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Pituitary Hyperplasia Secondary to Prolonged Undiagnosed Hypothyroidism in a 13-Year-Old Female

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Abstract

Background Pituitary hyperplasia is often overlooked as a potential complication of chronic hypothyroidism. When hypothyroidism persists, the disruption of the negative feedback loop from the thyroid can lead to increased thyrotropin production in the pituitary, resulting in hyperplasia.

Objective This case report aims to explore pituitary hyperplasia as a reversible complication of untreated primary hypothyroidism, highlighting the importance of timely diagnosis and appropriate treatment to prevent unnecessary interventions.

Case Description We reported a 13-year-old female presented with psychosis, crying spells, and emotional instability, which led to an initial psychiatric evaluation. Laboratory tests revealed severely elevated thyroid-stimulating hormone (TSH) levels greater than 100 mIU/L, low free thyroxine (T4) levels at 0.1 ng/dL, and high thyroid peroxidase antibodies (> 600 IU/mL), confirming a diagnosis of Hashimoto's thyroiditis and severe primary hypothyroidism. A pituitary magnetic resonance imaging showed signs of pituitary hyperplasia. Following the initiation of levothyroxine therapy, the patient's TSH levels normalized, and the pituitary hyperplasia significantly regressed. The patient has since remained stable and asymptomatic.

Conclusion This case report details a 13-year-old female diagnosed with Hashimoto's thyroiditis and pituitary hyperplasia. Following levothyroxine treatment, both thyroid function and pituitary size normalized, leading to significant clinical improvement. This case highlights the importance of recognizing pituitary hyperplasia as a reversible condition caused by hypothyroidism. It underscores the critical need for timely diagnosis and appropriate treatment to prevent unnecessary surgical interventions.

Keywords

- pituitary hyperplasia
- hypothyroidism
- Hashimoto's thyroiditis
- thyroid-related pituitary disorders
- psychiatric manifestations of hypothyroidism

Introduction

Pituitary hyperplasia is an often overlooked side effect of chronic hypothyroidism, despite the frequent occurrence of primary hypothyroidism.[1] Long-term primary hypothyroidism can cause pituitary hyperplasia because of the loss of negative feedback induced by the thyroid gland's decreased secretion of thyroxine (T4) and triiodothyronine (T3). This causes the hypothalamus to produce excessive amounts of thyrotropin-releasing hormone subsequently leading to thyrotroph pituitary hyperplasia.[2] Over time, patients may develop headaches, visual disturbances,

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and clinical manifestations of hypothyroidism, along with elevated prolactin secretion.[3] Some studies have shown that the incidence of pituitary hyperplasia in primary hypothyroidism ranges from 25% to 81%. One study found that 70% of patients with thyroid-stimulating hormone (TSH) levels exceeding 50 IU/mL had pituitary enlargement.[4]

Hypothyroidism can exhibit a wide range of neuropsychiatric signs and symptoms. Therefore, psychiatrists must recognize the diverse manifestations of hypothyroidism, properly assess thyroid function through laboratory tests, and be familiar with basic treatment options.[5]

Since overt hypothyroidism can manifest as mood or cognitive impairments, serum TSH levels should be checked in patients experiencing affective symptoms or mental decline. Distinguishing thyroid-related neurocognitive issues from other conditions can be challenging.[6]

Pituitary hyperplasia is often considered a rare condition that resembles a pituitary adenoma and can grow to significant sizes, potentially compressing the optic chiasm. A misdiagnosis could have serious consequences, and a pituitary resection might be performed mistakenly.[7] It is crucial to investigate endocrine factors, particularly hypothyroidism, as potential causes of pituitary hyperplasia.[8] Although imaging techniques continue to improve, distinguishing between pituitary adenomas and pituitary hyperplasia remains challenging. On magnetic resonance imaging (MRI), hyperplasia typically appears with homogeneous intensity and contrast enhancement,[9] and when a central protrusion is present, it is referred to as the nipple sign.[10] On the other hand, pituitary adenomas can be identified by their heterogeneous intensity, as well as T1-weighted and contrast-enhanced images that display hypointensity compared to the normal pituitary gland.[9]

The primary strategy for managing pituitary hyperplasia resulting from primary hypothyroidism is to provide thyroid hormone replacement therapy. It is essential to monitor these patients closely and a decrease in pituitary size should be noted after starting levothyroxine therapy to confirm the diagnosis of pituitary hyperplasia due to primary hypothyroidism.[11]

In this case report, we emphasize the importance of accurately distinguishing pituitary hyperplasia from other pituitary lesions to ensure proper diagnosis. Additionally, we highlight the need for careful monitoring during treatment to prevent mismanagement and unnecessary surgical interventions.

Case Description

History and Physical Examination

A 13-year-old girl was referred to Faiha Specialized Diabetes, Endocrine, and Metabolism Center (FDEMC) in Basrah, Southern Iraq, by a psychiatrist following a psychotic episode and crying spells. She reported a 2-year history of fatigue, lethargy, and poor intellectual performance in school. Her past medical and surgical histories were unremarkable. On examination, the patient was noted to have a height of 137 cm and a weight of 46 kg, placing her below the expected height range with a body mass index (BMI) of 24.5. Physical examination revealed a puffy face, periorbital puffiness, and an apathetic facial expression. She appeared depressed and exhibited signs of lethargy. Secondary sexual characteristics were normal, with breast development at Tanner stage 3. However, menarche had not yet occurred. The referral was made due to concerns raised by the abnormal TSH measurement of 100 mIU/L initially detected by the psychiatrist. Her family history was significant for thyroid disorders, including hyperthyroidism in her father and paternal aunt, and a history of goiter in her maternal grandmother.

Investigations and Workup

A thyroid ultrasound was performed, revealing diffuse enlargement of the thyroid gland with heterogeneous echogenicity, exhibiting a "giraffe-like appearance." Increased vascularity was also noted on color Doppler imaging. These findings are consistent with autoimmune thyroid disease, most likely Hashimoto's thyroiditis. ►**Table 1** shows the laboratory investigations done to the patient in the center at the presentation. We initially observed that the TSH level was greater than 100 mIU/L and upon performing a TSH dilution, we determined that the true value was 731 mIU/L. These results, combined with the ultrasound findings, confirm a diagnosis of Hashimoto's thyroiditis, an autoimmune thyroid disease. Considering the possibility of other conditions, we also evaluated kidney disease, but investigations including renal ultrasound and renal function tests were normal. Given the patient's prolonged disease course and overt presentation, we decided to perform a pituitary MRI, which revealed diffuse homogeneous enlargement of the pituitary gland (13×13 mm) with an upward protrusion that is dome-shaped "nipple sign" as shown in ►**Fig. 1**.

Management and Progress

We started levothyroxine treatment and scheduled monthly follow-up appointments. Over the 6-month course of treatment, the patient showed gradual and steady improvement in both her physical and emotional condition. At the start of treatment, she weighed 46 kg, was 137 cm height, and had a BMI of 24.5. Over the following months, there was a progressive increase in both weight and height, reaching 48 kg and 142 cm, respectively, by the end of the 6 months. This resulted in a slight decrease in BMI to 23.8. Psychologically, the patient exhibited a noticeable improvement in her emotional state and responsiveness. Initially, she demonstrated significant emotional distress, withdrawn behavior, and reduced engagement with her family. By the second month, she showed better interaction with her mother and increased engagement in daily activities. By the fourth month, there was continued improvement in communication and responsiveness. In the later stages of follow-up, the patient exhibited a marked reduction in psychiatric symptoms. Although no formal cognitive assessments were conducted, clinical observation indicated ongoing improvement.

Outcome

Six months after treatment, there was a significant improvement in the patient's condition. She no longer showed signs

Table 1 Laboratory investigations at presentation

Serum	Values	Reference ranges
LDL cholesterol	248 mg/dL	< 100 mg/dL
Triglycerides	154 mg/dL	< 150 mg/dL
HDL cholesterol	80 mg/dL	> 45 mg/dL
Aspartate aminotransferase (AST)	40 U/L	< 40 U/L
Alanine aminotransferase (ALT)	29 U/L	< 40 U/L
Alkaline phosphatase	Normal	44–147 U/L
Creatine phosphokinase (CPK)	700.2 U/L	< 200 U/L
Fasting plasma glucose	81 mg/dL	70–100 mg/dL
Serum ferritin	25.8 ng/mL	30–150 ng/mL
TSH level	> 100 mIU/L (initial)	0.4–4.0 mIU/L
TSH (after dilution)	731 mIU/L	0.4–4.0 mIU/L
Free thyroxine (free T4)	0.1 ng/dL	0.8–1.8 ng/dL
Total triiodothyronine (total T3)	23.9 ng/dL	80–180 ng/dL
Thyroid peroxidase antibodies (TPO)	> 600 IU/mL	< 35 IU/mL
Thyrotropin receptor antibodies (TRAb)	6.55 IU/L	< 1.75 IU/L
Prolactin	48.5 ng/mL	< 20 ng/mL (women)
Vitamin D	35 ng/mL	20–50 ng/mL

Abbreviations: HDL, high-density lipoprotein; LDL, low-density lipoprotein; TSH, thyroid-stimulating hormone.

of apathy, her cognitive function improved, and her depressive symptoms resolved. She was more engaged and appeared oriented when asked. Additionally, her TSH levels normalized. Given the ongoing concerns about the pituitary, a follow-up MRI was performed, revealing that the previously enlarged pituitary gland had reduced to a nearly normal size, measuring 6.7 mm, as shown in ►**Fig. 2**. The patient also began having regular cycles and returned to school, which she left due to her condition, showing further signs of recovery and progress.

Discussion

Pituitary hyperplasia is a frequently overlooked manifestation of primary hypothyroidism. It results from the absence of negative feedback on the pituitary and hypothalamus. Its clinical and imaging features can resemble those of a pituitary

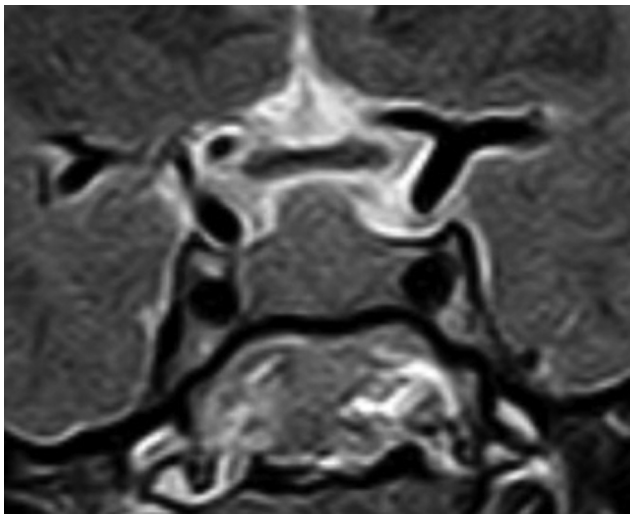

Fig. 1 Shows a coronal T2-weighted magnetic resonance imaging (MRI) of the pituitary gland, demonstrating a diffusely enlarged gland measuring 13 × 13 mm. The imaging reveals the characteristic "nipple sign", indicative of pituitary hyperplasia, commonly associated with untreated primary hypothyroidism, May 2024.

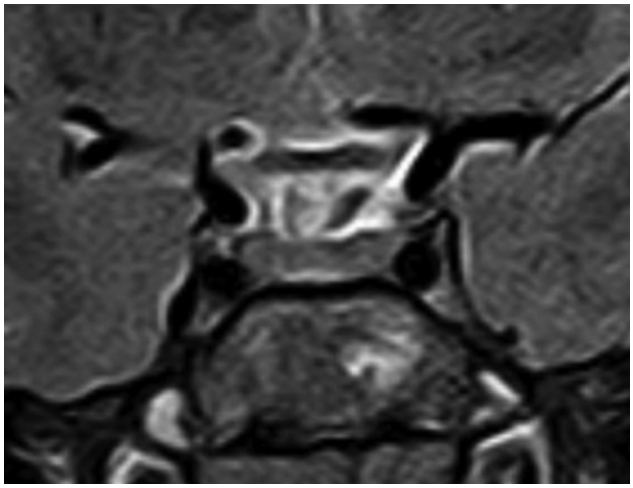

Fig. 2 Shows a coronal T2-weighted magnetic resonance imaging (MRI) of the pituitary gland, demonstrating a reduction in gland size to 6.7 mm height with the disappearance of "the nipple sign", indicating regression of pituitary hyperplasia, November 2024.

mass, making recognition crucial, as the primary treatment is thyroid hormone replacement rather than surgery.[4]

The link between thyroid deficiency and psychiatric symptoms is quite common and often goes unnoticed as a potential cause of changes in behavior, mood, and cognition.[12] We present a case of a 13-year-old female with prolonged undiagnosed Hashimoto's thyroiditis, initially referred from a psychiatric clinic after presenting with psychosis and crying spells. The referral was prompted by elevated TSH levels discovered during psychiatric evaluation, which led to further investigations at our endocrine center (FDEMC) as seen in ►**Table 1**. The initial MRI (►**Fig. 1**) revealed a diffused homogeneous enlargement of pituitary gland with a "nipple sign". This finding was crucial in guiding our diagnosis of pituitary hyperplasia, a unique but significant finding associated with longstanding hypothyroidism. A 6-month follow-up MRI, as shown in ►**Fig. 2**, revealed a significant reduction in the size of the pituitary gland, indicating a positive response to the treatment. This case highlights the psychiatric manifestations of untreated hypothyroidism, as well as examines pituitary hyperplasia as a reversible consequence of the condition, emphasizing the need for timely diagnosis and appropriate treatment to avoid unnecessary interventions.

Differentiating between pituitary hyperplasia and pituitary adenoma is essential because their treatment approaches differ significantly. Certain MRI features can help distinguish pituitary hyperplasia from adenomas, with the most indicative being the smooth midline projection of the pituitary mass, known as the "nipple sign" or "dome-shaped" pituitary enlargement.[11] Hyperplastic lesions are generally characterized by a symmetrical, dome-shaped structure with homogeneous enhancement, whereas nonfunctioning pituitary adenomas tend to display greater variability in both shape and signal homogeneity.[13]

Pituitary hyperplasia due to primary hypothyroidism, typically responds well to thyroid hormone replacement therapy, whereas pituitary adenoma may require surgical intervention and/or radiotherapy.[11] The presented case resembles previously reported cases of pituitary hyperplasia secondary to severe primary hypothyroidism, such as in the case reported by Rajwani and Ghalib of a 25-year-old woman with prolonged hypothyroidism (TSH 290 mIU/L), who presented with a pituitary lesion initially mimicking a macroadenoma. After thyroxine treatment and hormonal stabilization, follow-up imaging revealed complete resolution of the lesion, confirming pituitary hyperplasia. This highlights the importance of differentiating true pituitary adenomas from reversible pituitary hyperplasia caused by systemic endocrine dysfunction.[3]

The presented case is comparable to another two reports by Alonso et al. in which an 18-year-old female with severe autoimmune primary hypothyroidism (TSH 490 mIU/L), experienced spontaneous galactorrhea, headaches, and malaise. Initial imaging revealed pituitary enlargement compressing the optic chiasm. Following 5 months of levothyroxine therapy, both symptoms and biochemical abnormalities resolved, with a follow-up MRI showing a normal-sized pituitary and no evidence of compression. This case further underscores the importance of distinguishing between pituitary hyperplasia secondary to untreated hypothyroidism and true pituitary lesions, as timely hormonal correction can result in complete resolution of imaging and clinical findings.[14]

The other case, also by Alonso et al., was a report of a 24-year-old female with type 1 diabetes and autoimmune primary hypothyroidism, who presented with a 5-year history of galactorrhea and oligomenorrhea. Poor adherence to insulin and levothyroxine therapy led to persistently elevated TSH (500 mIU/L) and diffuse pituitary enlargement compressing the infundibulum and optic chiasm, initially misdiagnosed as a prolactinoma. After 17 months of consistent levothyroxine and liothyronine treatment, TSH normalized, symptoms resolved, and follow-up imaging revealed a normal pituitary gland. This case highlights the diagnostic challenges of distinguishing pituitary hyperplasia secondary to severe hypothyroidism from other sellar pathologies, particularly in cases of prolonged untreated endocrine dysfunction.[14]

The present case report is limited by its single-patient nature, which restricts the generalizability of findings. Additionally, while the resolution of pituitary hyperplasia following levothyroxine therapy supports the diagnosis of longstanding primary hypothyroidism, further studies are needed to better understand the association between severe hypothyroidism and pituitary changes in pediatric patients. Additionally, this case highlights the diagnostic challenge when psychiatric symptoms are the primary presentation of hypothyroidism, underscoring the need for greater clinical awareness in such scenarios. There is also a potential bias in the reliance on specific lab tests (e.g., TSH and T4 levels) for diagnosis. Since the patient was diagnosed in an endocrine center, the findings may not be fully applicable to primary care or less specialized settings. Further research is required to confirm these findings and evaluate the role of pituitary changes in broader pediatric populations.

Conclusion

Pituitary hyperplasia is a rare but significant complication of prolonged, undiagnosed hypothyroidism, often mimicking other sellar pathologies such as pituitary adenomas. Distinguishing hyperplasia from true pituitary lesions is essential to prevent unnecessary surgical interventions. Treatment with levothyroxine not only corrects the underlying hypothyroidism but also facilitates regression of pituitary hyperplasia and normalization of gland size in most cases. Regular monitoring with pituitary MRI and clinical follow-up is crucial for confirming the diagnosis and evaluating treatment response.

Authors' Contributions

S.M.AK.H contributed to case management and follow-up, manuscript drafting, critical review, literature review, manuscript editing, and final approval of the manuscript. A.A.M. was responsible for case diagnosis and management, figure preparation, supervision, manuscript revision, and final approval of the manuscript.

Compliance with Ethical Principles

This case report was reviewed and approved by the Institutional Review Board of Faiha Specialized Diabetes, Endocrine and Metabolism Center (FDEMC).

Patient's Consent

Written informed consent was obtained from the patient's father for the publication of this case report.

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None.

Conflict of Interest

None declared.

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