

## Surviving the Thyroid Storm: Role of Plasmapheresis

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### Abstract

### Case Report

Thyroid storm is a rare, but life-threatening condition that requires rapid diagnosis and emergent treatment. In the treatment of thyrotoxicosis, alternative treatment modalities are required when anti-thyroid drugs (ATD) cannot be used either because of their side effects or their inefficiencies, or when it is necessary to start a rapid action such as thyroid storm. By using plasmapheresis, it is possible to effectively and rapidly remove the thyroid hormones that have been increased in the blood. This observation aimed to illustrate the difficulties to treat a patient allergic to ATD who presented a thyroid storm caused by multinodular thyrotoxic goiter. She presented a cardiovascular compromise and massively elevated free thyroxin (FT4: 70 pmol/l). Corticosteroid, propranolol, lugol solution and antibiotic were administrated. Plasmapheresis was also indicated. After three sessions of plasma exchanges, FT4 declined and the patient's status was stable and allowed her to get surgery. Plasma exchanging appears to be effective in removing protein bound thyroid hormone when a thyroid storm occurs or when common ATD can't be used as it was the case of our patient.

Keywords: Thyroid storm, hyperthyroidism, plasmapheresis, thyrotoxicosis, allergy.

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## INTRODUCTION

Thyroid storm is a rare, but life-threatening condition that requires rapid diagnosis and emergent treatment [1-3]. It results from extreme thyroid hormone elevation. The condition manifests as decompensation of multiple organs with loss of consciousness, high fever, heart failure, diarrhea, and jaundice. The most common etiology of thyroid storm is Graves' disease, followed by other causes of hyperthyroidism such as a solitary toxic adenoma or toxic multinodular goiter [4]. Therapy is multifaceted and focuses on regulating the synthesis, release, peripheral conversion, and recycling of thyroid hormones in conjunction with supporting adrenergic tone and vasomotor response [5]. In the treatment of thyrotoxicosis, alternative treatment modalities are required when anti-thyroid drugs cannot be used either because of their side effects or their inefficiencies, or when it is necessary to start a rapid action such as thyroid storm. By using plasmapheresis, it is possible to effectively and rapidly remove the thyroid hormones that have been increased in the blood [6, 7]. Therapeutic plasma exchange (TPE) is an extracorporeal blood purification technique designed to remove large molecular weight substances bound to plasma proteins. Symptoms of apheresis only for thyrotoxicosis have been determined by the American Society for Apheresis indications category III [8].

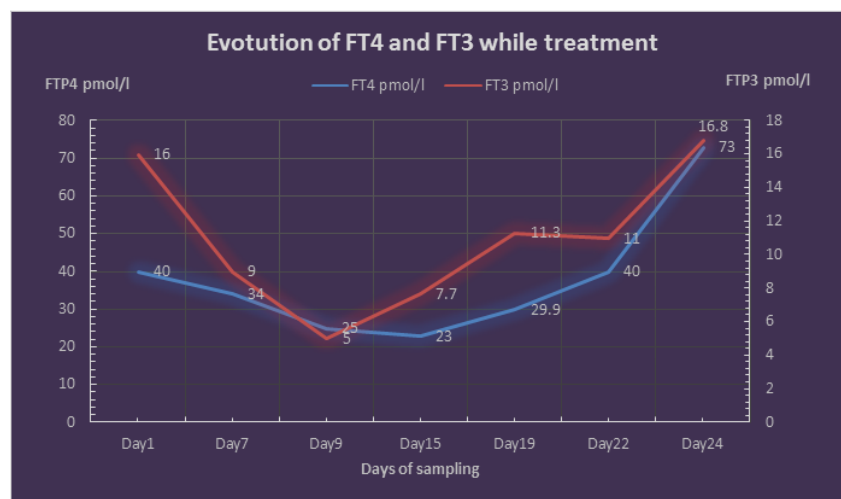
We report a case of a thyroid storm, where traditional therapy was insufficient and we highlight how plasmapheresis can help to prepare the patient to surgical intervention.

## CASE PRESENTATION

A 65-year-old woman known to have a multinodular goiter for about fifty years. She has consulted, when she started having symptoms of hyperthyroidism. Thyroid ultrasound showed a multinodular goiter with mediastinal extension and nodules graded TIRADS IV. She had no flush syndrome and normal calcitonemia. She was treated by carbimazol that she stopped taking after one month because occurrence of an urticary reaction. When she consulted six months later, she was suffering from cardiac arrhythmia by atrial fibrillation (ACFA), the patient was hospitalized, free thyroxin hormone (FT4) was high: 25 pmol/l with a reference range (RR) : 12-22 pmol/l, triiodothyronine (FT3) was high : 12,9 pmol (RR: 3,1-6,8 pmol/l). The thyroid-stimulating hormone (TSH) was low : < 0,005 µIU/l (RR: 0, 27-4,2 IU/l). She was putted on carbimazol 20mg/day and propranolol 10mg\*3/day. She presented a cutaneous reaction, with pruritus extended to all her body and did not respond well to anti-histaminic and dermo-corticoids. Since she was able to get another ATD from abroad, carbimazol; the only antithyroid drug available

in our country, was maintained for few weeks until she managed to get the alternative treatment. When benzylthiouracil was available, she was started on small doses (100mg) then the doses were increased to 200mg/day, she presented minimal rash so anti-histaminic drug was associated. In order to prepare her for surgery she was treated also with propranolol, dexamethasone and lugol solution. Because she did not respond to this protocol (Figure 1), plasmapheresis was indicated. As it was not available immediately, on the demand of the patient, she was authorized to leave the hospital for two days, but unfortunately she did not show up for her plasmapheresis's session. We were told that she no longer wanted to pursue this process. We insisted that she must continue the treatment by benzylthiouracil and control the FT4. But the patient never returned for follow up. Six months later, she consulted at emergency with a two days history of accentuated palpitations, dyspnea, heat intolerance, and hemoptysis of low abundance. She denied having chest pain, visual complaints. She had not taken her ATD for about three months prior to presentation and was taking anti-vitamin K, diuretics and beta-blocker. Physical examination revealed a thin agitated patient with a low BMI: 16,88Kg/m<sup>2</sup>. She had jaundice with conjunctival icterus. The heart rate was accelerated: 180 beats /min. The blood pressure was normal: 120/80 mmHg. The temperature was high: 38, 5°C. Respiratory rate was elevated: 26 breaths/min with normal oxygen saturation: 91%.She had a bilateral lower-extremity edema. Cardiac auscultation revealed tachycardia with a normal S1 and S2. There were no crackles over the lungs. The abdomen was soft, non-tender and non-distended, without hepatomegaly. The laboratory investigations showed severe hyperthyroidism with

suppressed thyroid-stimulating hormone TSH<0.05 $\mu$ UI/ml (RR: 0.4-4.0 IU/ml), a free thyroxin hormone T4 at 70.30pmol/l (RR: 8-22pmol/l). Liver transaminases were normal ,total bilirubin elevated: 29mg/l(RR:0-10mg/l); (direct: 20mg/l(RR:0-3mg/l),indirect:9,6mg/l(RR:0-8mg/l)). The white blood cells were elevated with a rate of 21700/ ml with neutrophils predominance (20200 / ml), platelets were normal as well as hemoglobin. C-reactive protein (CRP) was negative at 3,7mg / l.INR was at 1, 52 with a low protrombin rate (55%).The chest X-ray showed a systematized opacity of the middle lobe. Electrocardiogram demonstrated sinus tachycardia with auricular fibrillation. The echocardiography showed a conserved ejection fraction of the left ventricular with a hypertension in the pulmonary arteria associated with a dilated right ventricular. The diagnosis of thyroid storm was made, with a Burch and Wartofsky score of 85 (Table 2). The patient was shifted to the intensive care unit .Treatment for thyroid storm was immediately started, including propranolol 40 mg 3 times daily, Lugol's solution 10 drops every 8 hours and methylprednisolone 120mg/day. The antibiotics for pulmonary infection was started (moxifloxacin 400mg twice daily), and anti-coagulation (low molecular weight heparin) at curative doses. It was also decided to proceed with plasmapheresis in preparation for an urgent thyroidectomy. She received three plasmapheresis sessions. The jaundice has regressed progressively, the thyroid free thyroxin hormone levels also decreased. A total thyroidectomy was performed. The postsurgical course was simple, she was successfully extubated. She presented hypocalcemia and was substituted .The anatomopathological exam showed a goiter without signs of malignancy.



**Fig-1: Evolution of FT4 and FT3 while medical preparation for surgery**

**Table-1: The Burch-Wartofsky Point Scale for diagnosis of thyroid storm in the case our patient (colored): scored at 85 superior than 45 giving the diagnosis of a thyroid storm.**

Thermoregulatory dysfunction	Cardiovascular Dysfunction	Gastrointestinal-hepatic dysfunction	Central nervous system disturbance	Precipitating event
Temperature (°C) 37.2–37.7 5 37.8–38.3 10 38.4–38.8 15 38.9–39.4 20 39.4–39.9 25 ≥ 40.0 30	Tachycardia (beats per minute) 100–109 5 110–119 10 120–129 15 13–139 20 ≥ 140 25 Atrial fibrillation Absent 0 Present 10 Congestive heart failure Absent 0 Mild 5 Moderate 10 Severe 20	Manifestation Absent 0 Moderate (diarrhea, abdominal pain, nausea/vomiting) 10 Severe (jaundice) 15	Manifestation Absent 0 Mild (agitation) 10 Moderate (delirium, psychosis, extreme lethargy) 20 Severe (seizure, coma) 30	Status Absent 0 Present 10

## DISCUSSION

“Thyrotoxicosis”, “hyperthyroidism” and “thyroid storm”, each term refer to one specific condition: the term “thyrotoxicosis” refers to a clinical state that results from inappropriately high thyroid hormone action in tissues generally due to inappropriately high tissue thyroid hormone levels [9]. “Hyperthyroidism, ‘is a form of thyrotoxicosis due to inappropriately high synthesis and secretion of thyroid hormone(s) by the thyroid [9].”Thyroid storm” is a life-threatening complication of thyrotoxicosis. Diagnosis is based on the Burch–Wartofsky scoring [2] or by using the diagnostic criteria recently proposed by Akamizu and al [10]. A score of 45 or above is highly suggestive of thyroid storm, a score of 25 to 44 suggests an impending storm, and a score less than 25 is unlikely of being thyroid storm. This scoring system help to standardize the diagnostic because it is obvious that the point at which severe thyrotoxicosis becomes thyroid storm is controversial, and to some degree, subjective [9]. Our patient presented a hyperthyroidism that induced thyrotoxicosis and had been complicated with thyroid storm (score of 85). A precipitating event is usually identified that results in transition from hyperthyroid state to thyroid storm. In our case it was pneumonia. In the past, thyroid surgery during uncontrolled hyperthyroidism was the most common reason for thyroid storm; presently, infection is the most common precipitant, as it was for our patient. Other precipitating factors include myocardial infarction, pulmonary thromboembolism, parturition, surgery, trauma, diabetic ketoacidosis, withdrawal of antithyroid drugs, and administration of iodine (intravenous radio contrast dye or amiodarone) [11]. This observation aimed to illustrate the difficulties and challenges to treat a patient who was not only allergic to the only available anti thyroid drug (ATD) in our country but was not observant when putted on benzylthiouracil treatment and refused plasmapheresis when all medical treatment failed to prepare her to the surgery. Initially carbimazol was prescribed for the patient, but because of her

allergic reaction she stopped taking it. Indeed, it is recommended that minor cutaneous reactions may be managed with concurrent antihistamine therapy without stopping the ATD. Persistent symptomatic minor side effects of anti-thyroid medication should be managed by cessation of the medication and changing to radioactive iodine( RAI) or surgery, or switching to the other ATD when RAI or surgery are not options. In the case of a serious allergic reaction, prescribing the alternative drug is not recommended [9]. Our patient had an urticary reaction extended to all her body when treated with low doses of carbimazol (20mg) and that persisted even with anti-histaminic and corticosteroids. A recent study provided evidence that switching from one ATD to the other is safe in the case of minor side effects, although patients may develop similar side effects with the second ATD [12].Our patient got a minimal rash when treated with benzylthiouracil. However, one recent case report described a more severe reaction to Methimazol (MMI) consisting of rash, pruritis, and tongue and throat swelling that was successfully managed with antihistamine therapy, but this is not generally recommended because of the risk of anaphylaxis [13]. As a result of her poor compliance, and the occurrence of pneumonia she had a thyroid storm. She responded to the treatment, and was successeffuly prepared to the surgery, by using lugol solution, corticosteroids, and plasmapheresis. It’ s obvious that whenever possible, thyrotoxic patients who are undergoing thyroidectomy should be rendered euthyroid by MMI before undergoing surgery [14].Preoperative potassium iodine, or Lugol’s solution should be used before surgery in most patients. This treatment is beneficial because it decreases thyroid blood flow, vascularity, and intraoperative blood loss during thyroidectomy [15, 16].In addition, rapid preparation for emergent surgery can be facilitated by the use of corticosteroids [17] and potentially cholestyramine [18, 19].The recommended doses for hydrocortisone are 300mg bolus then 100 mg/ 8hours when a thyroid storm occurs. Dexamethasone can also be used [9]. Therapeutic plasma exchange (TPE) is an

alternative treatment for hyperthyroidism achieving rapid decline in plasma thyroid hormones and anti-thyroid antibodies. Guidelines and indication criteria for therapeutic plasma exchange (TPE) treatment in patients with hyperthyroidism are still lacking, although numerous reports on TPE treatment in thyrotoxic patients have been published [20, 21]. According to the 2016 Japanese guidelines from The Japan Thyroid Association and Japan Endocrine Society Taskforce, it is recommended that TPE be considered if thyrotoxic symptoms such as tachycardia, high fever, and disturbances of consciousness have not improved within 24–48 hours of initial intensive treatment, because these symptoms in patients with thyroid storm typically improve within 12–24 hours of appropriate initial therapy [3]. In this case, no other ATD was available excepting carbimazol, known to be allergenic for our patient so we couldn't use and plasmapheresis was indicated. After three plasma exchanges, the patient was eligible for surgery. Even if a normal level of freeT4 was not obtained yet, but seemed enough. The dosage of triiodothyronine FT3 couldn't be done because of the lack of reactivity at that time in the hospital. After surgery the patient had hypocalcemia, and was substituted with calcium.

Recent data suggest that supplementing oral calcium, vitamin D, or both preoperatively may reduce the risk of postoperative hypocalcemia due to parathyroid injury or increased bone turnover [22]. This was not performed in our case. A meta-analysis of risk factors for postoperative hypocalcemia identified preoperative vitamin D deficiency as a risk factor for postoperative hypocalcemia [22].

## CONCLUSION

We can conclude that plasmapheresis presents an effective alternative treatment option; when thyroid storms occur or when common ATD are insufficient or contraindicated, especially when we aim to prepare patients for surgery. It is a safe, fast and effective method, if performed in specialist centers.

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