INTERNAL MEDICINE

□ CASE REPORT □

Cowfish (Umisuzume, *Lactoria diaphana*) Poisoning with Rhabdomyolysis

Takeaki Shinzato[1], Akira Furusu[2], Tomoya Nishino[2], Katsushige Abe[2], Tetsuro Kanda[1], Takahiro Maeda[3] and Shigeru Kohno[2]

Abstract

A 40-year-old man developed weakness and myalgia of the shoulders and brachia nine hours after eating a cowfish (Umisuzume, *Lactoria diaphana*). A clinical symptom showed rhabdomyolysis and serum creatine phosphokinase was elevated to 180,000 IU/L on day 3. Cardiopulmonary arrest and acute renal failure developed after 59 hours and hemodiafiltration was performed. Cerebral death was diagnosed on day 9 and the patient died on day 16. The case has the characteristic clinical course of palytoxin poisoning, which has also been reported as blue humphead parrotfish poisoning from other kinds of fish.

Key words: acute renal failure, cowfish, palytoxin, rhabdomyolysis

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Introduction

Fish of the boxfish family have generally been considered to be non-toxic and grilled fillets and liver with miso (soybean paste) are regarded as a delicacy in Goto, Nagasaki. However, in 1992, Kamiyama et al first reported a case of boxfish poisoning; there were several reports in 2000 and thereafter in the Japanese literature. All of the patients in these cases showed myalgia and myoglobinuria, with a consequent diagnosis of rhabdomyolysis, with palytoxin (PTX) as a possible causative agent. Here, we report a case of rhabdomyolysis due to poisoning from cowfish (Umisuzume, *Lactoria diaphana*).

Case Report

The patient was a 40-year-old man with a chief complaint of myalgia from both shoulders to forearms, chest pressure and dyspnea. He had a medical history of type I diabetes. The patient was a fisherman by occupation, and on the end of August, 2007 at 7 AM. he returned home after fishing and cooked a cowfish that he had caught with a net. All organs other than the liver were removed and the fillet and liver were grilled with miso and eaten for breakfast. That evening, the patient felt sick and developed myalgia from the shoulders to forearms. He stayed quietly at home, but also developed chest pressure and dyspnea and visited our hospital on the morning of the next day. He was admitted to hospital for treatment due to macrohematuria and an abnormally high level of myogenic enzyme.

On admission, the patient was of height 175 cm and weight 69.5 kg, with blood pressure of 130/78 mmHg, a body temperature of 36.8℃, a regular pulse rate of 120/min, a respiration rate of 15/min, and SpO_2 of 97%. Other observations included palpebral conjunctiva: no anemia; palpebral conjunctiva: no jaundice; edema: none; heart sounds: normal; breath sounds: normal; abdomen: normal; neurological findings; normal, consciousness: alert. The test results on admission are summarized in Table 1.

On admission, the patient complained of subjective symptoms including severe myalgia from both shoulders to forearms, chest pressure and dyspnea. No digestive symptoms (i.e., diarrhea, nausea or vomiting) were observed. The patient was awake and alert and showed no neurological abnormalities. A blood test showed a marked increase in myogenic

[1]Department of Internal Medicine, Association of Far-off Islands Hospitals in Nagasaki Prefectural Goto Central Hospital, Goto, [2]The Second Department of Internal Medicine, Nagasaki University School of Medicine, Nagasaki and [3]Department of Island and Community Medicine, Nagasaki University Graduate School of Biomedical Sciences, Goto
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Correspondence to Dr. Akira Furusu, furusua-ngs@umin.ac.jp

Table 1.

Hematology			**Immunoserology**		
WBC	15,530	/μL	CRP	4.61	mg/dL
RBC	522×10^4	/μL			
Hb	14.9	g/dL	**Urine qualitative test**		
Ht	45.1	%	Color	Red brown	
Plt	13.4×10^4	/μL	Density	1.029	
			pH	5.5	
Serum chemistry			Protein	2+	
CK	51,172	IU/L	Blood	3+	
AST	1,066	IU/L	Sugar	4+	
ALT	272	IU/L	Ketone body	±	
LDH	900	IU/L			
ALP	295	IU/L	**Urinary sediment**		
γGTP	25	IU/L	RBC	1-4	/HPF
ChE	381	IU/L	WBC	0-1	/HPF
TP	8.3	g/dL	Squamous epithelium	0-1	/HPF
Alb	4.9	g/dL	Hyaline cast	0-1	/HPF
T-Bil	0.83	mg/dL			
BUN	21.2	mg/dL	**Arterial blood gas (room air)**		
Cr	0.89	mg/dL	pH	7.330	
Na	136.2	mEq/dL	pCO_2	39.4	Torr
K	4.48	mEq/dL	pO_2	97.7	Torr
Cl	93.6	mEq/dL	HCO_3	20.2	mmol/L
Ca	9.5	mg/dL	BE	-4.7	mmol/L
P	5.0	mg/dL			
TC	209	mg/dL	**12-lead ECG**		
TG	102	mg/dL	Regular sinus, No ST change		
Glucose	579	mg/dL			
HbA1c	7.9	%			

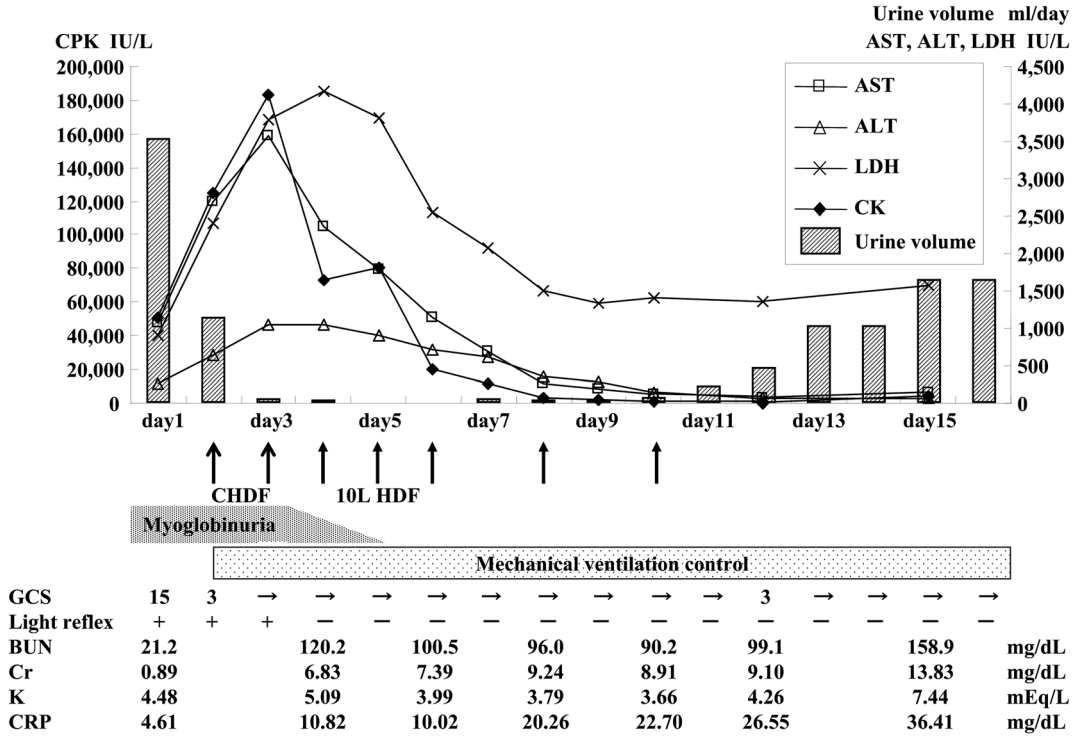
enzyme (Table 1) and macrohematuria was observed, but erythrocytes were not found in urine sediment; consequently, myoglobinuria was thought to be present and the patient was diagnosed with rhabdomyolysis. In a history interview, the patient explained that he had ate the liver of cowfish, and then PTX poisoning was suspected based on his symptoms (although a PTX hemolysis activity assay conducted using serum and urine on admission gave a negative result). Infusion of half saline (solita T1®) 4,000 mL/day was performed and urine was kept at 2,700 mL/day.

On hospital day 2, the patient still complained of myalgia in the upper body, chest pressure and dyspnea, but his vital signs were stable (blood pressure: around 120 mmHg, SpO_2: 96%). At 18: 35, however, the patient developed cardiopulmonary arrest. Circulation was restored by cardiac massage, but the patient fell into a coma (Glasgow Coma Scale: G1C 1S1). Spontaneous respiration stopped and mechanical ventilation was required. There was no abnormality on the electrocardiogram after anabiosis. Anuria developed and he showed symptoms of acute renal failure (BUN: 77.0 mg/dL, Cr: 4.26 mg/dL). Continuous hemodiafiltration (CHDF) (Fig. 1) was started, but CHDF alone did not improve hyperkalemia and hyperphosphatemia, which were probably induced by myocytolysis, and on hospital day 4 hemodiafiltration (HDF) with 10 L of displacement solution was initiated. The levels of myogenic enzyme peaked (CK: 182,910 IU/L, AST: 3,568 IU/L, ALT: 1,055 IU/L, and LDH: 4,589 IU/L) on hospital day 3 and then decreased, and myoglobinuria disappeared on hospital day 5.

The patient was in a coma and an EEG performed on hospital day 9 showed a flat brain wave in all regions, leading to diagnosis of cerebral death by a neurosurgeon. On hospital day 11, the urine volume began to increase and reached 1,300 mL/day on hospital day 14, showing a tendency for improvement of acute renal failure. His family was told that the patient had undergone cerebral death, and thereafter they requested no further positive treatment, including dialysis. After approval by the Institutional Review Board, dialysis was discontinued on hospital day 11. On hospital day 15, the patient showed severe hyperkalemia (BUN: 158.9 mg/dL, Cr: 13.83 mg/dL, K: 7.44 mEq/L), and on hospital day 16 at 7: 30 the patient died due to cardiac arrest caused by hyperkalemia.

Discussion

We encountered a case of rhabdomyolysis due to PTX poisoning from cowfish (Umisuzume, *Lactoria diaphana*). PTX is a neurotoxin with a molecular weight of 2,680 Da (1), which was discovered in Zoantharia, an order of cnidarians, in 1971 (2). It has 10 to 100-fold toxicity compared to tetrodotoxin (TTX), the common puffer toxin, and is one of the strongest fish toxins (2). Most reported cases of PTX poisoning involve eating of the knobsnout parrotfish (3, 4). but some cases have occurred after eating of mackerel and serranid. These kinds of fish prey directly on Zoantharia, or prey on fish that prey on Zoantharia, and consequently the toxin accumulates in the bowels and especially in the liver. Humans develop poisoning after eating the fish, and therefore this poisoning is caused by a food chain (4). Zoantharia



GCS	15	3	→	→	→	→	→	→	→	→	→	3	→	→	→	→	
Light reflex	+	+	+	−	−	−	−	−	−	−	−	−	−	−	−	−	
BUN	21.2			120.2		100.5		96.0		90.2		99.1			158.9		mg/dL
Cr	0.89			6.83		7.39		9.24		8.91		9.10			13.83		mg/dL
K	4.48			5.09		3.99		3.79		3.66		4.26			7.44		mEq/L
CRP	4.61			10.82		10.02		20.26		22.70		26.55			36.41		mg/dL

Figure 1. **Clinical course.**

was originally found in warm seas, but has recently been seen around the coastal area of western Japan, due to an increase in marine water temperature caused by global warming (5).

Binding of PTX to Na, K-ATPase on the cell surface causes Na channel opening, and secondary electrodependent opening of Ca channels and Na/Ca-exchange induces release of neurotransmitters from nerve termini, with resultant myocyte contraction (6). This action is not antagonized by TTX, a Na channel blocker (7). The clinical course of PTX poisoning includes development of rhabdomyolysis by several to 49 hours after PTX intake, with subsequent myalgia, myoglobinuria and dyspnea. In severe cases, the patient dies due to cardiopulmonary arrest. Spasm induced in the vascular smooth muscle has also been reported, resulting in myocardial infarction (3) and intestinal necrosis (unpublished observation in a man with knobsnout parrotfish poisoning in Kamigoto, Nagasaki in April 2007).

In the present case, a PTX hemolysis assay in serum and urine was negative; however, this assay has low sensitivity and PTX poisoning cannot be ruled out by a negative result (4). To confirm the diagnosis, DNA analysis of uneaten fish and detection of a PTX-like substance directly from the fish are required, but in this and most other cases the leftovers have already been thrown away. Differential diagnoses include ciguatera and TTX poisoning. Ciguatera poisoning induces digestive symptoms including diarrhea and vomiting (8), and TTX poisoning induces skeletal muscle paralysis but not rhabdomyolysis (9); therefore, both were unlikely in our case. Cardiopulmonary arrest more than 48 hours after eating of cowfish is unexpected, and the cardiopulmonary arrest seen after 59 hours in our patient may have occurred as follows: (1) respiratory muscle damage caused by rhabdomyolysis due to PTX; (2) brainstem damage, based on a report that PTX directly damages neurons (10), (3) PTX-induced vasospasm causing cerebral infarction; and (4) direct damage to the myocardium by PTX. An autopsy was not permitted by the patient's family, preventing identification of the cause.

At present, there is no specific treatment for PTX detoxification or efficient removal of PTX from the body. Therefore, when a case of PTX poisoning is suspected, cardiorespiration should be monitored, and mechanical ventilation under anesthesia should be given without hesitation when the patient complains of dyspnea. In addition, the Japanese food hygiene law states that the edible parts of the globefish family are only the fillet and a spermary; this must be widely publicized.

We reported this case for the purpose of improving awareness of such poisoning in future clinical practice.

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