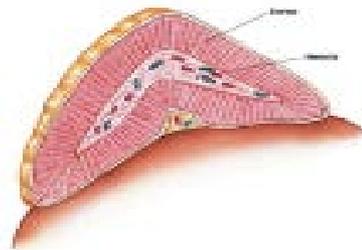
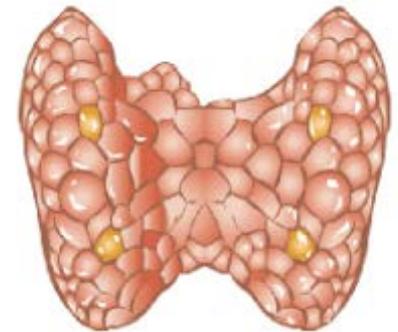
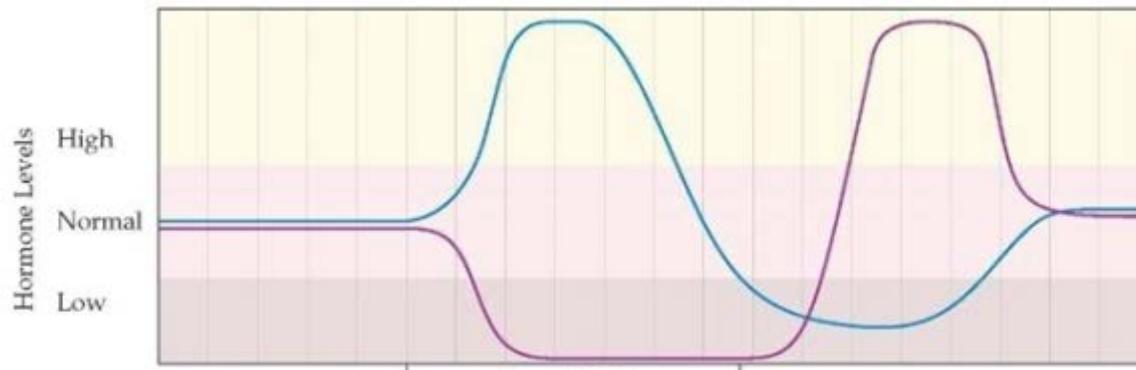




Blame it on the hormones

Ted Giles Clinical Vignettes – Canadian Society of Internal Medicine 2015 – Charlottetown, PEI



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➤ Case presentation

➤ Clinical issue 1

➤ Clinical issue 2

➤ Final diagnoses

➤ Literature review

➤ Learning points

Case presentation

- 29F, recent immigrant to Canada
- PMHx: Negative for endocrinopathies or mental health issues
- FHx: Mother with Hashimoto's thyroiditis
- July 2014: Presented to another hospital with a 1-month history of palpitations, 8 kg weight loss over 2 weeks and a sBP of 200 mmHg.
- Investigations: overt hyperthyroidism and a thyroid uptake scan showing diffusely increased uptake (41% at 24 h, normal range 10–25%),
- Dx: Hyperthyroidism secondary to Graves' disease.
- Rx: Propranolol 20 mg p.o. tid and Methimazole 5 mg p.o. bid

Case presentation

- One month later, patient received 370 MBq of radioactive iodine (I-131)
- Two months later, still mildly hyperthyroid with sBP ranging from 150 to 175 mmHg.
- Rx: Metoprolol SR 100 mg p.o. die and nifedipine XL 30 mg p.o. die.
- One month later (3 months post RAIA), she presented to ER at our hospital with a 1-week history of anxiety and paranoid ideations.
- Newly distrustful of everyone around her, extremely jealous, psychotic behaviours were witnessed in the emergency room.

Table 1 – Thyroid function tests

Date	TSH (mIU/l) (0.40–4.40)	Free T₄ (pmol/l) (8–18)	Free T₃ (pmol/l) (3.5–6.5)
July 23, 2014	0.03	21.1	6.8
August 4, 2014	0.05	12.5	5.4
October 8, 2014	0.30	14.4	3.8
November 1, 2014	> 100	< 1.90	2.46
November 11, 2014	> 100	6.30	
December 17, 2014	18.15	12.10	
January 5, 2015	28.90	11.10	
March 4, 2015	5.79	16.20	
April 9, 2015	3.80	14.90	

Case presentation

- Physical exam: Unremarkable except for a BP of 167/109, a HR of 157.
- No stigmata of hypo- or hyper- thyroidism.
- Normal neck exam, normal CVS, respiratory, abdominal, lower extremities and neurological exam (i.e. normal DTR)
- Bloodwork; hypokalemia at 2.4 mmol/l with other electrolytes within normal range.

Clinical issue 1

- Thyroid dysfunction
- Bloodwork; iatrogenic overt hypothyroidism secondary to radioactive iodine ablation
- With input from psychiatry and neurology, patient thought to have 'Acute psychosis secondary to a general medical condition' (acute hypothyroidism).
- Normal head CT and MRI.
- Not religious or cultural practices.

Clinical issue 1

- Hospitalised for 2 days on General Internal Medicine CTU.
- Rx: 200 mcg p.o. levothyroxine on D1, then 50 mcg p.o. die. Risperidone as an inpatient, but not at discharge.
- Rationale: Despite young age and absence of cardiovascular comorbidities, regimen chosen empirically given her psychotic state as several case reports have described the precipitation of psychosis or mania by levothyroxine replacement in hypothyroid patients.

Clinical issue 1

- Follow-up: Seen as an outpatient 1 week after discharge. Paranoid ideations and psychotic behaviours resolved with L-T4 supplementation alone and no antipsychotic medication.
- 1 week: fT4 still low, so L-T4 increased to 75 mcg p.o. die. 1 month: normalizing TFTs. 2 months: slight rise in TSH, L-T4 increased to 100 mcg po die. 5 months: euthyroid and normotensive.

Clinical issue 2

- Low K, Hypertensive, ???
- Serum renin, aldosterone levels and a random cortisol requested at first ER presentation.
- Renin 1.46 ng/l per s and aldosterone 1140 pmol/l for an aldosterone/renin ratio of 780 (pmol/l)/(ng/l per s), cortisol 376 nmol/l
- Follow-up: 24-h urine collection for metanephrines and catecholamines within normal range and C+ abdominal CT showed a 5 mm left adrenal gland nodule compatible with an adenoma. Normal 1 mg dexamethasone-suppression test.

Clinical issue 2

- Saline loading test: 2 L of i.v. NS were infused over 4h. Aldosterone level pre: 755 pmol/l and post: 599 pmol/l. Diagnosis of primary hyperaldosteronism confirmed.
- Bilateral adrenal vein sampling under ACTH stimulation (50 mcg/h) ordered.

Table 2 - Adrenal vein sampling results

Test	Result
Cortisol IVC	304 nmol/l
Cortisol LAV	6928 nmol/l
Cortisol RAV	7803 nmol/l
Selectivity index (cortisol RAV/IVC)	25.66 (SI > 3.0 denotes successful catheterization under ACTH stimulation)
Selectivity index (cortisol LAV/IVC)	22.78
Aldosterone IVC	2277 pmol/l
Aldosterone LAV	336 851 pmol/l
Aldosterone RAV	550 752 pmol/l
LAV aldosterone/cortisol ratio	48.62 nmol/l per pmol per l
RAV aldosterone/cortisol ratio	70.58 nmol/l per pmol per l
RAV/LAV A/C ratio (lateralization index)	1.45:1 (4:1 is diagnostic for lateralization)

IVC, inferior vena cava; LAV, left adrenal vein; RAV, right adrenal vein

Clinical issue 2

- Medical treatment preferable to surgical treatment.
- Amiloride (pregnancy category B) chosen over spironolactone (pregnancy category C).
- She remained on nifedipine XL 30 mg p.o. die, metoprolol SR was discontinued.
- PREGNANCY PLANNING: contraception until 6 months after RAI and until TSH levels at target (TSH < 2.5 for T1) for 3 months.
- Patient referred to obstetrical medicine clinic in November 2014 for joint follow-up and pregnancy planning.

Final diagnoses

1: Iatrogenic myxoedema madness (acute psychosis due to severe hypothyroidism following radioactive iodine ablation for Graves' disease)

2: Primary hyperaldosteronism secondary to bilateral idiopathic adrenal hyperplasia.

Literature review

- Myxoedema madness: First described by Asher in 1949. Most cases secondary to untreated longstanding Hashimoto's thyroiditis
- Only one case report suggesting a relationship between acute hypothyroidism following radioactive iodine ablation in a patient with Graves' disease and psychosis. Very similar to ours. Hyams et al (2013).

Literature review

- Association between Graves' disease and primary hyperaldosteronism: Two case reports with no abstract. Falls outside MEN syndromes or PGAS associations.
- Association between hypothyroidism and primary hyperaldosteronism: Two case reports found, but full articles not accessible.
- Association of primary hyperaldosteronism from bilateral idiopathic adrenal hyperplasia and psychosis due to iatrogenic hypothyroidism following radioactive iodine ablation of Graves' disease is extremely rare: our case report describes it for the first time.

Conclusion and learning points

- Psychosis (myxoedema madness) can present as a neuropsychiatric manifestation of acute hypothyroidism following radioactive iodine ablation of Graves' disease.
- Primary hyperaldosteronism may be caused by idiopathic bilateral adrenal hyperplasia even in the presence of an adrenal adenoma seen on imaging.
- Adrenal vein sampling is a useful tool to differentiate between an aldosterone-producing adenoma and idiopathic bilateral adrenal hyperplasia.

Conclusion and learning points

- The management of autoimmune hyperthyroidism, iatrogenic hypothyroidism and primary hyperaldosteronism from bilateral idiopathic adrenal hyperplasia in patients planning pregnancy includes:
 - Delaying pregnancy 6 months following radioactive iodine treatment and until patient is euthyroid for 3 months,
 - Using amiloride as opposed to spironolactone,
 - Controlling blood pressure with agents safe in pregnancy such as nifedipine and avoiding Beta- blockers.

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Questions

