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A case of a co-secreting TSH and growth hormone pituitary adenoma presenting with a thyroid nodule

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Summary

Co-secreting TSH and growth hormone pituitary adenomas are rare. We present a case of a 55-year-old woman who presented with symptoms of neck fullness. Ultrasound revealed multiple thyroid nodules and examination revealed several clinical features of acromegaly. She was found to have a co-secreting TSH and growth hormone pituitary macroadenoma. She underwent surgical resection followed by gamma knife radiation, which resulted in complete remission of her TSH and GH-secreting adenoma.

Learning points:

- TSH-secreting pituitary adenomas are rare and about one-third co-secrete other hormones.
- Thyroid nodules are common in acromegaly and can be the presenting sign of a growth hormone-secreting pituitary adenoma.
- In the workup of acromegaly, assessment of other pituitary hormones is essential, even in the absence of symptoms of other pituitary hormone dysfunction.
- Complete remission of co-secreting GH and TSH pituitary macroadenomas is possible with surgery and radiation alone.

Background

TSH and growth hormone co-secreting pituitary adenomas are a rare phenomenon. TSH-secreting pituitary adenomas account for less than 3% of all pituitary adenomas. They typically present with either symptoms of tumor growth or symptoms of hyperthyroidism. The patient in this case initially presented with a thyroid nodule and was eventually found to have a co-secreting TSH and GH pituitary macroadenoma. Our patient achieved remission without somatostatin analog therapy, which is unlike many other cases of TSH and GH co-secreting pituitary adenomas (1, 2, 3).

Case presentation

A 55-year-old woman with a medical history significant only for hypertension initially presented to her primary care physician with complaints of fullness in her upper neck for the past several months. She complained of no other symptoms at the time though she was concerned she may have a thyroid nodule. A thyroid ultrasound showed a heterogeneous and enlarged thyroid gland with several small cysts throughout the gland and two thyroid nodules. One nodule was a subcentimeter right-sided nodule, which was mixed cystic and solid with grade 1 vascularity without calcifications (Fig. 1). The other was a left-sided primarily

cystic nodule, which measured 2.3 cm in maximal dimension (Figs 2 and 3). Thyroid function tests were then checked and revealed a TSH of 1.7 μ IU/mL (normal range: 0.5–4.0) and free T4 of 1.8 ng/dL (normal range: 0.5–1.1). Total T3 was 270 ng/dL (normal range: 85–190). She was subsequently referred to Endocrinology for abnormal thyroid function tests and thyroid nodules. Upon examination, the patient was noted to have an enlarged jaw, coarse facial features, soft tissue thickening of her face and hands and bony enlargement of her hands and feet. The patient revealed that over the past 5 years, her shoe size had increased from a size 6 to a size 8. She had also recently noticed that her high school ring only fit around the tip of her fourth digit. She had had cessation of menses at the age of 42 years. She had also noted occasional headaches but had not had any recent vision loss. She had no arthralgias and no symptoms of obstructive sleep apnea. Additionally, she had no heat intolerance, palpitations or weight loss. Her height was 165 cm and weight was 74.2 kg. BMI was 27 kg/m². Her heart rate was 77 bpm and blood pressure was 139/94.

Investigation

Thyroid function tests were repeated and showed a TSH of 1.27 μ IU/mL (normal range: 0.5–4.0) and free T4 by equilibrium dialysis was 3.9 ng/dL (normal range: 0.8–2.0). Due to a suspicion for acromegaly based on examination,

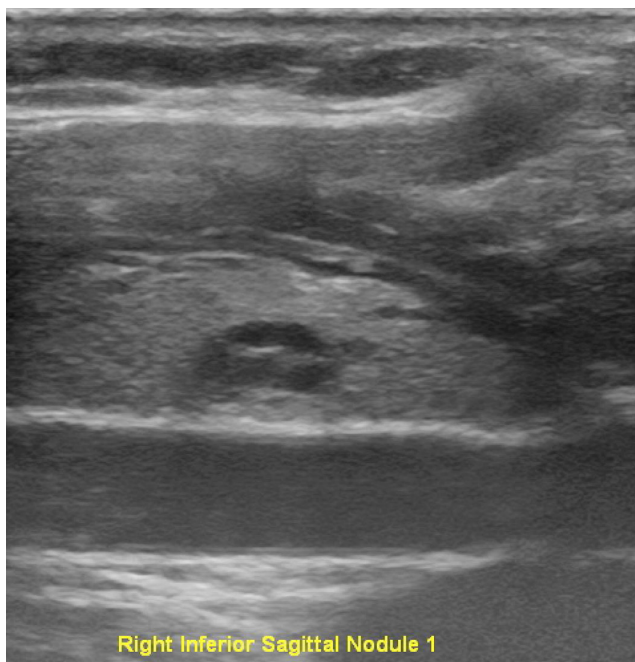


Figure 1
Patient's initial thyroid ultrasound images. Sagittal orientation of the right-sided subcentimeter nodule, which is mixed solid and cystic.

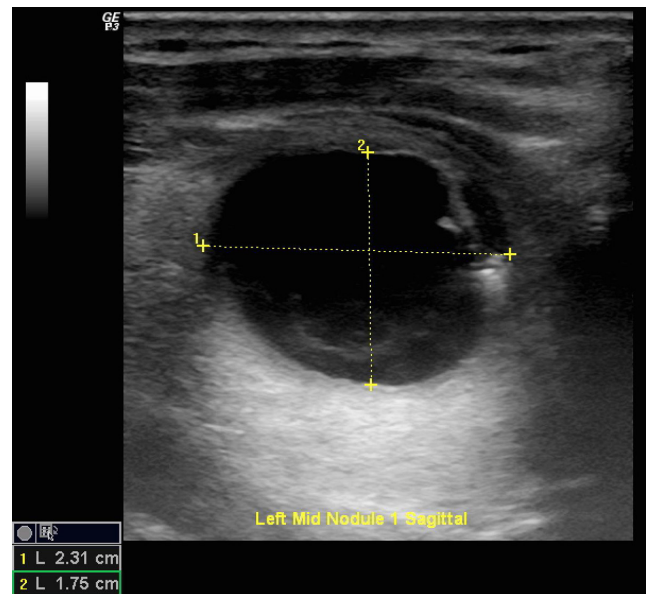


Figure 2
Patient's initial thyroid ultrasound images. Left-sided cystic nodule in sagittal orientation. It measures 2.31 cm longitudinally and 1.75 cm in anterior–posterior dimension.

a growth hormone level and insulin like growth factor were checked. Growth hormone was elevated at 17 ng/mL (normal range: 0.03–10.00). Insulin-like growth factor was elevated at 1292 ng/mL (normal range for age: 53–287). Other pituitary function was assessed with a prolactin, which was 25.4 ng/mL (normal range: 4–20), luteinizing

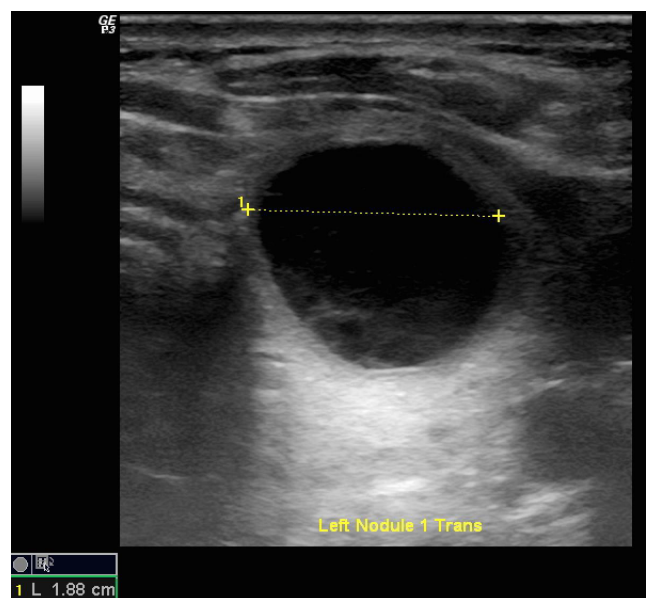


Figure 3
Patient's initial thyroid ultrasound images. Left-sided cystic nodule measuring 1.88 cm in the transverse plane.

hormone, which was 1.6 mIU/mL (normal post-menopausal range: 10–60), follicle stimulating hormone which was 7.3 mIU/mL (normal post-menopausal range: 16.7–113.6). ACTH stimulation test was normal with serum cortisol rising to 22.2 µg/dL 60 min after 250 µg of synthetic ACTH. She underwent formal visual field testing that showed no peripheral vision deficits. MRI of the pituitary showed a large sellar mass measuring 3.8 cm × 4.1 cm compressing the optic chiasm and optic nerves and invading into the left cavernous sinus (Fig. 4) consistent with the diagnosis of pituitary macroadenoma.

Treatment

Given the size of the macroadenoma and compression of the optic chiasm, the patient was urgently referred to neurosurgery for evaluation. She underwent transsphenoidal resection of the macroadenoma (Figs 5 and 6). Post operatively, the patient developed polyuria and was thought to have central diabetes insipidus. She was started on oral desmopressin 0.05 mg nightly. Additionally, as a precaution, she was also started on hydrocortisone 20 mg every morning and 10 mg every evening in the event that she developed adrenal insufficiency after resection of the large macroadenoma. At 6 weeks postoperatively, her 8 a.m. cortisol was 13 µg/dL

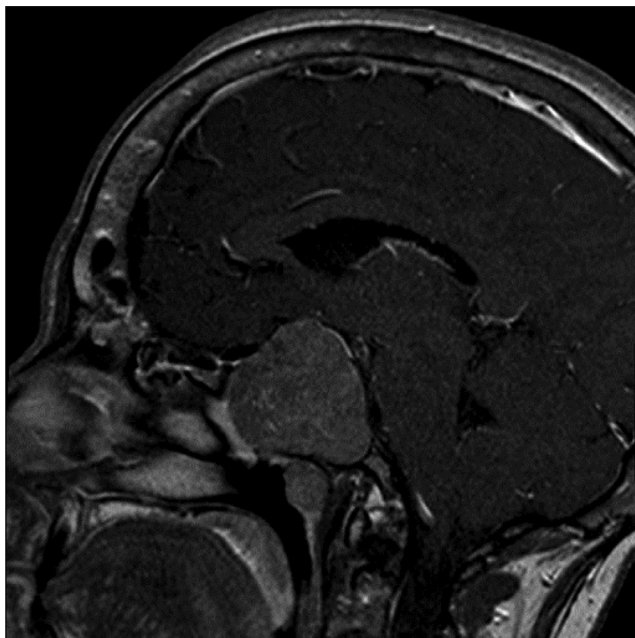


Figure 4
Preoperative T1-weighted sagittal MRI showing a heterogeneously enhancing 3.8 cm × 4.1 cm mass in the sella, which elevates and compresses the optic chiasm.

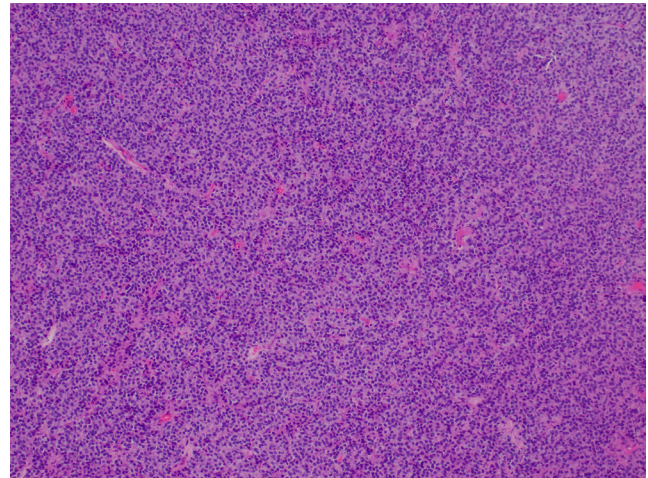


Figure 5
Pathology specimen of the patient's pituitary adenoma showing a typical solid growth pattern. Micrographs complementary of Dr Dianne Wilson MD, Department of Pathology, University of Kentucky.

(normal range: 6–25) after holding hydrocortisone for 36 h. Hydrocortisone was then discontinued. Her other labs 6 weeks after surgery showed a prolactin level of 6.7 ng/dL (normal range: 4–20), a free T4 of 0.7 ng/dL (normal range: 0.5–1.1) and a TSH of 0.8 µIU/mL (normal range: 0.5–4.0). Luteinizing hormone remained low at 0.7 ng/dL (normal post-menopausal range: 10–60) as did follicular-stimulating hormone at 3.2 mIU/mL (normal post-menopausal range: 16.7–113.6). Insulin-like growth factor had come down to 242 ng/mL (normal range: 53–287). About 2 months post operatively, her

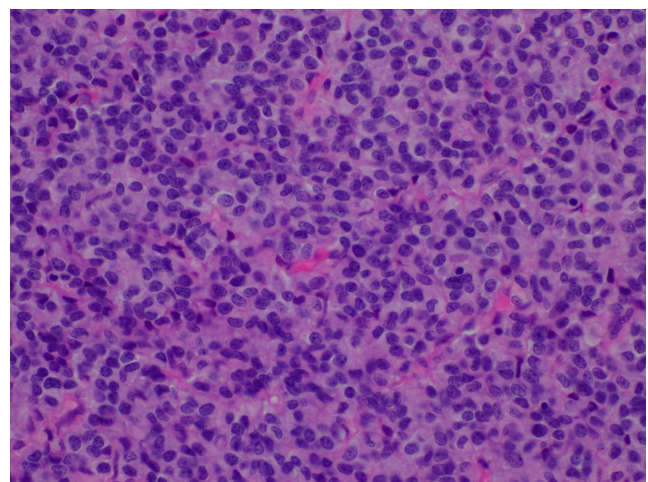


Figure 6
Higher power micrograph of the patient's pituitary adenoma showing small, monomorphous cells of the neuroendocrine cytophenotype. Micrographs complementary of Dr Dianne Wilson MD, Department of Pathology, University of Kentucky.

desmopressin was held for a trial off of the medication. After holding desmopressin for 1 week, her serum sodium increased to 145 mmol/L (from 143 mmol/L 2 weeks before), plasma osmolality was 297 mosmol/kg and urine osmolality was 602 mosmol/kg. Partial DI was suspected and she was restarted on desmopressin as a spray at 10 µg nightly.

Outcome and follow-up

MRI of the pituitary 3 months post operatively that showed evidence of residual tumor along the left aspect of the sella (Fig. 7). Given her residual tumor on MRI, she was treated with gamma knife radiation 4 months after transsphenoidal resection. Her 6-month post-operative IGF-1 level was normal at 206 ng/mL (normal range: 53–287). She remained without symptoms and comorbidities of acromegaly including the absence of OSA symptoms, signs of left ventricular dysfunction, or osteoarthritis. One year post operatively, her insulin like growth factor was 107 ng/mL, well within the normal range for age of 53–287 ng/mL. Her MRI done 10 months after gamma knife radiation showed the area of residual tumor was of similar size (16 mm in maximal diameter) but more confluent in appearance. Her TSH and free T4 remained normal at 0.79 µIU/mL (normal range:

0.4–4.2) and 1.0 (normal range: 0.9–1.6), respectively. She continued to have central hypogonadism, which was suspected to be from hormonal hyposecretion from the pituitary mass. In terms of her partial central DI, she failed another trial off desmopressin 15 months post operatively. After holding desmopressin for 3 days and remaining NPO for 8–10h overnight, her serum sodium was 149 mmol/L, plasma osmolality was 293 mosmol/kg and her urine osmolality was 486 mosmol/kg. She was continued on desmopressin 10 µg intranasally daily until 18 months after transsphenoidal resection. Repeat thyroid ultrasound done 9 months after transsphenoidal resection showed no evidence of the left-sided cyst and a stable appearance and size of her right-sided subcentimeter nodule. It did not meet criteria for fine needle aspiration. Two years after gamma knife radiation, MRI showed no evidence of tumor progression and IGF-1 level was 69 ng/mL (normal range: 53–287).

Discussion

This patient presented initially with a thyroid nodule and was found to have a TSH- and GH-secreting pituitary macroadenoma. This represents a unique presentation of a unique disease. TSH-secreting pituitary adenomas are rare. Their prevalence is estimated at about 2.8% of all pituitary adenomas (4). Not uncommonly, they co-secrete other pituitary hormones including growth hormone (in about 16% of cases), prolactin (in about 10% of cases), and gonadotropins (in about 1% of cases) (5). TSH-secreting adenomas are typically benign, however, more than 60% of them are locally invasive as our patient's was (6). TSH-secreting pituitary adenomas typically present with either symptoms of tumor growth like headache or visual field disturbance or symptoms of hyperthyroidism (4). While thyroid nodules are common in patients with TSHomas, they are not typically the presenting sign. Our patient presented with a thyroid nodule. She had occasional nonspecific headaches but no visual changes, palpitations, weight loss or tremor. In hindsight, she had multiple reasons to have structural thyroid disease.

Both TSH-secreting pituitary adenomas and growth hormone-secreting pituitary adenomas are associated with goiters. Acromegalic patients on average have larger thyroid glands compared to non-acromegalic controls (7). Goiters are more common as well with a prevalence of 25% in patients with acromegaly and 8.3% in controls (7). Both TSH- and GH-secreting pituitary adenomas are also associated with an increased incidence of thyroid



Figure 7
T1-weighted sagittal MRI done 3 months post operatively showing absence of the sellar mass but some enhancing tissue present along the inferior aspect of the sella representing residual tumor.



nodules. One case series of patients with TSH-secreting adenomas reported a frequency of thyroid nodules of 64% (6). The prevalence of thyroid nodules in patients with GH-secreting adenomas has been found to be similar at 64.6% in one cross sectional study (7). These figures compare with the prevalence of thyroid nodules in the general population, which has been reported to be about 30%. The mechanism by which acromegaly causes thyroid as well as other organ enlargement likely has to do with the fact that IGF-1 is associated with both increased cellular proliferation and decreased cellular apoptosis (8). Follicular cells of the thyroid, specifically, have IGF-1 receptors (7). However, serum IGF-1 levels are not necessarily correlated with the presence of thyromegaly (8). Our patient's large, predominantly cystic thyroid nodule resolved completely after surgical resection of her pituitary tumor. It is uncertain whether this was due to the treatment of acromegaly and central hyperthyroidism or if this was simply the natural history of her thyroid nodule. Her remaining nodule was <1 cm without concerning sonographic characteristics and did not require biopsy.

Thyroid cancer has rarely been found in patients with TSH-secreting adenomas (4). The frequency of thyroid cancer in patients with acromegaly, however, has been debated. Some studies have shown an increased rate of thyroid cancer in patients with acromegaly compared to controls without acromegaly (7). In one meta-analysis, the pooled odds ratio for thyroid cancer in acromegaly compared to normal controls was found to be 6.7. However, this same meta-analysis showed no difference in the relative risk of thyroid malignancy in acromegalics with thyroid nodules compared to non-acromegalics with thyroid nodules (9). Thus, the increased risk of malignancy in patients with acromegaly may just be due to the fact that they have more nodules. The 2014 Endocrine Society guidelines on treatment of acromegaly recommend a thyroid ultrasound in patients with acromegaly only if there is palpable thyroid nodularity.

In terms of treatment, our patient's GH- and TSH-producing pituitary macroadenoma went into remission after surgery and gamma knife radiation alone. The first-line treatment for both TSH and growth hormone-secreting pituitary adenomas is surgical resection. However, less than 60% of patients with TSH-secreting pituitary macroadenomas and less than 50% of GH-secreting macroadenomas achieve remission with surgery alone (4). Radiation therapy is used in addition to surgery to halt tumor growth and achieve biochemical

remission. In patients with TSH-secreting pituitary adenomas, about two-thirds will need only surgery and radiation (2). The medical treatment used to normalize TSH and FT4 levels is somatostatin analogs like octreotide. This is effective in about 90% of patients with TSH-secreting pituitary adenomas (4). Unlike many other case reports of co-secreting TSH and GH pituitary adenomas, our patient did not require somatostatin analog therapy (1, 2, 3).

Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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Patient consent

The patient has given written informed consent.

Author contribution statement

L H Adams: Author of case report; Endocrinology fellow currently taking care of the patient. D Adams: Editor of case report; Endocrinology attending currently taking care of patient.

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Megha Desai: Initial consulting Endocrinologist in the case.

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