Acta Cardiol Sin 2014;30:574–577
Case Report
doi: 10.6515/ACS20131218A

A Case of Takotsubo Cardiomyopathy Precipitated by Thyroid Storm and Diabetic Ketoacidosis with Poor Prognosis

Wei-Tsung Wu,[1] Po-Chao Hsu,[1,2,3] Hung-Ling Huang,[1] Ying-Chih Chen[1] and Shun-Ching Chien[4]

Takotsubo cardiomyopathy (TCMP) is known as stress cardiomyopathy, and long-term prognosis is generally excellent if recovering from an acute stage. Both thyroid storm and diabetic ketoacidosis (DKA) are reported to be rare causes of TCMP. However, there are no studies discussing TCMP as induced by a combination of thyroid storm and DKA, and the prognosis is unknown. Herein we report an 81-year-old female with type-2 diabetes mellitus initially presenting with palpitation, chest tightness, and gastrointestinal symptoms. She was further diagnosed as TCMP after echocardiogram and coronary angiography, and DKA was confirmed later. However, the patient's general condition didn't improve under proper treatment. Thereafter, thyroid storm was discovered fortuitously. Despite appropriate treatment, the patient finally expired due to acute respiratory distress syndrome progression. This rare case reminds us that despite TCMP being a transient cardiomyopathy with good prognosis, physicians should survey the possible underlying disease cautiously to avoid catastrophic clinical outcome.

Key Words: Acute respiratory distress syndrome • Diabetic ketoacidosis • Stress cardiomyopathy • Takotsubo cardiomyopathy • Thyroid storm

INTRODUCTION

Takotsubo cardiomyopathy (TCMP) is also recognized as stress cardiomyopathy, broken-heart syndrome, or apical ballooning syndrome, which is a form of reversible, transient systolic dysfunction over the left ventricle.[1,2] Generally, TCMP can be triggered by physical or emotional stress.[3] Both thyroid storm and diabetic ketoacidosis (DKA) are rare causes of TCMP.[4-7] Herein, we report a rare case of TCMP precipitated by thyroid storm and DKA simultaneously, finally leading to acute respiratory distress syndrome (ARDS) formation and catastrophic clinical outcome.

CASE REPORT

We report the case of a 81-year-old female with a case of type-2 diabetes mellitus (DM), hypertension and an old cerebral vascular accident. This time, she suffered from palpitation, chest tightness, and abdominal fullness in combination with vomiting and diarrhea, and was brought to our emergency department (ED) for assistance. The patient also complained of anxiety and excessive sweating in the last three months.

Upon arrival at our ED, the patient's vital signs were pulse rate 146 beats/min, respiratory rate 22/min, blood pressure 110/60 mmHg, and body temperature 38.5 °C. A subsequent electrocardiogram (ECG) revealed sinus

Received: July 28, 2013 Accepted: December 18, 2013
[1]Department of Internal Medicine, Kaohsiung Medical University Hospital; [2]Division of Cardiology, Department of Internal Medicine, Kaohsiung Medical University Hospital; [3]Graduate Institute of Medicine, School of Medicine, Kaohsiung Medical University; [4]Department of Emergency, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan.
Address correspondence and reprint requests to: Dr. Shun-Ching Chien, Department of Emergency Medicine, Kaohsiung Medical University Hospital, No. 100, Tzyou 1st Road, Kaohsiung 80708, Taiwan. Tel: 886-7-235-7227; Fax: 886-7-535-3978; E-mail: 990325kmuh@gmail.com

tachycardia with ST elevation over V_2-V_4 (Figure 1A). Chest X-ray (CXR) showed cardiomegaly and pulmonary congestion (Figure 1B). Because ST elevation myocardial infarction was strongly suspected, emergency coronary angiography was performed but revealed a virtually normal finding (Figures 2A and B). In addition, echocardiography revealed impaired left ventricular systolic function (ejection fraction: 35.4%) with apical hypokinesia to akinesia, which was compatible with apical ballooning sign of TCMP (Figures 2C and D).

Initial laboratory data revealed white blood cell count: 17100/μL, C-reactive protein (CRP): 24 mg/L, creatinine: 2.14 mg/dL, blood sugar: 566 mg/dL, blood osmolarity: 339 mOsm/kg, blood ketone 2.2 mmol/L, and elevated cardiac biomarkers (creatine kinase-MB: 17.5 ng/mL; troponin 8.75 ng/mL). Arterial blood gas showed high anion gap metabolic acidosis (PH: 7.16, HCO_3: 8.3 mmol/L) and urinalysis revealed glucosuria and strongly positive for urine acetone. Under the impression of DKA, insulin and fluid replacement were given to correct severe metabolic acidosis. However, the patient still suffered from progressive dyspnea and was then intubated due to impending respiratory failure. In addition, despite the gradual correction of hyperglycemia and metabolic acidosis, the patient's consciousness level became disturbed in combination with persistent hyperthermia, dyspnea, and anuria. We further checked the thyroid function and the data revealed elevated T4 level (6.14 ng/dl) but thyroid stimulating hormone (TSH) was below the detectable limit (< 0.03 uU/mL). Thyroperoxidase antibodies, thyroglobulin antibodies, and anti-microsomal antibodies were negative, while TSH antibodies were positive. Thyroid storm was highly suspected in part due to the Burch-Wartofsky-Score (60/140), and the thyroid storm diagnostic criteria of the Japan Thyroid Association was also satisfied. Therefore, the patient received intravenous hydrocortisone, oral propylthiouracil, potassium iodide and propranolol for treatment of thyroid storm. Propranolol was later discontinued due to unstable patient hemodynamic. The patient was then transferred to our intensive care unit (ICU) for further care.

During her ICU stay, we performed continuous veno-venous hemofiltration (CVVH) for anuria, metabolic acidosis and unstable hemodynamic. Vasopressor was given for shock status, and empirical antibiotic with ceftriaxone was also given for possible infection control. After 3 days of treatment, the patient's hemodynamics stabilized and we successfully weaned her off vasopressor and CVVH. Follow-up echocardiography revealed

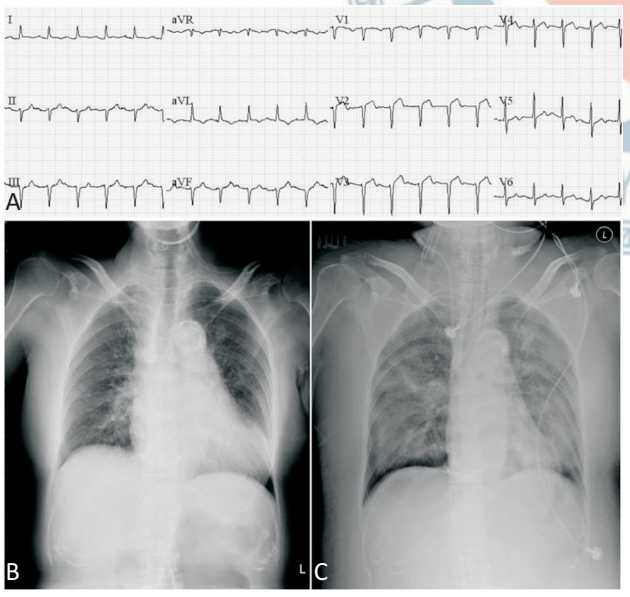

Figure 1. *(A) Electrocardiogram revealed sinus tachycardia with ST elevation over V2-V4. (B) Initial chest X-ray (CXR) showed cardiomegaly and pulmonary congestion. (C) CXR rapidly progressed to bilateral diffuse infiltration and patch after recovery of heart function, which is compatible with the diagnosis of adult respiratory distress syndrome.*

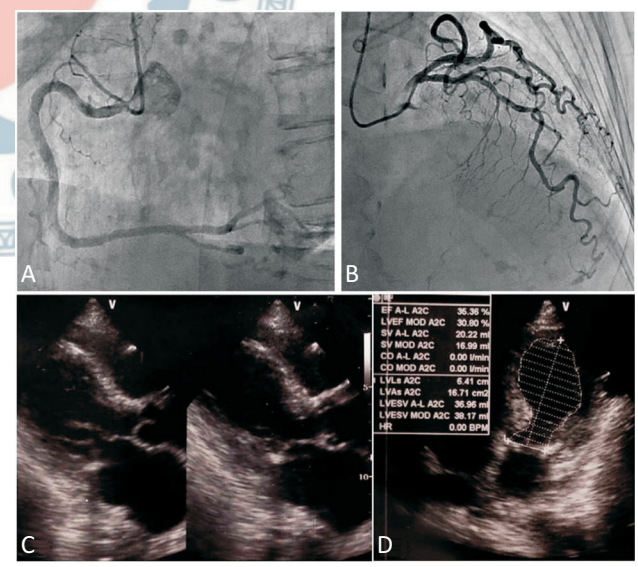

Figure 2. *Emergent coronary angiography showed nearly normal finding of right (A) and left coronary arteries (B). (C) Echocardiography revealed apical hypokinesia to akinesia, which was compatible with apical ballooning sign of takotsubo cardiomyopathy. (D) Left ventricular ejection fraction (LVEF) calculated by Simpson's method showed impaired systolic function (LVEF: 35.4%).*

improvement of apical ballooning sign and ejection fraction (59.2%). Laboratory data also revealed decreased free T4 level (2.8 ng/dl) and correction of metabolic acidosis. However, the patient's consciousness still deteriorated over time but computed tomography of brain did not reveal any remarkable finding.

Although the patient's fever pattern gradually subsided under intensive medical treatment and there was no obvious clinical evidence of the hospital-acquired pneumonia during treatment, CXR rapidly progressed to bilateral diffuse infiltration and patch (Figure 1C), and arterial blood gas revealed progression of hypoxemia (PaO_2/FiO_2 ratio < 200 mmHg) even under titrating up the setting of the mechanical ventilator. With a preliminary diagnosis of ARDS, we adjusted the ventilator setting to low tidal volume and high positive end-expiratory pressure. However, desaturation was still noted even under FiO_2 100% supply. The patient finally expired on the 8th day after admission.

DISCUSSION

TCMP was first described in 1991 in Japan, characterized by transient left ventricular dysfunction, electrocardiographic changes of ST segment elevation, and T wave inversion with elevation of cardiac enzymes that can mimic acute myocardial infarction.[1,2] However, TCMP frequently presents without obstructive coronary artery disease and is mainly seen in postmenopausal women. Several possible mechanisms regarding the pathophysiology of TCMP have been advocated, including myocardial stunning caused by catecholamine-mediated cardiotoxity, coronary vasospasm, and microvascular dysfunction, which lead to left ventricular outflow obstruction. Associated elevations in plasma catecholamines have been shown to induce reversible cardiomyopathy, and a higher density of left ventricular apical adrenoreceptors leads to a greater sympathetic response in this region and may explain focal dyskinesia and characteristic ballooning.[1] TCMP can be triggered by severe emotional or physiological stress such as an unexpected death in the family, a quarrel, exhausting work, and severe medical illness.[3]

Some cases of TCMP associated with hyperthyroidism have been reported,[4,5] and the causes of hyperthyroidism including Grave's disease, exogenous levothyroxine intake, Hashimoto's thyroiditis and toxic multinodular goiter. Biologically, hyperthyroidism mimics adrenergic excess status, and pathologically high levels of thyroid hormone promote exaggerated chronotropic and contractile responses to catecholamines,[4] which enhance myocardial sensitivity to sympathetic and vagal innervation and increased cAMP responses from b-adrenergic receptors in cardiac myocytes.[8] This indicates synergistic action with adrenergic hormones under the state of excess catecholamine will make the hyperthyroidism trigger TCMP attack.

Diabetic mellitus as well as thyroid disease are currently the most common endocrine diseases afflicting the general populace today, and have been known to have mutual influence and a complex interdependent relationship. Hyperthyroidism has been known to worsen the hyperglycemia status via several mechanisms, including but not limited to increased insulin degeneration rate, enhanced inactive insulin precursors level, defective proinsulin processing, and increased intestinal absorption of glucose. Therefore, hyperthyroidism might precipitate DKA in diabetes patients.[9] In addition, DKA has also been reported in the literature to be a rare cause of TCMP.[6,7] Despite the possible mechanism not being clearly clarified, Lin et al. reported that DKA results from relative or absolute insulin deficiency combined with counter-regulatory hormone excess, such as catecholamine excesses.[6] Nanda et al. also stated that in times of stress, tissues with high capacity for aerobic metabolism, like myocardium, can preferentially change their metabolic substrate to ketones, and the myocyte has a decreased ability to metabolize glucose and free fatty acids in TCMP.[7]

To our knowledge, our case should be the first case report of TCMP precipitated by thyroid storm and DKA simultaneously. As we mentioned previously, DM and thyroid disease have been known to have mutual influence and may aggravate each other, and therefore induce TCMP. Furthermore, although long-term prognosis is normally excellent in patients of TCMP, our case finally led to ARDS formation and caused catastrophic outcome. No studies have mentioned the association between thyroid storm and ARDS; however, some rare literature discussed the association between DKA and ARDS formation.[10] Excessive crystalloid infusion favors

the development of pulmonary edema. Patients with an increased alveolar to arterial oxygen gradient and patients with pulmonary rales may have increased risk for ARDS, especially in those patients with impaired left ventricular systolic function such as TCMP. In addition, we did not conclude that hospital-acquired pneumonia was the cause of ARDS formation because of the relatively low CRP level in our case, and no pathogen was identified from blood and sputum cultures.

In conclusion, TCMP precipitated by thyroid storm and DKA is extremely rare and could lead to poor prognosis. Physicians should survey the possible underlying disease cautiously in patients with TCMP to avoid the undesired and catastrophic clinical outcome.

CONFLICT OF INTERESTS

None declared.

REFERENCES

1. Gianni M, Dentali F, Grandi AM, et al. Apical ballooning syndrome or takotsubo cardiomyopathy: a systematic review. *Eur Heart J* 2006;27:1523-9.
2. Prasad A, Lerman A, Rihal CS. Apical ballooning syndrome (Tako-Tsubo or stress cardiomyopathy): a mimic of acute myocardial infarction. *Am Heart J* 2008;155:408-17.
3. Sharkey SW, Lesser JR, Zenovich AG, et al. Acute and reversible cardiomyopathy provoked by stress in women from the United States. *Circulation* 2005;111:472-9.
4. Rossor AM, Pearce SH, Adams PC. Left ventricular apical ballooning (takotsubo cardiomyopathy) in thyrotoxicosis. *Thyroid* 2007; 17:181-2.
5. Alidjan F, Ezzhati M, Bruggeling W, et al. Takotsubo cardiomyopathy precipitated by thyrotoxicosis. *Thyroid* 2010;20:1427-8.
6. Lin C, Chen C, Tsai M. Ampulla cardiomyopathy in a patient with diabetic ketoacidosis: a case report. *J Intern Med Taiwan* 2007; 18:120-4.
7. Nanda S, Longo S, Bhatt SP, et al. Stress cardiomyopathy – a unique presentation of diabetic ketoacidosis. *Ann Clin Biochem* 2009;46:257-60.
8. Silva JE, Bianco SD. Thyroid-adrenergic interactions: physiological and clinical implications. *Thyroid* 2008;18:157-65.
9. Sola E, Morillas C, Garzón S, et al. Association between diabetic ketoacidosis and thyrotoxicosis. *Acta Diabetol* 2002;39:235-7.
10. Kumar B, Ruff S. Adult respiratory distress syndrome in diabetic ketoacidosis. *Intensive Care Med* 1984;10:269.