Thyroid Storm Presenting as Multiple Organ Dysfunction Syndrome*  

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Thyroid storm is a rare disorder characterized by hypertension, hyperthermia, and multiple systems involvement. Early recognition and treatment of thyroid storm are essential in reducing morbidity and mortality from this disorder. We present the case of a patient with an atypical (normothermic, normotensive) presentation of thyroid storm, accompanied by multiple organ dysfunction syndrome, including lactic acidosis and liver dysfunction, both of which are very rare complications. This case highlights both the multiple organ systems that can be involved in thyroid storm and the importance of recognizing atypical presentations of thyroid storm.  

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Key words: fever; hyperthyroidism; lactic acidosis; thyroid crisis  
Abbreviations: BMR = basal metabolic rate; PTU = propylthiouracil

Thyroid storm, or crisis, refers to the sudden onset of life-threatening manifestations of hyperthyroidism. In this report, we describe a case of thyroid storm presenting with several atypical features, including multiple organ dysfunction syndrome, normothermia, rhabdomyolysis, lactic acidosis, elevated transaminases, and reversible cardiomyopathy. The atypical features of this case highlight the variable presentations of thyroid storm that may delay or impede timely diagnosis and lifesaving therapies.

Case Report

A 44-year-old African American female homemaker was admitted to the hospital following 2 months of progressively increasing dyspnea on exertion, fatigue, increased appetite, diarrhea, 10-lb weight loss, and heat intolerance. In the 2 weeks before admission, her dyspnea on exertion had worsened, and she had developed palpitations and a nonproductive cough. She had been amenorrheic for 8 months and had not seen a physician for several years. She was not taking any medications. Her past medical history was significant for anemia of undetermined etiology, >20 years ago. She was a 20-pack-year cigarette smoker and had used cocaine in the past.

Examination on admission revealed a thin, anxious woman, with vital signs as follows: oral temperature, 36.1°C; heart rate, 140 beats/min; BP, 130/70 mm Hg; and respiratory rate, 18 breaths/min. Oxygen saturation measured by pulse oximetry was 97% on room air. There was no exophthalmos, eyelid lag, or stare. The thyroid gland was palpable and diffusely enlarged with a bruit. Chest examination was normal. Cardiac examination revealed a slowly displaced point of maximal impulse that was 7 cm from sternalmidline, regular tachycardia, and a soft 2/6 systolic murmur at the apex. Her liver margins were palpated to 3 cm below the right costal margin. The liver edge was smooth and without tenderness. The extremities were warm and well perfused with brisk capillary refill. The peripheral pulses were normal. A fine resting tremor of the upper extremities and nonpitting pretilial edema were present. She had hyperactive brachial and radial tendon reflexes. A chest radiograph revealed cardiomegaly. ECG showed sinus tachycardia, with a rate of 130 beats/min, and was otherwise remarkable for voltage criteria of left ventricular hypertrophy. CBC count showed 8 × 10^9/L white cells, with a hemoglobin value of 6.3 g/dL, and platelet count of 287 × 10^9/L. Mean corpuscle volume was 59 U, and the corrected reticulocyte count was 0.9%. Blood chemistries were within normal limits, except for potassium concentration of 3.2 mEq/L. At the time of admission, hyperthyroidism was diagnosed, along with hypoprolactinemia, microcytic anemia. She received 50 mg oral metoprolol and 40 mEq oral potassium, as well as 1 U packed RBCs, by transfusion.

Four hours after admission, she remained afebrile, with a heart rate of 100 beats/min, BP, 130/70 mm Hg, and respiratory rate, 15 breaths/min. She reported less dyspnea. Eight hours after admission, she experienced increased restlessness, irritability, severe dyspnea, nausea, and vomiting, and she was incontinent of urine and feces. She was afebrile, tachycardic (110 beats/min), and tachypneic (35 breaths/min), with a BP of 130/60 mm Hg. She was lethargic but arousable. Her extremities were cold, with poor capillary refill. Bedside capillary glucose testing revealed serum glucose of 35 mg/dL, which was corrected with IV dextrose solution. Despite therapies, her mental status worsened, and she became anuric. She developed a metabolic acidosis with arterial blood gas: pH, 7.31; Pco_2_, 16 mm Hg; Po_2_, 131 mm Hg, while breathing 2 L of oxygen by nasal cannula. The anion gap had increased to 19 mEq/L (Table 1). A chest radiograph and ECG were repeated and showed no change since the time of her admission. Serum toxicology results were entirely negative.

She was transferred to the ICU, where she was treated with IV fluids, antibiotics, and hydrocortisone, with no improvement in her condition. Table 1 lists selected laboratory results. A repeat measure of arterial blood gases, obtained for increasing respiratory distress, revealed the following: pH, 7.15; Pco_2_, 21 mm Hg; and Po_2_, 76 mm Hg on a partial rebreathing face mask. Sernm CO_2_ had decreased to 12 mEq/L, anion gap was 23 mEq/L, lactic acid was 12 mmol/L, creatinine phosphokinase was 2,023 U/L, and her creatinine had risen from 0.4 mg/dL (on admission) to 1.3 mg/dL. Her prothrombin time was 26 s (international normalized ratio, 4.39), with a partial thromboplastin time of 51 s. Her hepatic aspartate aminotransferase rose from 52 U/L (on admission) to 213 U/L. Shortly after transfer to the ICU, an additional dose of 100 mg hydrocortisone was administered for presumed thyroid storm. She was increasingly obtunded and required elective endotracheal intubation for airway protection and mechanical ventilation for respiratory failure, as her Pco_2_ began to rise and her work of breathing appeared excessive. Thyroid function tests became available 20 h after admission and revealed a free T4 level of 9 ng/dL (normal range, 0.89 to 1.8 ng/dL) and a thyroid-stimulating hormone level of 0.1 U/mL (normal range, 0.4 to 5.5 U/mL; see Table 2). Twelve hours after transfer to the ICU, she was started on propylthiouracil (PTU), 200 mg every 4 h, and propranolol, 25 mg every 6 h.

During the next 10 h, she remained afebrile (97 to 99°F) and normotensive. Her arterial blood gases improved (Table 1). She began to produce 40 mL/h of urine shortly after receiving hydrocortisone, 200 mg in two separate doses, and 7 L of IV crystalloids. Her lactic acid and anion gap normalized. Her transaminases, coagulation parameters, and total creatine phosphokinase also began to decrease. She was successfully extubated.

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Table 1—Laboratory Test Results at Selected Intervals*

<table>
<thead>
<tr>
<th>Variables</th>
<th>pH/PCO₂</th>
<th>Anion Gap, mEq/L</th>
<th>Creatinine, mg/dL</th>
<th>Lactic Acid, mmol/L</th>
<th>Bilirubin, mg/dL</th>
<th>AST, U/L</th>
<th>ALK-phos, U/L</th>
<th>CPK/MB%, U/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reference values</td>
<td>7.4–7.6</td>
<td>0.7–1.2</td>
<td>0.7–2.1</td>
<td>0.2–1</td>
<td>14–36</td>
<td>38–126</td>
<td>30–135</td>
<td></td>
</tr>
<tr>
<td>Time</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Admission</td>
<td>7.31/16</td>
<td>19</td>
<td>0.8</td>
<td>0.6</td>
<td>52</td>
<td>229</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initial symptoms</td>
<td>7.5/16</td>
<td>20</td>
<td>1.1</td>
<td>12</td>
<td>3</td>
<td>213</td>
<td>310</td>
<td>2.623/1</td>
</tr>
<tr>
<td>Transfer to ICU</td>
<td>7.5/16</td>
<td>23</td>
<td>1.3</td>
<td>2.8</td>
<td>234</td>
<td>222</td>
<td>2.931/1</td>
<td></td>
</tr>
<tr>
<td>Intubation</td>
<td>7.5/12</td>
<td>16</td>
<td>1.6</td>
<td>3.4</td>
<td>4</td>
<td>1467</td>
<td>219</td>
<td>2.222/2</td>
</tr>
<tr>
<td>10 h after intubation</td>
<td>7.38/130</td>
<td>11</td>
<td>1.1</td>
<td>2.2</td>
<td>1.7</td>
<td>897</td>
<td>179</td>
<td></td>
</tr>
</tbody>
</table>

*AST = aspartate aminotransferase; ALK-phos = alkaline phosphatase; CPK-MB = creatine phosphokinase MB band.
†Normal range, 0 to 4 U/L.

After 30 h, all blood, urine, and stool cultures were negative for bacterial organisms. Her serum iron level was 34 μg/dL. An echocardiogram showed dilated cardiac chambers without regional wall motion abnormalities and an estimated ejection fraction of 25%. She was transferred to the hospital floor and was treated for congestive heart failure with diuretics and for hyperthyroidism with propranolol and PTU. The diagnosis of Grave’s disease was supported by the presence of thyroid-stimulating globulin in her serum. She was discharged home on the 10th day after admission, receiving PTU, propranolol, iron, and enalapril. Renal and pulmonary function were intact. A follow-up outpatient visit 2 months later, she was feeling well, had gained weight, and was clinically euthyroid. A repeat echocardiogram revealed nearly normal cardiac function. Radioactive iodine treatments are planned after PTU has been reduced to 10 mg/d.

**DISCUSSION**

Thyroid storm is a sudden, life-threatening exacerbation of thyrotoxicosis. The classic clinical presentation includes fever, tachycardia, tremor, nausea and vomiting, diarrhea, dehydration, delirium, and coma. The most characteristic feature is fever, where the temperature may rise above 40.6°C (105°F). Apathetic storm, which refers to a syndrome sometimes seen in elderly patients, is characterized by extreme weakness and emotional apathy. Fever, if present, does not reach the levels seen in classic storm. Variable presentations of typical hypermetabolic thyroid storm have also been reported, and these include congestive heart failure, hepatic failure, cerebral infarction, acute abdominal pain, seizures, stroke, rhabdomyolysis, coma, and shock. However, this is the first reported case of a young patient presenting with normothermic, normotensive thyroid storm accompanied by lactic acidosis and multiple organ dysfunction syndrome.

The patient’s history suggests that sepsis may have occurred simultaneously with thyroid storm. However, all cultures of body fluids (blood, sputum, and urine) demonstrated no growth, and she had no evident clinical focus of infection other than a history of mild, nonproductive cough prior to admission. We hypothesize that a viral upper respiratory infection precipitated thyroid storm (from simple underlying hyperthyroidism). The tachycardia, mental status changes, hypoglycemia, restlessness, and GI symptoms noted in her case are typical of thyroid storm. Her urinary and fecal incontinence are not typical, but they may be consistent with hyperautonoma associated with thyroid storm. Her rapid recovery following initiation of definitive antithyroid treatments suggests that thyroid storm was the primary etiology of her critical illness. However, we cannot exclude the possibility of superimposed culture-negative sepsis that responded to concurrent administration of antimicrobial agents. Thyroid function tests support the contention that she had hyperthyroidism; the point at which simple thyrotoxicosis ends and thyroid storm begins is an arbitrary clinical distinction. Her rapidly developing syndrome, clinical signs, and laboratory data, taken together, suggest that her underlying hyperthyroidism evolved to storm, perhaps as a result of infection, anemia, and/or even clinical palpation of her thyroid gland. Although reported in elderly patients with apathetic thyroid storm, normothermia has not been previously reported in a young patient with thyroid storm. This patient remained normothermic throughout her hospital stay. Some have suggested that definitive thermoregulation is universally

Table 2—Results of Thyroid Function Tests*

<table>
<thead>
<tr>
<th>Variables</th>
<th>TSH, IU/mL</th>
<th>TT₄, μg/dL</th>
<th>FT₄, ng/dL</th>
<th>FTI</th>
<th>T₃, U, %</th>
<th>TT₃, ng/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reference values</td>
<td>0.4–5.5</td>
<td>4.8–10.7</td>
<td>0.89–1.8</td>
<td>1.2–3.96</td>
<td>25–37</td>
<td>0.6–1.8</td>
</tr>
<tr>
<td>Time</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Admission</td>
<td>&lt;0.1</td>
<td>24</td>
<td>9</td>
<td>17</td>
<td>65</td>
<td></td>
</tr>
<tr>
<td>Intubation</td>
<td>&lt;0.1</td>
<td>14</td>
<td>4</td>
<td>9</td>
<td>67</td>
<td></td>
</tr>
<tr>
<td>24 h after intubation</td>
<td>&lt;0.1</td>
<td>13</td>
<td>4</td>
<td>9</td>
<td>70</td>
<td></td>
</tr>
<tr>
<td>Discharge</td>
<td>&lt;0.1</td>
<td>6.5</td>
<td>2.3</td>
<td>2.7</td>
<td>33</td>
<td></td>
</tr>
</tbody>
</table>

*TSH = thyroid-stimulating hormone; TT₄ = total thyroxine; FT₄ = free thyroxine; FTI = free thyroxine index; T₃, U = triiodothyronine resin uptake; TT₃ = total triiodothyronine.
†Reference values at our hospital.
present in thyroid storm. In one of the few published series on thyroid storm, Mazzaferrri and Skillman reported that fever above 38.4°C (101°F) was present in all 22 cases. It is unknown whether the fever is a response to the release of the thyroid crisis, which leads to the elevation of the basal metabolic rate (BMR) due to the body's inability to dissipate heat. In patients with thyroid storm, BMR was twice that measured in thyrotoxic individuals prior to development of crisis. These data suggest that increased thermogenesis in thyroid storm is due to elevations of BMR beyond elevated levels of uncomplicated thyrotoxicosis. However, it is unclear why our patient did not have a fever.

Lactic acidosis has also not been reported to occur in patients with thyroid storm. In our case, several factors could have contributed to lactic acidosis: (1) increased lactate production due to BMR greater than oxygen delivery, elevated work of breathing, muscular activity (associated with restlessness), or possibly reduced cardiac output (acute dilated cardiomyopathy); and (2) reduced hepatic clearance of lactic acid.

Mild elevations of creatinine phosphokinase and clinically apparent myopathy are common in both hypo- and hyperthyroidism. However, rhabdomyolysis has only been reported in two previous cases of thyroid storm. Although we did not test for myoglobin in her urine, mild rhabdomyolysis could have contributed to her acute renal failure. Even though isolated organ dysfunction has been reported in thyrotoxicosis, multiple organ dysfunction syndromes have not been described. Renal function is generally augmented in hyperthyroidism. Acute renal failure in this case probably resulted from her cardiopulmonary decompensation (potentially compounded by mild rhabdomyolysis) rather than from direct effects of hyperthyroidism. Hyperthyroidism can cause atrial fibrillation and cardiomyopathy. The increase in heart rate and myocardial contractility coupled with peripheral vasodilation associated with hyperthyroidism are known to events in dilated cardiomyopathy and heart failure if the thyroid disease is left untreated. As in our case, the cardiac abnormalities are reversible with antithyroid treatment. Mild elevations of liver enzymes are common in hyperthyroidism but hepatic failure is rare. The mechanism for liver enzyme elevations in thyrotoxicosis is not well understood, and the elevations noted in this case are unusual.

Thyroid crisis is rarely seen today. The mechanisms underlying the clinical progression from compensated thyrotoxicosis to thyroid storm have not been fully determined. It has long been recognized that a sudden increase in circulating thyroid hormone levels following the withdrawal of antithyroid drugs, the therapeutic use of iodine-131, or surgery in thyrotoxic patients, may proceed to thyroid storm. Thus, it seems that an acute elevation of free triiodothyronine or thyronine in thyrotoxic patients may produce systemic decompensation and may result in thyroid crisis. However, no absolute level of serum triiodothyronine or thyronine exists above which thyroid storm occurs inevitably. Thyroid storm is a systemic disease, and many of its clinical features result from overactivity of the sympathetic nervous system. The mechanisms to explain these responses are not well understood, since serum catecholamine levels are not increased. Studies suggest that the enhanced sympathetic activity in thyroid storm results from an increased number of β-adrenergic receptors on target organs, such as the myocardium, which contributes to a supersensitivity to even normal levels of catecholamines. The effectiveness of β-blockade in the control of thyrotoxic symptoms supports this hypothesis.

This case demonstrates that atypical (normothermic, normotensive) presentations do not preclude the diagnosis of thyroid storm in younger patients. Lactic acidosis, rhabdomyolysis, and multiple organ dysfunction syndromes can complicate this disease. Early recognition and prompt antithyroid therapies likely attenuated organ dysfunction, permitting this patient to recover fully.

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