Thyroid Storm

Pietro Princi and Ioannis Koutelidakis

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Case Presentation

A 38-year-old woman had been referred to the general practitioner because she was irritable with fever, upper abdominal pain, tachycardia, and previously unrecognized thyroid disease, before being referred to our hospital for emergency access.

At the emergency department, the patient is admitted to red room for the rapidly worsening clinical condition, because of highly elevated fever (>39 °C). The electrocardiogram (ECG) shows atrial fibrillation with over 140 beats per minute. Elevated values of serum liver function and creatinine are noted, but the myocardial enzymes are in the normal range.

The white blood cell (WBC) count is mildly elevated. Hydration and diuretics are started at the emergency department. Cardiologist evaluation and intensive care admission are necessary after 12 h for ulterior worsening condition. Serum T4 and T3 free fraction showed elevated value, and TSH are suppressed. Thyrostatic treatment with propylthiouracil and propranolol is administered.

After 48 h from admission in ICU, the vital signs are stabilized, the fever disappeared, and the patient is discharged from ICU after 4 days, but the consciousness of patient is not completely recovered. After 9 days, T3 and T4 become normal even if TSH is suppressed. Then an urgent neck exploration is planned with total thyroidectomy performed with prior administration for 5 days of Lugol's solution (ten drops three times per day).

The patient is discharged in a euthyroid condition and fully conscious state 18 days after admission with normal renal function and serum calcium. Calcium and vitamin D supplementation is necessary for 2 weeks.

Questions

1. Concerning the definition of thyroid storm:
   1. It is a life-threatening medical emergency that results from an extreme hyperthyroidism with possible multiorgan dysfunction.
   2. It is a really rare condition, but it could be extremely dangerous and fatal if not treated in time.
   3. It is related to hypothyroidism.
   4. It was first described by Lahey in 1926.
      (a) Only 1, 2, and 4 are correct.
      (b) Only 3 is correct.
      (c) Only 1, 2, and 3 are correct.
      (d) All answers are correct.
2. Regarding the clinical presentation of thyroid storm:
   1. Fever is the most uncommon symptoms.
   2. The main symptoms are related to the thyrotoxicosis crisis with all the aspects included.
   3. The finding of thyroid disease is evident in all cases.
   4. Atrial fibrillation has never been registered.
      (a) Only 1, 2, and 4 are correct.
      (b) Only 2 is correct.
      (c) Only 2 and 4 are correct.
      (d) Only 4 is correct.
3. Among symptoms related to thyroid storm:
   1. Psychological signs could be developed with tremor and severe agitation.
   2. They can progress to severe psychosis, stupor, and coma.

3. Epilepticus status and stroke are very common.
4. Confusion and delirium may be present.
   (a) All answers are correct.
   (b) Only 1, 2, and 3 are correct.
   (c) Only 1, 2, and 4 are correct.
   (d) Only 4 is correct.

4. Regarding gastrointestinal symptoms:
   1. Abdominal pain, vomiting, and nausea may be present.
   2. It could suggest an abdominal surgical emergency.
   3. Liver dysfunction is frequently reported.
   4. Jaundice has been registered.
      (a) Only 1, 3, and 4 are correct.
      (b) Only 2 and 3 are correct.
      (c) Only 1 is correct.
      (d) All are correct.

5. Regarding the etiology of thyroid storm:
   1. Thyroid surgery is considered the most common cause.
   2. Autonomous interruption of drug administration exposes the patients to a higher risk during surgery.
   3. Use of radioiodine increased the risk of thyroid storm.
   4. Better preoperative preparation increases its incidence.
      (a) Only 1 and 2 are correct.
      (b) Only 1, 2, and 3 are correct.
      (c) Only 2, 3, and 4 are correct.
      (d) Only 1 is correct.

6. Among all precipitating factors of thyroid storm:
   1. Infection is considered the most common.
   2. Delivery is reported as a factor in case of unrecognized thyrotoxicosis.
   3. Major trauma is not reported as precipitating factor.
   4. They are not clearly identified in 25–43% of the patients.
      (a) Only 4 is correct.
      (b) All are correct.
      (c) Only 1, 2, and 4 are correct.
      (d) Only 2 and 4 are correct.

7. Concerning the diagnosis of thyroid storm:
   1. Early diagnosis is fundamental to reduce the incidence of a fatal outcome.
   2. It is based on clinical features.
   3. Burch and Wartofsky introduced a specific scoring system in 1993.
   4. More than 45 points in Burch and Wartofsky score system indicate the diagnosis of thyroid storm.
      (a) Only 1 and 3 are correct.
      (b) Only 2 and 4 are correct.
      (c) All are correct.
      (d) Only 1, 3, and 4 are correct.

8. With regard to the diagnosis of thyroid storm according to the Japanese Thyroid Association, it can be stated:
   1. The diagnosis is based on the association of thyrotoxicosis with other symptoms (central nervous system symptoms, fever, tachycardia, hearth failure, and gastrointestinal/hepatic symptoms)
   2. The suspected patient does not need to have an underlying diagnosis of thyrotoxicosis.
   3. The diagnosis of TS2 thyroid storm could be related to, at least, five features.
   4. The Japanese Thyroid Association scoring system is more sensitive and more specific than the Burch and Wartofsky scoring system.
      (a) All are correct.
      (b) Only 2 and 3 are correct.
      (c) Only 4 is correct.
      (d) Only 1 is correct.
9. The treatment option of thyroid storm is:
   1. An urgent operation
   2. Mainly based on drugs
   3. Immediate use of glucocorticoids
   4. Only beta-blockers are useful
      (a) Only 1 is correct.
      (b) Only 2 is correct.
      (c) Only 3 is correct.
      (d) Only 4 is correct.
10. The initial treatment for patients with clinical features of thyroid storm or severe thyrotoxicosis who do not fully meet the criteria for thyroid storm is:
    1. A beta-blocker (propranolol) and either propylthiouracil (PTU) or methimazole
    2. Glucocorticoids and beta-blockers
    3. Propylthiouracil only
    4. Methimazole only
       (a) Only 1 is correct.
       (b) Only 2 is correct.
       (c) Only 3 is correct.
       (d) Only 4 is correct.
11. In patients with thyroid storm or severe thyrotoxicosis:
    1. Glucocorticoids and iodine solutions are mandatory.
    2. Only glucocorticoids must be administrated the first hours.
    3. It is better to use iodine 1 h after the first dose of thionamide.
    4. Iodine blocks the release of T4 and T3 from the gland within hours.
       (a) Only 1 and 2 are correct.
       (b) Only 1 is correct.
       (c) Only 3 is correct.
       (d) Only 3 and 4 are correct.

12. In patients with airway problems and thyroid storm:
    1. Cardio-selective beta-blockers such as metoprolol or atenolol could be considered but with care.
    2. ICU treatment is mandatory.
    3. Only propranolol is effective.
    4. In patients with severe asthma who cannot take beta-blockers, rate control can be achieved with calcium-channel blockers such as diltiazem.
        (a) Only 1 and 2 are correct.
        (b) Only 2 and 3 are correct.
        (c) Only 1 and 4 are correct.
        (d) Only 4 is correct.
13. The best operation for patients with thyroid storm:
    1. Is total thyroidectomy
    2. Is subtotal thyroidectomy
    3. Depends on the pathology of the thyroid
    4. Must be postponed for 3 months
        (a) Only 1 and 4 are correct.
        (b) Only 1 is correct.
        (c) Only 2 is correct.
        (d) Only 3 and 4 are correct.
14. The operation is urgent:
    1. In every condition when thyroid storm is present
    2. If the patient is unable to take antithyroid drugs
    3. If the patient has no comorbidities
    4. If the patient is under the age of 40
        (a) Only 1 and 2 and 3 are correct.
        (b) Only 1 and 4 are correct.
        (c) Only 1 and 3 are correct.
        (d) Only 2 is correct.
15. Concerning the prognosis of thyroid storm:
    1. Recent reviews reported the mortality of treated thyroid storm to be less than 10%.
    2. It depends on early recognition and treatment.
    3. It still has a poor prognosis and high mortality.
    4. Multiorgan failure develops very often in thyroid storm.
        (a) Only 3 and 4 are correct.
        (b) Only 1 and 2 are correct.
        (c) Only 1 correct.
        (d) Only 2 is correct.

40.1 Introduction

Thyroid storm is a life-threatening medical emergency that results from an extreme hyperthyroidism with possible multiorgan dysfunction [1–6]. Even if this is a rare condition, it could be extremely dangerous and fatal if not treated in time.

It was first described by Lahey in 1926 as the "crisis of exophthalmic goiter" related to the patients who presented exacerbation of symptoms for Basedow-Graves' disease [7].

Today, this condition rarely occurs after thyroid operations. Nevertheless, it is important for surgeons to understand its clinical manifestations, pathophysiology, and the effective treatment.

Furthermore, thyroid storm could be precipitated by trauma, infections, or other causes, and patients with untreated or inadequately treated preexisting hyperthyroidism may require urgent operations [8, 9].

The contemporary involvement of cardiovascular system as well as the thermoregulatory, gastrointestinal, hepatic, and central nervous system is included in the actual definition as reported by Burch and Wartofsky [3] who develop a specific scoring system for diagnosis.

Actually, the diagnosis of this clinical condition is difficult for physicians even if different teams around the world tried to define clear diagnostic criteria to improve the treatment of thyroid storm and to decrease its mortality with early aggressive therapy and ICU (intensive care unit) support, when necessary.

Thyroid storm accounts for between 1% and 2% of all hospital admissions for thyrotoxicosis, but some reports estimate the incidence may be as high as 10% [3].

The decrease of incidence in the last years may be due to more frequent screening for thyroid blood test with subsequent early diagnosis of hyperthyroidism and prevention of thyroid storm with administration of medical therapy.

40.2 Clinical Presentation

Thyroid storm must be early recognized for prompt definition of medical therapy because it could be burdened by a mortality ranged from 8% to 25% in hospitalized populations according to the most recent reports [4, 9, 10].

The clinical presentation is mainly the thyrotoxicosis crisis with all the aspects included.

Fever is one of the most common symptoms, with temperature occasionally exceeding 40 °C, and is usually considered a leading factor in differentiating thyroid storm from non-storm thyrotoxicosis [9]. It must be treated because, if not, it could lead to the death of patients within 48 h. Patients with thyroid storm present warm skin and often flushing, with profuse diaphoresis. The finding of thyroid disease with diffuse goiter as well as exophthalmos may not be evident. It is possible to register tachycardia higher than 150 beats/min and atrial fibrillation as well as tachypnea, acute pulmonary edema, and ventricular dysfunction or heart failure [11–17]. Psychic signs and symptoms could be developed with tremor and severe agi-

tation, emotional liability, confusion, and delirium that may progress to severe psychosis, stupor, and coma and rarely epilepticus status and stroke [18, 19].

Other symptoms could affect the gastrointestinal system like abdominal pain, vomiting, nausea, and diarrhea that should suggest an abdominal surgical emergency, and hepatomegaly, liver dysfunction, and jaundice sometimes indicate a hepatocellular dysfunction [20–24].

Leukocytosis occasionally is present especially with coexisting infections or trauma [25–27].

Diabetic ketoacidosis is rare in concomitancy of thyroid storm but could be dangerous for patients [28]. Then efforts should be made to maximize patient compliance to antithyroid and antidiabetic agents in treating such patients [4].

40.3 Natural History

Thyroid surgery has been considered the most common cause of thyroid storm, even if in the last years it has become rare because of a better preoperative therapeutic preparation of patients with administration of antithyroid and beta-blocker drugs. Furthermore, the increased use of radioiodine, especially in older patients, has decreased the incidence of this disorder. Among this subgroup of patients, there are some with incompletely treated hyperthyroidism or autonomous interruption of drug intake that expose them to an increased risk of thyroid storm during surgery [4].

A wide list of condition is reported in ▶ Box 40.1, like nonthyroidal surgery, major trauma, infection, imaging studies with iodinated contrast, and delivery in patients with unrecognized thyrotoxicosis [4, 29–32]. In all the cases, these conditions have the main role as precipitating factor of thyroid storm.

The basis of thyroid storm is essentially related to the pathophysiology of thyroid hormones.

The complete passages that lead from a simple toxicosis to a severe and multiorgan acute crisis are not well and completely known even if a major insult is required [32].

All the primary causes of hyperthyroidism can follow into acute crisis of thyroid storm even if the most common etiology is a history of Graves' disease [22, 33, 34]. Plummer disease and multinodular toxic goiter were reported as well as amiodarone-associated thyrotoxicosis or autoimmune thyroiditis.

Actually, infection is the most common cause of thyroid storm in the inpatient setting even if from 25% to 43% of the patients present without a clearly identifiable precipitating factor [3, 26, 30].

The mechanism underlying the pathogenesis of thyroid storm is not completely known. A dramatic increase in serum free T4 level is commonly observed and may precipitate the

onset of thyroid storm. Additional factors such as poor nutrition and complicating medical, surgical, and emotional effects on thyroid hormone binding are other important contributors as well as increased catecholamines [35].

The development of heart failure and cardiomyopathy in case of thyroid storm is reported in 20 cases even if the mortality rate is nearly 25%. Recognizing this condition is imperative in preventing left ventricular dysfunction and cardiogenic shock and for early treatment with specific medical therapy.

Thyroid storm combined with thyroid cancer, primary hyperparathyroidism, or hypercalcemic crisis is reported [36–38]. Elevated serum calcium level could increase the action of T4 through the second messenger way with subsequent set off the crisis.

Box 40.1: Factors Precipitating the Thyroid Storm

Thyroid surgery/surgical storm
Non-thyroidal surgery
Trauma and sepsis
Infections (pneumonia)
Vigorous manipulation of the thyroid gland
Thyroiditis
Parturition burn
Myocardial infarct and pulmonary embolism
Cerebrovascular incidents
Medications such as anesthetics, salicylates, pseudoephedrine, and amiodarone
Interferon treatment
Radioactive iodine treatment
Exposure to iodinated contrast
Withdrawal of antithyroid treatment
Diabetic ketoacidosis
Hypoglycemia acute ingestion of high doses of thyroid hormone
Metastatic thyroid cancer
Struma ovarii
Molar pregnancy
H1N1 infection
Emotional stress
Intense exercise
Extreme hyperparathyroidism

40.4 Diagnosis

The successful management of thyroid storm is based on early diagnosis and therapy that must be started as soon as possible because a delay may increase the risk of a fatal outcome.

Serum concentration of triiodothyronine (T3), thyroxine (T4), and free T4 is usually nondiagnostic, because these tests are similar in patients with storm and non-storm thyrotoxicosis.

The real challenge of this clinical condition is the diagnosis.

Characteristic features such as Bayley's symptom complex of insomnia, anorexia, vomiting, diarrhea, marked sweating, and great emotional instability are reliable in predicting impending storm [39]. A temperature greater than 38 ° C, marked tachycardia, accentuated symptoms and signs of thy-

rotoxicosis, and central nervous system (CNS), cardiovascular, or gastrointestinal system dysfunction indicate storm [9, 10].

In 1993, Burch and Wartofsky [2] introduced a specific scoring system for the diagnosis of thyroid storm:

- Temperature: 5 points per 1 °F above 99 F (no more than 30 points)
- Central nervous system dysfunction: 10 points for mild (agitation), 20 points for moderate (delirium, psychosis, or extreme lethargy), and 30 points for severe (seizure or coma)
- Tachycardia: 5 points for 99–109, 10 points for 110–119, 15 points for 120–129, 20 points for 130–139, and 25 points for frequency greater than 140
- Presence of atrial fibrillation:10 points
- Heart failure: 5 points for mild (pedal edema), 10 points for moderate (bi-basilar rales), 15 points for severe (pulmonary edema)
- Gastrointestinal dysfunction: 10 points for moderate (diarrhea, nausea/vomiting, or abdominal pain) and 20 for severe (unexplained jaundice)
- Presence of precipitating factor: 10 points

A score of 25 to 44 using the scale of "Burch and Wartofsky" is suggestive of impending storm, and a score of 45 or higher is highly suggestive of storm. A score less than 25 points does not suggest a thyroid storm status. One should be aware that patients rarely have thyroid storm and apathetic thyrotoxicosis, coma, cerebral infarction, status epilepticus, rhabdomyolysis, and acute renal failure.

Another score system based on similar clinical findings has been defined in 2012 by the Japanese Thyroid Association [3, 30]. Thyrotoxicosis (elevated FT3 and/or FT4) is fundamental, but other different symptoms are required:

- Central nervous system symptoms (restlessness, delirium, psychosis/mental aberration, lethargy/somnolence, coma)
- Fever (38 C/100.4 F or greater)
- Tachycardia (130/min or higher)
- Hearth failure (pulmonary edema, rales, cardiogenic shock, or NYHA class IV)
- GI/hepatic manifestation (nausea, vomiting, diarrhea, total bilirubin 3 mg/dl or more)

The diagnosis has been made for thyroid storm (TS1): thyrotoxicosis (elevated FT3 and/or FT4) combined with:

- At least one central nervous system manifestation and one or more other symptoms (fever, tachycardia, cardiologic disease, gastrointestinal/hepatic) *or* a combination of at least three symptoms among GI/hepatic, hearth failure or tachycardia, and fever

Thyroid storm (TS2) could be suspected with:

- Thyrotoxicosis (elevated FT3 and/or FT4)

- A combination of at least two features among tachycardia, hearth failure, gastrointestinal or liver dysfunction, and fever *or* a patient with thyroid disease and presence of goiter and exophthalmos who meets criteria for TS1 but TF hormones are not available

These scoring systems are guidelines albeit the actual diagnosis is based on clinical judgment. According to the Burch and Wartofsky 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 chest X-ray may be done to assess heart failure. Head CT scan may help exclude a neurological cause in some patients. An ECG is often done to monitor arrhythmias.

Differential diagnosis could be made with sepsis, infection, psychosis, cocaine abuse, pheochromocytoma, neuroleptic malignant syndrome, and hyperthermia.

40.5 Treatment

The treatment options of thyroid storm are mainly based on drugs [1, 3, 4]. The therapeutic options for thyroid storm are varying from those used for uncomplicated hyperthyroidism, with additional drugs often used such as glucocorticoids and an iodine solution. Also support of the patient in an ICU is essential sometimes since the mortality rate of thyroid storm is 2.5–7% [5, 9, 11, 14]. The principles of treatment are based on clinical experience and case studies since there are no prospective studies. They are mostly used to patients with severe hyperthyroidism who do not fully suffer from thyroid storm. The therapeutic drugs are numerous, each of which has a different mechanism of action:

- A beta-blocker for the symptoms and signs provoked by increased adrenergic tone.
- A thionamide to block new hormone synthesis.
- An iodine solution for blocking the release of thyroid hormone.
- An iodinated radiocontrast agent (if available) to stop the peripheral conversion of T4 to T3.
- Glucocorticoids to reduce T4 to T3 conversion, activate vasomotor stability, reduce the autoimmune process in Graves' disease, and treat an associated relative adrenal insufficiency.
- Bile acid sequestrants may also benefit in severe cases the decrease of enterohepatic recycling of thyroid hormones [31–33, 39].

For patients with clinical features of thyroid storm or severe thyrotoxicosis who do not fully meet the criteria for thyroid

storm, we begin treatment with a beta-blocker (propranolol) and either propylthiouracil (PTU) or methimazole. PTU is better than methimazole because of PTU's effect to decrease T4 to T3 conversion. One hour after the first dose of thionamide is taken, we administer iodine (saturated solution of potassium iodide [SSKI] or Lugol's solution) [40].

For patients with symptoms of thyroid storm, we also administer glucocorticoids (hydrocortisone). Cholestyramine may also be beneficial in severe cases to reduce enterohepatic recycling of thyroid hormones. Many patients require high amounts of fluid, but others may require diuresis because of congestive heart failure. Infection has to be identified and treated, and hyperpyrexia should be immediately corrected mainly with acetaminophen.

In patients with thyroid storm or severe thyrotoxicosis, it is mandatory immediate treatment with a beta-blocker. Japanese guidelines recommend esmolol over propranolol due to increased mortality in patients with congestive heart failure treated with propranolol [3, 40, 41]. If thyroid storm is accompanied by reactive airway disease, cardio-selective beta-blockers such as metoprolol or atenolol could be considered but with care. In patients with severe asthma who cannot take beta-blockers, rate control can be achieved with calcium-channel blockers such as diltiazem [41].

Thionamides inhibit thyroid hormone synthesis in 1–2 h after administration. But they have no effect on the release of hormones from the thyroid gland. For patients with thyroid storm or severe thyrotoxicosis, we begin immediate treatment with either PTU or methimazole [41, 42]:

- PTU is suggested for the acute treatment of life-threatening thyroid storm in an ICU setting.
- Methimazole is better for severe, but not life-threatening, hyperthyroidism due to longer duration of action and, after weeks of treatment, leads to more rapid normalization of serum T3 compared with PTU and also is less hepatotoxic.

The dose of thionamide given to patients with thyroid storm should be higher than that required to fully block thyroid hormone synthesis [43, 44].

Iopanoic acid and other iodinated radiocontrast agents used for oral cholecystography have been used to treat hyperthyroidism but with little data published for their use in thyroid storm. They are strong inhibitors of T4 to T3 conversion, and release of iodine in pharmacologic quantities from these agents has the important benefit of blocking thyroid hormone release [45, 46]. They have been useful in treating severe hyperthyroidism and preparing hyperthyroid patients for urgent surgery. Due to their iodinization, they should be given 1 h after the thionamide in order to prevent the iodine from being used as substrate for new hormone synthesis [47].

Iodine-containing solutions have mostly been used for the treatment of thyroid storm since iodine blocks the release of T4 and T3 from the gland within hours. In patients with thyroid storm or severe thyrotoxicosis, it is better to use iodine 1 h after the first dose of thionamide. Oral doses are potassium iodide-iodine (Lugol's) solution, or SSKI [48, 49].

Glucocorticoids also reduce the T4 to T3 conversion. In addition, they may have a direct effect on the underlying autoimmune process if the reason of thyroid storm is Graves' disease and treat potentially associated limited adrenal reserve. Glucocorticoids should not be used in patients with severe, but not life-threatening, hyperthyroidism [42, 50].

Thyroid hormones are metabolized in the liver and conjugated with glucuronide and sulfate, and their products are excreted in the bile. Free thyroid hormones are released and reabsorbed in the intestine. Bile acid sequestrants such as cholestyramine have been found to reduce thyroid hormone levels in thyrotoxic patients by interfering with enterohepatic circulation and recycling of thyroid hormone. They are useful adjunctive therapy in patients with thyroid storm but mostly in patients who are intolerant of thionamides [44, 51, 52].

Other therapies such plasmapheresis has been tried when traditional therapy has not been successful [12, 39, 53–56]. Plasmapheresis removes cytokines, antibodies, and thyroid hormones from plasma. Lithium also is used to block the release of thyroid hormone. However, it may provoke renal and neurologic toxicity [57–60].

In patients with Graves' disease, radioactive iodine or thyroidectomy as definitive therapy is important to prevent a recurrence of thyroid storm. Radioiodine therapy could be suggested as first choice for definitive therapy of hyperthyroidism in the absence of orbitopathy due to its lower cost and lower complication rate compared with surgery.

In summary, the treatment of thyroid storm is based on the reduction of thyroid hormone production and secretion. Further, the therapy must be directed against systemic disturbances, amelioration of the peripheral actions of thyroid hormones, and treatment of any precipitating or underlying illness (► Box 40.2).

After the thyroid storm has been treated, permanent treatment of the hyperthyroidism should be administered. The initial therapy should be slowly diminished after the acute hospitalization, and the patient should be closely followed as an outpatient before definitive therapy. Many of the patients will receive iodine therapy as part of their acute treatment strategy. During this interval period, it is important to continue thionamides and check thyroid function to assess stabilization. If surgery is planned, preparation and control of hyperthyroidism should be accomplished prior to operation. Finally, continuation of therapy with thionamide agents is an alternative in those patients.

Box 40.2: Treatment of Thyroid Storm

1. *Reduction of thyroid hormone synthesis and secretion*
   Inhibition of T4 and T3 synthesis: propylthiouracil and methimazole
   Inhibition of T4 and T3 secretion: potassium iodide, Lugol's solution, radiographic contrast agents, iopanoic, acid, lithium, thyroidectomy
2. *Therapy directed against systemic disorders*
   Treatment of fever: acetaminophen
   Correction of volume and nutrition: iv fluids and electrolytes, glucose, vitamins
   Supportive therapy: oxygen, vasopressor drugs
   Treatment of congestive heart failure: diuretics, digoxin
3. *Amelioration of the peripheral actions of thyroid hormones*
   Inhibition of extrathyroidal conversion of T4 to T3: propylthiouracil, radiographic contrast agents, glucocorticoids, propranolol
   Removal of T4 and T3 from serum: cholestyramine, plasmapheresis, hemodialysis, hemoperfusion
4. *Treatment of any precipitating or underlying illness*

40.6 Indications for Surgery and Surgical Details

The indications for surgery are the same with those who have to be operated on due to hyperthyroidism. The operation indicated is total thyroidectomy. Before surgery though, thyroid storm must be treated and the patient should be euthyroid. The main indication for urgent operation is if the patient is unable to take antithyroid drugs and all the drugs mentioned above. Also another category of urgent operation is those patients who clinically deteriorate or do not improve within 24–48 h despite intensive medical treatment, develop side effects from the treatment, or need immediate treatment of their hyperthyroidism due to severe underlying cardiac or pulmonary comorbidities. Surgery is mandatory for patients with hyperthyroidism due to a very large or obstructive goiter [9, 41, 61].

Some patients are unable to continue thionamides due to side effects such as agranulocytosis or hepatotoxicity or because of allergy. In those patients who need urgent treatment of hyperthyroidism, thyroidectomy is the treatment of choice. Also, there is a category of patients who are in coma due to hyperthyroidism and cannot be treated with drugs, and plasmapheresis might be a treatment of choice. In case reports, when therapy with drugs mentioned above has not been successful, plasmapheresis has been used to prepare patients with thyroid storm for thyroid surgery. Iodinated contrast agents have also been used to prepare patients for urgent surgery, but they are no longer available in many countries. In those patients, total thyroidectomy might be a useful addition in the definitive treatment of thyroid storm [5, 39, 55].

If an operation is mandatory, treatment is recommended to be continued for up to 5–7 days. Surgery should not be delayed for more than 8–10 days. The reason is a phenome-

non called escape from the Wolff-Chaikoff effect. High doses of exogenous iodine inhibit the organification of iodine in the thyroid gland (the Wolff-Chaikoff effect). This effect is mostly transient. The iodide transport system is able to adapt to higher concentrations of iodine, allowing thyroid hormone synthesis, with potential exacerbation of thyrotoxicosis [41, 62].

40.7 Outcomes and Prognosis

The outcomes of thyroid storm depend mainly on the immediate delivery of the appropriate treatments described previously. Initial case series described mortality rates as high as 37.5%, but more recent reviews report the mortality of treated thyroid storm to be at 10.7%. This can be due to the advances made in treatment options and in earlier recognition of this endocrine emergency. In a Japanese survey with cases of thyroid storm, multiorgan failure and congestive heart failure were the main causes of death [41].

Even when mortality is avoided, significant morbidity, such as brain injury, diffuse atrophy of the muscles, cerebrovascular disease, renal function impairment, and even psychosis, can lead to long-term complications.

Answers to the Questions

1. (a); 2. (b); 3. (c); 4. (d); 5. (a); 6. (c); 7. (c); 8. (d); 9. (b); 10. (a); 11. (d); 12. (c); 13. (b); 14. (d); 15. (b)

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