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A case of refractory ventricular fibrillation after caffeine poisoning successfully treated by supportive care

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ABSTRACT

Caffeine (1,3,7-trimethylxantine), a structural analog of adenosine, is widely used as a central nervous system stimulant in beverages and drugs. Caffeine overdose induces hypokalemia, fatal ventricular fibrillation, and cardiac arrest, resulting in death. We describe a case of caffeine overdose that presented with refractory ventricular fibrillation that was treated with supportive care because invasive care for severely ill patients was limited due to the COVID-19 pandemic. A 20-year-old woman with no underlying medical history ingested 90,200-mg caffeine tablets (total dose 18 g) in a suicide attempt. She was transported to the emergency department 45 min after ingestion with dizziness, palpitations, nausea, and vomiting. She developed cardiac arrest 80 min after ingesting the caffeine, with refractory ventricular tachycardia that recurred for about 2.5 h. Advanced life support including defibrillation was started immediately and we gave intravenous Intralipid emulsion, potassium chloride, amiodarone, and esmolol, without hemodialysis or extracorporeal membrane oxygenation (ECMO). The ventricular fibrillation was stopped 4 h after ingestion. As supportive care, mechanical ventilation, sedatives, and neuromuscular blockade were continued until 12 h after ingestion. Although she suffered from prolonged, refractory ventricular tachycardia, she recovered without complications. This case report describes the clinical course of severe caffeine intoxication without an active elimination method, such as hemodialysis or ECMO and explores the treatment of caffeine intoxication with a literature review.

1. Introduction

Acute caffeine poisoning can result in various ways, from the regular consumption of coffee or energy drinks to intentional poisoning with caffeine pills. Patients taking a potentially lethal dose of caffeine (≥ 10 g) have been successfully treated with hemodialysis, hemoperfusion, or extracorporeal circulation [1–3]. However, in a medical environment where hemodialysis or perfusion is impossible due to limited medical resources, supportive treatment is the only option for critical patients. We describe a case of caffeine overdose that presented with refractory ventricular fibrillation (V. fib) with supportive care in a situation where invasive care for severely ill patients was limited due to the COVID-19 pandemic.

2. Case presentation

A 20-year-old woman with no psychiatric or underlying medical history ingested 90,200-mg caffeine tablets (total dose 18 g, 332 mg/kg) in a suicide attempt. She was transported to the emergency department 45 min after ingestion, complaining of dizziness, palpitations, nausea, and vomiting in the ambulance.

On arrival at the emergency department, the Glasgow Coma Scale was 14 (E4V4M6) with a blood pressure of 112/70 mmHg, oxygen saturation of 97% on ambient air, and an electrocardiogram showed sinus tachycardia at a rate of 139 beats/minute. An arterial blood gas analysis showed mild metabolic acidosis (bicarbonate 17.3 mmol/L) and other laboratory data showed hypokalemia (potassium 2.2 mmol/L) and hypophosphatemia (phosphorus 1.0 mmol/L). Serum creatinine (0.64 mg/dL), aspartate aminotransferase (AST) (14 IU/L), alanine aminotransferase (ALT) (7 IU/L), creatine kinase (103 IU/L), and troponin I (<

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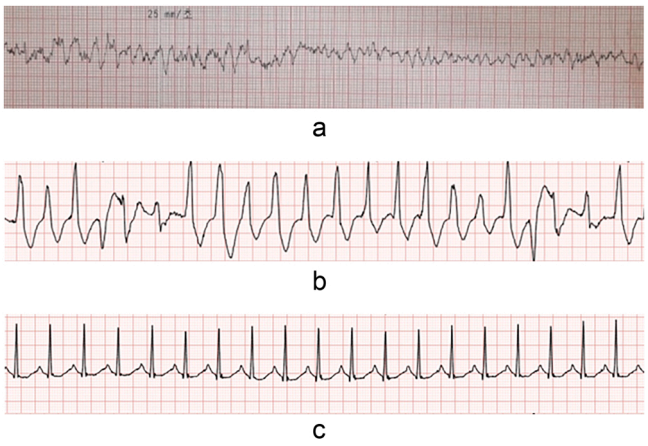

Fig. 1. ECG obtained at 25 mm/second, 10 mm/mV. ECG at (A) the first ventricular fibrillation, (B) first ROSC, and (C) 5 h after the first ROSC. ECG, electrocardiogram; ROSC, return of spontaneous circulation.

2.3 pg/mL) were all normal.

During 4 L of gastric lavage, she vomited three to four times and suddenly developed generalized clonic movements for several seconds and V. fib 25 min after arrival (80 min after ingestion) (Fig. 1). Chest compressions, intubation, and 200-J defibrillation twice resulted in a return of spontaneous circulation (ROSC) after 6 min of advanced cardiovascular life support (Fig. 1). Immediately after ROSC, irritability and endotracheal holder biting worsened, and teeth 21 and 22 were avulsed. We administered an intravenous (IV) midazolam (3 mg) bolus for sedation. At 45 min after arrival (90 min after ingestion), she developed recurrent V. fib. We gave a 200-J shock, IV infusions of amiodarone (300 and 150 mg), lidocaine (50 and 25 mg), magnesium (2 g), and a lipid emulsion containing 80 mg of purified soybean oil (250 mL of Lipidem 20%). The initial laboratory data showed hypokalemia; therefore, we added an IV potassium chloride infusion. IV infusions of midazolam (5 mg/hour) and vecuronium (5 mg/hour) were administered and IV norepinephrine was used to treat hypotension. Continuous IV amiodarone (started at 1 mg/minute for 6 h and then at 0.5 mg/minute for 18 h) and esmolol (started at 50 μg/kg/minute) were added for uncontrolled tachyarrhythmia. Until 4 h after ingestion, V. fib and ROSC with defibrillation occurred 12 times. Fig. 2 describes the clinical course and treatment with time. At 7 h after ingestion, serum creatine (1.39 mg/dL), AST/ALT (228 IU/L/191 IU/L), and troponin I (159 pg/mL) were elevated. An electrocardiogram showed sinus tachycardia at a rate of 124 beats/minute and a bedside echocardiogram showed an ejection fraction > 60%, but no regional wall motion abnormality. For supportive care, mechanical ventilation, sedatives, and neuromuscular blockade were continued until 12 h after ingestion. At 12 h after ingestion, the serum (90.6 mg/L) and urine (91.9 mg/L) caffeine concentrations were elevated and the serum (0.45 mg/L) and urine (4.72 mg/L) theophylline concentrations were also mildly elevated. The serum and urine samples were sent to an external poisoning center and we received the results 22 h after ingestion. At this time, the patient's mental status had recovered fully and she was extubated. At 20 h after ingestion, laboratory tests showed rhabdomyolysis (creatine kinase 11,444 IU/L). At 30 h after ingestion, the acute kidney injury had improved (serum creatinine 0.71 mg/dL), but the creatine kinase level was increased (25,270 IU/L). The creatine kinase level decreased thereafter and was 1660 IU/L 6 days after ingestion. Hospitalization was delayed due to lack of a general ward bed and occurred 45 h after arrival. Only hydration and supportive care were done on the ward. On day 4 of admission, Holter monitoring showed sinus rhythm and no ventricular premature beats, and an echocardiogram was normal. On day 6 of admission, she was discharged without medical complications and planned psychiatric outpatient treatment.

3Discussion

Caffeine, a structural analog of adenosine, is a widely used central nervous system stimulant in beverages or drugs. It is rapidly absorbed with early peak levels, crosses the blood–brain barrier, and the maximum plasma concentration is reached within 30–60 min after ingestion [4]. An average cup of coffee contains 100–200 mg of caffeine and up to 400 mg daily is unlikely to cause serious harm in a healthy adult. There is no defined toxic dose or level of caffeine; however, ingestion of 100–150 mg/kg or serum levels > 100 μg/mL are likely to cause life-threatening toxicity, and the acute ingestion of > 200 mg/kg can be lethal [5,6].

We report a patient with a supra-lethal caffeine overdose and severe life-threatening cardiovascular instability that was successfully treated only with medical treatment, without renal replacement treatment or ECMO. Although severe caffeine poisoning after taking 18 g (332 mg/kg) of caffeine tablets caused cardiac arrest about 1 h later, and refractory ventricular tachycardia continued for 2.5 h, the patient recovered without complications with supportive care only. This patient presented to the hospital during the night and it was impossible to perform dialysis at the hospital; due to the COVID-19 pandemic, it was also impossible to find an intensive care unit bed at another hospital.

The findings of acute caffeine intoxication range from mild symptoms such as nausea, vomiting, and tachycardia to serious signs, including hypokalemia, hypophosphatemia, metabolic imbalance, ventricular tachycardia, convulsions, and cardiac arrest. Fatal arrhythmias are the most common cause of death in acute caffeine intoxication [7]. In severe poisoning with life-threatening complications, an active elimination method such as hemodialysis or hemoperfusion should be used to reduce the blood caffeine concentration rapidly in addition to symptomatic therapy, such as electrolyte imbalance correction, beta-blockers for tachycardia control, and cardioversion or defibrillation for fatal arrhythmias. Ishigaki et al. reported a patient who took a 15.6-g caffeine overdose in whom a combination of hemoperfusion and hemodialysis improved the ventricular tachycardia within 2 h [1]. In a 20-g caffeine overdose, Yasuda et al. reported that early hemodialysis and venoarterial ECMO corrected a subsequent arrhythmia [2].

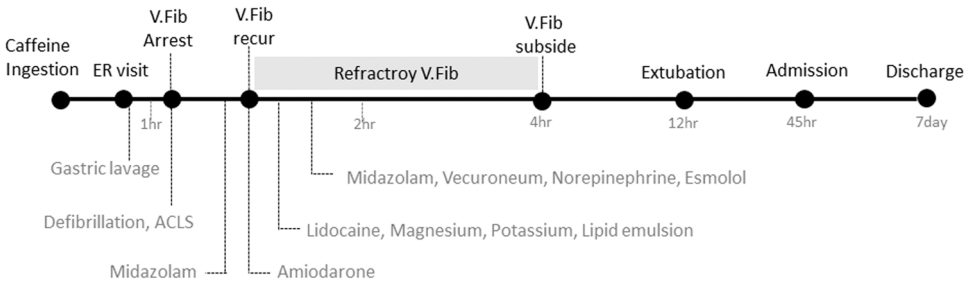

Fig. 2. The patient's clinical course and treatment. The patient needed defibrillation due to ventricular fibrillation several times between 80 min and 4 h after caffeine ingestion. V Fib, ventricular fibrillation; ACLS, advanced cardiovascular life support; AKI, acute kidney injury.

Table 1
Successful treatment cases of caffeine intoxication with refractory ventricular fibrillation from previous literature.

Author (Published year)	Caffeine dose	Caffeine concentration	Treatment
Ishigaki et al. [1]	15.6 g	237 mg/L	Hemoperfusion & Hemodialysis
Yasuda et al. [2]	15.4 g	42 mg/L	VA ECMO & Hemodialysis
Benjamin et al. (2020) [3]	50.0 g	254 mg/L	Hemodialysis
Muraro et al. [10]	40.0 g	> 120 mg/L	Intralipid (120 + 250 + 100 mg)
Terashima et al. [11]	23.2 g	unchecked	Propofol (20 mg/h~100 mg/h)

However, if mechanical elimination methods for caffeine intoxication, such as hemodialysis or hemoperfusion, are unavailable, active symptomatic treatment must wait for the blood concentration to decrease. In this case, dialysis was judged necessary, but there were no available intensive care units or continuous renal replacement therapy treatment facilities in 15 nearby hospitals due to the COVID-19 pandemic. ECMO would have been helpful, but as the patient presented at night, ECMO treatment was not available. Thus, we could perform only conventional defibrillation and CPR for recurrent V. fib arrest and administered IV medication, such as amiodarone, lidocaine, magnesium, and esmolol, for the recurrent V. fib and potassium for hypokalemia. This worked and the patient recovered without any complications with supportive care only.

During resuscitation, our patient was also given IV Intralipid. Recent studies have suggested that Intralipid emulsion acts as a vehicle to move drugs from the heart and brain to less well-perfused organs [8,9]. Muraro et al. reported a 40-g caffeine overdose with severe cardiovascular collapse that was successfully resuscitated with Intralipid infusion [10]. An Intralipid dose of 6 mL/kg was administered and had an immediate positive effect on the patient's blood pressure. In that case, Intralipid also reduced the vasodilatation, decreased renal and cardiac toxicity due to the caffeine overdose, and prevented rhabdomyolysis and seizures, and the patient did not require hemodialysis for complete recovery. The table shows reported successful treatments of patients with caffeine intoxication with refractory ventricular fibrillation.

Although it was not administered in our patient, propofol infusion for severe caffeine intoxication has also been reported to result in prompt improvement of potentially fatal ventricular arrhythmias. Terashima et al. reported that administering propofol immediately improved V. fib in a 23-g caffeine overdose [11]. Propofol has several cardiovascular effects, such as baroreflex activity and direct peripheral vasodilatation [12], and may act as an IV lipid emulsion via the "lipid sink" phenomenon. Via this mechanism, a lipid emulsion infusion creates an expanded lipid phase and extracts toxic drugs from tissues. As a result, toxic drugs cannot exert their pharmacological actions [13].

In summary, during a period of limited medical resources due to the pandemic, we experienced a case of acute caffeine intoxication with refractory ventricular tachycardia, and a combination of intralipid emulsion and anti-arrhythmic agents and full supportive care without a mechanical elimination method led to the patient's recovery Table. 1

Ethical approval

This study was approved by the Institutional Review Board of SMG-SNU Boramae Medical Center and the necessity to obtain written consent was waived (IRB no. 10–2022–74).

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data Availability

No data was used for the research described in the article.

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