Thyroid Storm with Heart Failure Treated with a Short-acting Beta-adrenoreceptor Blocker, Landiolol Hydrochloride

Yugo Yamashita¹, Moritake Iguchi¹, Rieko Nakatani², Takeshi Usui³, Daisuke Takagi¹, Yasuhiro Hamatani¹, Takashi Unoki¹, Mitsuru Ishii¹, Hisashi Ogawa¹, Nobutoyo Masunaga¹, Mitsuru Abe¹ and Masaharu Akao¹

Abstract

Beta-adrenoceptor blockers are essential in controlling the peripheral actions of thyroid hormones and a rapid heart rate in patients with thyroid storm, although they should be used with great caution when there is the potential for heart failure. A 67-year-old woman was diagnosed as having thyroid storm in addition to marked tachycardia with atrial fibrillation and heart failure associated with a reduced left ventricular function. The administration of an oral beta blocker, bisoprolol fumarate, induced hypotension and was not tolerable for the patient, whereas landiolol hydrochloride, a short-acting intravenous beta-adrenoceptor blocker with high cardioselectivity and a short elimination half-life, was useful for controlling the patient’s tachycardia and heart failure without causing hemodynamic deterioration.

Key words: thyroid storm, heart failure, atrial fibrillation, beta-adrenoceptor blocker, landiolol hydrochloride

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Introduction

Thyroid storm is one of the most critical illnesses within the spectrum of endocrine emergencies. This condition is characterized by a markedly enhanced thyroid function that presents with several specific clinical features (1). In terms of the incidence of thyroid storm, this disorder has been noted to occur in less than 10% of patients hospitalized for hyperthyroidism, although the overall mortality is estimated to be 20-30% (2). Heart failure and tachycardia with atrial fibrillation are the typical complications of thyroid storm.

There are several conventional forms of treatment for hyperthyroidism, including antithyroid drugs, radioiodine and total thyroidectomy. Beta-adrenoceptor blockers are essential for controlling the peripheral actions of thyroid hormones. However, contraindications for the use of these agents include moderate to severe heart failure.

We herein present a case of thyroid storm resulting in marked tachycardia with atrial fibrillation and severe heart failure in which treatment with a short-acting beta-adrenoceptor blocker, landiolol hydrochloride, was useful for controlling the patient’s tachycardia and heart failure.

Case Report

A 67-year-old woman had been diagnosed with Graves’ disease 20 years previously and followed with an antithyroid drug, thiamazole, by her general practitioner. She had no past medical history of paroxysmal atrial fibrillation. Two months before the current admission, she visited another hospital, where she was diagnosed with hypothyroidism and received thyroid hormone replacement therapy. However, she subsequently developed general fatigue and palpitations...
On admission, the patient was found to be 157 cm in height and 49 kg in weight, with a body temperature of 36.0°C, blood pressure of 123/43 mmHg, pulse rate of 87/min with irregularity and heart rate of 220/min. She was restless and exhibited a Glasgow Coma Scale of 15 points (E4V5M6), which is equivalent to grade 1 on the Japan Coma Scale. Her skin was edematous and moist with cold sweating. Although the conjunctiva was not anemic or icteric, pulmonary vesicular rales and a systolic cardiac murmur were audible.

A chest X-ray showed pulmonary congestion with a marked increase in the cardiothoracic ratio (Fig. 1). In addition, an electrocardiogram showed marked tachycardia with atrial fibrillation, and the patient’s heart rate was approximately 220/min (Fig. 2). The laboratory data (Table 1) showed moderately increased total bilirubin, aspartate-aminotransferase and alanine-aminotransferase levels, while the N-terminal pro-B-type natriuretic peptide level was markedly elevated. Regarding endocrinological tests (Table 2), thyroid function tests showed high levels of free triiodothyronine (fT3) and free thyroxin (fT4) and a low level of thyroid-stimulating hormone (TSH). Furthermore, very high levels of thyroglobulin (Tg), anti-Tg antibodies, antithyroid peroxidase (TPO) antibodies and thyrotropin receptor antibodies (TRAbs) were observed, whereas a blood gas analysis showed normal values for blood pH, HCO₃⁻ and
The patient’s clinical course during hospitalization is shown in Fig. 3. After admission, furosemide was given intravenously to treat the congestive heart failure and bisoprolol fumarate (2.5 mg/day) was given orally to control her heart rate. Therapy with iodine and hydrocortisone was started immediately in order to rapidly lower the levels of thyroid hormones, and treatment with thiamazole was initiated at a low dose (15 mg/day), since we could not rule out the possibility of overlapping iatrogenic thyrotoxicosis due to the administration of thyroid hormone replacement therapy at her first visit to our hospital. The high TRAb titer suggested that both iatrogenic thyrotoxicosis and autoimmune stimulation had induced the thyrotoxicosis. After the completion of these treatments, the fT3 and fT4 levels returned to the normal ranges within two days. However, the patient continued to show marked tachycardia, with no improvements in the heart failure. Bolus digoxin was subsequently given intravenously (0.25 mg); however, we were unable to control the rapid heart rate. Treatment with oral bisoprolol fumarate was only minimally effective in lowering the heart rate and instead caused an acute drop in systolic blood pressure from 120 to 70 mmHg. We considered that increasing the dose of oral bisoprolol fumarate would be rather harmful, so we decided to initiate therapy with intravenous landiolol hydrochloride under monitoring of the arterial blood pressure. We carefully adjusted the dose of landiolol hydrochloride within the range of 1-5 μg/kg/min in response to the patient’s heart rate and blood pressure and were successfully able to control the heart rate without causing remarkable hypotension. After stabilizing the heart rate, echocardiography showed an improvement in the EF (55%), with a left atrial diameter of 39 mm and left ventricular end-diastolic dimension of 41 mm. On day 30, we performed electrical countershock, which resulted in successful conversion to a normal sinus rhythm (Fig. 2). A chest obtained X-ray on day 30 showed right atelectasis with persistent right pleural effusion and an improvement in the pulmonary congestion (Fig. 1). Thereafter, the thyroid hormone levels were maintained within the normal ranges; however, the atrial fibrillation and hyperthyroidism gradually recurred, despite the continuous administration of iodine and thiamazole. Total thyroidectomy was then performed on day 58, and the patient subsequently maintained a euthyroid state under treatment with thyroid hormone replacement therapy. In addition, she showed spontaneous conversion of the atrial fibrillation to a normal sinus rhythm and was discharged on day 72.

**Table 1. Laboratory Data on Admission (1).**

<table>
<thead>
<tr>
<th>Hematology test</th>
<th>Biochemistry test</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC 5,000/μL</td>
<td>TP 6.3 g/dL</td>
</tr>
<tr>
<td>RBC 423*10⁶/μL</td>
<td>Alb 2.8 g/dL</td>
</tr>
<tr>
<td>Hb 12.5 g/dL</td>
<td>T-Bil 2.3 mg/dL</td>
</tr>
<tr>
<td>Pt 12.6*10⁹/μL</td>
<td>AST 51 U/L</td>
</tr>
<tr>
<td>Coagulation test</td>
<td>CRP 0.10 mg/dL</td>
</tr>
<tr>
<td>PT 13.3 sec</td>
<td>ALT 44 U/L</td>
</tr>
<tr>
<td>PT-INR 1.14</td>
<td>TC 95 mg/dL</td>
</tr>
<tr>
<td>APTT 25.6 sec</td>
<td>LDL 234 mg/dL</td>
</tr>
<tr>
<td>Coagulation test</td>
<td>LDL-C 54 mg/dL</td>
</tr>
<tr>
<td>PT-INR 1.14</td>
<td>BUN 33 mg/dL</td>
</tr>
<tr>
<td>APTT 25.6 sec</td>
<td>NT-proBNP 6,101 pg/mL</td>
</tr>
<tr>
<td>Cr 0.43 mg/dL</td>
<td>Tn-I 48.8 pg/mL</td>
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</tbody>
</table>

**Table 2. Laboratory Data on Admission (2).**

<table>
<thead>
<tr>
<th>Endocrinological test</th>
<th>Blood Gas Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>fT3 24.3 pg/mL (O2:4l/min with mask)</td>
<td>PCO₂ 46.0 mmHg</td>
</tr>
<tr>
<td>fT4 2.5 ng/dL</td>
<td>HCO₃⁻ 26.5 mmol/L</td>
</tr>
<tr>
<td>TSH 0.003 μU/mL</td>
<td>Lactate 1.5 mmol/L</td>
</tr>
<tr>
<td>Tg 6,356 ng/mL</td>
<td>PO₂ 167.0 mmHg</td>
</tr>
<tr>
<td>anti-Tg antibody 48.5 pg/mL</td>
<td>pH 7.378</td>
</tr>
<tr>
<td>anti-TPO antibody 312.0 IU/mL</td>
<td>PCO₂ 46.0 mmHg</td>
</tr>
<tr>
<td>TRAb 207.0 IU/L</td>
<td>HCO₃⁻ 26.5 mmol/L</td>
</tr>
</tbody>
</table>


**Definition and treatment of thyroid storm**

Thyroid storm is a medical emergency resulting from the exacerbation of a hyperthyroid state characterized by the decompensation of one or more organ systems (3). Early rec-
Figure 3. Clinical course after admission. The upper panel shows sequential changes in the free triiodothyronine (fT3), free thyroxine (fT4) and thyroid-stimulating hormone (TSH) levels. The lower panel shows sequential changes in the heart rate (HR), systolic blood pressure (sBP) and ejection fraction (EF).

Ongoing and intensive treatment are essential for limiting the morbidity and mortality associated with this condition. Thyroid storm has an abrupt onset, provoked by a precipitating factor, such as infectious disease, ketoacidosis, acute trauma, thyroid surgery, 131-I radiometabolic treatment, the administration of iodine-containing materials (amiodarone) and/or parturition (4). Clinically, it is characterized by four main features: fever, tachycardia or supraventricular arrhythmias, central nervous system symptoms and gastrointestinal symptoms (5). The Burch and Wartofsky diagnostic criteria are widely used in such cases (6); the Burch and Wartofsky score in this case was 65 points, which represents a critical condition requiring intensive treatment.

The medical management of thyroid storm consists of an array of medications that act to halt the synthesis, release and peripheral effects of thyroid hormones. Rapidly lowering the serum thyroid hormone levels is important for treating thyrotoxicosis, and the administration of beta-adrenoreceptor blockers is useful for controlling the peripheral actions of thyroid hormones. These agents are also effective in controlling a rapid heart rate. The application of a beta-adrenoreceptor blocker in the management of thyroid storm was first reported in 1966, with the agent pronethalol (7). Contraindications for the use of beta-adrenoreceptor blockers include a reduced cardiac function and history of moderate to severe heart failure.

Thyroid storm and heart failure

Patients with hyperthyroidism may display signs and symptoms indicative of heart failure (8). The effects of thyroid hormones on the heart and peripheral vasculature include a decrease in systemic vascular resistance and increases in the resting heart rate, left ventricular contractility and blood volume. In patients with hyperthyroidism, these combined effects increase the cardiac output by 50% to 300% above the baseline level; the prior literature refers to this phenomenon as high-output failure (9). However, in a subset of patients with both severe and chronic hyperthyroidism, exaggerated sinus tachycardia or atrial fibrillation can further aggravate left ventricular dysfunction and heart failure (8). Furthermore, patients with hyperthyroidism may develop complications of congestive heart failure at a rate of 5-6% and EF depression at a rate of 3% (10). Left ventricular systolic dysfunction associated with thyrotoxic heart failure frequently improves when the patient becomes euthyroid (11-13).

Beta-adrenoreceptor blocker therapy for thyroid storm presenting with heart failure

The administration of beta-adrenoreceptor blockers in patients with heart failure and a decreased left ventricular function should be performed with caution. Indeed, there are three reported cases of thyroid storm in which the patients developed sudden cardiorespiratory arrest soon after receiving oral propranolol (14). In addition, there is another report of a young hyperthyroid man with atrial flutter who was treated with propranolol and developed cardiovascular collapse (12). However, beta-adrenoreceptor blockers are par-
particularly useful in cases in which tachycardia itself aggravates heart failure. The use of intravenous short-acting beta-adrenoceptor blockers, versus oral drugs, is advantageous in fine-tuning the dose of the drug in such situations (15). It has also been reported that esmolol, a short-acting intravenous beta-adrenoceptor blocker, is a therapeutic option in patients with thyroid storm (16).

Landiolol hydrochloride is an ultra-short-acting intravenous beta-blocker exclusively used in Japan, with high cardioselectivity (beta1/beta2 selectivity: 255) and a short elimination half-life (4 min) (17). These features make it easy to titrate the dose of the drug and better manage the patient, especially during the perioperative period. Several previous case reports have demonstrated the usefulness of landiolol hydrochloride in patients with hyperthyroidism presenting with tachycardia during the perioperative and postoperative periods (18-21). Since landiolol exhibits higher cardioselectivity and fewer cardiodepressant effects than esmolol, its clinical indications may be broader. The J-Land study reported that landiolol hydrochloride is more effective for controlling a rapid heart rate than digoxin in patients with atrial fibrillation or atrial flutter associated with left ventricular dysfunction (22). Another study suggested that the continuous infusion of low-dose landiolol may be useful as a first-line therapy in cases of acute decompensated heart failure involving rapid atrial fibrillation (23). To the best of our knowledge, the current report is the first to describe the use of landiolol hydrochloride for thyroid storm in a patient with acute decompensated heart failure in the emergency setting.

Summary

The current patient demonstrated marked tachycardia with atrial fibrillation and heart failure associated with a reduced left ventricular function. Even after normalization of the thyroid hormone levels, the patient continued to show marked tachycardia, with no improvements in heart failure. Whereas the administration of bisoprolol fumarate induced hypotension and was not tolerable for the patient, landiolol hydrochloride was useful for controlling the tachycardia and heart failure without causing hemodynamic deterioration.

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

References