A Hidden Solution

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- 51-year-old woman presented to emergency room with a 6-month history of intermittent and gradually onset palpitations, which had worsened that day. She described her pulse as fast (it was approximately 140 beats/minute) but regular.

- She also reported recent worsening fatigue, heat intolerance and 18-kgs weight loss despite a good appetite

- No dyspnea, orthopnea, syncopal episodes, headaches, tremors or profuse sweating. She reported no fever, neck pain or swelling, difficult swallowing or ophthalmopathy.

- The patient had a spinal cord injury from a car accident at the age of 21 years. The injury resulted in paraplegia with associated fecal and urinary incontinence, for which she underwent a colostomy and a urinary diversion with an ileal pouch that required self-catheterization several times daily.

- No history of medications or substances that may increase the heart rate, no DM or HTN. No history of cardiovascular, thyroid or psychiatric disorders. No family history of thyroid disease.

- On physical examination, her pulse was 110b/m (regular), and her BP was 120/80 mmHg. The patient appeared well nourished and comfortable. There was no tremors.
- Her thyroid gland was slightly enlarged, non tender and firm on palpation with a smooth surface and no discrete palpable nodules. There was no exophthalmos . The skin examination was normal.
- Cardiovascular examination revealed a regular tachycardia with normal heart sounds and no murmurs. The abdomen was soft and non tender. The sites of her colostomy and ileal conduit appeared normal. The rest of the examination was unremarkable.

- **Most common causes of palpitation are :**

1) Cardiac
2) Endocrine & Metabolic
3) Psychiatric
4) Drug induced

D.D. OF PALPITATIONS

- Cardiac 43%

1) Premature atrial/ventricular contraction
2) Atrial flutter/fibrillation
3) Sick sinus syndrome
4) Sinus tachycardia
5) WPW syndrome
6) Vent tachycardia/fibrillation
7) Structural heart diseases
   - LVF
   - AA
   - MVP, Valve regurge
   - CHD
   - Prosthetic valves
   - Pulmonary embolism

- Psychiatric causes 30%

1) Depression
2) Panic disorders
3) Somatization disorders
4) Generalized anxiety
5) Social phobia

Madhuri Y, et al. Hospital physician. 2003

D.D. OF PALPITATIONS

- **Endocrine & Metabolic**

1) Hypoglycemia
2) Hyperthyroidism
3) Pheochromocytoma
4) Hypo/hyper calcemia
5) Hypo/hyper kalemia
6) Hypo/hyper magnesemia

- **Drug induced**

1) Nitrates
2) Epinephrine
3) Cardiac glycosides
4) Caffeine,alcohol

- **High COP states**

1) Fever
2) Anemia
3) Pregnancy

- **Other causes**

1) Postmenopausal period
2) Hyperventilation
3) Emotional stress

27%

Madhuri Y, et al. Hospital physician. 2003

Investigation

- ECG revealed sinus tachycardia

- TSH was undetectable
- Total (T4) = 14.2 µg /dl
- Total (T3) = 197 ng /dl

- ***Neck US***

- Slightly enlarged thyroid gland but diffusely hypoechoic, findings suggestive of autoimmune thyroid disease
- There was no evidence of a marked increase in intraglandular vascular flow
- 0.7-cm hypoechoic nodule without increased intranodular vascularity was seen in the left thyroid lobe

- **The ratio of total T3 to total T4 (ng/mcg) is usually >20 in**

1) Graves disease

2) Toxic nodular goiter

3) Painless or postpartum thyroiditis

4) 1&2

$$\frac{\text{(T3) = 197 ng /dl}}{\text{(T4) = 14.2 µg /dl}} = 13.8$$

Shigemasa C, Abe K, Taniguchi S, et al. J Clin Endocrinol Metab. 1987;65:359-363.

- **Next step ?**

1) Treatment with B blockers and ATD
2) Treatment with B blockers alone
3) RAIU
4) FNAC
5) Test for thyroid antibodies

- A radioactive iodine uptake should be performed when the clinical presentation of thyrotoxicosis is not diagnostic of GD

Hyperthyroidism Management Guidelines, Endocr Pract. 2011;17

FNA biopsy is recommended for :

1. **Nodule(s) >1.0 cm** that is solid and hypoechoic on US
2. **Of any size** with **US** findings suggestive of extra capsular growth or metastatic cervical LN
3. **Of any size** with **history** of neck irradiation in childhood or adolescence; PTC, MTC, or MEN 2 in first-degree relatives; previous thyroid surgery for cancer; increased calcitonin levels
4. **Of < 1.0 cm** with **US** findings associated with malignancy (hypoechoic pattern and/or irregular margins, a more-tall-than-wide shape, micro-calcifications, or intranodular vascular spots). the coexistence of 2 or more suspicious US criteria greatly increases the risk of thyroid cancer

Nodules that are hot on scintigraphy should be excluded from FNA biopsy

AACE/AME/ETA Thyroid Nodule Guidelines, Endocr Pract. 2010;16(Suppl 1)

- **The iodine-123 uptake at 24 hours was 1.8% (15 to 30), so differential diagnosis may be one of the following except:**

1) Subacute viral thyroiditis
2) Silent lymphocytic thyroiditis
3) HCG-mediated hyperthyroidism
4) Thyrotoxicosis factitia
5) Drug induced thyrotoxicosis
6) Iodine-induced hyperthyroidism

D.D. of Thyrotoxicosis

Cause	Thyroid Iodine-123 Uptake
Graves' disease	Elevated
Toxic nodular goiter	Elevated
Thyrotropin-secreting pituitary adenoma	Elevated
Trophoblastic tumor	Elevated
Hyperemesis gravidarum	Elevated
Painful thyroiditis	Low
Silent lymphocytic thyroiditis	Low
Drugs (amiodarone, interferon alfa, and lithium)	Low
Iodine-induced hyperthyroidism	Low
Struma ovarii	Low
Thyrotoxicosis factitia	Low

HCG-mediated

- **Tests of thyroid peroxidase antibodies, thyroglobulin antibodies were negative. This can exclude :**

1) Subacute viral thyroiditis
2) Silent lymphocytic thyroiditis
3) Thyrotoxicosis factitia
4) Iodine-induced hyperthyroidism
5) Drug- induced hyperthyroidism
6) Struma ovarii

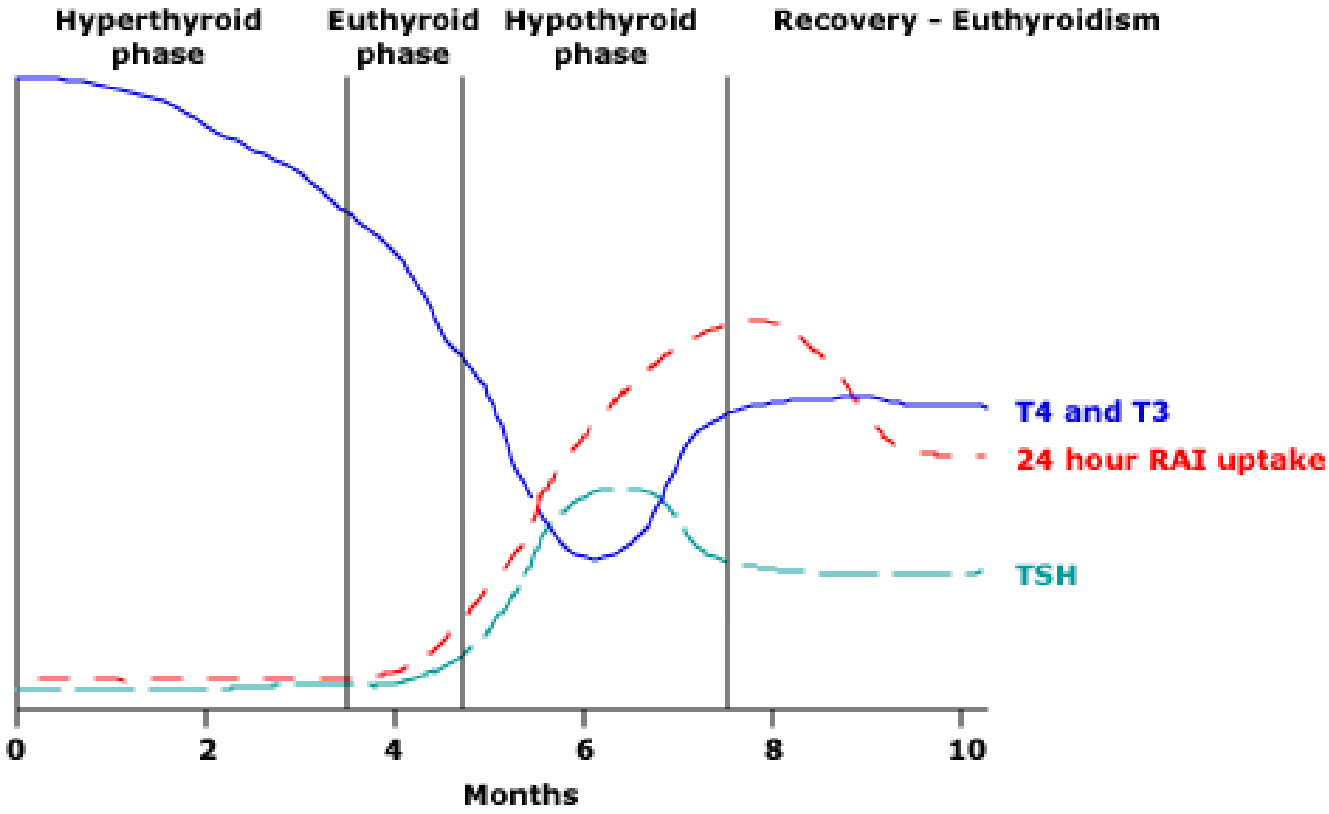
D.D. of Thyrotoxicosis

Cause	Thyroid Iodine-123 Uptake	Thyroid Peroxidase Antibodies	Thyroid-Stimulating Immunoglobulin
Painful thyroiditis	Low	Negative	Negative
Silent lymphocytic thyroiditis	Low	Usually positive	Negative
Drugs (amiodarone, interferon alfa, and lithium)	Low	Usually negative	Negative
Iodine-induced hyperthyroidism	Low	Usually negative	Negative
Struma ovarii	Low	Negative	Negative
Thyrotoxicosis factitia	Low	Negative	Negative

Pornpoj, et al. A Hidden Solution. N Engl J Med 2011;364:2123-7.

SUBACUTE THYROIDITIS

1. Subacute nonsuppurative thyroiditis
2. De Quervain's thyroiditis
3. Subacute granulomatous thyroiditis



SUBACUTE THYROIDITIS

- Diagnosis is based primarily upon clinical manifestations (neck pain radiating upward to the jaw, marked thyroid tenderness and diffuse goiter).

- Thyroid function tests.

- Low radioiodine uptake during the hyperthyroid phase and a high (ESR) confirm the diagnosis.

Pearce EN, Farwell AP, Braverman LE. Thyroiditis. N Engl J Med 2003; 348:2646.

PAINLESS (SILENT, LYMPHOCYTIC) THYROIDITIS

- Autoimmune disease manifested by triphasic pattern
- Postpartum period is the most common time, but painless thyroiditis can also occur in non pregnant patients and men.
- Described in some types of drug-induced thyroid dysfunction (lithium , IFN-α or interleukin-2).

Pearce EN, Farwell AP, Braverman LE. Thyroiditis. N Engl J Med 2003; 348:2646.

PAINLESS (SILENT, LYMPHOCYTIC) THYROIDITIS

- The patient may have any manifestation of hyperthyroidism. However, the symptoms are usually mild. Some patients have no symptoms or signs.
- The thyroid gland is not painful or tender, but is usually minimally diffusely enlarged and sometimes firm in texture.
- Thyroid function tests
- Do not routinely measure anti TPO, since they are nonspecific. (Graves' disease)
- Shorter duration, minimal thyroid enlargement, and low thyroid RAIU

Pearce EN, Farwell AP, Braverman LE. Thyroiditis. N Engl J Med 2003; 348:2646.

D.D

Drugs (amiodarone, interferon alfa, and lithium)	Low
Iodine-induced hyperthyroidism	Low
Struma ovarii	Low
Thyrotoxicosis factitia	Low

STRUMA OVARII

- Ectopic thyroid tissue existing as a component of an ovarian tumor. (<1% of all ovarian tumors)
- 5%–10% of patients with struma ovarii present with thyrotoxicosis due to either autonomous ectopic thyroid function or the coexistence of GD.
- 25% of struma ovarii tumors contain elements of papillary thyroid cancer.

- Diagnosis made by radioiodine imaging of the pelvis.
- Surgical treatment is indicated due to the risk of malignancy and to cure hyperthyroidism. Preoperative treatment with beta blockers and antithyroid drugs.

Hyperthyroidism Management Guidelines, Endocr Pract. 2011;17

D.D

Drugs (amiodarone, interferon alfa, and lithium)	Low
Iodine-induced hyperthyroidism	Low
Thyrotoxicosis factitia	Low

- The patient reported no ingestion of exogenous thyroid hormone, thyroid extract, or any medications

- No dietary supplements that may have contained iodine, or recent radiographic studies that required the use of iodine-containing contrast agents

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- **In this patient, slightly elevated thyroglobulin level in the absence of thyroglobulin antibodies essentially rules out:**

1) Thyrotoxicosis factitia

2) Iodine-induced hyperthyroidism

3) Drug- induced hyperthyroidism

D.D. of Thyrotoxicosis

Cause	Thyroid Iodine-123 Uptake	Thyroglobulin
Painful thyroiditis	Low	Increased
Silent lymphocytic thyroiditis	Low	Increased
Drugs (amiodarone, interferon alfa, and lithium)	Low	Increased
Iodine-induced hyperthyroidism	Low	Increased
Struma ovarii	Low	Increased
Thyrotoxicosis factitia	Low	Decreased

Pornpoj, et al. A Hidden Solution. N Engl J Med 2011;364:2123-7.

THYROTOXICOSIS FACTITIA

- Thyrotoxicosis due to ingestion of thyroid hormone.

1. Intentional ingestion of thyroid hormone either surreptitious or iatrogenic.

2. Unintentional ingestion either accidentally, such as in pediatric poisoning or pharmacy error, or through ingestion of supplements that contain thyroid extracts.

Hedberg CW, et al. An outbreak of thyrotoxicosis caused by consumption of bovine thyroid gland in ground beef. N Engl J Med. 1987; 316:993-998.

THYROTOXICOSIS FACTITIA

- Iatrogenic causes of thyrotoxicosis factitia are easily identified, but surreptitious use of thyroid hormone may present a diagnostic problem.

  - Absence of goiter
  - Suppressed serum thyroglobulin
  - Low uptake of radioactive iodine

Hyperthyroidism Management Guidelines, Endocr Pract. 2011;17

D.D

Drugs (amiodarone, interferon alfa, and lithium)	Low
Iodine-induced hyperthyroidism	Low

- ***Iodine concentration in urine :***

  Elevated

- On detailed questioning regarding possible sources of excess iodine, the patient stated that she had been using povidone–iodine swabs for many years immediately before urinary self catheterization four to five times daily.

- ***Serum inorganic iodide concentration :***

  57 µg/L(normal range, <2)

- **Iodine-induced hyperthyroidism is believed to occur in except**

1) Patients with underlying thyroid autonomy
2) Those living in areas with iodine deficiency
3) Those living in areas with sufficient dietary iodine

- In regions of iodine deficiency, hyperthyroidism was reported after introduction of iodine. (1 to 20 %)

- In individuals with nodular goiter living in areas of iodine deficiency. (10 to 20 %)

- Thyrotoxicosis occurs because of underlying areas of autonomy. When the iodine supply increases, the autonomous areas produce thyroid hormone independent of normal regulatory mechanisms

(Jod-Basedow phenomenon)

- Such patients may had subclinical hyperthyroidism before iodine repletion.

Roti E, Uberti ED. Iodine excess and hyperthyroidism. Thyroid 2001; 11:493.

- The recommended iodine intake for healthy, non pregnant adults *(150 µg per day)*

- The tolerable upper level of iodine intake in most persons (1100 µg per day)

Institute of Medicine. Dietary reference intakes. Washington, DC: National Academies Press, 2006.

- **<u>Common sources of excess iodine include:</u>**

- Iodinated radiographic contrast agents

  1 ml contains 350 mg of iodine
- Iodine containing medications (e.g., amiodarone)

  200-mg tablet contains 75 mg of iodine

  Because of its long half-life and high lipid solubility, it may cause iodine-induced thyrotoxicosis long after its discontinuation.
- Topical antiseptics (Povidone–iodine 10% topical solution) vaginal douching, mouth rinsing or surgical wounds

  1 ml containing 10 mg of iodine
- Dietary supplements
- Water enriched with iodine for purification purposes

Drug	*Mechanism(s)*	*Timing of onset following initiation of the drug*	*Therapy*
Amiodarone	Iodine induced (type 1)	Months to Years	Supportive care[a] Antithyroid drugs; perchlora Surgery
Iodinated contrast	Underlying thyroid autonomy	Weeks to months	Antithyroid drugs
Radioactive iodine, early	Destruction	1–4 weeks	Observation; if severe, administer corticosteroids
Radioactive iodine for TMNG, late	GD	3–6 months	Antithyroid drugs Repeat radioactive iodine Surgery

Hyperthyroidism Management Guidelines, Endocr Pract. 2011;17

- **Iodine-induced hyperthyroidism is treated by removal of iodine source plus:**

1) Beta blockers alone

2) Beta blockers in combination with methimazole

3) 1 or 2

Hyperthyroidism Management Guidelines, Endocr Pract. 2011;17

- The patient was asked to stop using povidone–iodine swabs. A beta-adrenergic blocker was prescribed to manage the patient's tachycardia.

- Eight weeks later, thyroid hormone level had normalized, the thyrotropin level became detectable and all symptoms of thyrotoxicosis were relieved

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- Treatment of the underlying thyroid disease should be addressed.
- Iodine concentration in urine
- RAIU

- **Underlying Graves' disease**

  (methimazole, radioiodine ablation, or surgery)

- **Underlying autonomous adenoma or multinodular goiter**
  - Who return to euthyroidism after discontinuation of iodine do not necessarily require definitive treatment.
  - However, these patients are at risk for recurrent hyperthyroidism if given iodine again.
  - So, many clinicians prefer to treat with surgery or radioiodine, particularly if they develop persistent subclinical hyperthyroidism

Burman KD, Wartofsky L. Iodine effects on the thyroid gland: biochemical and clinical aspects. Rev Endocr Metab Disord 2000; 1:19.

THANK YOU