Thyroid storm complicated by multisystem organ failure requiring plasmapheresis to bridge to thyroidectomy: A case report and literature review

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Abstract

Objective: Emphasizing awareness about the importance of prompt clinical identification, diagnosis, and updated medical management of thyroid storm.

Background: Thyroid storm is a life-threatening complication of hyperthyroidism, usually associated with Grave's disease but can be secondary to toxic multinoval goiter or solitary toxic adenomas. Thyroid storm is diagnosed by history, physical examination and laboratory data. Treatment options differ depending upon severity and include treatment of the precipitating event, thionamides, beta receptor blocking agents, bile acids sequestrants, steroids, high dose potassium iodide and in severe cases plasmapheresis. Here, we present a case of thyroid storm refractory to medical management requiring plasmapheresis to bridge to total thyroidectomy.

Case report: A 40-year-old man with a known history of Graves’ disease and poor adherence to methimazole and propranolol who presented to the emergency department with tingling and numbness in bilateral upper extremities, shortness of breath and palpitations that had been progressively worsening over the past couple months. Review of systems revealed weight loss of 150 pounds, bilateral swelling of his feet and ankles, bulging of his eyes and heat intolerance. Laboratory data at admission revealed TSH of <0.01. Initially, treated with conventional optimal medical therapy, but he still required plasmapheresis to ultimately bridge to total thyroidectomy.

Conclusions: Thyroid storm is one of the rare and lethal complications of untreated or undertreated Graves’ disease with a mortality rate of up to 10-30%. Potential catastrophic consequences of untreated Graves’ disease include thyroid storm, shock and death. It is important for clinicians to be aware and knowledgeable of the diversity of presentation, severity of the conditions and updated management including plasmapheresis.

Introduction

Thyroid storm is a rare life-threatening medical emergency. It is associated with high mortality (10 to 30%) [1]. It is characterized by severe thyrotoxicosis and systemic hemodynamic decompensation. There are multiple risk factors but usually patients with Graves’ disease are at a greater risk [1]. Patients can present with diverse signs and symptoms and varying degrees of organ decompensation. Treatment should be initiated promptly by targeting all steps of thyroid hormone synthesis, release and action. Patients who are not responding appropriately to medical therapy should be treated with therapeutic plasma exchange and later thyroidectomy once the patient is stabilized [2]. Here, we report a case of thyroid storm secondary to noncompliance with medication for Graves’ disease which was managed appropriately in an intensive care unit (ICU) setting initially with medical therapy, then plasmapheresis and ultimately thyroidectomy.

Case presentation

A 40-year-old man with a known history of Graves’ disease, who stopped taking his prescribed methimazole and propranolol for four months, presented to the emergency department with tingling and numbness in both of his upper extremities, shortness of breath and palpitations that had been progressively worsening over the past few months. Review of systems revealed that he had lost over 150 pounds in four years and has swelling of his feet and ankles, bulging of his eyes and heat intolerance. On presentation to the emergency department, initial vital signs were: blood pressure 118/64 mmHg, heart rate 146 bpm, respiratory rate 17, oral temperature 98.1 degrees Fahrenheit, oxygen saturation 99% on room air. On physical examination, the patient was skinny, diaphoretic and in mild distress. Head and neck exam revealed proptosis, lid lag and a diffusely enlarged nontender thyroid without skin depression. There was audible bruits. His pulse was irregular and he was tachycardic without an audible murmur. Lungs were clear to auscultation. There were non-pitting edema of the feet and ankles bilaterally. Tremors were visible upon outstretched arms. Neurologically, he was completely oriented and was able to provide a detailed history. Deep tendon reflexes were 3+ in both patellar and Achilles tendons. Laboratory values on admission and after treatment with methimazole for 24 hours are summarized below (Table 1). Chest radiograph showed cardiomegaly with clear lung fields. Echocardiogram showed systolic dysfunction with an ejection fraction of 30-35%. He was started on propranolol and methimazole in four months and has swelling of his feet and ankles, bulging of his eyes and heat intolerance. On presentation to the emergency department, initial vital signs were: blood pressure 118/64 mmHg, heart rate 146 bpm, respiratory rate 17, oral temperature 98.1 degrees Fahrenheit, oxygen saturation 99% on room air. On physical examination, the patient was skinny, diaphoretic and in mild distress. Head and neck exam revealed proptosis, lid lag and a diffusely enlarged nontender thyroid without audible bruits. His pulse was irregular and he was tachycardic without an audible murmur. Lungs were clear to auscultation. There was non-pitting edema of the feet and ankles bilaterally. Tremors were visible upon outstretched arms. Neurologically, he was completely oriented and was able to provide a detailed history. Deep tendon reflexes were 3+ in both patellar and Achilles tendons. Laboratory values on admission and after treatment with methimazole for 24 hours are summarized below (Table 1). Chest radiograph showed cardiomegaly with clear lung fields. Echocardiogram showed systolic dysfunction with an ejection fraction of 30-35%. He was started on propranolol and methimazole in the emergency department and was urgently seen by endocrinologist.

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Table 1. Laboratory values on admission, after medical treatment and after plasmapheresis.

| LABS                  | On admission | After 24 hours of medical management | After plasmapheresis | Reference ranges               |
|-----------------------|--------------|-------------------------------------|-----------------------|--------------------------------|
| Sodium (mmol/L)       | 138          | 133                                 | 134                   | 136-145                        |
| Potassium (mmol/L)    | 4.1          | 5.9                                 | 5.1                   | 3.5-5.2                        |
| CO2 (mmol/L)          | 26           | 16                                  | 20                    | 24-31                          |
| Anion gap             | 3            | 3                                   | 8                     | 8-16                           |
| Glucose (mg/dL)       | 103          | 79                                  | 169                   | 70-110                         |
| BUN (mg/dL)           | 10           | 50                                  | 54                    | 5-25                           |
| Creatinine (mg/dL)    | 0.87         | 2.22                                | 1.71                  | 0.61-1.24                      |
| Phosphorous (mg/dL)   | 4.8          | 7.2                                 | 5                     | 2.5-4.6                        |
| Calcium (mg/dL)       | 9.1          | 8.3                                 | 8.5                   | 8.5-10.5                       |
| Albumin (g/dL)        | 3.0          | 3.2                                 | 4                     | 3.5-5                          |
| Total bilirubin (mg/dL)| 3.5         | 9.6                                 | 7                     | 0.2-1.3                        |
| Alkaline Phosphatase (iU/L) | 382          | 407                                 | 194                   | 38-126                         |
| AST (iU/L)            | 35           | 2439                                | 2070                  | 10-42                          |
| ALT (iU/L)            | 35           | 1473                                | 1253                  | 10-60                          |
| LDH (iU/L)            | -            | 2368                                | -                     | 91-200                         |
| TSH (iU/mL)           | <0.01        | -                                   | 0.300-4.500           |
| Free T4 (NG/DL)       | 5.23         | 4.54                                | -                     | 0.50-1.26                      |
| Free T3 (pg/ml)       | 12.9         | -                                   | 2.28-3.96             |
| WBC (K/uL)            | 5.5          | 14.0                                | 14.9                  | 4.5-11.0                       |
| Hemoglobin (gm/dL)/Hematocrit (%) | 12.5/37.8 | 14.1/41.8 | 13.3/40.4 | 13.2-17.5/40.3-53.0 |
| Platelet count (K/uL) | 146          | 89                                  | 40.4                  | 140-450                        |
| INR                   | -            | 3.71                                | 4.75                  | 0.88-1.15                      |
| Fibrinogen            | -            | -                                   | 157                   | 232-519                        |
| Peripheral Smear       | No schistocytes | No schistocytes | No schistocytes | -                              |

The Burch-Wartofsky point scale for thyrotoxicosis was calculated to be 45, which was highly suggestive of thyroid storm and he was started on methimazole, cholestyramine and intravenous hydrocortisone 100mg every eight hours. Within 24 hours, the patient developed altered mental status, lethargy, multiorgan failure, disseminated intravascular coagulopathy and hyperkalemia. He was intubated for airway protection and transferred to intensive care unit. Potassium iodine was contra-indicated due to hyperkalemia and methimazole was discontinued due to liver failure. Lithium was considered as a treatment option, however due to his rapid decline and worsening renal function, lithium was not started and the decision was made to urgently place a vascular catheter and proceed with plasmapheresis. Two sessions of plasmapheresis were performed. After plasmapheresis, the renal and liver function were improved. Meanwhile, the patient was evaluated by an endocrine surgeon for thyroidectomy. His platelet count and international normal ratio (INR) stabilized and the patient’s neurological function improved on the ventilator after plasma exchange. He was successfully extubated and was taken to surgery on following day. After thyroidectomy, levothyroxine and calcium supplementation were started. Cholestyramine was discontinued, and hydrocortisone was tapered. Still, atrial fibrillation with rapid ventricular response continued requiring continuous diltiazem infusion. He underwent transthoracic echocardiogram (TEE) with cardioversion and was successfully converted to normal sinus rhythm. He was transitioned to an oral regimen of diltiazem and propranolol by cardiology. He was discharged with the instruction to continue apixaban for anticoagulation for one month as per cardiologist.

**Discussion**

Thyroid storm is the most severe form of thyrotoxicosis. It is a hypermetabolic condition associated with significant morbidity and mortality. At times, diagnosis can be challenging due to the diversity of symptoms specifically in younger patients or patients with altered mental status, which can be mistaken for substance abuse [3]. Thyroid hormone is the key regulating hormone in our body’s metabolism. It increases tissue thermogenesis and our basal metabolic rate. Triiodothyronine (T3) and thyroxine (T4) have widespread multiorgan effects [3]. Younger patients tend to present with symptoms of sympathetic stimulation such as anxiety, restlessness and tremor, whereas older patients tend to present with less obvious clinical manifestations. Elderly patients may lack adrenergic symptoms and report depression, fatigue and weight loss, which is termed apathetic hyperthyroidism [3]. Cardiovascular symptoms include tachycardia that can exceed 140 beats/minute resulting in high output systolic heart failure. Hypotension, cardiac arrhythmias and death from cardiovascular collapse may also occur [4]. A variety of atrial and ventricular tachycardias have been described in hyperthyroidism, but the most common arrhythmia is atrial fibrillation [5]. Hyperpyrexia ranging from 104-106°F is common due to the overall hypermetabolic state. Agitation, anxiety, delirium, psychosis, stupor or coma are also seen and are considered by many to be essential to the diagnosis. Other symptoms may include hepatic failure with jaundice [6-8].

Graves’ disease, toxic multinodular goiter or solitary toxic adenomas are associated with a hyperthyroid state [9]. If left untreated, thyroid storm can develop in these patients. Among these, thyroid storm associated with Graves’ disease is most reported [10] and is generally precipitated by an event such as surgery, trauma, infection or parturition [11]. Poor compliance with antithyroid medications is a commonly reported precipitant of thyroid storm associated with Graves’ disease.

The diagnosis of thyroid storm is based upon the presence of symptoms with biochemical evidence of hyperthyroidism i.e. elevation of free T4 and/or T3 and suppression of thyroid stimulating hormone (TSH). In 1993, Burch and Wartofsky introduced a scoring system using precise clinical criteria for the identification of thyroid storm [12].

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A score of 45 or more is highly suggestive of thyroid storm whereas a score below 25 makes thyroid storm unlikely. A score of 25 to 44 is suggestive of impending storm. In our patient, the Burch Wartofsky score was 45 [9,12].

The diagnosis of thyroid storm can be overlooked due to the varying presentations, which can lead to serious consequences. Therefore, diagnosing a patient in a timely manner with adequate management is crucial to minimize the associated mortality. Treatment should be started immediately in ICU setting. A multidrug approach is the most effective way of treatment. Therapeutic plasma exchange should be considered earlier in patients who are not responding to optimum medical therapy and the internist should be aware of this option. In patients with thyroid storm secondary to uncontrolled Graves’ disease, definitive treatment options such as iodine ablation and total thyroidectomy should be considered to prevent recurrence.

Author Contributions
R.S (Rabail Soomro), N.C (Natasha Campbell), S.C(Stuart Campbell), C.L(Christopher Lesniak) were involved in the case selection, in addition to planning and drafting the manuscript.
R.S (Rabail Soomro), N.C (Natasha Campbell), M.S(Michael Sullivan)- Were involved in the case discussion.
R.O(Raquel Ong), J.C(Jennifer Cheng)- worked on the case discussion, case presentation and discussion.
M.A.H (Mohammad A. Hossain) - worked on the planning, manuscript revision and final approval.

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