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Reversible Pituitary Hyperplasia Mimicking a Macroadenoma in Severe Autoimmune Primary Hypothyroidism

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Abstract

Pituitary hyperplasia is a reversible but underrecognized consequence of severe primary hypothyroidism that may closely mimic a pituitary macroadenoma; radiological overlap with hypophysitis can further complicate the differential diagnosis. A 26-year-old man underwent brain magnetic resonance imaging (MRI) for headache and balance disturbance, which revealed an approximately 18 × 12 mm sellar enlargement with suprasellar extension. The initial radiological interpretation favored a macroadenoma. Endocrine evaluation demonstrated profound autoimmune primary hypothyroidism, with markedly elevated thyroid-stimulating hormone (TSH), reduced free thyroxine (FT4), positive thyroid autoantibodies, and mild hyperprolactinemia. Levothyroxine replacement was initiated; no dopamine agonist, glucocorticoid treatment, or pituitary-directed intervention was administered. Follow-up MRI on Day 175 showed normal pituitary morphology despite residual biochemical abnormalities, and long-term imaging confirmed sustained resolution. Hypophysitis was considered retrospectively because of the radiological overlap. However, preservation of the posterior pituitary bright spot, absence of reported cavernous sinus involvement, lack of documented arginine vasopressin deficiency, and complete resolution during levothyroxine replacement favored reactive thyrotroph hyperplasia. A complete baseline etiological work-up for secondary hypophysitis and histological confirmation were not available, preventing absolute exclusion of an inflammatory pituitary disorder. This case emphasizes the need for integrated endocrine and imaging assessment of sellar enlargement before pituitary-directed treatment.

Categories: Radiology, Neurosurgery, Endocrinology/Diabetes/Metabolism
Keywords: autoimmune thyroiditis, pituitary hyperplasia, pituitary macroadenoma, primary hypothyroidism, sellar mass

Introduction

Pituitary hyperplasia is a non-neoplastic enlargement of the pituitary gland that may occur in response to chronic trophic stimulation. Severe primary hypothyroidism is a well-recognized cause: loss of thyroid hormone negative feedback increases hypothalamic thyrotropin-releasing hormone (TRH) stimulation and promotes thyrotroph hyperplasia, while increased TRH drive may also contribute to hyperprolactinemia [1,2]. The degree of pituitary enlargement appears to correlate with the severity of hypothyroidism, and regression is commonly observed after thyroid hormone replacement [1,2].

The differential diagnosis of sellar enlargement is broad and includes pituitary neuroendocrine tumors, reactive pituitary hyperplasia, and inflammatory or infiltrative disorders. Pituitary hyperplasia represents diffuse non-neoplastic enlargement, whereas a pituitary macroadenoma is conventionally defined by a pituitary adenoma measuring at least 10 mm. Imaging alone does not always reliably distinguish hypothyroidism-related hyperplasia from a pituitary adenoma [3]. Hypophysitis is also important in this differential because diffuse or symmetric enlargement and homogeneous contrast enhancement may overlap with reactive hyperplasia. Features that may support hypophysitis include pituitary stalk thickening, loss of the posterior pituitary bright spot, arginine vasopressin deficiency, anterior pituitary hormone deficiencies, and associated autoimmune or systemic inflammatory disease; however, none of these findings is individually diagnostic [4,5].

Current Pituitary Society guidelines recommend systematic endocrine assessment of sellar lesions, including free thyroxine (FT4) and thyroid-stimulating hormone (TSH), morning cortisol, adrenocorticotropic hormone, gonadotropins, insulin-like growth factor 1, and prolactin assessment as appropriate [6]. Identifying primary hypothyroidism is therefore directly relevant when pituitary enlargement is discovered because hypothyroidism-related hyperplasia may regress with levothyroxine, thereby avoiding unnecessary pituitary-directed treatment.

We report a 26-year-old man with severe autoimmune primary hypothyroidism, hyperprolactinemia, and an 18-mm sellar enlargement initially interpreted as a pituitary macroadenoma. The pituitary enlargement

resolved during levothyroxine replacement and remained absent on long-term follow-up without dopamine agonist therapy, glucocorticoid treatment, or pituitary surgery. Particular attention is given to the differential diagnosis with hypophysitis and to the limitations of establishing this diagnosis without histological confirmation.

Case Presentation

A 26-year-old man with no relevant documented medical history was referred after a brain magnetic resonance imaging (MRI) obtained for headache, distal paresthesias, and balance disturbance revealed a sellar lesion. Day 1 was defined as the date of the initial MRI. The MRI showed an approximately 18 × 12 mm sellar lesion with suprasellar extension and elevation of the optic chiasm. No cavernous sinus involvement was reported; the posterior pituitary bright spot was preserved; and pituitary stalk thickening was not described in the baseline radiology report. The available record did not document polyuria, polydipsia, or other symptoms suggestive of arginine vasopressin deficiency. The available baseline images showed an enhancing, predominantly midline sellar mass with suprasellar extension. The initial radiological interpretation was consistent with a pituitary macroadenoma (Figure *1*). A contemporaneous formal bilateral visual-field examination was not available.

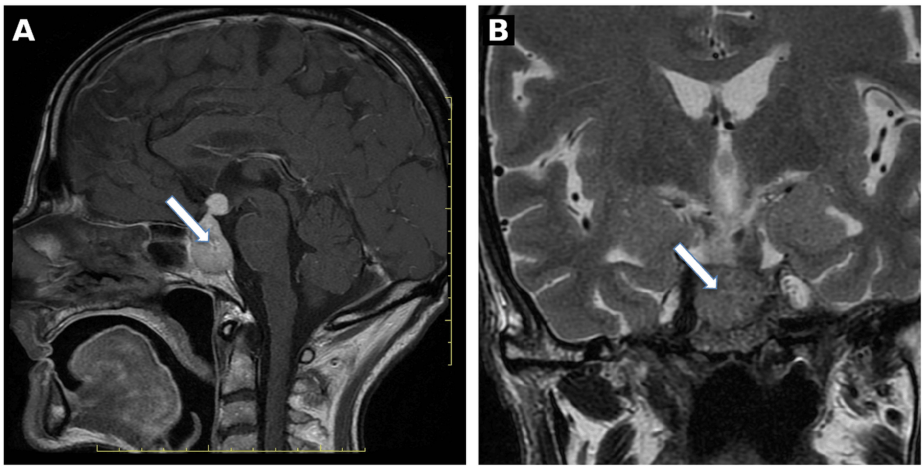


FIGURE 1: Pituitary magnetic resonance imaging at diagnosis

(A) Sagittal contrast-enhanced T1-weighted MRI demonstrating an enhancing sellar mass with suprasellar extension (arrow). (B) Coronal T2-weighted MRI showing the predominantly midline sellar enlargement with suprasellar extension (arrow), initially interpreted as consistent with a pituitary macroadenoma.

Further history revealed a 5 kg weight gain over six months, chronic constipation, cold intolerance, and reported nocturnal apneic episodes. Physical examination showed bradycardia at 52 beats/minute and macroglossia. As part of the endocrine evaluation of the sellar lesion, the thyroid axis was assessed using both TSH and FT4. On Day 8, testing showed markedly increased TSH, FT4 at the lower end of the laboratory reference interval, mild hyperprolactinemia, and markedly elevated thyroid peroxidase and thyroglobulin antibodies (Table *1*). Repeat thyroid testing on Day 12 documented persistent marked TSH elevation with frankly decreased FT4. This repeat measurement was obtained clinically to document the persistence and severity of the biochemical abnormality before treatment and was not required as a separate diagnostic criterion for autoimmune thyroiditis. The combination of markedly elevated TSH and reduced FT4 established primary hypothyroidism, while the positive thyroid autoantibodies supported an autoimmune etiology.

Follow-up day	Parameter	Result	Reference range	Interpretation
Day 8	TSH	>100 mIU/L	0.40-4.50 mIU/L	Markedly increased
Day 8	FT4	0.74 ng/dL	0.70-1.48 ng/dL	Low-normal
Day 8	Prolactin	45.3 ng/mL	3.3-13.5 ng/mL	Increased
Day 8	Thyroid peroxidase antibodies	149.2 IU/mL	<8 IU/mL	Positive/increased
Day 8	Thyroglobulin antibodies	287.5 IU/mL	<18 IU/mL	Positive/increased
Day 12	TSH	>100 mIU/L	0.40-4.50 mIU/L	Markedly increased
Day 12	FT4	<0.40 ng/dL	0.70-1.48 ng/dL	Decreased
Day 61	TSH	43.40 mIU/L	0.40-4.50 mIU/L	Increased
Day 61	FT4	1.00 ng/dL	0.70-1.48 ng/dL	Within range
Day 61	Prolactin	47.1 ng/mL	3.3-13.5 ng/mL	Increased
Day 165	TSH	9.50 mIU/L	0.40-4.50 mIU/L	Increased
Day 165	FT4	1.10 ng/dL	0.70-1.50 ng/dL	Within range
Day 165	Prolactin	68.5 ng/mL	3.3-13.5 ng/mL	Increased
Early follow-up	Morning cortisol	11.60 µg/dL	Not available in source record	Clinical interpretation discussed in the "Discussion" section
Mid-follow-up	Morning cortisol	9.9 µg/dL	Not available in source record	Clinical interpretation discussed in the "Discussion" section
Day 786	TSH	4.045 mIU/L	0.35-4.94 mIU/L	Within range
Day 786	FT4	1.43 ng/dL	0.70-1.48 ng/dL	Within range
Day 786	Prolactin	3.39 ng/mL	3.5-19.4 ng/mL	Slightly below lower limit; hyperprolactinemia resolved
Day 786	Morning cortisol	16.30 µg/dL	Not available in source record	Reference interval unavailable

TABLE 1: Serial endocrine laboratory findings during follow-up

Values and reference intervals are reproduced from the source laboratory records when available.

TSH: Thyroid-stimulating hormone; FT4: Free thyroxine.

Given the association between severe primary hypothyroidism and pituitary enlargement, reactive thyrotroph hyperplasia was considered the leading diagnosis; however, a nonfunctioning pituitary adenoma and hypophysitis remained relevant differential diagnoses. Levothyroxine replacement was initiated and subsequently adjusted toward a weight-based replacement dose of approximately 1.6 µg/kg/day. Detailed stepwise dose adjustments and adherence data were not fully available in the medical record. No cabergoline or other dopamine agonist, glucocorticoid treatment, or pituitary-directed intervention was administered. Hypothyroid symptoms improved within approximately three months.

Biochemical recovery was gradual. By Day 61, TSH had decreased but remained markedly elevated; FT4 had increased compared with Day 12; and prolactin remained elevated. On Day 165, TSH remained above the reference range, FT4 was within range, and prolactin remained elevated (Table *1*). A dedicated hypothalamic-pituitary MRI on Day 175 described a pituitary gland of normal size with homogeneous enhancement, no sellar or parasellar mass, a midline pituitary stalk, and a normal optic chiasm. Thus, structural normalization had occurred before complete biochemical normalization.

Long-term reassessment confirmed sustained radiological resolution. Pituitary MRI on Day 781 again showed a normal anterior pituitary gland without a focal lesion, with a normal stalk and optic chiasm (Figure *2*).

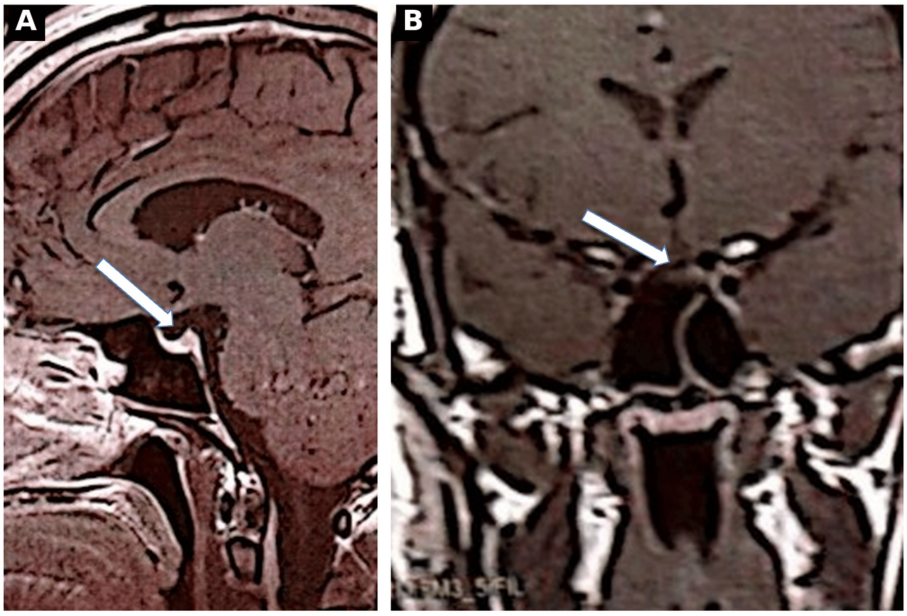


FIGURE 2: Follow-up pituitary magnetic resonance imaging demonstrating sustained radiological resolution

Contrast-enhanced T1-weighted pituitary MRI obtained on Day 781 showing normal pituitary morphology on sagittal (A) and coronal (B) views (arrows), with no recurrent focal sellar lesion and a normal relationship to the optic chiasm.

By Day 786, thyroid function was within the laboratory reference range, and hyperprolactinemia had resolved. Morning cortisol measurements obtained during follow-up included values that were indeterminate for excluding central adrenal insufficiency at earlier time points; no dynamic assessment of the hypothalamic-pituitary-adrenal axis was documented. The serial laboratory findings are summarized in Table *1*, and the longitudinal TSH, FT4, and prolactin trends are shown in Figure *3*.

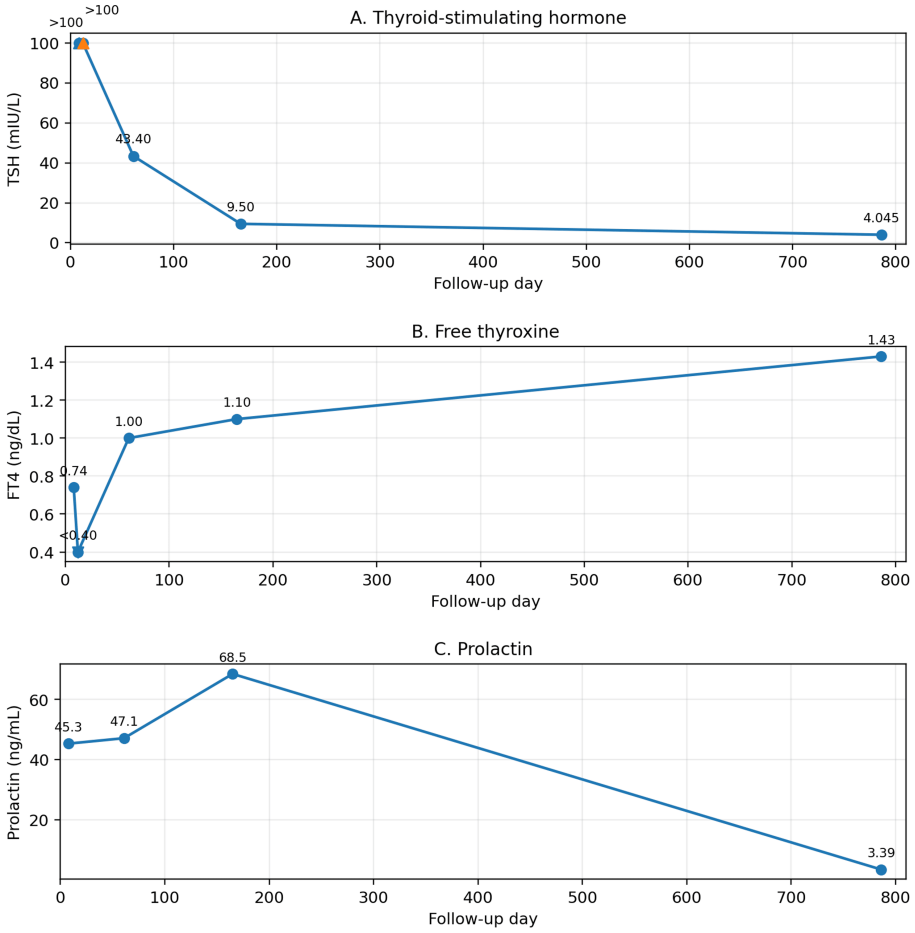


FIGURE 3: Longitudinal biochemical evolution during follow-up

Serial TSH (A), FT4 (B), and prolactin (C) values are plotted against follow-up day. Results reported as >100 mIU/L for TSH and <0.40 ng/dL for FT4 are displayed at the assay boundary values solely for graphical placement; the inequality labels preserve the original reported results. Prolactin was not measured on Day 12.

TSH: Thyroid-stimulating hormone; FT4: Free thyroxine.

Discussion

This case illustrates reversible pituitary enlargement associated with severe autoimmune primary hypothyroidism. The pathophysiological basis of hypothyroidism-related pituitary hyperplasia is chronic thyrotroph stimulation resulting from loss of thyroid hormone negative feedback, with increased hypothalamic TRH drive and subsequent expansion of thyrotroph cells. Increased TRH stimulation may also enhance prolactin secretion and contribute to the associated hyperprolactinemia [1].

The principal diagnostic challenge was not only to distinguish reactive pituitary hyperplasia from a pituitary adenoma but also from hypophysitis. Current approaches to sellar lesions emphasize integration of clinical findings, dedicated pituitary imaging, and endocrine testing rather than interpretation of MRI morphology in isolation [3-6]. In this context, TSH was not used as a marker of the sellar mass itself. It was measured together with FT4 to determine whether thyroid-axis dysfunction was primary or central. The combination of markedly elevated TSH and decreased FT4 established severe primary hypothyroidism and was therefore directly relevant to the differential diagnosis. This approach is consistent with the 2025 Pituitary Society consensus, which recommends measurement of both TSH and FT4 as part of baseline pituitary testing in patients with sellar lesions [6].

Hypophysitis encompasses a heterogeneous group of inflammatory disorders affecting the pituitary gland and/or infundibulum. Lymphocytic hypophysitis is the most common primary form and can be associated with other autoimmune disorders. Imaging findings that may favor hypophysitis include diffuse symmetric enlargement, homogeneous enhancement, pituitary stalk thickening, and loss of the posterior pituitary bright spot. Arginine vasopressin deficiency and anterior pituitary hormone deficiencies also increase suspicion, particularly when stalk involvement is present [4,5,7]. Secondary hypophysitis may occur in

association with systemic inflammatory, granulomatous, infectious, or drug-related disorders, including sarcoidosis, granulomatosis with polyangiitis, IgG4-related disease, tuberculosis, syphilis, and immune checkpoint inhibitor therapy [4,5,7].

In the present patient, several documented findings were less typical of hypophysitis: he was male; the posterior pituitary bright spot was preserved; no cavernous sinus involvement was reported; baseline stalk thickening was not described; and the available record did not document arginine vasopressin deficiency. Moreover, pituitary morphology completely normalized during levothyroxine replacement without glucocorticoid or other anti-inflammatory treatment. These observations favor reactive thyrotroph hyperplasia. However, radiological regression is not pathognomonic, as spontaneous or treatment-associated regression can also occur in hypophysitis [5]. Accordingly, hypophysitis cannot be excluded with absolute certainty in the absence of histological confirmation.

To further address this differential diagnosis, the predictive score proposed by Taieb et al. in 2025 was retrospectively considered using the reliably documented baseline data (Table *2*) [8]. The score incorporates female sex (+3), headache (−2), visual disturbances (−2), corticotropic insufficiency (+1), pituitary volume < 7 cm^3 (+0.5), loss of the posterior pituitary bright spot (+0.5), cavernous sinus invasion (−0.5), pituitary stalk thickening (+4.5), and optic pathway compression (−2). A score ⩾ 0.5 was associated with a high probability of hypophysitis, with an area under the receiver operating characteristic curve of 0.967, sensitivity of 93.8%, and specificity of 87.5% [8]. Using only variables that could be established reliably in our patient, the available-data subtotal was −2, attributable to headache. Male sex contributed no points; corticotropic status could not be reliably classified for scoring because basal cortisol values were indeterminate and no dynamic testing was performed; the posterior pituitary bright spot was preserved; and cavernous sinus invasion was not reported. Pituitary volume, corticotropic status, stalk thickening, and definite optic pathway compression could not be scored reliably from the available baseline documentation. Therefore, this was an incomplete retrospective application rather than a formal validated score, and it cannot independently exclude hypophysitis. Importantly, the score was developed to differentiate predominantly lymphocytic hypophysitis from nonfunctioning pituitary macroadenoma and has not been specifically validated to distinguish hypophysitis from hypothyroidism-induced thyrotroph hyperplasia.

Criterion	Baseline finding	Points used	Comment
Female sex	Male	0	No points
Headache	Present	−2	Documented at presentation
Visual disturbances	No visual symptoms documented	0	Formal contemporaneous bilateral visual-field testing unavailable
Corticotropic insufficiency	Not reliably assessable	Not scored	Morning cortisol values were indeterminate; no dynamic testing was performed
Pituitary volume < 7 cm^3	Not assessable	Not scored	Three-dimensional measurements unavailable
Loss of posterior pituitary bright spot	No; bright spot preserved	0	Documented on baseline imaging report
Cavernous sinus invasion	Not reported	0	No cavernous sinus involvement reported
Pituitary stalk thickening	Not described	Not scored	Baseline report did not characterize stalk thickness
Optic pathway compression	Chiasm elevation described	Not scored	Definite compression was not documented
Available data subtotal		−2	Incomplete application; not a formal validated total score

TABLE 2: Retrospective application of the Taieb et al. hypophysitis prediction score using available baseline data

The score was developed to distinguish predominantly lymphocytic hypophysitis from nonfunctioning pituitary macroadenoma. Because several variables were not reliably assessable in this patient, the subtotal shown here is descriptive and should not be interpreted as a complete validated score [8].

The presence of autoimmune thyroiditis also raised the question of a broader autoimmune disorder. Autoimmune thyroid disease can coexist with other autoimmune endocrinopathies, including within

autoimmune polyglandular syndromes [9]. However, isolated autoimmune thyroid disease does not establish an autoimmune polyglandular syndrome, and no additional autoimmune endocrine or systemic disorder was documented in the available record. Therefore, autoimmune polyglandular syndrome type 3 or type 4 could not be established in this patient. A systematic screening panel for additional autoimmune diseases was not documented in the available record, which remains a limitation of the retrospective assessment. Similarly, no temporal association with SARS-CoV-2 infection or another recognized trigger of secondary hypophysitis was documented in the available record [10].

The possibility of secondary granulomatous or systemic hypophysitis also merits consideration. Neurosarcoidosis can involve the hypothalamic-pituitary region and mimic a pituitary macroadenoma, including reported cases that led to transsphenoidal surgery before the diagnosis was recognized [11]. Granulomatosis with polyangiitis can similarly present as a sellar mass with pituitary dysfunction and arginine vasopressin deficiency [12]. Baseline testing for angiotensin-converting enzyme, antineutrophil cytoplasmic antibodies, serum IgG4, or tuberculosis-directed investigations was not documented in the available medical record. This limits retrospective exclusion of sarcoidosis, granulomatosis with polyangiitis, IgG4-related disease, and infectious granulomatous hypophysitis. No systemic inflammatory or granulomatous manifestations were documented in the available record, and the absence of reported stalk involvement or arginine vasopressin deficiency reduced the level of clinical suspicion at presentation. We therefore acknowledge the lack of a complete baseline etiological work-up as a limitation rather than inferring negative results retrospectively. A targeted approach that integrates clinical, endocrine, and imaging features is also important to avoid low-yield investigations and unnecessary cost [4-7].

Diagnostic confusion between hypothyroidism-related pituitary hyperplasia and pituitary adenoma is well documented. In the review by Roux et al., 93 adult cases of pituitary hyperplasia associated with longstanding primary hypothyroidism were identified; among cases with a reported initial radiological interpretation, 58.6% had initially been considered pituitary adenomas [1]. Among 77 patients with follow-up MRI, complete radiological regression was observed in 55 and partial regression in 17 patients [1]. In the series by Khawaja et al., pituitary enlargement was present in 37 of 53 patients with marked primary hypothyroidism, and gland size decreased after thyroxine treatment in most patients who underwent follow-up imaging [2]. Nikith et al. further showed that symmetric enlargement, homogeneous enhancement, and reduction in gland size after levothyroxine favor hyperplasia, whereas heterogeneous enhancement, cystic or hemorrhagic changes, and more advanced cavernous sinus invasion are more suggestive of adenoma [3].

An important feature of the present case is the dissociation between structural and biochemical recovery. Clinical symptoms improved within approximately three months, whereas the first documented normal pituitary MRI was obtained on Day 175. At that time, TSH remained above the reference range, and prolactin was still elevated. Rapid radiological regression after thyroid hormone replacement has nevertheless been reported: Neves et al. described marked regression by approximately three months, and Rajput et al. reported complete regression at 12 weeks [13,14]. These observations support reversibility as a useful diagnostic clue while emphasizing that clinical, biochemical, and radiological recovery may occur on different timelines.

The prolactin trajectory should also be interpreted cautiously. In a systematic review of thyroid disorders associated with hyperprolactinemia, Khan et al. reported complete resolution of hyperprolactinemia in 38 of 54 patients with individual follow-up data and improvement in 10 additional patients after treatment of the underlying thyroid disorder [15]. In the present patient, prolactin remained elevated on Day 165, when complete biochemical euthyroidism had not yet been achieved. This value should therefore not be interpreted as persistent hyperprolactinemia following complete correction of hypothyroidism. When prolactin remains unexpectedly elevated, medication effects, venipuncture-related stress, and macroprolactinemia should also be considered [16].

Evaluation of the remaining pituitary axes is particularly important when a large sellar lesion is present. Hypopituitarism and, rarely, clinically significant adrenal insufficiency have been reported in severe hypothyroidism-associated pituitary hyperplasia [17]. In this patient, two earlier morning cortisol measurements fell within a range that is indeterminate when central adrenal insufficiency is suspected. Endocrine Society Guidelines recommend dynamic testing when morning cortisol is between 3 and 15 µg/dL in this context [18]. Because no stimulation test was documented, the available basal cortisol values cannot confirm complete preservation of corticotroph reserve. Likewise, a complete contemporaneous baseline assessment of the gonadal and growth hormone axes was not available, which represents an additional limitation.

This report therefore has several limitations. The diagnosis was not histologically confirmed. A complete baseline etiological work-up for primary or secondary hypophysitis was not documented, and formal contemporaneous bilateral visual-field assessment and complete pituitary hormonal testing were unavailable. Baseline MRI was available as exported images rather than the complete original DICOM (Digital Imaging and Communications in Medicine) dataset, precluding standardized volumetric analysis and retrospective expert reassessment of all imaging criteria. Detailed levothyroxine dose adjustments and adherence data were incomplete, and some serial hormonal measurements were performed in different laboratories with differing or unavailable reference intervals. These limitations preclude absolute exclusion

of hypophysitis or a coincidental pituitary lesion. Nevertheless, the combination of profound primary hypothyroidism, preserved posterior pituitary bright spot, absence of reported cavernous sinus involvement, complete radiological resolution during levothyroxine replacement without glucocorticoid or pituitary-directed treatment, and sustained normal pituitary morphology during long-term follow-up collectively provides strong clinical support for reactive pituitary hyperplasia secondary to severe primary hypothyroidism.

Future research directions

Future research should aim to improve the non-invasive distinction between reactive pituitary hyperplasia, pituitary neuroendocrine tumors, and inflammatory pituitary lesions. MRI-based radiomics combined with machine-learning approaches represents a promising avenue. Quantitative extraction of first-order intensity and histogram features, shape descriptors, texture features, and higher-order imaging characteristics from T1-weighted, T2-weighted, and contrast-enhanced MRI may capture information that is not apparent on routine visual assessment. Radiomics has already been investigated extensively in pituitary adenomas for tumor characterization, subtype prediction, invasiveness, consistency, treatment response, and recurrence prediction. However, most published studies remain retrospective and external validation is uncommon, and no radiomics model has yet been specifically validated to distinguish hypothyroidism-related pituitary hyperplasia from pituitary adenoma or hypophysitis [19]. Future studies should therefore include reactive pituitary hyperplasia as a predefined diagnostic category and evaluate such models prospectively across multiple centers.

Advanced MRI techniques may provide complementary information beyond conventional structural imaging. Dynamic contrast-enhanced MRI could be investigated to determine whether enhancement kinetics, perfusion characteristics, or quantitative permeability parameters differ between reactive hyperplastic tissue and autonomous neoplastic tissue. Proton MR spectroscopy could similarly be explored for metabolic signatures that might distinguish reactive cellular proliferation from neoplasia or inflammatory pituitary disease. Although these techniques have been used in the evaluation of pituitary lesions, their ability to differentiate hypothyroidism-related pituitary hyperplasia from adenoma or hypophysitis has not been established. Their role in this specific differential diagnosis should therefore be considered investigational.

Circulating molecular biomarkers represent another potential research direction. Circulating microRNAs have been investigated in pituitary tumors; for example, miR-20a-5p has recently been identified as a potential circulating biomarker in patients with prolactinoma and hyperprolactinemia [20]. However, no circulating microRNA has been validated for distinguishing reactive thyrotroph hyperplasia from autonomous pituitary neoplasia. Future studies could investigate candidate microRNA signatures in conjunction with endocrine and imaging parameters. The potential diagnostic value of circulating hypothalamic- or pituitary-derived peptides, molecular fragments, or other serum biomarkers is even less established and should currently be regarded as hypothesis-generating. Genetic susceptibility also warrants exploration. Variants affecting the thyrotropin-releasing hormone receptor (TRHR), thyroid hormone receptors, or other components of hypothalamic-pituitary-thyroid feedback could theoretically modify the magnitude or duration of thyrotroph proliferation during prolonged thyroid hormone deficiency. At present, however, no such genetic variant has been established as a determinant of acquired hypothyroidism-related pituitary hyperplasia, and adequately powered replication studies would be required before any clinical implication could be inferred.

Finally, prospective multicenter studies using standardized endocrine assessment and serial volumetric pituitary MRI are needed to characterize the kinetics of pituitary regression more precisely. Existing reports demonstrate substantial radiological reversibility after thyroid hormone replacement, but the timing and magnitude of recovery vary between patients [1]. Future studies should evaluate whether regression kinetics are associated with the severity and duration of hypothyroidism, baseline pituitary volume, treatment adherence, or levothyroxine replacement strategy. Severe hypothyroidism-related pituitary hyperplasia may also be accompanied by deficiencies of other pituitary axes, including clinically significant corticotropic dysfunction [17]. Although functional recovery may occur after correction of hypothyroidism, future studies should clarify why hormonal recovery may be incomplete or persistent in some patients and determine whether this reflects prolonged cellular or compressive injury, delayed functional recovery, or an unrecognized coexisting pituitary disorder. Integrating longitudinal endocrine phenotyping, quantitative imaging, radiomics, and selected molecular biomarkers may ultimately improve identification of patients in whom thyroid hormone replacement and surveillance alone are appropriate [19,20].

Conclusions

Severe primary hypothyroidism should be included in the differential diagnosis of pituitary enlargement before a sellar lesion is classified as a pituitary macroadenoma. Hypophysitis should also be considered, particularly when pituitary stalk thickening, loss of the posterior pituitary bright spot, arginine vasopressin deficiency, multiple pituitary hormone deficits, or systemic inflammatory or autoimmune features are present.

In this single case, the combination of profound primary hypothyroidism, preservation of the posterior

pituitary bright spot, absence of reported cavernous sinus involvement, and complete sustained radiological resolution during levothyroxine replacement without glucocorticoid or pituitary-directed therapy strongly favored reactive pituitary hyperplasia. However, the absence of histological confirmation, incomplete applicability of the hypophysitis prediction score, and absence of a complete baseline etiological work-up for secondary hypophysitis prevent absolute exclusion of an inflammatory pituitary disorder. Clinical improvement, pituitary morphological regression, normalization of TSH, and normalization of prolactin may occur at different times. A structured and individualized clinical, endocrine, visual, and radiological reassessment is therefore preferable to premature pituitary-directed therapy or indiscriminate diagnostic testing.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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Disclosures

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References

1. Roux A, Rosso D, Cuboni D, Maccario M, Grottoli S, Arvat E, Gasco V: Pituitary hyperplasia due to longstanding primary hypothyroidism: a case report and comprehensive review of the literature. Biomedicines. 2024, 12:1368. 10.3390/biomedicines12061368
2. Khawaja NM, Taher BM, Barham ME, et al.: Pituitary enlargement in patients with primary hypothyroidism . Endocr Pract. 2006, 12:29-34. 10.4158/EP.12.1.29
3. Nikith S, Krishnappa B, Lakkundi S, et al.: Radiological evolution of pituitary hyperplasia in primary hypothyroidism and its differentiation from nonfunctioning pituitary adenoma coexisting with primary hypothyroidism. Endocrine. 2024, 86:358-68. 10.1007/s12020-024-03983-1
4. Perez-Guzman MC, Szuman G, Altwijri A, Shek K, Asa SL, Ezzat S: Mimickers of pituitary tumors . Neurooncol Adv. 2025, 7:i48-57. 10.1093/noajnl/vdae085
5. Miquel L, Testud B, Albarel F, et al.: An update on hypophysitis . Nat Rev Endocrinol. 2026, 22:287-301. 10.1038/s41574-025-01200-1
6. Fleseriu M, Gurnell M, McCormack A, et al.: Pituitary incidentaloma: a Pituitary Society international consensus guideline statement. Nat Rev Endocrinol. 2025, 21:638-55. 10.1038/s41574-025-01134-8
7. Iglesias P, Biagetti B, Guerrero-Pérez F, Vicente A, Cordido F, Díez JJ: Executive summary of the consensus document on hypophysitis of the Neuroendocrinology Area of Knowledge of the Spanish Society of Endocrinology and Nutrition. Endocrinol Diabetes Nutr (Engl Ed). 2023, 70:116-25. 10.1016/j.endien.2023.01.001
8. Taieb A, Bouzaouache I, Gasmi A, et al.: A predictive score incorporating clinical, radiologic, and hormonal parameters to discriminate lymphocytic hypophysitis from non-functioning pituitary macroadenomas.

Diagnostics (Basel). 2025, 15:2334. 10.3390/diagnostics15182334
9. Frommer L, Kahaly GJ: Autoimmune polyendocrinopathy. J Clin Endocrinol Metab. 2019, 104:4769-82. 10.1210/jc.2019-00602
10. Menotti S, di Filippo L, Terenzi U, Chiloiro S, De Marinis L: Hypophysitis in COVID-19: a systematic review. Pituitary. 2024, 27:874-88. 10.1007/s11102-024-01462-4
11. Ach T, Ben Yahia W, Halloul I, Sghaier F, Atig A: Neurosarcoidosis-induced hypophysitis mimicking pituitary macroadenoma. Cureus. 2023, 15:e39865. 10.7759/cureus.39865
12. de Sousa Torraca F, Hypolito NM, de Azevedo FV, Brito AC, Ochtrop ML, Tavares AB: Pituitary involvement in granulomatosis with polyangiitis: a diagnostic and therapeutic challenge. Mod Rheumatol Case Rep. 2026, 10:rxag042. 10.1093/mrcr/rxag042
13. Neves CP, Massolt ET, Peeters RP, Neggers SJ, de Herder WW: Pituitary hyperplasia: an uncommon presentation of a common disease. Endocrinol Diabetes Metab Case Rep. 2015, 2015:150056. 10.1530/EDM-15-0056
14. Rajput R, Sehgal A, Gahlan D: Reversible thyrotroph hyperplasia with hyperprolactinemia: a rare presenting manifestation of primary hypothyroidism. Indian J Endocrinol Metab. 2012, 16:1037-9. 10.4103/2230-8210.103036
15. Khan AA, Sharma R, Ata F, et al.: Systematic review of the association between thyroid disorders and hyperprolactinemia. Thyroid Res. 2025, 18:1. 10.1186/s13044-024-00214-7
16. Petersenn S, Fleseriu M, Casanueva FF, et al.: Diagnosis and management of prolactin-secreting pituitary adenomas: a Pituitary Society international consensus statement. Nat Rev Endocrinol. 2023, 19:722-40. 10.1038/s41574-023-00886-5
17. Hakami Y, AlJaman A: Thyrotroph hyperplasia caused by severe primary hypothyroidism leading to adrenal crisis. JCEM Case Rep. 2024, 2:luae187. 10.1210/jcemcr/luae187
18. Fleseriu M, Hashim IA, Karavitaki N, Melmed S, Murad MH, Salvatori R, Samuels MH: Hormonal replacement in hypopituitarism in adults: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2016, 101:3888-921. 10.1210/jc.2016-2118
19. Agosti E, Mangili M, Panciani PP, et al.: Radiomics in pituitary adenomas: a systematic review of clinical applications and predictive models. J Clin Med. 2025, 14:6595. 10.3390/jcm14186595
20. Lee YJ, Hong JW, Kim Y, et al.: Circulating miR-20a-5p as a biomarker associated with cabergoline responsiveness in patients with hyperprolactinemia and pituitary adenomas. Eur J Endocrinol. 2025, 192:335-45. 10.1093/ejendo/lvaf025