

Causes and Clinical Picture of Thyrotoxic Crisis

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Annotation: Thyrotoxic crisis, also known as thyroid storm, is an acute, life-threatening complication of hyperthyroidism. It is an exaggerated presentation of thyrotoxicosis, and it comes with sudden multisystem involvement. The mortality associated with thyroid storm is estimated to be 8 to 25% despite modern advancements in its treatment and supportive measures. Thus, it is very important to recognize it early and start aggressive treatment to reduce mortality. The diagnosis of thyroid storm is clinical.

Keywords: crisis, thyroid storm, thyrotoxicosis, multinodular goiter, Graves' disease, toxic adenoma.

Thyrotoxicosis is defined as the state of thyroid hormone excess and is not synonymous with hyperthyroidism, which is the result of excessive thyroid function. However, the major etiologies of thyrotoxicosis are hyperthyroidism caused by Graves' disease, toxic MNG, and toxic adenomas.

Etiology:

Superimposed precipitating factors cause thyroid storms in patients with diagnosed or undiagnosed hyperthyroidism. It is more common with Graves disease but can occur with other etiologies of hyperthyroidism, such as toxic multinodular goiter and toxic thyroid adenoma. The precipitating factors are:

- Abrupt discontinuation of antithyroid medicine
- Thyroid surgery
- Non-thyroid surgery
- Trauma
- Acute illnesses like infections, including COVID-19, diabetic ketoacidosis, acute myocardial infarction, cardiovascular accident, cardiac failure, and drug reactions
- Parturition

- Recent use of Iodinated contrast medium
- Radioiodine therapy (rare)
- Burns
- Stroke or traumatic brain injury
- Medication side effects, eg, amiodarone, anesthetics, salicylates
- Hyperemesis gravidarum in pregnancy

Causes of thyrotoxicosis :

Primary hyperthyroidism:

- Graves' disease
- Toxic multinodular goiter
- Toxic adenoma
- Functioning thyroid carcinoma metastases
- Activating mutation of the TSH receptor
- Activating mutation of G_{α} (McCune-Albright syndrome)
- Struma ovarii
- Drugs: iodine excess (Jod-Basedow phenomenon)

Thyrotoxicosis without hyperthyroidism:

- Subacute thyroiditis
- Silent thyroiditis
- Other causes of thyroid destruction: amiodarone, radiation, infarction of adenoma
- Ingestion of excess thyroid hormone (thyrotoxicosis factitia) or thyroid tissue

Secondary hyperthyroidism:

- TSH-secreting pituitary adenoma
- Thyroid hormone resistance syndrome: occasional patients may have features of thyrotoxicosis
- Chorionic gonadotropin-secreting tumours
- Gestational thyrotoxicosis

Clinical features:

The diagnosis of thyroid storm needs clinical suspicion based on the presentation mentioned above in a patient with hyperthyroidism or suspected hyperthyroidism. One should not wait for lab results before starting treatment. Thyroid function tests can be obtained, which usually show high FT4/FT3 and low TSH. It is not necessary to have a very high level of thyroid hormone to cause a thyroid storm. Other lab abnormalities may include hypercalcemia, hyperglycemia (due to inhibition of insulin release and increased glycogenolysis), abnormal LFTs, and high or low white blood cell (WBC) count.

Burch-Wartofsky Point Scale (BWPS)

In 1993, the following scoring system for the diagnosis of thyroid storm was introduced:

- Temperature: 5 points per 1 F above 99 F (maximum 30 points)
- CNS dysfunction: 10 points for mild (agitation), 20 for moderate (delirium, psychosis, or extreme lethargy), and 30 for severe (seizure or coma)

- Tachycardia: 5 (99-109), 10 (110 -119), 15 (120 -129), 20 (130 -139) and 25 (greater than 140)
- Presence of atrial fibrillation:10
- Heart failure: 5 for mild (pedal edema), 10 for moderate (bi-basilar rales), 15 for severe (pulmonary edema)
- GI dysfunction: 10 for moderate (diarrhea, nausea/vomiting, or abdominal pain) and 20 for severe (unexplained jaundice)
- Presence of Precipitating factor: 10 points

Diagnosis: A score of more than 45 highly suggests thyroid storm, 25 to 44 supports the diagnosis, and less than 25 makes the diagnosis unlikely.

The Japanese Thyroid Association (JTA)

This is a different scoring system based on similar clinical findings.[8] Thyrotoxicosis (elevated FT3 and/or FT4) is a prerequisite, and it requires various combinations of the following symptoms:

- CNS manifestation (restlessness, delirium, psychosis/mental aberration, lethargy/somnolence, coma)
- Fever (38 C/100.4 F or greater)
- Tachycardia (130/min or higher)
- CHF (pulmonary edema, rales, cardiogenic shock, or NYHA class IV)
- GI/Hepatic Manifestation (Nausea, vomiting, diarrhea, total Bilirubin 3 mg/dl or more)

Diagnosis:

Definite Thyroid Storm (TS1): Thyrotoxicosis (elevated FT3 and/or FT4) plus

- At least 1 CNS manifestation plus 1 or more other symptoms (fever, tachycardia, CHF, GI/Hepatic) ‘OR’ A combination of at least 3 features among fever, GI/Hepatic, CHF, or tachycardia
- Suspected Thyroid Storm (TS2): Thyrotoxicosis (elevated FT3 and/or FT4) plus
- A combination of at least 2 features among tachycardia, CHF, GI/Hepatic, Fever ‘OR’ A patient with h/o thyroid disease, presence of goiter and exophthalmos who meets criteria for TS1 but TFTs not available

These scoring systems are just guidelines. The actual diagnosis is based on clinical judgment. Based on the BWPS scoring system, a score of 45 or more is more sensitive but less specific than JTA scoring systems TS1 or TS2 to detect thyroid storm cases. A BWPS score of 25 to 45 may suggest an impending storm. A chest X-ray may help assess heart failure, and a head CT may help exclude a neurological cause in some patients. An ECG is often done to monitor for arrhythmias.

Treatment:

The primary treatment strategies:

1. Symptomatic Management

- Beta-blockers: Used to control symptoms such as tachycardia, tremors, and anxiety.
- Propranolol: Commonly used, as it also inhibits peripheral conversion of T4 to T3.

Alternatives: Atenolol, metoprolol, or nadolol.

2. Antithyroid Medications:

These drugs inhibit thyroid hormone synthesis and are the first-line treatment in many cases.

- Methimazole (MMI): Preferred due to its lower side effect profile (except in the first trimester of pregnancy).
- Propylthiouracil (PTU): Preferred in the first trimester of pregnancy and in thyroid storm because it also inhibits T4 to T3 conversion.

Monitoring: Regular thyroid function tests (TFTs) are necessary to adjust dosing and avoid hypothyroidism.

3. Radioactive Iodine (RAI) Therapy

Often used for definitive treatment, particularly in Graves' disease or toxic nodular goiter.

Contraindicated in pregnancy and lactation.

May lead to hypothyroidism, requiring lifelong thyroid hormone replacement.

4. Surgery (Thyroidectomy)

- Indicated in cases where:

There are compressive symptoms.

RAI is contraindicated (e.g., pregnancy).

A large goiter or suspicion of malignancy exists.

Patient preference or failure of other treatments.

- Pre-operative preparation with antithyroid drugs and iodine is essential to reduce thyroid hormone levels and vascularity of the gland.

5. Thyroid Storm Management

A life-threatening complication requiring intensive care:

- Supportive care: IV fluids, oxygen, and cooling measures.
- Beta-blockers: IV propranolol or esmolol for rapid control.
- High-dose antithyroid drugs: PTU is preferred for its dual mechanism.
- Iodine solution: Lugol's iodine or potassium iodide to inhibit thyroid hormone release (administered after antithyroid drugs to avoid worsening the storm).
- Corticosteroids: To reduce T4 to T3 conversion and treat associated adrenal insufficiency.
- Treat precipitating factors (e.g., infection or surgery).

6. Special Considerations:

- Pregnancy: PTU in the first trimester, then switch to methimazole; avoid RAI.
- Thyroiditis: Often transient; treatment focuses on symptom management (e.g., beta-blockers).

Conclusion: A thyroid storm is a true medical emergency that is fatal if left untreated. The cause of death may be heart failure, arrhythmias, or multiple organ failure. However, with treatment, most patients see an improvement within 24 hours.

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