A Case of Thyroid Storm with Multiple Organ Failure Effectively Treated with Plasma Exchange

Kazuki Sasaki¹, Akira Yoshida¹, Yukiko Nakata², Isamu Mizote¹, Yasushi Sakata¹ and Issei Komuro¹

Abstract

We describe a 48-year-old man with thyroid storm presenting with heart failure. He presented severely impaired left ventricular wall motion and a marked increase in the liver enzymes. He developed disseminated intravascular coagulation on day 2. Due to elevated serum thyroid hormone level, anti-thyroid hormone receptor antibody positivity, and his clinical symptoms, he was diagnosed as thyroid storm due to untreated Graves’ disease. His condition did not improve even after 6 days of conventional therapy including steroids. After therapeutic plasma exchange was carried out, his thyroid hormone level decreased markedly. Consequently, his condition recovered gradually, and he was discharged at day 43.

Key words: thyroid storm, heart failure, plasma exchange


Introduction

Thyroid storm is defined as thyroid function that is markedly enhanced, and the clinical features are central nervous system dysfunction, high fever, tachycardia, heart failure, and gastrointestinal dysfunction (1). The overall mortality is estimated 10-20%. It has become generally accepted that there should be no delay in therapy because the mortality rate may rise to 75% (2).

There are three conventional forms of treatment for thyrotoxicosis due to Graves’ disease such as antithyroid drugs, radioiodine therapy, and total thyroidectomy. In cases of uncontrollable thyroid storm, some reports have described the effectiveness of plasma exchange (3-5). We encountered a case of thyroid storm accompanied with heart failure and liver dysfunction which was effectively treated with plasma exchange.

Case Report

A 48-year-old man was admitted for general malaise, jaundice and gastrointestinal symptoms. His father, mother and two sisters had Graves’ disease. He had noticed thirst, fatigue and irritability for previous 5 years; however he had left his symptoms unchecked. On the day before admission, he had severe nausea, frequent vomiting and diarrhea. He became restless and in a mentally irritable state. He was examined by a local doctor. Prolonged activated partial thromboplastin time (APTT) and prothrombin time (PT), elevated aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were pointed out. Because of suspected fulminant hepatitis, he was carried to our hospital by ambulance.

On admission he was found to be 164 cm in height and 47.5 kg in weight. His body temperature was 38.1°C, blood pressure 133/74 mmHg, pulse was regular at 146/min, respiratory rate was at 38/min, and arterial oxygen saturation by pulse oximetry (SpO₂) values were 99% in room air. His Glasgow Coma Scale was 14 (E4, V4, M6). He appeared moist with sweating. Conjunctiva was not anemic but slightly icteric. Exophthalmos was negative. His anterior cervix was markedly swollen. Pulmonary vesicular rales and systolic cardiac murmur were audible. His abdomen was flat and ascites were not detected physically. No pretibial edema was found in either leg. Laboratory data (Table 1) showed leukocytosis and moderately increased C-reactive protein
Table 1. Laboratory Data on Admission

<table>
<thead>
<tr>
<th>Test</th>
<th>Unit</th>
<th>Value</th>
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<tbody>
<tr>
<td>Hematology test</td>
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<tr>
<td>WBC</td>
<td>/µL</td>
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<tr>
<td>RBC</td>
<td>/µL</td>
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<td>%</td>
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<tr>
<td>Pt</td>
<td>/µL</td>
<td>13.3×10⁴</td>
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<tr>
<td>Coagulation test</td>
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<td>APTT</td>
<td>sec</td>
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</tr>
<tr>
<td>PT</td>
<td>%</td>
<td>15</td>
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<tr>
<td>FDP</td>
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<tr>
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</tr>
<tr>
<td>Alb</td>
<td>g/dL</td>
<td>3.6</td>
</tr>
<tr>
<td>D-Bil</td>
<td>mg/dL</td>
<td>2.0</td>
</tr>
</tbody>
</table>
| Table 1. Laboratory Data on Admission

On admission we first noticed sinus tachycardia and a restless state. Echocardiography revealed dilatation of both atria and ventricles. Abdominal ultrasonography showed the liver with a sharp edge and smooth surface. Abdominal computed tomography (CT) revealed very slight ascites but no other abnormality, denying fulminate hepatitis. Cervical CT showed a diffuse thyroid goiter.

Clinical course after admission (Fig. 2)

On admission we first noticed sinus tachycardia and a restless state. Echocardiography revealed dilatation of both atria and ventricles. His left ventricular wall motion was generally severely hypokinetic and LV ejection fraction was
In a short time his respiratory state deteriorated and arterial blood gas analysis showed inadequate oxygenation despite the use of an oxygen mask with reservoir bag (O2 10 L/min). He required endotracheal intubation for assisted ventilation. Intraaortic balloon pump (IABP) was started to stabilize circulation. Coronary angiography was performed using a small amount of contrast media, which showed a normal coronary artery. Consecutively right heart catheter examination showed that the cardiac index (CI) was 4.3 L/min/m², pulmonary artery pressure (PAP) was 55/25/35 mmHg (systolic/diastolic/mean), right atrium pressure (RAP) was 20 mmHg and pulmonary capillary wedge pressure (PCWP) was 22 mmHg. Unaware of the etiology, we began to treat him as acute decompensated heart failure with fulminant myocarditis. At first, carbipilide 0.025 μg/kg/min, furosemide 100 mg/day and dobutamine 2 μg/kg/min were administered intravenously.

On day 2 his hyperthermia persisted, heart rate increased to 200/min and the rhythm was converted to atrial fibrillation. Digitalis and randiolol were administered intravenously, but atrial fibrillation continued. Even direct current cardioversion was not effective. In laboratory data, leukocytosis, thrombocytopenia, prolonged PT and increased FDP were observed, which fulfilled disseminated intravascular coagulation (DIC) diagnostic criteria established by the Japanese Association for Acute Medicine (6). Blood culture was sterile and he had no clinical evidence of active infection. On the same day, to exclude fulminant myocarditis, endomyocardial biopsy was performed. Histological data of myocardial biopsy revealed mild lymphocytic infiltration and moderate fibrosis, which did not support myocarditis. Thyroid function tests showed high levels of free triiodothyronine (fT3), free thyroxin (fT4), anti-thyroid-stimulating hormone receptor antibody (TRAb), and a low level of thyroid-stimulating hormone (TSH) matched with thyrotoxicosis due to Graves’ disease. Therefore he was diagnosed as thyroid storm. The Burch & Wartofsky score was more than 105. Immediately he was given oral thiamazole (1-methyl 2-mercapto imidazole: MMI) 30 mg/day, Lugol’s iodine solution 20 mg/day and methylprednisolone (1 g/day). Because his body temperature persisted above 37°C, tachycardia continued and no significant improvement of LV function was observed.

Figure 2. Clinical course after admission. Upper panel shows sequential changes in ejection fraction (EF), heart rate (HR) and total bilirubin (T-Bil). Lower panel shows sequential changes in free thyroxine (fT4) and free triiodothyronine (fT3) levels. MMI: 1-methyl 2-mercapto imidazole (thiamazole), mPSL: methylprednisolone, PE: plasma exchange, TRAb: anti-thyroid-stimulating hormone receptor antibody
observed, thiamazole was increased to 90 mg/day and Lugol’s iodine solution to 30 mg/day. Afterwards, PT was lower than 40% and T-Bil was gradually increased to 15.5 mg/dL on day 6. We recognized that it is difficult to control multiple organ failure due to thyrotoxicosis using only antithyroid drugs, although the thyroid hormone began to decrease. Therefore, therapeutic plasma exchange was carried out using 40 units of fresh frozen plasma on days 7 and 8, resulting in rapid decreases in FT4, FT3 and TRAb. Soon after the second plasma exchange, atrial fibrillation was converted to sinus rhythm and the heart rate was decreased to approximately 90/min. He was relieved from DIC on day 15. CTR was reduced to 48% (Fig. 1) and EF was increased to 57% by day 16. His general condition gradually improved and thyroid hormone was normalized at day 25. T-Bil was slowly decreased to 1.9 mg/dL on day 40. Consequently, he was discharged on day 43.

**Discussion**

Thyroid storm is a sudden, life-threatening exacerbation of thyrotoxicosis. The clinical presentation includes fever, tachycardia, tremor, nausea and vomiting, diarrhea, dehydration, delirium, and coma. The pathogenesis is poorly understood, but a plausible explanation is acute and rapid increases in the serum thyroid hormone by precipitating causes such as infection, metabolic acidosis, surgery and hypoglycemia (7). In the present case, the precise trigger of the thyroid storm could not be identified, but it was considered that his familial history, which his father, mother, and two sisters had Graves’ disease, indicated his high risk of morbidity (8) and his untreated Graves’ disease made him vulnerable to thyroid storm development.

On admission, his cardiac and liver function was severely damaged. In hyperthyroidism, congestive heart failure is complicated in 5-6%, and EF depression in 3% (9). In some cases, decreased cardiac performance could be reversible after the establishment of euthyroid state (10-12). The thyroid hormone directly mediates tachycardia and the expression of both structural and regulatory genes, such as α-myosin heavy chain, sarcoplasmic reticulum Ca$^{2+}$-ATPase, β1-adrenergic receptors in cardiac myocytes. It also indirectly leads to thermogenesis, dilates peripheral vasculature, activates renin-angiotensin-aldosterone system and gives rise to volume retention (13). Thus excessive thyroid hormone results in high output heart failure through increased work imposed on the heart. In addition, severe liver dysfunction such as cardiogenic ischemic hepatitis could be complicated in association with thyroid storm (14, 15). Rapid removal of thyroid hormone is necessary for the treatment of thyroid storm with severe cardiac and liver dysfunction.

The three conventional forms of treatment for hyperthyroidism are antithyroid drugs, radioiodine therapy, and total thyroidectomy. Thyroidectomy is the definitive treatment for thyrotoxicosis. Because surgery in hyperthyroidism could exacerbate the general condition, it is necessary that the thyroid hormone should be adjusted to euthyroid state before thyroidectomy (16). Antithyroid drugs are often prescribed for hyperthyroidism, but they have slow acting propensity (1). In the present case, because only drug therapy was insufficient to control multi organ failure due to thyrotoxicosis, therapeutic plasma exchange was necessary. As previously mentioned, some reports have described the effectiveness of plasma exchange to thyroid storm (3-5). In plasma exchange a large amount of thyroid hormone binds serum protein and supplies fresh plasma to circulation instead of reducing thyroid hormone. Generally, thyroid hormone infrequently is increased again after plasma exchange in spite of its transient decrease (16). A re-increase of thyroid hormone was observed in the present case as well, but to a lower level than that before plasma exchange. We consider the transient decrease of the level of thyroid hormone due to plasma exchange improved his cardiac and liver dysfunction, and led to the early recovery from DIC. Plasma exchange should be considered when a patient is suffering from thyroid storm along with DIC because plasma exchange is also beneficial for treatment of DIC.

We effectively treated a case of thyroid storm with multiple organ failure with plasma exchange. EF improved as a decrease of thyroid hormone. Although plasma exchange has problems, such as infection, cost and invasiveness, plasma exchange is worth considering especially in patients resistant to conventional medical treatments.

**The authors state that they have no Conflict of Interest (COI).**

**Acknowledgement**

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