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症 例 報 告

A case of ventricular fibrillation caused by accidental hypothermia due to stimulant intoxication and alcohol intake

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——Summary——（Jpn J Clin Toxicol 2021；34：108–112）

Context：We resuscitated a patient with ventricular fibrillation（Vf）from extreme accidental hypothermia resulting from amphetamine intoxication. For cardiac patients with dilated pupils, abuse of stimulant drugs should be considered.

Case details：A 50–year–old female with depression was found in the kitchen of an unheated home in winter with a leather belt fastened around her throat. Her Glasgow coma scale value was 3 and she had Vf. A scar was noted on her left arm. Defibrillation at 150 J was repeated with 300 mg of amiodarone i.v. Her body temperature was 21℃ and warming was started. Her spouse refused permission to administer veno–arterial extracorporeal membrane oxygenation（VA ECMO）. After the return of spontaneous circulation, her body temperature increased to 22℃ . After admission, her spouse stated that she had been convicted for stimulant use and had a history of hospitalization. The TRIAGE® panel of drugs of abuse revealed amphetamine positivity. Both pupils remained dilated at 5 mm even after stabilizing her circulation dynamics. She recalled passing out from stimulant and alcohol intake. The scar on her left arm resulted from surgery to treat an arteriovenous fistula caused by stimulant abuse.

Discussion：It is suggested that we should keep the possibility of abuse of stimulant drugs in mind while we treat cardiac arrest patients with dilated pupils.

Key words：amphetamine, drug addiction, life–threatening arrythmia

INTRODUCTION

Accidental hypothermia is a typical complication of acute drug intoxication. For cardiac patients with dilated pupils, abuse of stimulant drugs should be considered. We describe the resuscitation of a patient with ventricular fibrillation（Vf）accompanied by extreme hypothermia due to amphetamine intoxication. After the return of spontaneous circulation（ROSC）, her vital signs remained unstable. However, her spouse refused permission to administer veno–arterial extracorporeal membrane oxygenation（VA ECMO）. She recovered after warming with Arctic Sun 5000® and a warm drip infusion and her hospital stay was uneventful thereafter. We considered how amphetamine was involved in the hypothermia and onset of Vf in this patient as well as how medical in-

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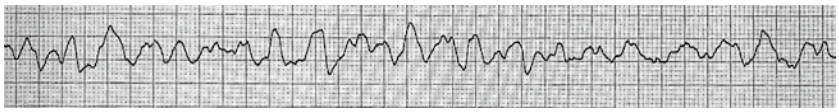

Fig. 1 Cardiac monitoring in ambulance shows Vf

Table 1 Blood findings reveal only elevated CPK and PT

WBC	5,300/mm^3	TP	7.4 g/dL	T-Bil	0.4 mg/dL
RBC	531×10^4/mm	Alb	4.3 g/dL	BUN	11.4 mg/dL
Hb	13.6 g/dL	AST	44 U/L	Cre	0.53 mg/dL
Ht	39.7%	ALT	32 U/L	Na	133 mEq/L
Plt	18.8	LDH	237 U/L	K	4.2 mEq/L
PT/INR	1.21	ALP	193 U/L	Cl	101 mEq/L
PT	14.2 s	γ-GTP	13 U/L	CRP	0.05 mg/dL
Fib	196 mg/dL	CPK	788 U/L	HbAlc	5.0%
HCV	positive				

stitutions and governments can help patients with stimulant intoxication based on a literature search.

CASE REPORT

A 50-year-old female was found with a leather belt fastened around her throat in the kitchen of her unheated home in December 2017, when the outside temperature was 6.8℃. She had depression and a surgical scar was noted on her left arm.

When an emergency medical technician arrived at the scene, her Glasgow coma scale value was 3 and a cardiac monitor showed Vf (**Fig. 1**). Her body temperature could not be measured because of extreme hypothermia. She was defibrillated and resuscitated at the scene and transferred to our hospital. The Vf and ventricular tachycardia (VT) continued in the ambulance. Upon arrival, her consciousness level was 3 on the Glasgow coma scale, and both pupils were dilated to 6 mm without light reflection, palpebral conjunctiva, or strangulation marks on the neck. Cardiac monitoring confirmed continued Vf and 150 J of defibrillation was repeatedly applied, with 300 mg of amiodarone i.v. Warming with temperature management system Arctic Sun 5000® and a warm drip infusion was started, because her body (bladder) temperature was 21℃. Cardiopulmonary assistance and inner warming by VA ECMO did not proceed because we were unable to contact any relatives and her spouse refused permission for invasive treatment. Sinus rhythm normalized after ROSC, when rewarming increased her body temperature to 22℃. The cause of the cardiac arrest was investigated using whole body CT imaging before admission to the ICU. Blood findings showed high CPK and PT values and no other abnormal values (**Table 1**). Chest X-ray and head CT findings were also normal on arrival. After admission, her common-law spouse stated that she had been convicted for stimulant use three years previously and had a history of hospitalization. **Fig. 2** shows the processes during the acute period. It is put on time on horizontal axis from the arrival time at our hospital (0hr). The results of qualitative tests revealed that she was amphetamine positive on the TRIAGE® panel of drugs of abuse. Even after her circulation dynamics stabilized, both pupils remained dilated at 5 mm. On hospital day 1, her consciousness became E4VTM6. She was weaned from a ventilator and extubated on hospital day 4 so that food intake could resume. Ultrasound cardiography showed that the cardiac function was normal and the ejection fraction was 67%. She recalled passing out from stimulant and alcohol intake. An enquiry at her family consultation hospital revealed that the scar on her left arm resulted from surgery to treat an arteriovenous fistula caused by stimulant abuse. Venous thromboembolism (VTE) was confirmed by contrast CT im-

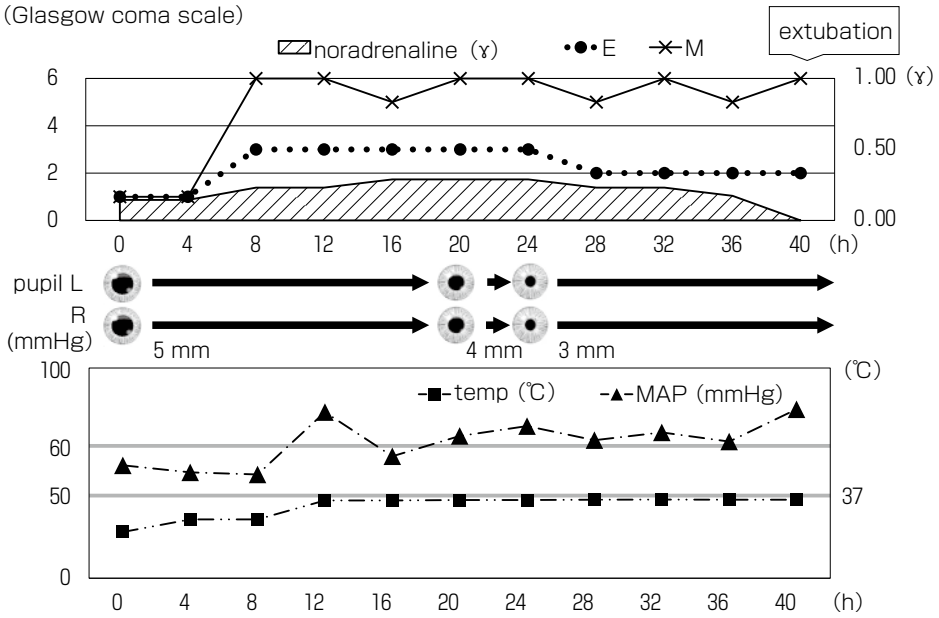

Fig. 2 Chart during acute stage indicates good course after ROSC despite persistently dilated pupils

aging on hospital day 6, and direct-acting oral anticoagulants (DOAC) were started. Her consciousness remained clear after extubation and her subsequent course was good. She was transferred to a psychiatric facility on hospital day 22.

DISCUSSION

The first wave of drug abuse in Japan was caused after World War II in 1950s by the spread of Philopon, a form of methamphetamine that caused significant social problems. A third wave has hit Japan from 1970s up to now because of increasing abuses of not only illegal drugs such as stimulants but also of legal drugs. The largest and most problematic abused drug in Japan remains stimulants, which cause about 10 acute poisonings annually. Furthermore, about 20,000 individuals are arrested annually, and numerous abusers follow behind[1].

Kalant et al. stated that the pharmacological actions of stimulants comprise a central stimulatory effect, sympathetic nervous system excitement, and anorectic activity[2]. Kojima et al. described the symptoms of highly concentrated methamphetamine poisoning as high blood pressure, tachycardia, arrhythmia, marked temperature increase, convulsions, coma, secondary hypotension, collapse, and death[3,4]. Stimulants can also increase body temperature to 40℃. The results of animal studies have shown that body temperature is reduced by low-dose amphetamine action on the anterior hypothalamus and the involvement of methylamphetamine in serotonin receptors. Cardiovascular diseases caused by stimulants include myocardial dysfunction and infarction, as well as infective endocarditis. Myocardial dysfunction is attributed to acute myocardial injury, dilated cardiomyopathy, and hypertrophic cardiomyopathy. Acute myocardial injury results in sudden heart failure and pulmonary edema in healthy adults, and diffuse and highly depressed left ventricular wall motion leads to acute circulatory failure. Life-saving is complicated by the rapid progress of intoxication with most stimulants. The mechanism of action is as follows. Methamphetamine promotes noradrenaline release from sympathetic nerve endings, resulting in coronary artery spasm and elevated blood pressure. Furthermore, calcium overload and direct damage to cardiomyocytes via free radicals might also cause acute myocardial damage. On the other hand, the

lives of some patients with acute myocardial damage have been saved, and their myocardial functions became normalized as in Takotsubo cardiomyopathy. Excess sympathetic stimulation by amphetamine seems to cause Takotsubo cardiomyopathy. Hypertrophic cardiomyopathy and the dilated cardiomyopathy seen among stimulant addicts are also thought to be the effects of excess catecholamines and post-load increases due to hypertension. Direct amphetamine toxicity without a catecholamine excess has also been proposed[1]. Details of vital signs and the amount and number of ingested stimulants were unknown when the present patient was admitted to the hospital. After we determined the pupillary status of the patient and her history of stimulant abuse, the TRIAGE® drug panel revealed that she was positive for amphetamine. The half-life of amphetamine in blood ranges from 5 to 30 hours, and it remains detectable in the bloodstream for 2-8 days after use[1]. She admitted using stimulants daily after release from prison. It is suggested that we should keep the possibility of abuse of stimulant drugs in mind while we treat cardiac arrest patients with dilated pupils. Our patient achieved a full recovery without sequelae. Therefore, that Vf was caused by acute myocardial injury due to amphetamine seems unlikely. Stimulant abusers have an overwhelmingly low tolerance for alcohol. Stimulant and concurrent alcohol intake could have easily reduced the consciousness level in our patient and the extreme hypothermia might have caused Vf under conditions of prolonged cold exposure. Accidental hypothermia generally causes organ dysfunction with a significant decrease in metabolism at body temperatures < 35℃, resulting in mortality rates of 30-90%. Accidental hypothermia is not necessarily associated with an extremely cold climate, climatic conditions such as wind speed and humidity, physical conditions such as nutrition, fatigue, alcohol intake, drug abuse, or thermoregulatory dysfunction caused by hypothyroidism and central nerve system disease. Many victims of accidental hypothermia in cold climates are found asleep and intoxicated with alcohol outdoors, near seas, lakes, mountains, rivers, etc. For severely hypothermic patients with cardiopulmonary arrest, electrical defibrillation is usually ineffective at temperatures < 28℃ and then rapid rewarming with VA ECMO is absolutely indicated. Generally, Vf, asystole, and respiratory arrest occur at < 28℃, < 20℃, and < 24℃, respectively. Warming with VA ECMO is considered more effective than repeated defibrillation with high energy in terms of minimizing cardiac damage[5].

Our approach to the increasing prevalence of drug abuse is to strengthen drug analysis systems in laboratories at emergency hospitals. Blood concentrations of amphetamine and alcohol should be measured as soon as possible after admission. Furthermore, drug analysis equipment such as liquid chromatographs should be placed in hospitals to analyze various addictive drugs. Our patient lived alone and her clinical condition and medical history were difficult to determine. For example, the scar on her left arm appeared to be self-inflicted, whereas in fact it was due to surgery to repair an arteriovenous fistula caused by stimulant abuse. Because the number of injuries, including those that are self-inflicted, that involve drug abuse has been increasing, we consider that police, fire, and medical agencies should be in close communication to prevent recurrent drug addiction and promote national security.

CONCLUSION

We describe the resuscitation of a patient who presented with Vf and extreme hypothermia caused by amphetamine intoxication and alcohol. Such patients rarely recover by heating with a warm air blanket and warm drip infusion without VA ECMO. The cause of hypothermia is important to determine when patients live alone and their medical history is obscure. It is also suggested that we should keep the

possibility of abuse of stimulant drugs in mind while we treat cardiac arrest patients with dilated pupils.

Declaration of interests

The authors have no interests to declare.

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要旨

【はじめに】今回，急性覚醒剤中毒により寒冷曝露で重度低体温症から Vf をきたしたが，能動的復温のみで良好な経過をたどった 1 例を経験した。瞳孔散大している心停止患者に薬物中毒を考慮すべき症例であったため報告する。
【症例】症例は 50 代女性。既往症：うつ病。現病歴：平成 29 年 12 月某日，首に革ベルトが巻き付いた状態で倒れているのを発見され Vf 症例で当院三次救急搬送された。来院時現症：意識レベル GCS 3，瞳孔左右 6 mm，対光反射なし，左上肢に瘢痕を認めた。モニター上 Vf 継続しており 150J の除細動とアミオダロン 300 mg 静注した。体温 21℃（膀胱温）で温生食と電気毛布で加温を開始した。PCPS は内縁の夫が希望せず施行しなかった。体温 22℃で自己心拍再開したが循環動態安定後も左右とも散瞳していた。トライエージではアンフェタミン陽性であった。内縁の夫に病歴聴取をしたところ覚醒剤使用歴があり，左上肢の瘢痕は覚醒剤乱用による動静脈瘻に対する手術創とのことであった。第 2 病日意識清明となり第 4 病日人工呼吸器離脱し抜管，経口摂取が可能となった。意識回復後の病歴聴取で，「ベルトを首に巻いて死のうとしたが死ねなかった。アルコールと一緒に覚醒剤を使用した」と供述があった。
【結語】瞳孔散大している心停止患者の治療に際し，薬物中毒も原因の一つとして考慮すべきである。