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Case Report

Advanced Magnetic Resonance Imaging Techniques for Localization of a Small Thyrotropin-Secreting Pituitary Tumor

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Abstract

Thyrotropin (TSH)-secreting pituitary tumors (TSH-omas) are a rare cause of hyperthyroidism. Historically, the majority have been macroadenomas (>1 cm); however, microadenomas (<1 cm) are increasing in frequency. Localization of TSH-secreting microadenomas can be challenging. We report the first case employing advanced pituitary magnetic resonance imaging (MRI) sequences to localize a TSH-secreting microadenoma, leading to successful resection. The patient presented with mild symptoms of hyperthyroidism and biochemistry confirming secondary hyperthyroidism. α-Glycoprotein subunit and sex hormone–binding globulin were elevated; however, cross-linked C-telopeptide of type I collagen was within the reference range. No pathogenic variants in thyroid hormone resistance genes were detected. A triiodothyronine suppression test, thyroid hormone–releasing hormone stimulation test, and short-acting octreotide suppression test were consistent with a TSH-oma. Initial pituitary MRI did not demonstrate a pituitary tumor. However, advanced imaging techniques including coronal T1 3-dimensional volumetric interpolated breath-hold sequence (VIBE) thin-slice scans confirmed a small, right-sided pituitary tumor. Transsphenoidal surgery was performed, and histopathology confirmed a TSH-oma. The patient remains in biochemical remission. TSH-secreting microadenomas are increasing in frequency and localization is likely to become an increasing challenge. Advanced MRI imaging techniques appear beneficial in the localization of TSH-secreting microadenomas.

Key Words: TSH-secreting pituitary tumors, TSH-oma, localization of small pituitary tumors, advanced pituitary MRI techniques

Abbreviations: ACTH, adrenocorticotropin hormone; CTX, cross-linked C-telopeptide of type I collagen; fT3, free triiodothyronine; fT4, free thyroxine; ^{68}GA, gallium-68; Gd, gadolinium; MRI, magnetic resonance imaging; PET, positron emission tomography; SHBG, sex hormone–binding globulin; SPACE, sampling perfection with application-optimized contrasts using different flip angle evolutions; TRH, thyroid hormone–releasing hormone; TSH, thyrotropin; TSH-oma, thyrotropin-secreting pituitary tumor; VIBE, volumetric interpolated breath-hold sequence.

Introduction

Thyrotropin (TSH)-secreting pituitary tumors (TSH-omas) account for only 0.5% to 2% of pituitary tumors [1]. Historically, most TSH-omas were macroadenomas [2]. However, with the increased availability of ultrasensitive immunometric assays for thyroid function tests, and frequent imaging [3], the prevalence of TSH-omas has increased and more are being diagnosed earlier in the natural history as microadenomas [4]. This case describes the challenging localization of a small TSH-oma, initially not visible on standard pituitary magnetic resonance imaging (MRI) sequences. It is the first to report the use of advanced MRI techniques to successfully localize a TSH-secreting microadenoma, leading to successful transsphenoidal surgery and biochemical remission.

Case Presentation

A 60-year-old man was referred to our tertiary endocrinology service with secondary hyperthyroidism dating back at least 5 years. He reported occasional palpitations, night sweats, and heat intolerance, but no other symptoms of hyperthyroidism, headaches, or visual disturbances. His background history was significant only for hypertension, and medications included perindopril 10 mg daily, amlodipine 10 mg daily, and hydrochlorothiazide 25 mg daily. He was not taking any complementary medications or supplements. His father had amiodarone-induced thyroiditis, and there was no other family history of thyroid conditions. On examination, the patient's body weight was 105 kg, heart rate was 66 beats per minute, and blood pressure was 160/90 mm Hg. There were no signs of hyperthyroidism and he appeared eupituitary. Visual fields were normal to confrontation.

Diagnostic Assessment

Laboratory investigations (Table 1) confirmed secondary hyperthyroidism (free thyroxine [fT4] 31.3 pmol/L (2.4 ng/dL) [reference range, 11.5-22.7 pmol/L (0.9-1.8 ng/mL)], (free triiodothyronine (fT3) 11.4 pmol/L (0.74 ng/dL) [reference range, 3.5-6.5 pmol/L (2.8-0.4 ng/dL)] and TSH 1.5 mIU/L (1.5 µIU/mL) [reference range, 0.6-4.8 mIU/L (0.6-4.8 µIU/mL)]) and otherwise normal pituitary function (see Table 1). Interference studies excluded heterophile antibody and assay interference in the thyroid function tests. Sex hormone–binding globulin (SHBG) was 55.0 nmol/L (522.5 µg/dL)

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(reference range, 10.0-50.0 nmol/L [95.0-475.0 µg/dL]), α-glycoprotein subunit was 0.9 IU/L (107.7 ng/dL) (reference range, 0.0-0.7 IU/L [0.0-84.7 ng/mL]), and serum cross-linked C-telopeptide of type I collagen (CTX) was 0.2 µg/L (200.0 ng/L) (0.1-0.6 µg/L [100.0-600.0 ng/L]) (Table 2). Genetic testing (see Table 2) for thyroid hormone resistance genes (*ALB*, *SECISBP2*, *SLC16A2*, *THRA*, *THRB*, and *TSHR* genes) did not identify any pathogenic variants.

Dynamic testing was consistent with a TSH-oma (see Table 2). There was no suppression of TSH following tertroxin administration (TSH 1.1 mIU/L [1.1 µIU/mL] at baseline, and 1.3 mIU/L [1.3 µIU/mL] following tertroxin), and no stimulation of TSH following administration of thyrotropin-releasing hormone (TRH) (TSH 1.1 mIU/L [1.1 µIU/mL] at baseline, 1.0 mIU/L [1.0 µIU/mL] at 20 minutes, and 0.9 mIU/L [0.9 µIU/mL] at 60 minutes following TRH). Suppression ratio of TSH was 85.2% following administration of a short-acting somatostatin analogue (TSH 1.7 mIU/L [1.7 µIU/mL] at baseline and 0.3 mIU/L [0.3 µIU/mL] following 3 doses of 100 mg octreotide every 8 hours).

Thyroid ultrasonography showed an enlarged thyroid gland with multiple small nodules. A thyroid uptake scan demonstrated homogenously increased uptake of 16.4% (reference range, 3%-8%). Initial pituitary MRI using (fast) spin echo ([F]SE) T1-[± gadolinium [Gd] enhancement) and T2-weighted sequences performed at a regional center did not report any pituitary tumors. On our review of these images, there was asymmetric fullness on the right side of the pituitary gland, but no definitive pituitary tumor or deviation of the pituitary stalk (Fig. 1). A gallium-68-DOTATATE positron emission tomography (^{68}Ga-DOTATATE PET)/MRI, performed to exclude an ectopic TSH-secreting tumor, showed physiological pituitary DOTATATE uptake and no abnormal DOTATATE-avid lesions (Fig. 2). A further pituitary MRI using advanced MRI sequences implemented recently at our institution for localization of adrenocorticotropin

Table 1. Results of thyroid function tests and pituitary hormones

Parameters	Values	Reference range
TSH	1.5 mIU/L (1.5 µIU/mL)	0.6-4.8 mIU/L (0.6-4.8 µIU/mL)
fT4	31.3 pmol/L (2.4 ng/dL)	11.5-22.7 pmol/L (0.9-1.8 ng/dL)
fT3	11.4 pmol/L (0.7 ng/dL)	3.5-6.5 pmol/L (2.8-0.4 ng/dL)
IGF-1	16.0 nmol/L (122.0 ng/mL)	7.2-26 nmol/L (55.1-198.9 ng/mL)
GH	0.2 µg/L (20.0 ng/dL)	0.05-3.0 µg/L (5.0-300.0 ng/dL)
TSH receptor antibodies	<0.3 IU/L (<0.3 mIU/mL)	<1.8 IU/L (<1.8 mIU/mL)
Cortisol	226.0 nmol/L (8.2 µg/dL)	100.0-535.0 nmol/L (3.6-19.4 µg/dL)
Prolactin	86.0 mLU/L (4.0 ng/mL)	55.0-300.0 mLU/L (2.6-14.1 ng/mL)
ACTH	14.0 ng/L (14.0 pg/mL)	9.0-51.0 ng/L (14.0-51.0 pg/mL)
LH	5.2 IU/L (5.2 mIU/mL)	1.5-9.3 IU/L (1.5-9.3 mIU/mL)
FSH	7.2 IU/L (7.2 mIU/mL)	1.4-18 IU/L (1.4-18.0 mIU/mL)
Testosterone	22.0 nmol/L (634.5 ng/dL)	11.0-40.0 nmol/L (317.3-1153.7 ng/dL)

Abbreviations: ACTH, adrenocorticotropin; fT3, free triiodothyronine; fT4, free thyroxine; FSH, follicle-stimulating hormone; GH, growth hormone; IGF-1, insulin-like growth factor 1; LH, luteinizing hormone; TSH, thyrotropin.

Table 2. Results of pathology and dynamic testing to differentiate between thyrotropin-secreting pituitary tumor and thyrotropin resistance

Parameters	Values	Reference range
SHBG	55.0 nmol/L (522.5 µg/dL)	10.0-50.0 nmol/L (95-475.0 µg/dL)
α-Glycoprotein subunit	0.9 IU/L (107.7 ng/dL)	0.0-0.7 IU/L (0.0-84.7 ng/dL)
CTx	0.2 ug/L (200.0 ng/L)	0.1-0.6 mg/L (100.0-600.0 ng/L)
TRH stimulation	TSH: Baseline: 1.1 mIU/L (1.1 µIU/mL) 20 min: 1.0 mIU/L (1.0 µIU/mL) 60 min: 0.9 mIU/L (0.9 µIU/mL)	<2-fold increase is consistent with TSH-oma
T3 suppression test	TSH: Baseline: 1.1 mIU/L (1.1 µIU/mL) Post tertroxin: 1.3 mIU/L (1.3 µIU/mL)	Failure to suppress TSH to any degree is suggestive of TSH-oma
Octreotide stimulation test	TSH: 2 h: 1.7 mIU/L (1.7 µIU/mL) 24 h: 0.3 mIU/L (0.3 µIU/mL) Suppression ratio of TSH at 24 vs 2 h: 85.2%	TSH 24- vs 2-h suppression ratio of >44.5% is consistent with TSH-oma [5]
Genetic testing for thyroid hormone resistance (*ALB*, *SECISBP2*, *SLC16A2*, *THRA*, *THRB*, and *TSHR* genes)	No pathogenic variants detected	

Abbreviations: CTx, cross-linked C-telopeptide of type I collagen; SHBG, sex hormone–binding globulin; T3, triiodothyronine; TRH, thyrotropin-releasing hormone.

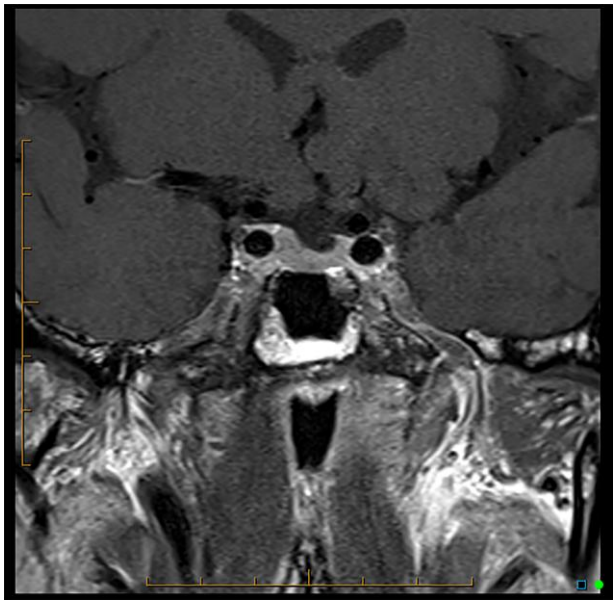

Figure 1. Magnetic resonance imaging scans of the pituitary. Coronal T1-weighted scan following gadolinium in 2023 showing asymmetric fullness on the right side of the pituitary gland, but no definitive pituitary lesion.

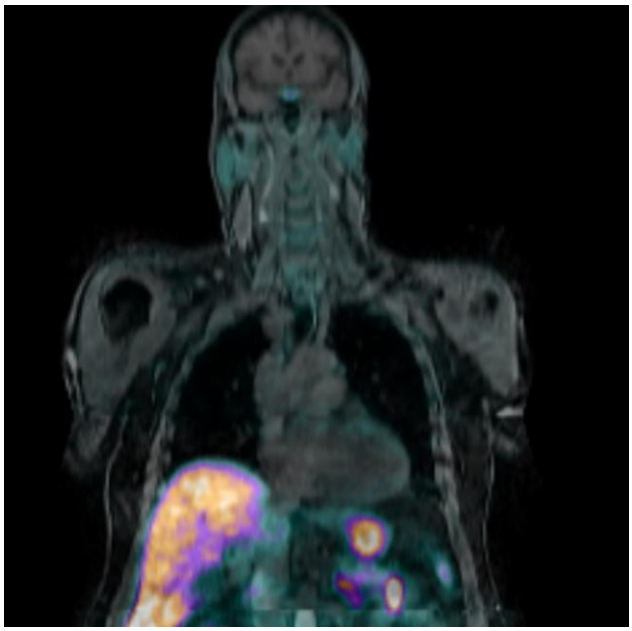

Figure 2. Ga68-DOTATATE positron emission tomography/magnetic resonance imaging showing physiological uptake in the pituitary gland. No DOTATATE avid lesions suggestive of an ectopic TSH-oma.

(ACTH)-secreting microadenomas was performed the following month after the initial pituitary MRI. The advanced MRI pituitary protocol includes Gd-enhanced coronal dynamics, T1-volumetric interpolated breath-hold examination (VIBE), and T2 sampling perfection with application-optimized contrasts using different flip angle evolutions (SPACE) scans [6]. This demonstrated heterogeneous enhancement of the right side of the pituitary and a 4- × 3-mm hypoenhancing lesion suggestive of a pituitary tumor, evident on coronal T1-VIBE thin-slice scans (Fig. 3). There was no T2 signal abnormality.

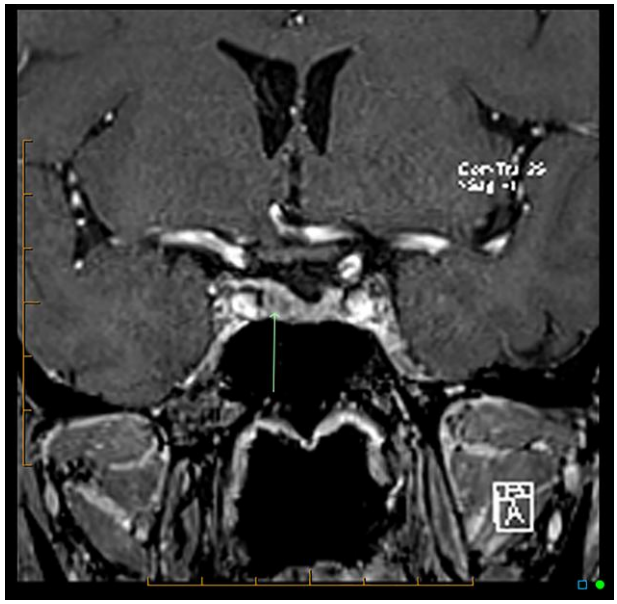

Figure 3. Magnetic resonance imaging (MRI) scans of the pituitary. Dedicated advanced pituitary protocol MRI scans with T1-VIBE scan post gadolinium showing a 4- × 3-mm hypoenhancing lesion on the right side of the pituitary gland consistent with a pituitary microadenoma.

Treatment

Lantreotide (60 mg subcutaneously every 4 weeks) was commenced to achieve euthyroidism preoperatively. Transsphenoidal resection was performed. A small pituitary tumor was visualized on the right hemipituitary and excised. Histopathology demonstrated a pituitary neuroendocrine tumor; immunohistochemistry was positive for TSH and pituitary-specific positive transcription factor 1 (PIT1) and negative for ACTH, growth hormone, prolactin, luteinizing hormone, follicle-stimulating hormone, T-box transcription factor (Tpit), and steroidogenic factor (SF1), confirming a TSH-oma.

Outcome and Follow-up

Postoperative biochemical testing demonstrated normalization of thyroid function (TSH 0.1 mIU/L, fT4 10.4 pmol/L [0.8 ng/dL], fT3 3.7 pmol/L [0.2 ng/dL]), and otherwise normal pituitary function. MRI of the pituitary postoperatively showed complete resection of the right-sided TSH-oma. The patient remains in biochemical remission 18 months following transsphenoidal surgery.

Discussion

We present a case of a TSH-secreting microadenoma, with no clearly identifiable lesion on standard pituitary MRI imaging. This is the first reported case to use advanced MRI pituitary sequences [6] to localize a TSH-secreting microadenoma, leading to successful resection. TSH-omas have increased in frequency and more are being diagnosed as microadenomas due to the availability of ultrasensitive immunometric assays for measurement of TSH, fT4, and fT3 [3]. Challenging localization of TSH-microadenomas is therefore likely to become an increasing problem.

Initial pituitary MRIs for our patient were performed using a combination of (F)SE T1- ± Gd enhancement and T2-weighted

sequences at a regional center. Experience from Cushing disease has shown that small ACTH-secreting pituitary tumors, particularly those smaller than 5 mm, can be difficult to localize on MRI, especially when using lower field strength MRI with 2-to 3-mm slice intervals, and false-negative rates occur in up to 50% of cases [7, 8]. We have recently implemented advanced MRI sequences for the localization of small ACTH-secreting tumors at our center. This protocol includes T1 VIBE and contrast-enhanced SPACE T2 scans with coronal dynamics in addition to Gd enhancement. To date, the T1 VIBE sequence and the addition of contrast-enhanced SPACE sequences have both improved the detection of ACTH-secreting pituitary microadenomas [6, 9, 10]. This is the first case report to extend the use of these sequences to TSH-secreting microadenomas to assist in successful localization.

A ^{68}Ga-DOTATATE PET/MRI was performed on our patient to exclude an extrasellar or ectopic TSH-secreting tumor. Ectopic pituitary tumors are rare, with approximately 180 cases described in the literature. Although most ectopic pituitary tumors are hormonally active, there are only 14 reported cases of ectopic TSH-secreting tumors [11]. TSH-omas express somatostatin receptors [12], which are the targets for somatostatin analogues [13]. ^{68}Ga-DOTATATE is a radio conjugate consisting of a somatostatin analogue labeled with a gallium position-emitting isotope. ^{68}Ga-DOTATATE PET/computed tomography scan has been previously reported to be able to identify ectopic TSH-omas [14]. Studies evaluating somatostatin receptor imaging in pituitary tumors are limited. A small number of cases showed a positive (but nonsignificant) correlation between the intensity of ^{111}Indium-pentetreotide uptake and degree of TSH suppression after acute administration of octreotide [15]. ^{68}Ga-DOTATATE PET/MRI did not improve identification of a small TSH-oma in our case, likely due to the small tumor size and physiological DOTATATE uptake in the normal pituitary.

In conclusion, we describe a case of a small TSH-oma in a patient who presented with secondary hyperthyroidism and diagnostic dynamic testing, but without a definitive pituitary lesion seen on initial standard MRI. We report the first case of employing advanced pituitary MRI sequences, previously shown to enhance the identification of ACTH-secreting pituitary tumors [6], to localize a small TSH-oma. As TSH-omas are increasing in prevalence and being detected earlier in their natural history [4], identification of TSH-secreting microadenomas is likely to become an increasing challenge and advanced imaging techniques will be needed. We propose that the use of these advanced MRI sequences be a routine part of the radiological evaluation of biochemically proven TSH-omas, where standard imaging fails to identify a definitive pituitary lesion, similar to the current practice for Cushing disease.

Learning Points

- Historically, most TSH-omas have been macroadenomas; however, microadenomas are increasing in frequency due to improved assays for assessing thyroid function.
- Localization of TSH-secreting microadenomas can be challenging.
- Advanced MRI sequences are useful to localize TSH-secreting microadenomas.
- Ectopic TSH-secreting tumors are rare but can occur, and imaging with 68Ga-DOTATATE PET can be useful to exclude these tumors.

Contributors

All authors made individual contributions to authorship. C.L. was involved in manuscript drafting and submission. E.B. was responsible for the diagnosis and management of the patient and manuscript submission. W.I. assisted with diagnosis and management of the patient and manuscript submission. B.O. was involved in radiological imaging and manuscript submission. All authors reviewed and approved the final draft.

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Disclosures

None declared.

Informed Patient Consent for Publication

Signed informed consent obtained directly from the patient.

Data Availability Statement

Original data generated and analyzed during this study are included in this published article.

References

1. Beck-Peccoz P, Giavoli C, Lania A. A 2019 update on TSH-secreting pituitary adenomas. *J Endocrinol Invest*. 2019;42(12):1401-1406.
2. De Herdt C, Philipse E, De Block C. ENDOCRINE TUMOURS: thyrotropin-secreting pituitary adenoma: a structured review of 535 adult cases. *Eur J Endocrinol*. 2021;185(2):R65-r74.
3. Socin HV, Chanson P, Delemer B, *et al*. The changing spectrum of TSH-secreting pituitary adenomas: diagnosis and management in 43 patients. *Eur J Endocrinol*. 2003;148(4):433-442.
4. Ónnestam L, Berinder K, Burman P, *et al*. National incidence and prevalence of TSH-secreting pituitary adenomas in Sweden. *J Clin Endocrinol Metab*. 2013;98(2):626-635.
5. Han R, Shen L, Zhang J, *et al*. Diagnosing thyrotropin-secreting pituitary adenomas by short-term somatostatin analogue test. *Thyroid*. 2020;30(9):1236-1244.
6. Bonneville JF, Potorac I, Petrossians P, Tshibanda L, Beckers A. Pituitary MRI in Cushing's disease—an update. *J Neuroendocrinol*. 2022;34(8):e13123.
7. Lacroix A, Feelders RA, Stratakis CA, Nieman LK. Cushing's syndrome. *Lancet*. 2015;386(9996):913-927.
8. Boscaro M, Arnaldi G. Approach to the patient with possible Cushing's syndrome. *J Clin Endocrinol Metab*. 2009;94(9):3121-3131.
9. Wang J, Wu Y, Yao Z, Yang Z. Assessment of pituitary microlesions using 3D sampling perfection with application-optimized contrasts using different flip-angle evolutions. *Neuroradiology*. 2014;56(12):1047-1053.
10. Wu Y, Cai Y, Rui W, *et al*. Contrast-enhanced 3D-T2-weighted SPACE sequence for MRI detection and localization of adrenocorticotropin (ACTH)-secreting pituitary microadenomas. *Clin Endocrinol (Oxf)*. 2022;96(4):578-588.
11. Kumar S, Phang CA, Ni H, Diamond T. A patient with an ectopic sphenoid bone TSH secretory adenoma: case report and review of the literature. *Front Endocrinol (Lausanne)*. 2022;13:961256.
12. Yu B, Zhang Z, Song H, Chi Y, Shi C, Xu M. Clinical importance of somatostatin receptor 2 (SSTR2) and somatostatin receptor 5

(SSTR5) expression in thyrotropin-producing pituitary adenoma (TSHoma). *Med Sci Monit*. 2017;23:1947-1955.
13. Fukuhara N, Horiguchi K, Nishioka H, *et al.* Short-term preoperative octreotide treatment for TSH-secreting pituitary adenoma. *Endocr J*. 2015;62(1):21-27.
14. Kim S, Dillon WP, Hope TA, *et al.* Ectopic thyroid-stimulating hormone-secreting pituitary adenoma of the nasopharynx diagnosed by gallium 68 DOTATATE positron emission tomography/computed tomography. *World Neurosurg*. 2019;125:400-404.
15. Losa M, Magnani P, Mortini P, *et al.* Indium-111 pentetreotide single-photon emission tomography in patients with TSH-secreting pituitary adenomas: correlation with the effect of a single administration of octreotide on serum TSH levels. *Eur J Nucl Med*. 1997;24(7):728-731.