CASE REPORT

A CASE OF TAKOTSUBO SYNDROME PRECIPITATED BY DIABETIC KETOACIDOSIS

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Takotsubo syndrome (TTS), Takotsubo cardiomyopathy, or stress-induced cardiomyopathy are interchangeable terms characterized by transient left ventricular systolic dysfunction, electrocardiographic changes, and cardiac biomarker elevation similar to acute coronary syndrome (ACS), without the presence of obstructive epicardial coronary artery disease. It predominantly affects postmenopausal females and manifests in the presence of stressful triggers such as severe physical or emotional stress, natural disasters, unexpected death of relatives, acute medical illnesses, etc. TTS was initially considered to be a benign condition however recent studies have shown that it may be associated with complications and mortality similar to ACS. Rare reports of TTS triggered by diabetic ketoacidosis (DKA) have been published. Herein we describe a case of an elderly female with a history of type II diabetes mellitus (DM) who was admitted with DKA and subsequently developed TTS that resolved after treatment of DKA and implementation of heart failure therapies.

Keywords: Takotsubo syndrome; Cardiomyopathy; ACS; DKA

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INTRODUCTION

TCM was initially described in Japan.[1] Since its recognition and better understanding of the disease, its prevalence has increased in the US. Approximately, 90% of the cases of the patients with TCM are females. The pathophysiology of TCM is still questionable. However, it has been proposed that TCM is a result of excess sympathetic stimulation in addition to catecholamine over-secretion.[2] Several studies with sample sizes greater than 100 have reported that the prevalence of diabetes in patients with TCM ranges from 1.6% to 25.5% with a mean of 16.8%.[3] It has been proposed that DM has a protective effect on TCM, due to autonomic dysfunction, adrenal hyposecretion and hyperglycaemic suppression of vascular vasodilators. This is supported by the last International Takotsubo Registry report (N=1750), where 89.8% were females, with overall 46.8% having neurological or psychiatric disorders and 14.2% with DM.[1] Contrary to this there have been reports showing no difference in TCM amongst diabetes vs non-diabetes. Here, we present an interesting case of TCM in a patient with diabetes where DKA was the trigger.

CASE PRESENTATION

A 70-year-old woman with a history of non-compliance, DM, hypertension, and dyslipidaemia presented to the emergency department with intermittent weakness, dizziness, polyuria, and polydipsia for a few days. Vital signs were within normal limits except for a heart rate of 108 beats per minute; physical examination showed dry mucous membranes. Laboratory data revealed the following: glucose 846 mg/dL, haemoglobin A1c 31.1%, anion gap 12.7 mEq/L, lactic acid 5.4 mmol/L, potassium 3.2 mEq/L, sodium 131 mEq/L, creatinine 2.76 mg/dL, blood urea nitrogen 74 mg/dL. Arterial blood gases showed a pH of 7.46, pCO2 29.8 mmHg, pO2 85.6 mmHg, and HCO3 3.3 mEq/L. Urinalysis showed glucosuria and ketonuria. Brain natriuretic peptide was 18053 pg/mL and high-sensitivity troponin-I 4004.3 ng/mL. Initial electrocardiogram (ECG) showed sinus tachycardia with ST and T changes not meeting the ST-elevation myocardial infarction (STEMI) criteria (Figure 1). Initial diagnoses of DKA, non-STEMI (NSTEMI), and acute kidney injury (AKI) were made. The patient was started on intravenous insulin, normal saline, atorvastatin, metoprolol succinate, heparin, aspirin, and clopidogrel and admitted to the intensive care unit (ICU). Repeat ECG showed dynamic changes with ST elevation concerning STEMI. Cardiac catheterization revealed angiographically normal epicardial coronary arteries (Figure 1, Panel X). Left ventriculography showed basal hyperkinesis and apical hypokinesis concerning TTS (Figure 1, Panel X). Transthoracic echocardiogram showed severe LV dysfunction with an ejection fraction of 25-30% (Figure 1, Panel X), basal hyperkinesis, and

apical akinesis consistent with TTS. She was transferred back to the ICU and overnight had brief runs of torsades and atrial fibrillation with rapid ventricular response that was treated with amiodarone and diltiazem infusions. Once the heart rate was controlled and her blood pressure was stable, she was transitioned to oral metoprolol succinate, spironolactone, and sacubitril-valsartan. After her anion gap normalized, the insulin infusion was stopped and she was transitioned to subcutaneous insulin with the addition of dapagliflozin. After spending 5 days in the hospital, she was discharged on guideline-directed quadruple therapy for heart failure with reduced ejection fraction. The patient was seen in the outpatient cardiology clinic three weeks later. A repeat echocardiogram done in the clinic showed a recovered LV ejection fraction between 60–65% (Figure 1, Panel X).

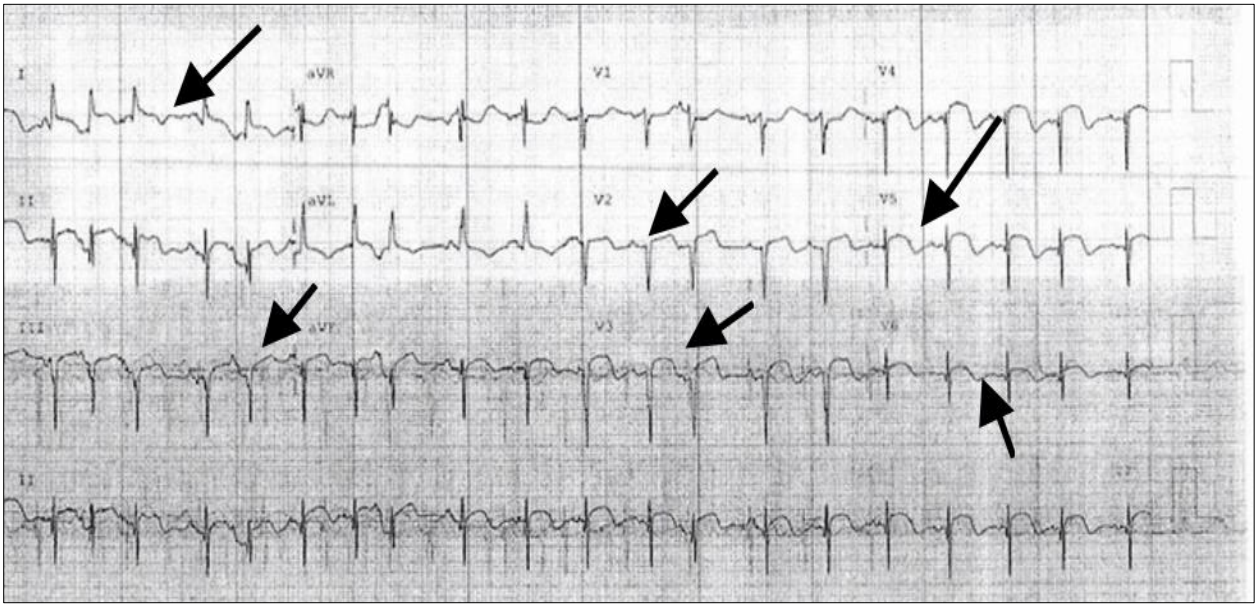

Figure-1: Initial EKG showed sinus tachycardia (heart rate of 115 beats per minute) with ST elevations in multiple leads (I, III, V2, V3, V5) suggestive of left ventricular hypertrophy

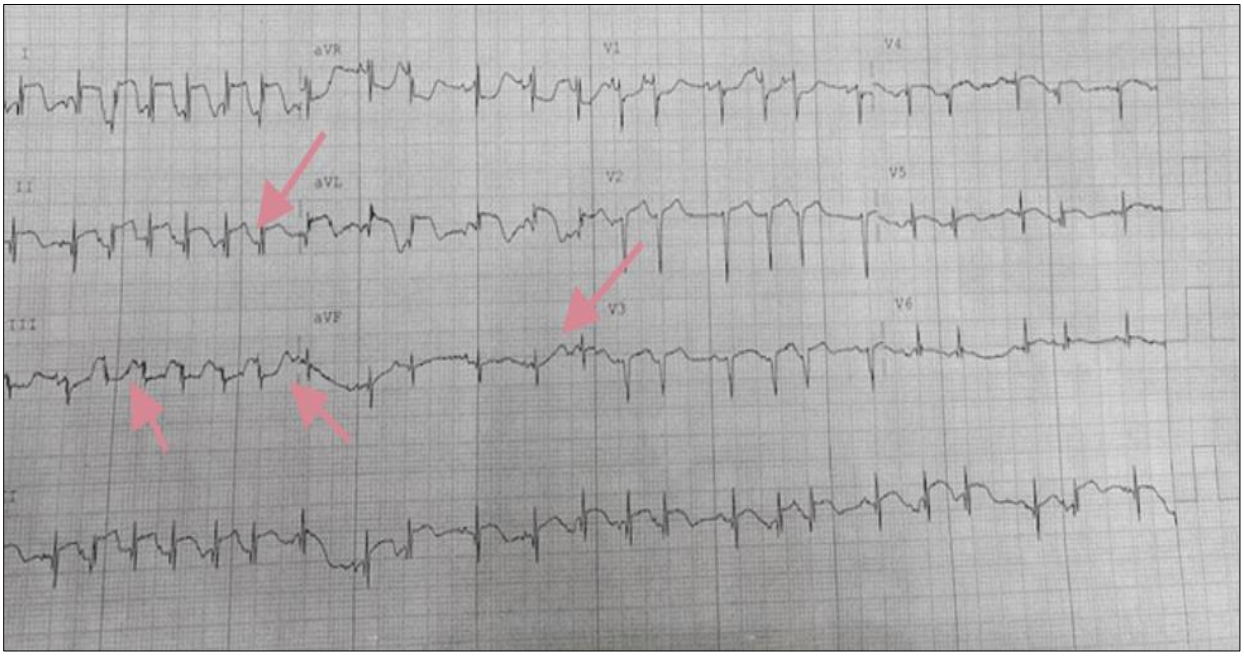

Figure-2: The second EKG showed ST elevation in the inferior leads (II, III, avF) concerning for myocardial infarction

Figure-3: Panels A-C: Left heart catheterization showed normal findings of (a)left main coronary, (a)left anterior descending, (a)left circumflex, and (b) right coronary artery.
Panels D-E: Left ventriculography showed apical hypokinesis and basal hyperkinesis of the left ventricle.
Panels F-G: Initial echocardiogram showed severely reduced left ventricular ejection fraction of 25-30% along with basal hyperkinesis and apical hypokinesis.
Follow-up echocardiogram showed normal left ventricular systolic function with a normalized ejection fraction between 60-65%

DISCUSSION

Initially reported in Japan in 1991, the word "Takotsubo" comes from the name of a pot used by the Japanese to trap octopuses. This shape resembles the shape of the left ventricle (LV) in cardiac imaging. TTS is more common in women than in men and typically occurs in individuals over the age of 50.[1,4] TTS is most prevalent in postmenopausal Caucasian women. Several mechanisms have been proposed for the development of TTS and include coronary vasospasm, microvascular dysfunction verified by abnormal Thrombolysis in Myocardial Infarction (TIMI) Frame Count or TIMI perfusion grade, neurogenic stunned myocardium with underlying enhanced sympathetic activity, supraphysiologic levels of circulating plasma catecholamines and neuropeptides (norepinephrine, epinephrine, and dopamine), inflammation, and oestrogen deficiency.[5–8] Inflammatory aetiology is supported by the presence of myocardial oedema, necrosis, and fibrosis on Cardiac magnetic resonance (CMR) imaging as well as the presence of focal (patchy) late gadolinium enhancement in about 10% of the patients.[2,9] Concomitant cases of myocarditis, pericarditis, or autoimmune conditions such as systemic lupus erythematosus have also been reported.[10] Risk factor profiles of TTS are similar to coronary artery disease although some reports suggest that DM may exert a possible protective mechanism however this remains controversial.[11,12]

Stress due to medical conditions such as psychological and pulmonary diseases, and malignancies has been known to cause 36% of cases according to the International Takotsubo Registry Study.[1] Few studies of DKA-induced TTS have been reported.[13] With the development of DKA, there is a rise in ketones, catecholamines, cortisol, glucagon, and growth hormones. The kidneys try to compensate for the rise in ketones with the resultant loss of electrolytes (potassium, sodium, magnesium, and phosphate) and the development of acute kidney injury. These electrolytes are essential for normal cell function. Many cells are affected including the cardiomyocytes leading to abnormal myocardial contractility. Excess catecholamines due to DKA have the most effect on the apex of the heart due to the high presence of beta-1 adrenoceptors.[14] Beta-1 adrenoceptors are activated by catecholamines. The combination of electrolyte loss and excess catecholamines secondary to DKA contributes to apical hypokinesis and reduced myocardial contractility. In our case, the patient has had DM for years but recently had been noncompliant with diabetic medications that contributed to the development of DKA.

It is estimated that the prevalence of TTS is 1-2% in patients presenting with ACS.[15] ECG changes in TTS typically have temporal evolution with four distinct stages.[15] Our patient presented with notably elevated troponin levels along with ST-segment elevation in the inferior leads on ECG. Left ventricular apical hypokinesis was noted on both left ventriculography and transthoracic echocardiogram with normal coronary arteries confirming the diagnosis of TTS. She was treated medically with remarkable recovery. Medication compliance was stressed. Insulin has been shown to reduce the inotropic effect of catecholamines on cardiomyocytes.[14] Administration of IV fluids, electrolytes, and insulin is expected to lead to the resolution of DKA and improvement in TTS. Supportive treatment with medications along with the resolution of DKA led to the resolution of TTS in this patient with repeat transthoracic echocardiogram showing recovered LV ejection fraction.

CONCLUSION

A possible association between DKA and TTS exists. Excess catecholamine release along with electrolyte loss secondary to DKA leads to TTS. Prompt recognition and treatment lead to favourable prognoses and long-term outcomes. Further investigation into the relationship between DKA and TTS is necessary to better understand the correlation between these two conditions.

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Ethical approval: Not required

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