Thyrotrophynoma induced hyperthyroidism: what is the best management?

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- TSH-secreting pituitary adenomas are a **rare cause of hyperthyroidism**, accounting for **< 1%** of all cases of hyperthyroidism.
- TSH is usually normal or high; total and free T4 and T3 are high; in some cases plasma alpha subunit of glycoprotein hormones is elevated.
- **Definitive therapy** of TSH-secreting pituitary adenomas can be achieved through **transsphenoidal resection of the tumor**. The role of somatostatin analogs as a primary treatment requires further investigation.
- **Medical therapy** is used to **restore euthyroidism prior to surgery**. Typically, **long-acting somatostatin analogs** are used, but dopamine agonists are an alternative. Beta blockers are given to ameliorate the symptoms and signs of hyperthyroidism.

A **63-year old woman** was sent to an Endocrinology appointment due to incidental **thyroid nodules**.

She had a history of hypertension, chronic gastritis and osteoporosis.

She was taking losartan, hydrochlorothiazide and omeprazol.

A few months earlier, she was medicated with bisoprolol due to complaints of palpitations. An EKG identified a sinus tachycardia.

She presented with no other symptoms of thyroid dysfunction.

INITIAL TESTING

TSH 3.97 uUI/L [0.35-4.94]
Free T4 2.10 ng/dL [0.70-1.48] ↑
Free T3 8.02 pg/mL [1.71-3.71] ↑
TPO antibodies 0.5 UI/mL
TRAbs <0.5 µUI/mL
FSH 43.9 µIU/mL [25.8-34.8]
LH 28.3 µUI/mL [14.2-52.3]
Prolactin 11.4 ng/mL [3.4-24.1]
Morning serum cortisol 12.3 µg/mL [6.2-19.4]
ACTH 11.2 pg/mL [<46]
IGF-1 68.6 ng/ml [75-212]

At presentation

6 Months
TSH 3.6 **N**
Free T4 1.99 ↑
Free T3 5.3 ↑

Clinical hyperthyroidism with inappropriately normal TSH

The patient started **propylthiouracil 50mg daily**

8 Months
TSH 6.47 ↑
Free T4 1.68 ↑
Free T3 4.29 ↑

The patient complained of new onset **visual disturbances**

TSH-secreting tumor vs Resistance to thyroid hormones

The patient stopped **propylthiouracil**

10 Months
TSH 3.32 **N**
Free T4 2.06 ↑
Free T3 6.09 ↑

TRH stimulation test: absence of response [maximum TSH 7.32]
Alpha subunit 1.0 UI/L [<1.6]

MRI: 8mm pituitary adenoma

Octreotide response test: positive (57% reduction of TSH during the test)

Overall results suggestive of a TSH-SECRETING TUMOR

12 Months
TSH 1.28 **N**
Free T4 0.98 **N**
Free T3 2.83 **N**

Normalization of thyroid function with octreotide LAR

The patient started Octreotide LAR

1 Month Post-op
TSH 1.51 **N**
Free T4 1.09 **N**
Free T3 2.83 **N**

Biochemical cure of central hyperhyroidism

Transphenoidal surgery

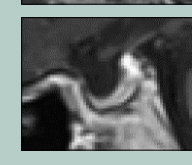
Octerotide LAR was stopped

Histology: insufficient tissue sample, no evidence of a tumor

2 Month Post-op
TSH 3.32 **N**
Free T4 2.06 ↑
Free T3 6.09 ↑

Recurrence of hyperhyroidism

MRI: image of empty sella turca, **possible 3mm adenoma**

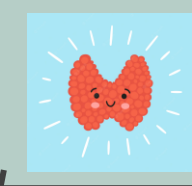


1 Year Post-op
TSH 2.86 **N**
Free T4 1.91 **N**
Free T3 2.87 **N**

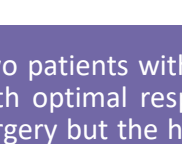
Biochemical euthyroidism with **Octreotide LAR**

Restart of Octreotide LAR

µUI/L [0.35-4.94]
ng/dL [0.70-3.71]
pg/mL [1.71-3.71]



20 Yrs Post-op
TSH 1.55
FT4 1.55
FT3 2.63
MRI: identical findings

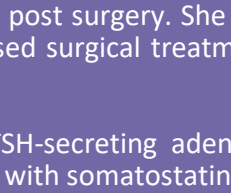


A **67-year old man** was referred to an Endocrinology appointment to study a **pituitary incidentaloma**.

The adenoma was initially identified on a head CT scan ordered in the ER following a head trauma.

He had a history of hypertension, atrial fibrillation and benign prostatic hyperplasia.

He was taking bisoprolol, warfarin, hydrochlorothiazide and lisinopril.



INITIAL TESTING

TSH 1.62 uUI/L [0.35-4.94]
Free T4 2.33 ng/dL [0.70-3.71]
Free T3 6.90 pg/mL [1.71-3.71]
TRH stimulation test: absence of response [maximum TSH 7.32]
Alpha subunit 0.20 uUI/mL [<1.6]
OGTT - nadir GH 0.50 ng/mL [N]
FSH 4.66 uUI/mL [N]
LH 3.07 uUI/mL [N]
TT 302.3 ng/dL [241-827]
Prolactin 26.7 ng/mL [3.4-24.1]
Morning serum cortisol 12.0 ug/mL [6.2-19.4]
ACTH 43.1 pg/mL [<46]

1. Clinical hyperthyroidism + inappropriately normal TSH
2. Normal alpha subunit
3. No response to TRH stimulation
4. Pituitary macroadenoma

⇨ Overall results suggestive of a TSH-SECRETING ADENOMA

At Presentation
TSH 1.62
Free T4 2.33 ↑
Free T3 6.90 ↑

MRI: 28 mm adenoma

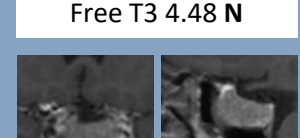
Reevaluation after 1 month
TSH 1.77
Free T4 2.18 ↑
Free T3 7.30 ↑

Surgery was offered to the patient, which he **refused**

The patient started **Octreotide LAR**

1 Month after starting therapy
TSH 0.12 ↓
Free T4 1.02 **N**
Free T3 3.39 **N**

6 Months after starting therapy
TSH 0.004 ↓
Free T4 1.38 **N**
Free T3 4.48 **N**

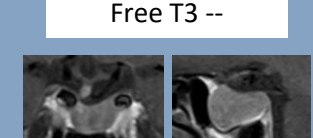


MRI: 26 mm adenoma

2 Years after starting therapy
TSH 0.96 **N**
Free T4 0.77 **N**
Free T3 2.21 **N**

MRI: 23 mm adenoma

15 Years after starting therapy
TSH 0.55 **N**
Free T4 1.45 **N**
Free T3 --



MRI: 24 mm adenoma

µUI/L [0.35-4.94]
ng/dL [0.70-3.71]
pg/mL [1.71-3.71]

Two patients with a history of a TSH-secreting adenoma were presented. The **first patient** had a microadenoma and was initially treated with octreotide LAR, with optimal response. After biochemical control of the hyperthyroidism, the patient underwent transsphenoidal surgery. The patient was euthyroid after surgery but the hyperthyroidism relapsed 2 months post surgery. She restarted treatment with octreotide LAR, again with an optimal and sustained response. **The second patient** had a macroadenoma and refused surgical treatment. He was treated solely with octreotide LAR, and also had an optimal and sustained response to medical treatment.

Although **surgery** is the definitive treatment for TSH-secreting adenomas, **cure will only occur in one third** of these individuals. Often, maintenance of euthyroidism depends on the use of medical therapy with somatostatin analogs, and **medical management as a primary therapy can be an alternative**.

BIBLIOGRAPHY

TPO = Thyroid peroxidase. TRAb = TSH receptor autoantibodies. TT = total testosterone