coronal image shows hypointense smooth and enlarged pituitary gland with central protrusion of pituitary lesion ("nipple sign") (yellow arrow); b) T1-weighted mid-sagittal image shows hypointense enlarged and lobular pituitary gland with mild reduction in size measuring 10.5×12 mm (Craniocaudal×Transverse) and shows displaced posterior pituitary bright spot (yellow arrow); c) T1-weighted post-contrast image shows uniform homogeneous enhancement of the pituitary gland with no obvious hypo-enhancing/ non-enhancing lesion (yellow arrow).

hypogonadism and long-term oestrogen use. All these conditions lead to low thyroid hormone levels, which are compensated by pituitary gland enlargement through positive feedback loops [1]. Desai et al., were among the first to report the association of hypothyroidism with PH in 1996 [2].

The most common cause of hypothyroidism in children and adolescents is Hashimoto's Thyroiditis (HT). The severity of HT is linked to antithyroid antibodies, primarily anti-thyroperoxidase (TPO) and anti-thyroglobulin (Tg). These antibodies provoke an inflammatory process in the gland, resulting in the infiltration of haematopoietic mononuclear cells, mainly lymphocytes, into the thyroid follicle interstitium, leading to subsequent thyroid cell atrophy. The low production of thyroid hormones diminishes the negative feedback to the hypothalamus, leading to the oversecretion of Thyrotropin-Releasing Hormone (TRH) and proliferation of Thyroid Stimulating Hormone (TSH)-secreting cells, resulting in reactive hyperplasia of the anterior pituitary, known as PH [3].

Accurate differentiation of PH from pituitary adenomas is crucial, yet challenging, based on clinical presentation, laboratory tests and radiological imaging. This distinction is critical because their treatments differ significantly; pituitary adenomas typically require surgical resection, while PH often resolves with thyroid hormone replacement therapy. Misdiagnosis leading to surgery in a patient with PH can cause irreversible pituitary dysfunction, resulting in growth impairment and mental retardation in children [4]. In the present case, the diagnosis of PH was confirmed by the presence of the 'nipple sign' on imaging, referring to a midline convexity of the superior pituitary border, which is thought to reflect hyperplasia rather than displacement or distortion caused by a mass lesion [5]. This, coupled with the spontaneous resolution of the size of the gland after thyroxine therapy, confirmed the diagnosis of PH. Several studies have echoed these findings. Cao J et al., and Simşek E et al., reported adolescent cases where long-standing hypothyroidism led to pituitary enlargement that reversed with thyroxine therapy [2,6].

Further strengthening the diagnostic reasoning, we systematically considered and excluded other potential causes of sellar enlargement. Rathke's cleft cysts, which are non neoplastic remnants of embryological origin, typically appear as non-enhancing midline cystic lesions on MRI, sometimes with intracystic nodules or variable signal intensity [7]. Non functioning pituitary cysts and craniopharyngiomas—often presenting with calcifications, mixed solid and cystic components, or evidence of compression—were similarly ruled out based on the lack of such features in the present patient's imaging [8]. The homogeneous and diffuse nature of the gland's enlargement was most compatible with hyperplasia, particularly in the context of longstanding, untreated hypothyroidism.

An additional diagnostic clue lies in the endocrine profile, particularly regarding prolactin levels. TRH stimulates both thyrotrophs and lactotrophs; thus, transient hyperprolactinaemia is common in PH [9]. This contrasts with prolactin-secreting pituitary adenomas, where hyperprolactinaemia is typically profound and unresponsive to thyroxine therapy. Recognition of this difference is essential to avoid misclassification, as the treatment pathways diverge significantly [10]. Franceschi R et al., reported normalisation of prolactin levels following levothyroxine replacement therapy, similar to the present case [11].

Of note, the impact of PH may extend beyond thyrotroph and lactotroph hyperplasia. Prolonged overstimulation of the anterior pituitary can affect other hormonal axes, including Growth Hormone (GH), Adrenocorticotropic Hormone (ACTH) and gonadotropins (LH/FSH) as well as cortisol. In paediatric patients, this may manifest as delayed growth, altered pubertal progression, or adrenal insufficiency [12]. Although the present patient did not exhibit overt signs of panhypopituitarism, clinicians should remain vigilant and perform comprehensive endocrine assessments in similar presentations.

In summary, PH in children, often secondary to HT, presents a diagnostic challenge in distinguishing it from pituitary adenomas. Accurate differentiation, aided by imaging characteristics like the 'nipple sign' and hormonal profiles along with a favourable response to thyroid hormone replacement, is crucial to avoid unnecessary surgery. Even with thyroid hormone replacement, some children with severe dysplasia or short stature may continue to experience developmental challenges. Therefore, there is a pressing need for further research to facilitate earlier diagnosis of PH in children.

CONCLUSION(S)

The present case illustrates the diagnostic challenge of differentiating PH from pituitary adenomas in children with HT. The presence of the 'nipple sign' and the resolution of pituitary enlargement following thyroxine therapy were crucial in establishing the correct diagnosis. Clinicians should be vigilant for PH in paediatric patients presenting with pituitary enlargement and hypothyroidism. Accurate identification of PH is essential to guide appropriate management and prevent unnecessary surgical intervention, ensuring optimal outcomes.

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