CASE DETECTIVE Series

Acute anxiety and tachycardia in a hospitalized 59-year-old woman

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PMH

- 59-year-old woman was hospitalized after 3 days of neck pain, painful swallowing, headache, and fever.
- Three years earlier she had received a liver transplant because of chronic liver disease due to hepatitis C, and afterward had contracted posttransplant lymphoproliferative disease.
- Because she needed frequent blood tests, a subclavian port had been placed 7 months before the current presentation and last accessed 6 weeks ago.
- She also had stage 3 chronic kidney disease.
- She had no history of thyroid disease or alcohol or tobacco use.

• Her medications at home included :

- Tacrolimus
- Oxycodone
- Oxymorphone
- Modafinil
- Promethazine
- A multivitamin, fish oil, vitamin D, and calcium supplements daily

Presentation symptoms & PE

- Temperature was 38.7°C, heart rate 103 bpm, blood pressure 129/64 mm Hg, and respiratory rate 22 bpm
- She was alert and oriented and answered questions appropriately.
- Her neck was tender to palpation all over but particularly in the left anterior area. There were no palpable masses or swollen glands or lymph nodes.
- The area around the subclavian port was red and tender.
- Cardiovascular and pulmonary examinations were **normal**.
- She had a surgical scar on the abdominal wall.
- The rest of the abdominal examination was normal.

Test	Value ^a	Reference range	
Hemoglobin	8.5 g/dL	11.6-15.0 g/dL	
White blood cell count	5.2 × 10 ⁹ /L	3.4-9.6 × 10 ⁹ /L	
Segmented neutrophils	82%	40%-60%	
Platelet count	219 × 10 ⁹ /L	157-371 × 10 ⁹ /L	
Thyroid-stimulating hormone (TSH)	1.04 mIU/L	0.3-4.2 mIU/L	
Thyroxine (free T ₄)	1.8 ng/dL	0.9–1.7 ng/dL	
Lactate	0.8 mmol/L	0.5-2.2 mmol/L	
C-reactive protein	64 mg/L	≤ 8 mg/L	
Erythrocyte sedimentation rate	78 mm/hour	0–30 mm/hour	
Sodium	138 mmol/L	135-145 mmol/L	
Potassium	4.2 mmol/L	3.6–5.2 mmol/L	
Chloride	102 mmol/L	98–107 mmol/L	
Bicarbonate	25 mmol/L	22–29 mmol/L	
Magnesium	1.9 mg/dL	1.7-2.3 mg/dL	
Calcium	8.9 mg/dL	8.6–9.6 mg/dL	
Blood urea nitrogen	27 mg/dL	6-21 mg/dL	
Serum creatinine	1.2 mg/dL	0.59-1.04 mg/dL	
Glucose	95 mg/dL	70–140 mg/dL	
Alanine aminotransferase	53 U/L	7–45 U/L	
Aspartate aminotransferase	49 U/L	8-48 U/L	
Alkaline phosphatase	121 U/L	46–118 U/L	
Albumin	3.7 g/dL	3.5–5.0 g/dL	
Total protein	6.5 g/dL	6.3–7.9 g/dL	
Bilirubin	0.8 mg/dL	≤ 1.2 g/dL	
Gamma-glutamyl transferase	42 U/L	5–36 U/L	
Lactate dehydrogenase	216 U/L	122–222 U/L	
Prothrombin time	10.3 seconds	9.4-12.5 seconds	

TABLE 1

"Abnormal results are shown in bold.

Presentation symptoms & PE

- Contrast-enhanced computed tomography (CT) of the head and neck revealed soft-tissue inflammation tracking from the left anterior chest wall, encompassing the thyroid, and reaching into the retropharyngeal space
- Blood cultures from the subclavian port grew methicillin-resistant Staphylococcus aureus after 15 hours, as did cultures from the peripheral blood after 30 hours.



Figure 1. Sagittal (left) and horizontal (right) views on computed tomography demonstrate inflammatory changes arising from the chest and tracking superiorly along the neck (arrows).

Progress note

- The team **removed her subclavian port**, started **intravenous vancomycin**, and admitted her to the hospital.
- Three days later, **contrast-enhanced CT showed marked improvement**: the thyroid gland was smaller, and the inflammatory fat-stranding previously seen surrounding the gland had resolved.
- However, on the patient's fourth day in the hospital, she became increasingly short of breath, confused, agitated, and anxious.
- She had **no focal neurologic deficits**, but her **mental status waxed and waned**, with **intermittent delirium** and **loss of orientation to time**.

Progress note

- Her temperature was still 38.4°C, but her heart rate had risen to 153 bpm, blood pressure 153/107 mm Hg, and respiratory rate 33 breaths per minute.
- Fine inspiratory crackles at the bases of both lungs
- Eyelid lag (the top eyelids remaining high when the patient looks down)
- Pitting edema in both ankles, rated 1+ (mild)
- Generalized hyperreflexia.

Progress note

- Electrocardiography revealed sinus tachycardia without ST-T-wave changes.
- Her white blood cell count was 12.8 × 10⁹/L with 78% neutrophils
- Transthoracic echocardiography revealed an ejection fraction of 45% but no wall-motion abnormalities.
- CT angiography of the chest was negative for pulmonary embolism.

Which one of the following conditions is the most likely diagnosis?

- A) Thyrotoxicosis, thyroid storm
- B) Pheochromocytoma
- C) Adrenal crisis
- D) Delirium tremens (withdrawal from heavy alcohol use)

Common features of thyroid storm

- **Central nervous system**: **anxiety, confusion**, delirium, generalized tremors, coma
- Cardiovascular: tachyarrhythmia (most commonly atrial fibrillation), Means-Lerman scratch (a murmur produced by a hyperdynamic pericardium rubbing against the pleura), congestive heart failure, cardiac shock
- Gastrointestinal: nausea, vomiting, diarrhea, abdominal pain
- Respiratory: dyspnea, tachypnea
- Others: fever, hyperhidrosis, skin hyperemia.

TABLE 2 Burch-Wartofsky Point Scale

Temperature (°F)		Cardiovascular dysfunction	
99-99.9	5 points	Tachycardia (beats/min)	
100-100.9	10	99-109	5
101-101.9	15	110-119	10
102-102.9	20	120-129	15
103-103.9	25	130-139	20
≥ 104.0	30	≥ 140	25
Central nervous system effects		Atrial fibrillation	10
Absent	0	Heart failure	
Mild (agitation)	10	Mild (nedal edema)	5
Moderate (delirium, psychosis, extreme lethargy)	20	Moderate (bibasilar rales)	10
Severe (seizure, coma)	30	Severe (pulmonary edema)	15
Gastrointestinal-hepatic dysfunction		Precipitant history	
Moderate (diarrhea, nausea/	50.00	Positive	0
vomiting, abdominal pain)	10	Negative	10
Severe (unexplained jaundice)	20	277.	

Total: < 25, storm unlikely; 25 – 45, impending storm; > 45, thyroid storm

Source: Burch, Wartofsky. Endocrinol Metab Clin North Am. 1993.²

Which one of the following would further support the diagnosis of hyperthyroidism?

- A) Low uptake on radioactive iodine uptake scanning
- B) Thyroperoxidase antibodies in the serum
- C) Elevated reverse triiodothyronine (T3) level
- D) A low thyroid-stimulating hormone (TSH) level and high free thyroxine (T4) level

nonspecific laboratory findings during thyroid storm

- mild hyperglycemia (due to inhibition of insulin release and increased glycogenolysis caused by catecholamines),
- mild hypercalcemia (secondary to increased bone resorption),
- elevated aminotransferase and alkaline phosphatase levels (related to liver dysfunction or from increased bone turnover),
- leukocytosis or, conversely, leukopenia.

Which of the following most likely placed this patient at risk of

thyroid storm?

- A) Vancomycin
- B) Liver transplant
- C) Absence of preexisting thyroid illness
- D) Contrast-enhanced CT
- E) Systemic infection

Underlying causes of thyrotoxicosis

• Primary hyperthyroidism

- Graves disease
- Toxic multinodular goiter
- Toxic adenoma
- Functioning thyroid carcinoma metastases
- Activating mutation of the TSH receptor
- Struma ovarii

Secondary hyperthyroidism

- TSH-secreting pituitary adenoma
- Chorionic gonadotropin-secreting tumors
- Gestational thyrotoxicosis

Thyrotoxicosis without hyperthyroidism

- Subacute thyroiditis
- Silent thyroiditis including postpartumthyroiditis
- ingestion of excess thyroid hormone (thyrotoxicosis factitia)
- Thyroid destruction such as amiodarone, radiation, and adenoma infarction.

Precipitants of thyroid storm

- **Surgery**: thyroid surgery ("surgical storm"), non-thyroid surgery, manipulation of the thyroid gland
- Cerebrovascular causes: myocardial infarction, venous thromboembolism, cerebrovascular disease
- Neoplasms: struma ovarii, metastatic thyroid cancer
- Endocrine diseases: Graves disease, thyroiditis, multinodular goiter, solitary toxic adenoma, diabetic ketoacidosis, hypoglycemia
- **Drugs**: interferon, amiodarone, abrupt cessation of thionamide therapy (rare), interleukin 2 therapy, anesthetics, salicylates, pseudoephedrine
- Others: systemic infections, thyroiditis, pregnancy, parturition, trauma, burns, radiocontrast dye, emotional stress
- No known precipitant in many patients

Which one of the following is the <u>most appropriate</u> next step in this patient's treatment?

- A) A beta-blocker and a thionamide
- B) An iodide solution
- C) Anticoagulation
- D) Aspirin

Optimal treatment of thyroid storm

- Patients with thyroid storm are critically ill and have a high mortality risk. Therefore, treatment and resuscitative measures should begin as early as possible.
- Management of thyroid storm involves the same principles that apply to uncomplicated hyperthyroidism, but additional medications and higher and more frequent dosing are often required.
- Optimal treatment of thyroid storm has the following **5 main goals**:
 - Reduce thyroid hormone synthesis and secretion
 - Block thyroid hormone actions at the cellular level
 - Reverse systemic decompensation (eg, hyperthermia, dehydration, congestive heart failure, arrhythmia)
 - Treat the precipitating event
 - Establish long-term therapy.

Treatment agents

- Thionamides
- Exogenous iodine
- Glucocorticoids
- Beta-blockers (first choice propranolol, atenolol and metoprolol alternatives, decomp HF esmolol)
- Bile acid sequestrants
- Plasmapheresis and surgery
- Supportive care
 - Antipyretics
 - Volume resuscitation

After the patient is clinically stable, which one of the following would be the <u>most appropriate</u> next step in her management?

- A) Continue propylthiouracil indefinitely
- **B)** Thyroidectomy
- C) Discontinue propylthiouracil, start methimazole, and evaluate for preexisting thyroid pathology such as Graves disease
- **D)** Radioactive iodine treatment

Thionamide side effects

- Common side effects of both medications include pruritus, rash,
- urticaria, arthritis, fever, nausea, and vomiting.
- More serious side effects include agranulocytosis, antineutrophil cytoplasmic antibody-positive vasculitis, and hepatotoxicity, all of which are more frequent with propylthiouracil
- Hepatotoxicity due to propylthiouracil use is associated with hepatocellular inflammation and necrosis, likely explaining higher rates of liver failure with this drug compared with methimazole, which is associated with cholestatic dysfunction
- Propylthiouracil should be discontinued at any time if aminotransferase levels reach more than 3 times the upper limit of normal, or if elevated levels at the onset of therapy increase further.

TAKE-HOME POINTS

- Thyroid storm requires a high level of suspicion (particularly in patients with preexisting thyroid disease), prompt recognition, and intensive medical therapy, in view of its high mortality rate. Its symptoms are not specific.
- Most cases of thyroid storm happen in the setting of underlying Graves disease; however, it may also occur in patients with normal thyroid function if they are exposed to the right triggers.
- TSH is the best single test to evaluate thyroid function.
- Hormone levels in patients experiencing thyroid storm are comparable to those in patients with stable thyrotoxicosis. Therefore, no cutoff values for the diagnosis exist.
- Management of thyroid storm is complex, based on the specifics of each case, and usually involves multiple treatments.