A case of cardiopulmonary arrest on arrival due to pilsicainide intoxication

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Abstract

A 22-year-old male was admitted to our hospital after taking 2450 mg of pilsicainide. On admission, the patient was in cardiac arrest, and percutaneous cardiopulmonary support was introduced to maintain his circulation. After three days of intensive care, he was no impaired consciousness and transferred another hospital for psychological problem.

1. Introduction

Pilsicainide hydrochloride is classified into the class IC antiarrhythmic drug group [1)]. Pilsicainide increases the PQ interval, QRS width and QTc, and its serum concentration correlates well with the rate of PQ interval prolongation[2)]. Pilsicainide was developed in Japan and launched in 1991, and until not long ago, it was one of the most frequently used arrhythmic drugs in Japan. We report a case of a patient who took a large dose of pilsicainide in a suicide attempt.

2. Case report

A 22-year-old male patient was transported to our hospital after taking a large amount of drugs. Upon the initial contact with the patient by the Emergency Medical System team, his Glasgow Coma Scale was 3, heart rate (HR) was 47/min, and blood pressure was 153/111 mmHg. The patient was in cardiac arrest with pulseless electrical activity on arrival at the hospital. He was found to have taken a high dose of pilsicainide hydrochloride (2450 mg), which was prescribed for his mother. He had a medical history of psychiatric disease and methamphetamine use.

On admission, the patient's height was 180 cm and weight was 77.7 kg. Laboratory findings showed the Table 1.

Table1. Laboratory findings on admission

Blood gas analysis (FiO_2:0.21)	Blood gas analysis (FiO_2:0.21)	Blood gas analysis (FiO_2:0.21)	Biochemistry	Bio
PH	7.295		TP	6.5
PaO_2	33.1	mmHg	Alb	4.1
$PaCO_2$	43.7	mmHg	Na	139
HCO_3^-	20.6	mmol/L	K	3.9
BE	-5.5	mmol/L	Cl	101
Anion Gap	11.7		BUN	4.9
Glu	152	mmol/L	Cre	32
Lac	6.7	mmol/L	AST	15
Blood count	Blood count	Blood count	ALT	5

WBC	10460	μL	LDH	153
Seg	45.6	%	γ-GT	7
Ly	2.6	%	CK	132
Eo	2.3	%	CRP	<0.
Ba	0.5	%	Urine drug screen	Uri
Hb	15.4	g/dL	METH	-
Plt	22.2	$\times 10^4/\mu L$	BAR	-
Coagulation	Coagulation	Coagulation	BZO	-
PT	11.7	sec	COC	-
PT-INR	1.03		THC	-
APTT	25.3	sec	TCA	-
Fib	141.7	mg/dL	MOR	-

The electrocardiogram showed bradycardia with a wide QRS of 146 msec and HR 40/min (Figure 1). The initial serum concentration of pilsicainide hydrochloride was abnormally high at 12.46 μg/mL (therapeutic range: 0.2–0.9 μg/mL).

The patient's clinical course is shown in Figure 2. As he was in cardiac arrest on hospital arrival, a peripheral venous catheter was inserted and tracheal intubation was performed. A total of 10 A of adrenaline was administered for resuscitation, but return of spontaneous circulation did not occur, so percutaneous cardiopulmonary support (PCPS) (Getinge CS300 with TERUMO CAPIOX ME-SP200C) was established 40 minutes after arrival to maintain circulation. A contrast-enhanced computed tomography scan showed no findings affecting respiration and circulation. The patient was admitted to the intensive care unit (ICU), and hemodialysis (HD) with a NIKKISO DBB-100NX was introduced for drug removal, and intra-aortic balloon pumping (IABP) with a Getinge CS300 was used to support circulation. Echocardiography in the ICU showed a visual ejection fraction (EF) of about 10–15%. After induction of HD, ventricular tachycardia (VT) was observed (Figure 1). Cardioversion at 200 J with a Stryker LIFEPAK 20e was performed to restore normal sinus rhythm, and magnesium sulfate (20 mEq/L) was administered for arrhythmia prevention. His visual EF on echocardiography began to show gradual improvement. There was no recurrence of arrhythmia, and after 8 total hours of HD, the serum concentration of pilsicainide had decreased to 2.98 μg/mL. The patient was withdrawn from PCPS and IABP 24 hours after arrival at our hospital, and after 28 hours, the patient was weaned from mechanical ventilation. On the third hospital day, the patient's serum concentration of pilsicainide had decreased to 1.51 μg/mL, and he was transferred to another hospital for treatment of his psychological problems. On the transfer to another hospital, his vital signs remained stable, and he experienced no disturbance of consciousness. Five months later, we followed up the patient and his neurological prognosis is favorable and had no recurrent arrhythmias.

3. Discussion

Pilsicainide hydrochloride was one of the most frequently used antiarrhythmic drugs in Japan. The effective serum concentration of pilsicainide hydrochloride is 0.2–0.9 μg/ml, with marked PQ prolongation reported at levels of 0.98 μg/ml or higher and adverse effects likely to occur at levels exceeding 0.9 μg/ml[3)]. The highest serum concentration in our patient was 12.46 μg/ml, and PCPS was established because of the difficulty in maintaining his circulation on admission.

The reported cases of poisoning by pilsicainide overdose are summarized in Table 2.

Table2. Reported case of Pilsicainide hydrocholoride overdose

Author
(year)
sex
or

JCS (mmHg)	(mg/dL)	(mg)	serum concentration (μg/mL)
Kanda (1997)			
Nakajima (2001)			
Nakata[4] (2006)			
Matsuda (2014)			
Fujii (2015)			
Oshima[5] (2019)			
Tsuru[6] (2019)			
Our case (2021)			

IABP : Intra-Aortic Ballon Pumpimg. PCPS : Percutaneous cardio-pulmonary support. DHP : Direct hemoperfusion. CHD

In all cases, electrocardiographic abnormalities such as VT and wide QRS were reported. Except for that in an autopsy report[4], the serum concentration of pilsicainide on admission was highest in our case. There is a report of a patient who suffered severe shock after taking 2000 mg of pilsicainide and whose maximum serum concentration rose to 4.81 μg/ml and was saved by PCPS and IABP, as in our case. Temporary pacing and HD have also been reported as other treatments.

Pilsicainide is excreted renally at a high urinary excretion rate of unchanged drug of 80%[5] and has a blood half-life of 3.4 ± 0.2 hours. The blood half-life is markedly prolonged to 23.7 ± 0.2 hours when creatinine clearance is less than 20 ml/min. There are no antidotes or antagonists for pilsicainide, and its removal rate is reported to be as low as 37% on HD, 25% on hemofiltration dialysis, and 45% on plasma exchange. Because a slight decrease in the serum concentration of pilsicainide has been reported to improve symptoms [6]and repeated polymorphic VT occurred in our case, we intervened with HD to try to immediately decrease the serum concentration. Magnesium sulfate was reported [7] as another treatment option. We consider it to be effective and thus administered it for arrhythmia prophylaxis in our case.

4. Conclusion

We report a rare case of pilsicainide intoxication due to overdose. Temporary support by PCPS and other multidisciplinary treatments maintained the patient's circulatory status, and he recovered with no impaired consciousness.

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Disclosure

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Permission to reproduce material from other sources: N/A

Clinical trial registration: N/A

References

1) Hashimoto H, Satoh N, Nakashima M: Effects of SUN-1165, N-(2,6-dimethylphenyl)-8-pyrrolizidine acetamide hydrochloride hemihydrate, a new class i antiarrhythmic drug, on ventricular arrhythmias, intraventricular conduction, and the refractory period in canine myocardial infarction. J Cardiovasc Pharmacol. 1992; 19(3): 417-24.

2) Ino T, Atarashi H, Kuruma A, et al: Electrophysiologic and hemodynamic effects of a single oral dose of pilsicainide hydrochloride, a new class 1c antiarrhythmic agent. J Cardiovasc Pharmacol. 1998; 31(1): 157-64.

3) Shimizu M: Study on the optimal dosage and effectiveness of pilsicainide hydrochloride in patients with premature ventricular contractions and renal dysfunction. Japanese Pharmacology & Therapeutics. 1994; 22(8): 3717-25.

4) K. Nakata, R. Moriwaki, A. Yamaguchi, et al: Case in which magnesium sulfare effectively treated ventricular tachycardia due to overdose of pilsicainide hydrochloride. Chudoku Kenkyu. 2006; 16(1): 49-53.

5) Kiyohiro Oshima, Masato Murata, Makoto Aoki, et al: Ventricular tachycardia due to overdose of pilsicaide. J Jpn Soc Intensive care Med. 2019; 26: 191-2.

6) Shota Tsuru, Hiroshi Adachi, Toshiki Hiramatsu, et al: A case of intoxication relapse of pilsicainide after the transient recovery using hemoperfusion from the toxicity with electrocardiogram (ECG) abnormalities. J Jpn Soc Intensive care Med. 2019; 26: 405-6.

7) Fukasawa M, Ninomiya K, Kawakami Y, et al: Pilsicainide poisoning: an autopsy case and review of literature. Am J Forensic Med Pathol. 2018; 39(4) :357-9.

8) Shiga T, Hashiguchi M, Urae A, et al: Effect of cimetidine and probenecid on pilsicainide renal clearance in humans. Clin Pharmacol Ther. 2000; 67(3): 222-8.

9) Yasuda H, Mishima M, Yonemoto T, et al: Serious polymorphic ventricular tachycardia induced by pilsicainide intoxication with hyperkalemia treated with continuous hemodiafiltration. Journal of the Japanese Society of Intensive Care Medicine. 2010; 17(3): 327-32.

10) Nakata K, Moriwaki R, Yamaguchi A, et al: Case in which magnesium sulfate effectively treated ventricular tachycardia due to overdose of pilsicainide hydrochloride. Chudoku Kenkyu. 2006; 19(1): 49-53.

Figure legends

Fig. 1. Electrocardiographic findings.

(A) On admission.

(B) Electrocardiogram with a wide QRS complex of 210 ms before starting dialysis.

(C) Ventricular tachycardia on the monitor.

(D) After hemodialysis.

Fig. 2. Clinical course of the patient.

FFP: fresh frozen plasma, HD: hemodialysis, HR: heart rate, IABP: intra-aortic balloon pumping, NAd: noradrenaline, PCPS: percutaneous cardiopulmonary support, sBP: systolic blood pressure, VT: ventricular tachycardia.

Figure 2. Clinical course of the patient.

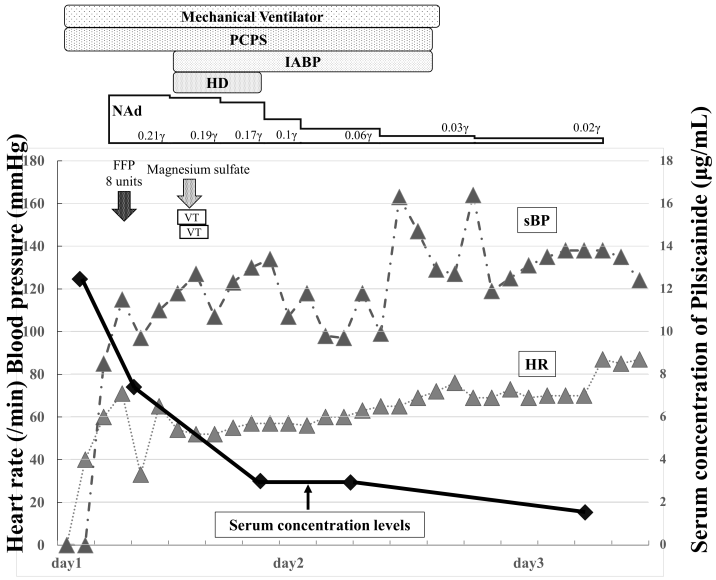
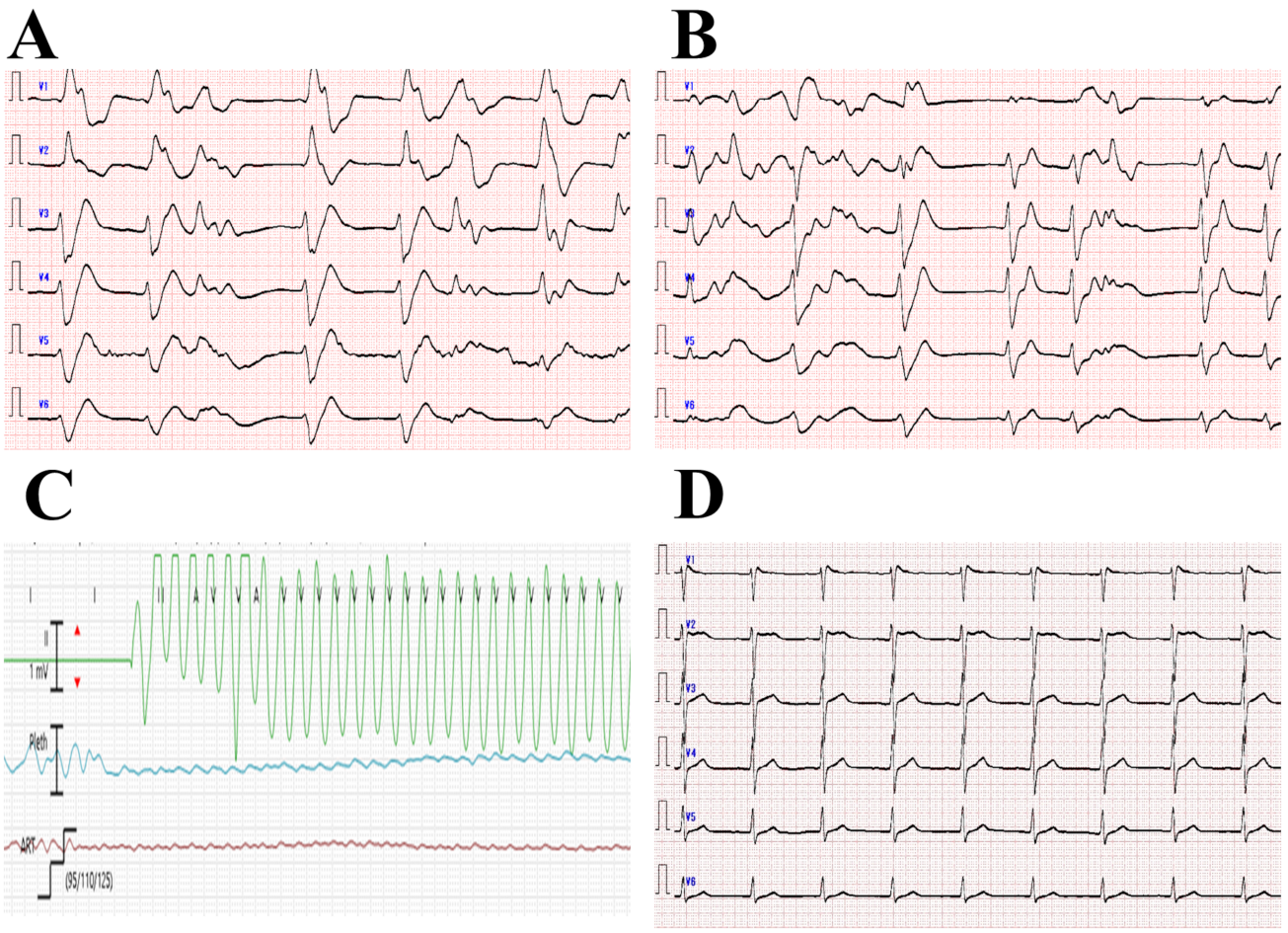


Figure 1.


A
V1
V2
V3
V4
V5
V6
B
V1
V2
V3
V4
V5
V6
C
II
1 mV
Pleth
ART
(95/110/125)
D
V1
V2
V3
V4
V5
V6