


## Case Report

# Caffeine poisoning successfully treated by venoarterial extracorporeal membrane oxygenation and emergency hemodialysis

Shinichi Yasuda,<sup>1</sup> Masaki Hisamura,<sup>2</sup>  Takahisa Hirano,<sup>1</sup> Yuriko Kukihara,<sup>1</sup> Keita Kodama,<sup>3</sup> Kazuki Konishi,<sup>3</sup> Motohiro Nakamura,<sup>2</sup> Gentaro Hiramatsu,<sup>2</sup> and Kenji Koshimizu<sup>2</sup>

<sup>1</sup>Department of Critical and Emergency Medicine, <sup>2</sup>Department of Emergency Medicine, and <sup>3</sup>Department of Clinical Engineering, Saitama Medical Center, Saitama Medical University, Kawagoe, Japan

**Background:** Caffeine overdose can cause life-threatening circulatory failure, neurological abnormalities, and ventricular fibrillation. We report the case of a patient with caffeine poisoning who was successfully treated with early hemodialysis and venoarterial extracorporeal membrane oxygenation.

**Case Presentation:** A 43-year-old man who had ingested pills containing 20 g caffeine was transported to the hospital 100 min after ingestion. Hemodynamic collapse and refractory arrhythmia were most likely the potential complications. The patient developed ventricular fibrillation when placed in the left lateral decubitus position. Return of spontaneous circulation with defibrillation and introduction of venoarterial extracorporeal membrane oxygenation were followed by emergency dialysis, which led to rapid improvement in the clinical findings.

**Conclusion:** Acute caffeine poisoning in a patient who developed an arrhythmia was successfully treated using an indwelling arterial and venous sheath followed by venoarterial extracorporeal membrane oxygenation.

**Key words:** arrhythmia, caffeine, hemodialysis, venoarterial extracorporeal membrane oxygenation, ventricular fibrillation

## INTRODUCTION

CAFFEINE OVERDOSE can cause lethal arrhythmias, which are often refractory.<sup>1</sup> There are several case reports in which hemodialysis was effective for refractory arrhythmias caused by caffeine poisoning in the context of suicide, and hemodialysis is becoming common as a means of treatment in other contexts.<sup>2</sup> There are currently few case reports in which patients who developed arrhythmias were saved using venoarterial extracorporeal membrane oxygenation (VA-ECMO); furthermore, to the best of our knowledge, no other study has reported on a shorter time used to initiate VA-ECMO for caffeine poisoning compared to that reported in our study, with a subsequent arrhythmia

corrected using an indwelling arterial and venous sheath and VA-ECMO.

## CASE PRESENTATION

A 43-YEAR-OLD MAN with a 20-year history of bipolar disorder attempted suicide by ingesting pills containing 20 g caffeine. He arrived at our hospital 100 min after ingestion. Vital signs included: respiratory rate, 30 breaths/min; SpO<sub>2</sub>, 97% (ambient air); heart rate, 130 b.p.m.; blood pressure, 126/69 mmHg; and Glasgow Coma Scale score, E4V5M6. The patient had 10 bouts of watery vomit. He was 176 cm tall and weighed 60 kg.

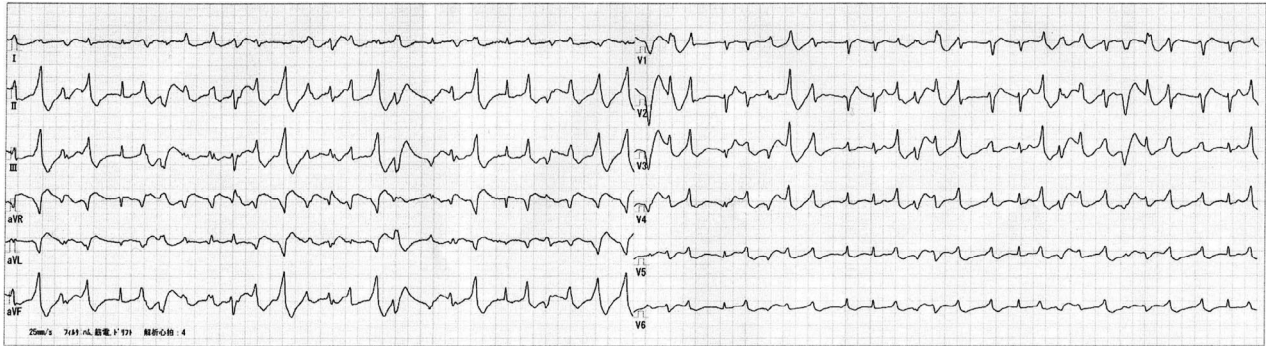
Premature ventricular contractions were observed on electrocardiography (Fig. 1). Blood examination revealed: white blood cell count, 7500/ $\mu$ L; creatine phosphokinase, 66 IU/L; and potassium, 2.6 mEq/L. Arterial blood gas analysis revealed respiratory alkalosis and metabolic acidosis: pH 7.43; PCO<sub>2</sub>, 27.3 mmHg; PO<sub>2</sub>, 124 mmHg; HCO<sub>3</sub><sup>-</sup>, 17.7 nEq/L; and lactate, 6.5 mmol/L. He had ingested 333 mg/kg of caffeine, with blood levels showing 42  $\mu$ g/mL (poisoning range  $\geq$ 25  $\mu$ g/mL) 2 h after ingestion. Blood

**Corresponding:** Masaki Hisamura, MD, PhD, Department of Emergency Medicine, Saitama Medical Center, Saitama Medical University, 1981 Kamoda, Kawagoe, Saitama 350-8550, Japan. E-mail: hisamura@msj.biglobe.ne.jp.

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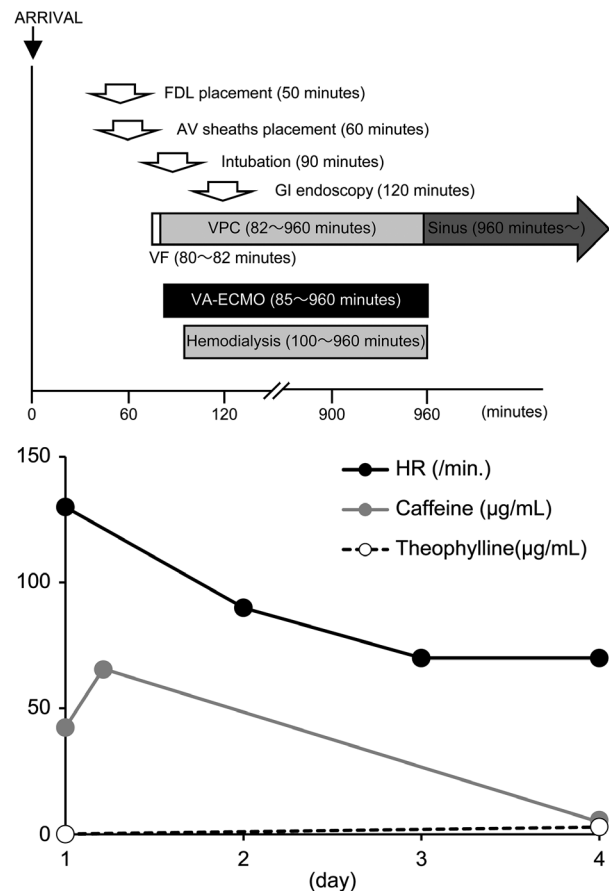
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**Fig. 1.** Electrocardiogram on admission of a 43-year-old man with caffeine overdose, showing premature ventricular contractions.

theophylline levels, a metabolite of caffeine, were at or below measurement sensitivity (poisoning range  $\geq 20$   $\mu\text{g}/\text{mL}$ ). Although a normal blood pressure at arrival was maintained, a wide QRS complex and a pulse rate of 130 b.p.m. were observed.

At 50 min after arrival, a flexible double-lumen catheter was placed in the right internal jugular for emergency hemodialysis. Sixty minutes after arrival, when the arrhythmia occurred, a catheter sheath was placed in the right femoral vein and left femoral artery to enable rapid introduction of extracorporeal membrane oxygenation (ECMO). Sixty-five minutes after arrival, midazolam (10 mg), fentanyl (0.1 mg), and rocuronium (50 mg) were used to initiate tracheal intubation and artificial respiratory management. Eighty minutes after arrival, when he was placed in the left lateral decubitus position during endoscopy, he developed pulseless ventricular tachycardia. Eighty-two minutes after arrival, chest compressions and defibrillation yielded successful return of spontaneous circulation; however, he developed ventricular fibrillation. Eighty-five minutes after arrival, VA-ECMO was introduced from the sheath catheter site, ensuring a blood supply of 3.5 L/min at 2000 rpm. Because potassium levels were low, they were replenished, which eliminated premature ventricular contractions. One hundred minutes after arrival, hemodialysis was introduced at a flow rate of 100 mL/min from the flexible double-lumen catheter and a dialysate flow rate of 4000 mL/h. After hemodialysis, the patient's tachycardia began to improve. Sixteen hours after arrival, the premature ventricular contractions decreased and hemodialysis was terminated. The premature ventricular contractions did not reappear after termination of dialysis, and his heart rate maintained a sinus rhythm at 90 b.p.m. Dialysis was terminated when the  $\text{PaO}_2/\text{FiO}_2$  ratio was at 450 mmHg, and the patient was weaned off ECMO. On hospital day 2, ECMO was



**Fig. 2.** Clinical course after hospital arrival of a 43-year-old man with caffeine overdose (top panel) and serum concentrations of caffeine and theophylline (bottom panel). AV, arterial venous; FDL, flexible double-lumen catheter; GI, gastrointestinal; HR, heart rate; VA-ECMO, venoarterial extracorporeal membrane oxygenation; VF, ventricular fibrillation; VPC, ventricular premature contraction.

terminated when the patient had a heart rate of 70 b.p.m., blood pressure of 130/80 mmHg, respiration rate of 16 breaths/min, and electrocardiographic waveform with sinus rhythm, suggesting he had escaped the acute poisoning state (Fig. 2). He also returned to a lucid state of consciousness. Extubation was carried out on hospital day 4, and the serum caffeine level was 5.5 µg/mL, with a serum theophylline level of 3.7 µg/mL (Fig. 2). Rehabilitation was started on the day of extubation, and he was transferred to a psychiatric hospital on day 21.

## DISCUSSION

**T**HE HALF-LIFE OF caffeine in the human body blood is 3–7 h in adults but is reportedly up to 16 h in the case of an overdose.<sup>2</sup> The lethal dose is  $\geq 150$  mg/kg for an adult, with blood levels  $\geq 70$  µg/mL.<sup>2</sup> Caffeine levels have been estimated by measuring serum theophylline, a metabolite of caffeine, but only 4% of caffeine is metabolized to theophylline, and possibly none in the early stages after ingestion.<sup>3</sup> The theophylline levels in this case were also below the detection level, and although levels had risen by hospital day 4, they were not useful for estimating caffeine levels or for devising a treatment plan. In the acute stages of caffeine poisoning, it might not be useful to measure theophylline levels for estimating caffeine levels.

Caffeine poisoning is frequently refractory, and hemodialysis is reported to be effective for lowering blood caffeine levels.<sup>2</sup> Caffeine has a protein binding rate of 36%, a molecular weight of 194, and a volume of distribution of 0.6–0.8 L/kg, which is relatively low, thereby increasing the effectiveness of hemadsorption and hemodialysis. The most common cause of death from caffeine poisoning is lethal arrhythmia, which persists until blood caffeine levels decrease. The use of VA-ECMO and hemodialysis to save a patient's life after refractory arrhythmia due to caffeine poisoning was recently published.<sup>4</sup>

As caffeine has a wide range of reported serum concentrations<sup>3</sup> and because Japan has few facilities capable of measuring caffeine levels,<sup>5</sup> treatment strategies should be determined based on caffeine poisoning in terms of either milligrams per kilogram of body weight or the absolute amount ingested.

If the amount of caffeine ingested has exceeded 150 mg/kg or 6.0 g, it would be preferable to combine hemodialysis and catheter sheath placement for VA-ECMO until symptoms improve. Catheter sheath placement is a relatively easy operation, but the difficulty increases when cardiac arrest or shock occurs.<sup>6</sup> In this case, a catheter sheath was implanted for VA-ECMO at the time of diagnosis of caffeine intoxication. This is the first study to report on such a rapid decision

**Table 1.** Comparison of results of previous studies on caffeine poisoning, treated using venoarterial extracorporeal membrane oxygenation (ECMO), with those of our study

Case no.	Author (year)	Age (years)/sex	Ingested dose (mg)	Amount of caffeine per 1 kg (mg/kg)	Serum concentration (µg/mL)	Time after poisoning (h)	Arrhythmia	Time of ECMO initiation after arrival (min)	Catheter sheath placement before cardiac arrest	Sequelae
1	Riku (2018) <sup>9</sup>	30/F	12,000	Unknown	172.0	1–2	VF	Unknown	None	None
2	Kato (2019) <sup>2</sup>	43/F	15,360	190	251.9	12	VF	120	None	Right peroneal nerve paralysis
	This case (2020)	43/M	20,000	333	66.0	1.6	VF	85	Yes	None

F, female; M, male; VF, ventricular fibrillation.

to carry out VA-ECMO (Table 1). Lethal arrhythmia from caffeine is refractory<sup>7</sup> and the chances of survival are extremely low unless extracorporeal life support is provided, specifically if extracorporeal cardiopulmonary resuscitation is undertaken.<sup>8</sup> Extracorporeal cardiopulmonary resuscitation with prompt VA-ECMO reportedly also improves neurological prognosis.<sup>4</sup>

## CONCLUSIONS

**WE PRESENTED** A case of acute caffeine poisoning in a patient successfully treated with hemodialysis and VA-ECMO. Our results suggest that advance placement of catheter sheaths for VA-ECMO can be beneficial in cases of caffeine poisoning.

## DISCLOSURE

Approval of the research protocol: N/A.

Informed consent: Verbal and written informed consent was obtained from the patient.

Registry and registration no. of the study/trial: N/A.

Animal Studies: N/A.

Conflict of interest: None.

## REFERENCES

1 Sato T, Nakagawa T, Nishina M, *et al.* Two cases who survived acute, potentially fatal caffeine overdose. *J. Jap. Assoc. Acute Med.* 2009; 20: 941–7.

- 2 Kato Y, Kuriyama A, Hata R, Ikegami T. Extracorporeal membrane oxygenation for hypokalemia and refractory ventricular fibrillation associated with caffeine intoxication. *J. Emerg. Med.* 2020; 58: 59–62.
- 3 Birkett DJ, Miners JO. Caffeine renal clearance and urine caffeine concentrations during steady state dosing. Implications for monitoring caffeine intake during sports events. *Br. J. Clin. Pharmacol.* 1991; 31: 405–8.
- 4 Inoue A, Hifumi T, Sakamoto T, Kuroda Y. Extracorporeal cardiopulmonary resuscitation for out-of-hospital cardiac arrest in adult patient. *J. Am. Heart. Assoc.* 2020; 9: e015291.
- 5 Yamamoto Y, Yamamoto M, Toda S. Severe caffeine poisoning in which theophylline levels helped as an indicator of treatment progress. *Med. J. Aizawa Hosp.* 2019; 17: 57–9.
- 6 Matsumura Y, Matsumoto J, Kondo H, *et al.* Early arterial access for resuscitative endovascular balloon occlusion of the aorta is related to survival outcome in trauma. *J. Trauma Acute Care Surg.* 2018; 85: 507–11.
- 7 Kamijo Y, Soma K (eds). *Clinical Toxicology (Japanese)*, 1st edn. Tokyo: Igaku-shoin Ltd, 2009.
- 8 Nakamura K. Extracorporeal cardiopulmonary resuscitation and maintenance management in patients with cardiac arrest. *J. Wakayama Med. Soc.* 2018; 69: 142–7.
- 9 Riku S, Yamamoto T, Kubota Y, *et al.* Refractory ventricular fibrillation caused by caffeine intoxication. *J. Cardiol. Cases.* 2018; 18: 210–2.