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Case Report

Cardiac arrest from acute myocardial infarction complicated with sodium-glucose cotransporter 2 inhibitor-associated ketoacidosis

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ABSTRACT

Euglycemic diabetic ketoacidosis (DKA) has been recognized as a potentially fatal complication related to sodium-glucose cotransporter 2 (SGLT2) inhibitors. Herein, we report a patient of out-of-hospital cardiac arrest, with an initial cardiac rhythm of ventricular fibrillation, who was subsequently diagnosed with acute myocardial infarction, complicated with SGLT2 inhibitor-associated euglycemic DKA. The patient survived and achieved nearly full functional recovery. This report calls for increased attention to SGLT2 inhibitors' fatal complications, as well as their proper use.

<**Learning objective:** Euglycemic diabetic ketoacidosis could develop in patients using sodium-glucose cotransporter 2 inhibitors. It is a potentially lethal complication and needs more attention. Physicians who prescribe this class of drugs should be aware of this complication. Meanwhile, research to elucidate patient characteristics that are more susceptible to this complication is urgently awaited.>

Introduction

Sodium-glucose cotransporter-2 (SGLT2) inhibitors are a new class of antidiabetic drug that have pleiotropic effects including improving cardiovascular outcomes [1]. Medicines of this class are known to have several adverse effects, including euglycemic diabetic ketoacidosis (DKA), which has been reported increasingly [2]. Here, we report a case of SGLT2 inhibitor-associated euglycemic DKA that was complicated with cardiac arrest from acute myocardial infarction.

Case report

A 49-year-old Asian man with a 1-year history of type 2 diabetes mellitus and vasospastic angina, whose body mass index was 22.1 kg/m^2, suddenly lost consciousness while sightseeing, shortly after he complained of nausea. An automated external defibrillator was initiated 5 min later, without bystander cardiopulmonary resuscitation. On the basis of initial cardiac rhythm of ventricular fibrillation, the automated external defibrillator delivered 2 shocks. The emergency medical service arrived and started basic life support, and delivered 4 shocks. Return of spontaneous circulation was achieved after a total resuscitation time of 16 min. He was rushed to the emergency department (ED) of our hospital while unconscious.

Upon arrival at the ED, his Glasgow coma scale was E1V2M2. His blood pressure was 136/90 mmHg and heart rate was 85 beats/min. His respiration rate was 20 breaths/min, and peripheral oxygen saturation was 100% on 100% oxygen delivery. His initial 12-lead electrocardiograms showed ST-segment elevation in precordial leads, I, and aVL and reciprocal ST-segment depression in III and aVF (Fig. 1A). A transthoracic echocardiography demonstrated hypokinesis of basal to apical left ventricular (LV) anteroseptal wall. We, therefore, diagnosed him as having acute anteroseptal myocardial infarction. After intubation and a brain computed tomography ruling out an intracranial event, we initiated targeted temperature (34 °C) management (TTM). Emergency coronary angiography revealed a subtotal stenosis in proximal left anterior descending (LAD) artery under nitrate administration (Fig. 1B), which was most likely to be organic stenosis. We did not utilize intravascular imaging modalities, in

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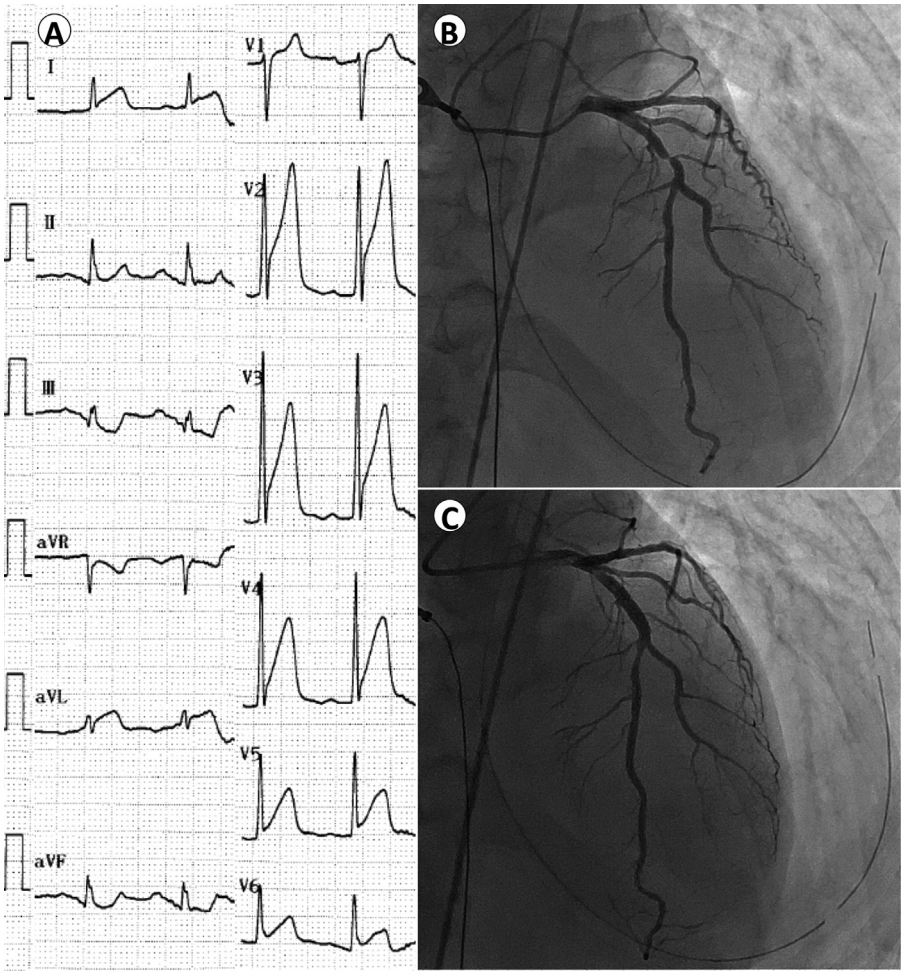

Fig. 1. Twelve-lead electrocardiograms on admission, and angiographic findings. The initial 12-lead electrocardiograms showed ST-segment elevation in V1–V6, I, and aVL, and reciprocal ST-segment depression in III and aVF (A) emergency coronary angiography revealed a subtotal occlusion of the proximal left anterior descending artery (B), which was then successfully stented (C).

order to achieve early revascularization to minimize the influence of hypoxic-ischemic encephalopathy. We subsequently performed percutaneous coronary intervention (PCI) successfully using an everolimus-eluting stent with a door-to-balloon time of 44 min, and gained good angiographic results with a Thrombolysis In Myocardial Infarction grade 3 flow (Fig. 1C). After the procedure, the patient was transferred to the intensive care unit (ICU), with 34 °C TTM being continued for 24 h.

In the first 24 h in the ICU, despite the fact that his blood pressure was maintained well without using catecholamine, and his lactate level was constantly below 2.0 mmol/L, the patient developed a high anion gap metabolic acidosis (Fig. 2A). The urinalysis showed that ketone was 3+, and other laboratory data 10 h after PCI are depicted in Table 1. We were informed that he had been taking aspirin 100 mg daily, isosorbide mononitrate 20 mg twice a day, nicorandil 5 mg 3 times a day, benidipine 4 mg twice a day, amlodipine 5 mg daily, pitavastatin 1 mg daily, metformin 500 mg 3 times a day, miglitol 50 mg 3 times a day, linagliptin 5 mg daily, and using isosorbide mononitrate 40 mg tape daily. With the evidence of ketonuria, ketonemia, the relatively low blood glucose level in spite of the severe ketoacidosis, and the fact that the patient was taking ipragliflozin 50 mg daily, an SGLT2 inhibitor, we concluded that he was experiencing SGLT2 inhibitor-associated euglycemic DKA, and started to correct it by 8.4% sodium bicarbonate. We did not initiate hypoglycemic therapy during the first 24 h because the blood glucose level was constantly less than 180 mg/dL (Fig. 2A). Shortly after the discontinuation of sodium bicarbonate on the 24th hour, the acidosis worsened temporarily, but improved favorably by extracellular fluid replacement solely (Fig. 2B). The creatine kinase (CK)-MB level declined with a peak level of 83 U/L 24 h after PCI, at which point we started rewarming. He was able to respond to simple verbal orders on post-PCI day 2, and was extubated 70 h after PCI, on post-PCI day 3. He had weakness in all extremities and hoarseness, but no disorientation or dysphagia. On post-PCI day 4, with his white blood cell count of 12,000/μL, and C-reactive protein level of 23.18 mg/dL, representing delayed inflammation in spite of aggressive antibiotic treatment with piperacillin–tazobactam, and vancomycin, he underwent a contrast computed tomography, which revealed a hepatic subcapsular hematoma in the caudate lobe caused by chest compression during cardiopulmonary resuscitation. This also explained the elevation of liver enzymes, as well as the discrepancy between CK and CK-MB (Table 1).

A transthoracic echocardiography on post-PCI day 4 demonstrated increased echogenicity and mild hypokinesis of mid to apical LV anteroseptal wall, an LV ejection fraction of 64.0% (modified Simpson's method), but neither significant valvular disease nor pulmonary hypertension.

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