Clinical Case Report

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Rapid Improvement of thyroid storm-related hemodynamic collapse by aggressive anti-thyroid therapy including steroid pulse

A case report

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Abstract

Rationale: Heart failure is relatively common in patients with hyperthyroidism, but thyrotoxic cardiomyopathy with poor left ventricular (LV) systolic function is very rare.

Patient concerns: We experienced a representative case of a patient who presented with severe LV dysfunction related to thyroid storm and needed extracorporeal membrane oxygenation (ECMO) temporally.

Diagnosis: Thyrotoxic cardiomyopathy.

Interventions and Outcomes: Aggressive antithyroid therapy, including steroid pulse to hyperthyroidism, leads to the dramatic improvement of cardiac function and she was successfully weaned from ECMO.

Lessons: The most outstanding feature of the current case was the rapid decrease of cardiac injury and improvement of cardiac function by strengthening antithyroid therapy, including steroid pulse, without thyroid hormone level normalization. In thyroid storm, various systemic inflammatory reactions have different time courses and among them, the cardiac phenotype emerges in most striking and critical ways.

Abbreviations: BNP = brain natriuretic peptide, ECMO = extracorporeal membrane oxygenation, fT3 = triiodothyronine, fT4 = free thyroxine, IABP = intra-aortic balloon pump, LVEF = left ventricular ejection fraction, MRI = magnetic resonance imaging, sIL-2R = soluble interleukin-2 receptor, SUV max = maximum standardized uptake value, TSH = thyroid-stimulating hormone, TTE = transthoracic echocardiography.

Keywords: extracorporeal membrane oxygenation, heart failure, hyperthyroidism, steroid pulse, thyrotoxic cardiomyopathy

1. Introduction

Hyperthyroidism is a common metabolic disorder with cardiovascular manifestations. It often causes classical high-output heart diseases because of decreased systemic vascular resistance and increased resting heart rate, left ventricular (LV) contractility, blood volume, and cardiac output.[1,2] However, thyrotoxic cardiomyopathy with severe LV dysfunction is rare. We report the case of a patient who presented with severe LV dysfunction related to thyroid storm and needed extracorporeal membrane oxygenation (ECMO); her condition was significantly improved by aggressive antithyroid therapy, including steroid pulse therapy. The case report conformed to the Declaration of Helsinki and was reviewed and approved by the University of Tokyo Institutional Review Board (2650). Written informed consent was obtained from the subject.

2. Case presentation

A 54-year-old Japanese female with no history of previous disease and no family history was admitted to a hospital because of fever, nausea, and vomiting for 7 days. Her systolic blood pressure was 70 mm Hg with a sinus rhythm of 130 bpm, suggesting a hemodynamic shock state, and appropriate treatment was started immediately after hospitalization. A transthoracic echocardiography (TTE) revealed severely reduced LV ejection fraction (LVEF < 20%) with normal LV size. Coronary angiography showed no organic stenosis, and she was immediately placed on mechanical circulatory support with venoarterial (VA)-ECMO and intra-aortic balloon pump (IABP) under the assessment of severe hemodynamic collapse. Furthermore, her thyroid-stimulating hormone (TSH < 0.01 μIU/mL) levels were severely suppressed, whereas free thyroxine (fT4 3.83 ng/dL) and

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triiodothyronine (fT3 4.58 pg/mL) levels were markedly elevated; thus, therapy with 10 mg of thiamazole was started. On the 6th day after hospitalization, her LV function remained severely impaired even after the normalization of tachycardia, and her circulatory hemodynamics was dependent on VA-ECMO (Fig. 1A). Her electrocardiogram generally showed sinus rhythm with short terms of atrial fibrillation. She was transferred to our hospital for considering implanting a LV-assist device. Laboratory evaluation still showed suppressed TSH and elevated fT4 and fT3 levels (with a high value of anti-TSH receptor antibodies); therefore, we strengthened the antithyroid therapy at the diagnosis of Graves disease, increasing thiamazole to 80 mg and initiating potassium iodide (400 mg/d) and colestyramine (27 g/d) in addition to steroid pulse therapy (1000 mg of methylprednisolone × 3 days). Other laboratory data showed elevated troponin I (12,163 pg/mL) and brain natriuretic peptide (BNP) levels (1303 pg/mL), whereas creatinine kinase levels did not increase consistently during the course. Her ultrasonography demonstrated severely reduced biventricular contraction with little dilation or edematous change. After the 3rd day of strengthening antithyroid therapy, TTE showed that LVEF had improved to 35%, and the troponin I level was significantly decreased (478 pg/mL). On the 6th day, LVEF had improved to within an almost normal level (Fig. 1B). We removed VA-ECMO and IABP 18 days after its implantation. Cardiac magnetic resonance imaging (MRI) showed normal LV contraction with few lesions of myocardial edema and late gadolinium enhancement (Fig. 1C and D), suggesting that the residual myocardial lesion could not be detectable by cardiac MRI. LV biopsy revealed mild lymphocytic infiltration with mild interstitial fibrosis (Fig. 1E and F). After the recovery of heart function, the BNP level was continuously increased, and it took 4 weeks for the level to be decreased to fit in with her recovered systolic function. In addition, a marked increase in the soluble interleukin-2 receptor (sIL-2R) level was observed (peak 6816 U/mL; 6 weeks after hospitalization), which decreased 3 months later (Fig. 2). The gamma glutamyl transpeptidase level (peak 495 U/L, 6 weeks after hospitalization) changed in a manner parallel with the sIL-2R level. 18F-fluorodeoxy glucose positron emission computed tomography demonstrated uptake at the bilateral neck (maximum standardized uptake value [SUV max]: 3.1), mediastinal (SUV max: 2.9), and para-aortic (SUV max: 3.6) lymph nodes (6 weeks after hospitalization) that disappeared 3 months later (Fig. 1G).

3. Discussion

Severe cardiac dysfunction in hyperthyroidism, as observed in the current case, could be presented as low-output heart failure. However, it is a very rare manifestation, and the most effective treatment for this LV dysfunction is suppression of thyroid hormone by antithyroid therapy.[3]

The mechanism about the severe derangement of systolic function in thyrotoxic cardiomyopathy as seen in this case had not been elucidated. The most effective modality of treatment for heart failure is antithyroid therapy, such as propylthiouracil and

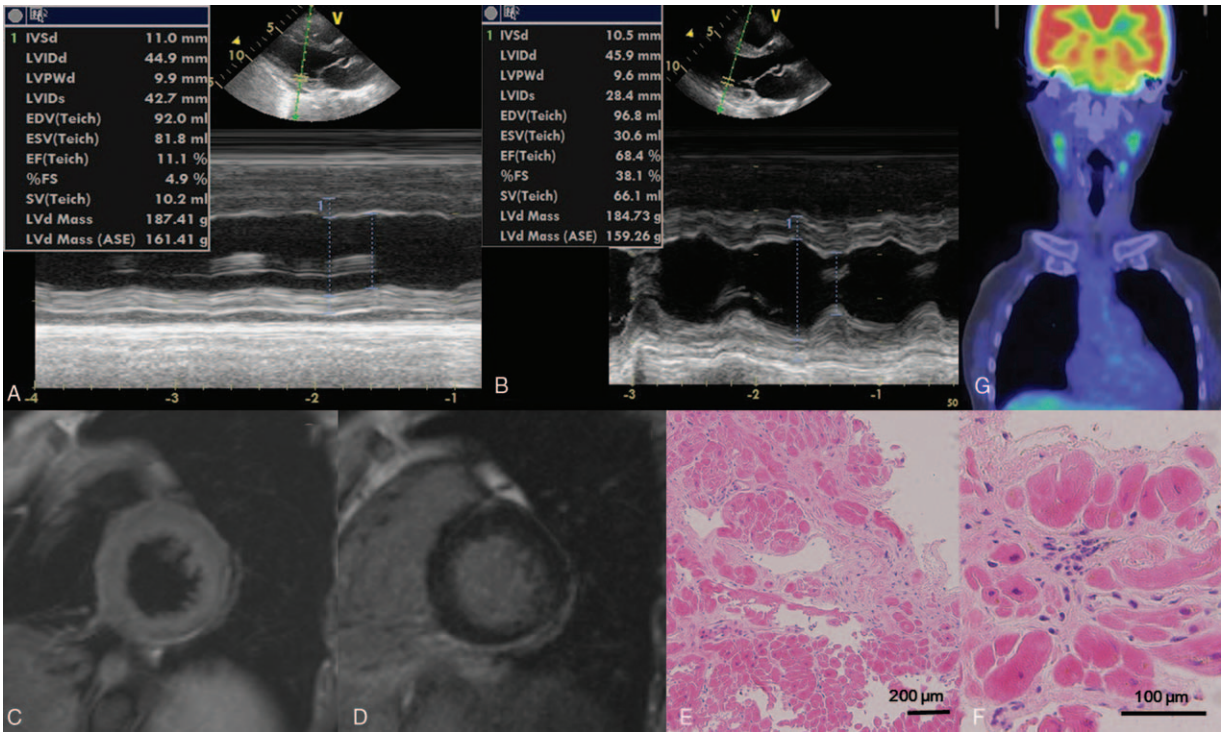

Figure 1. (A) M-mode echocardiographic finding of the left ventricle (LV) on the 6th day after hospitalization. LV ejection fraction (LVEF)* was severely reduced to 11%. LV diameter in diastole was 45 mm, which was within the normal range. (B) M-mode echocardiographic finding of the LV on the 14th day after hospitalization. LVEF was markedly increased up to 63%. (C) T2-weighted image of cardiac magnetic resonance imaging after weaning off of venoarterial-extracorporeal membrane oxygenation (venoarterial-ECMO) (3 weeks after hospitalization). There was no lesion of myocardial edema. (D) Late gadolinium enhancement image after weaning off of venoarterial-ECMO, demonstrating that there were few lesions of high signal intensity in her LV. (E and F) Pathologic finding (hematoxylin eosin staining) extracted from her right ventricle after weaning off of venoarterial-ECMO (4 weeks after hospitalization), demonstrating mild immune cell infiltration (focused in F) with a mild increase in fibrosis with generally maintained cardiomyocyte architecture. (G) 18F-fluorodeoxy glucose positron emission computed tomography performed 6 weeks after hospitalization demonstrating inflammation in the bilateral neck lymph node.

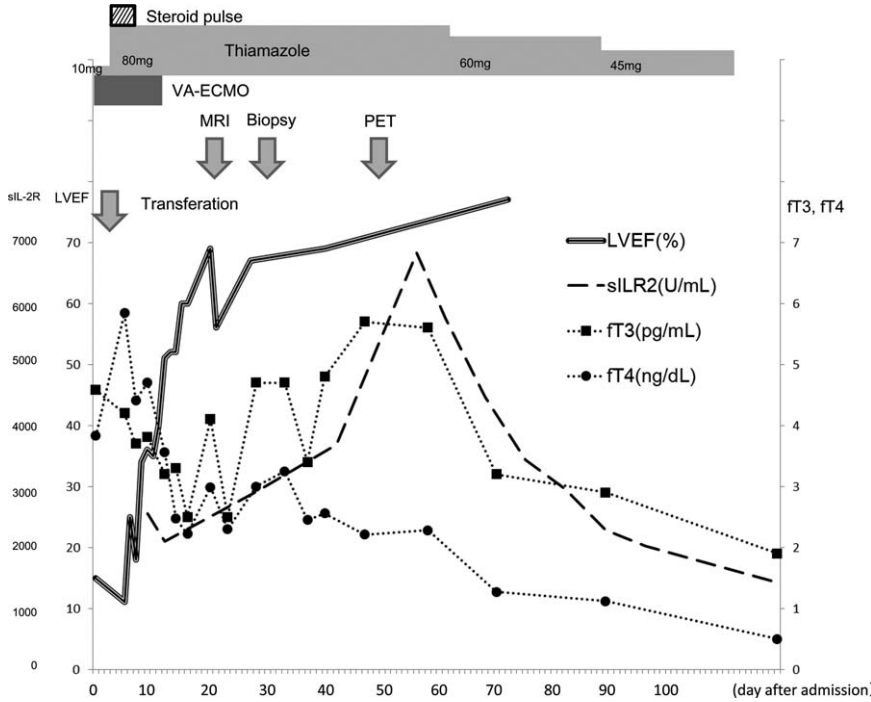

Figure 2. Time course of laboratory data, including left ventricular ejection fraction (LVEF), thyroid function (free thyroxine and triiodothyronine levels), and soluble interleukin-2 receptor (sIL-2R) levels, after hospitalization. On the 10th day, LVEF dramatically increased from 11% to 60%, whereas thyroid function decreased only slightly and did not reach beyond the normal range. In addition, sIL-2R† level continuously increased for approxiamately 3 months after hospitalization. *LVEF = left ventricular ejection fraction, ‡sIL-2R = soluble interleukin-2 receptor.

thiamazole, which correct the primary hemodynamic disturbance.[4] In a study of a series of 7 patients with hyperthyroidism and congestive heart failure, the mean LVEF increased from 28% to 55% after treatment for thyrotoxicosis.[5] There were other similar reports so that it is generally accepted that an appropriate treatment with hyperthyroidism leads to reverse LV contractility.

In contrast, the most outstanding feature of the cardiovascular phenotype in the current case was the rapid decrease of cardiac injury and improvement of cardiac function by strengthening antithyroid therapy, including steroid pulse, without thyroid hormone level normalization. The discrepancy between the time course of thyroid hormone level normalization and cardiac function strongly suggested that this cardiac derangement was not derived from the direct effect of the thyroid hormone but was caused by other contributions such as inflammatory reactions. Several reports demonstrated that myocardial derangement was induced by autoimmune mechanism in the setting of autoimmune thyroid dysfunction.[6,7] The response of myocardial lesion to therapy in this case was dramatically demonstrated, which might have been derived from an anti-inflammatory effect of steroid pulse therapy. On the other hand, extracardiac inflammatory reactions, such as marked sIL-2R level increase, liver dysfunction, and lymph node swelling, were prolonged for several months after the initiation of therapy.[8] This multiple organ dysfunction might be explained by the autoimmune disorder related to Graves disease.[9] However, the mechanism of different time course between each phenotype has not been clarified.[10] In any event, various systemic inflammatory reactions have different time courses and among them, the cardiac phenotype emerges in most striking and critical ways in a thyroid storm. Therefore, rapid and sufficient pharmacological interventions seem to be the critical issue.

In conclusion, thyrotoxic cardiomyopathy may cause a very severe LV dysfunction that needs an ECMO like this case. A prompt assessment of thyroid hormone status in patients with clinical manifestations of cardiomyopathy of unknown etiology is very important. The key for reversible LV dysfunction is the earlier treatment with hyperthyroidism.

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