CASE REPORT

Intoxication Following Minor Stabs from the Spines of a Porcupine Fish

Teetske F. van Gorcum, M.Sc.*¹, Max Janse, M.Sc.², Marianne E.C. Leenders, M.D.^{1, 3}, Irma de Vries, M.D.^{1, 3} and Jan Meulenbelt, M.D., Ph.D.^{1, 3}

¹National Poisons Information Centre, National Institute for Public Health and the Environment, Bilthoven, The Netherlands.

²Burgers' Zoo, Arnhem, The Netherlands.

³Department of Intensive Care & Clinical Toxicology, University Medical Centre Utrecht, Utrecht, The Netherlands.

*Correspondence: Teetske F. van Gorcum, M.Sc., National Poisons Information Centre, National Institute for Public Health and the Environment, PO Box 1, BA, 3720, Bilthoven, The Netherlands; E-mail: teetske.van.gorcum@rivm.nl

Abstract

We report an unusual intoxication by tetrodotoxin (TTX). A curator of an aquarium sustained minor punctures in his finger from the spines of a porcupine fish during an autopsy of a dead porcupine fish. He developed paresthesias, numbness, paresis, dizziness and headache. The death of the fish might have caused some autolysis, leading to increased availability of TTX. In combination with direct contact with the organ fluids, this probably led to TTX exposure via minor wounds.

Abstract presented at the congress of the European Association of Poisons Centres and Clinical Toxicologists in Berlin, May 2005.

INTRODUCTION

Tetrodotoxin (TTX) is a potent non-protein neurotoxin that is found in certain marine animals, such as puffer fish, porcupine fish, and blue-ringed octopuses. Intoxications with TTX (tetrodotoxination) occur with regularity in East Asian countries, especially in Japan, where a puffer fish of the genus *Fugu* is considered a delicacy. To minimize the number of intoxications, special training and a license are required to prepare *Fugu* [1]. Despite this legislation, the number of annual deaths in Japan from puffer fish poisoning lies around 10. At the start of the previous century more than 50% of the poisoned persons died, but since 1982 the mortality rate has decreased to less than 6% [2]. This decline is probably due to better knowledge of the native population about the toxicity of the fish and availability of better medical support. TTX is not degraded by cooking, freezing or commercial canning [3].

In the puffer fish, TTX is primarily located in the ovaries and liver, with smaller concentrations in other organs such as the intestine and skin [4]. There is a considerable seasonal variation in the toxicity of the fish, which is influenced by the reproductive cycle. Furthermore, toxicity fluctuates with location and species [3].

TTX is well absorbed by mucosa in the mouth and the gastrointestinal tract, and is probably largely eliminated via the kidneys. TTX is a powerful axonal blocking agent. It prevents depolarization and propagation of the action-potential by

blocking sodium channels. The clinical effects of tetrodotoxication are caused by this blockade and include paresthesias, numbness, dizziness, muscle weakness, hypotension, gastrointestinal problems, muscle paresis and paralysis, which may be responsible for respiratory failure without diminution of consciousness [4].

Case Report

A porcupine fish (*Diodon hystrix*) kept at an aquarium of Burgers' Zoo in the Netherlands died of a skin infection by a ciliate (*Cryptocaryon spec.*). The curator of the aquarium (co-author of this report) performed an autopsy on the fish to verify the cause of death. Unfortunately, while handling the dead fish, the spines of the fish penetrated his latex gloves resulting in 3 to 4 minor punctures of his left middle finger. He continued dissecting the fish and came in direct contact with the organ fluids by cutting and handling the organs. After 1.5 hours, the patient experienced paresthesia and numbness in this finger. He was familiar with the toxicity of TTX and went to a nearby hospital. In the following hour, the paresthesia gradually spread from the finger to his arm and shoulder. Two hours later it reached the left upper side of his back. In this period, the paresthesia became less intense and the patient developed paresis of his left arm and dizziness that persisted for approximately 4 hours. He had no respiratory insufficiency. The patient noticed an increase in urine production during the first 48 hours. The fluid intake was approximately 2 liters per day, and no intravenous fluid was administered. Laboratory investigations revealed normal values for hemoglobin, leukocytes, thrombocytes, potassium, creatinine, and gamma-GT, AST, ALT, LDH, CRP. BUN was 16.2 mg/dL (5.8 mmol/L) and glucose 93.6 mg/dL (5.2 mmol/L). Sodium was slightly increased to 146 mmol/L. The calculated plasma osmolality, 303 mosmol/kg, was also slightly increased. No urine analysis was available. Headache developed 7 hours after exposure and persisted for three days, while numbness persisted for two days. No other clinical signs were observed. No specific supportive therapy was indicated. The patient fully recovered after three days.

DISCUSSION

Porcupine fish (Fig. 1) and puffer fish belong to the order of Tetraodontiformes. Porcupine fish inhabit coral reefs and shoal areas in warm seas. Most porcupine fish range from 20 to 50 cm in length. In defense mode, the porcupine fish inflates itself with water or air to a spherical form, during which the spines are extended [3].

FIG. 1 Porcupine fish (*Diodon hystrix*). Photo by Robert A. Patzner, University of Salzburg, Austria

The mechanism of induction of toxicity of TTX-containing animals has not been completely described. It appears to be that an exogenous origin of TTX is generally accepted. Thus, TTX-bearing animals accumulate TTX via the food chain or through a symbiotic way from TTX-producing bacteria [5]. It is known that TTX is situated in the skin and intestines of porcupine fishes. The secretion of the skin of *Diodon hystrix* also contains TTX and some other neurotoxins [6]. Unique TTX-secreting glands in the skin of puffer fish have been identified. Kodama et al. suggested that TTX-secreting glands may play an important role for disposal of TTX, and the excreted TTX might act as a repellent against predators [7]. It can be speculated that in our patient, TTX entered the body directly via the skin and, more plausibly, via minor skin wounds. The death of the fish might have caused some autolysis, leading to an increased availability of TTX. In combination with direct contact with the organ fluids, this probably led to contamination of the wounds.

With regard to this incident, only one comparable intoxication was found in the international literature. In 1922, Phisalix et al. presented a case report about a scientist who developed malaise, headache, itching and rash of face and hands, and gastrointestinal symptoms after spending 2 days dissecting a large puffer fish. The skin of the patient was not damaged during dissection and thus the conclusion was drawn that the poison was absorbed through the skin [8].

Several studies have detected saxitoxin (STX) instead of TTX, or sometimes both toxins, in various species of puffer fish [9]. STX is a component of the well-known paralytic shellfish poison (PSP). The chemical structure of STX is different from that of TTX. Nevertheless, clinical effects of both toxins are very similar; both block the sodium channels and, therefore, the action-potential of nerves and skeletal muscle. The similarity of clinical effects makes the distinction between STX and TTX poisoning difficult [10]. No analysis of TTX, STX or related substances was performed in the remains of the fish or blood or urine samples of our patient, because the facility to analyze these toxins was not available. It is therefore possible that STX or related substances have contributed to this intoxication.

The onset, duration and seriousness of intoxication with TTX depend on the amount of absorbed toxin and the health of the patient. After ingestion, numbness and paresthesia develop, as in our patient, within a few minutes. In a mild intoxication, other symptoms will appear after a few hours. Prognosis is good in cases where the patient survives the first 24-hours with adequate supportive care. In severely intoxicated patients, clinical effects can be prolonged for days [3].

The rise of urine production and slight increase of sodium and calculated plasma osmolality in our patient were described only once before, as far as we know. Tambyah et al. presented a case in which tetrodotoxication led to cranial diabetes insipidus. They suggested that TTX might block the sodium channels of the neurons of the supraoptic nuclei in the hypothalamus, inhibiting the release of vasopressin and causing central diabetes insipidus [11].

Our patient did not develop any symptoms that required particular treatment. Treatment of more severe tetrodotoxication in general is supportive. A monoclonal antibody against TTX has been tested on mice, but not on humans [12]. Some case reports describe a positive effect of anticholinesterase drugs, which may be the result of a competitive reversible blockade of TTX at the motor end-plate, as well as at the motor axon and muscle membrane [1]. Chew et al. suggest that the blockade can be reversed by increasing the release of acetylcholine at the neuromuscular junction. This therapy appeared effective if given early and during recovery [1]. Kao et al., however, reported that TTX blocks sodium channels at the axons and muscle membranes, and does not have any influence at the end-plates [4].

The discussed patient, co-author of this report, has described the symptomatology himself. After he had handled the fish, he experienced the described phenomena and since then has not experienced them again. The other authors, who have interviewed the patient, were convinced that a causal connection between exposure and presented symptoms was very plausible.

In conclusion, the course of this intoxication indicated that a TTX intoxication is very plausible. TTX probably entered the body directly via the skin and/or via minor wounds. Autolysis might have caused a better availability of TTX. In combination with direct contact with the organ fluids, by cutting and handling these organs, this probably led to contamination of the wound. Unfortunately, the intoxication could not be proven by laboratory analyses because TTX analysis is not available in the Netherlands.

REFERENCES

1. Chew, SK, Goh, CH, Wang, KW, Mah, PK, and Tan, BY Puffer fish (tetrodotoxin) poisoning: clinical report and role of anti-cholinesterase drugs in therapy. *Singapore Med J.* (1983), **24**: 168–171
2. Noguchi, T, and Ebesu, JSM Puffer poisoning: epidemiology and treatment. *J Toxicol Tox Rev* (2001), **20**: 1–10
3. Halstead, BW *Poisonous and venomous marine animals of the world* The Darwin Press: Princeton, NJ, (1978): 437–548.
4. Kao, CY Tetrodotoxin, saxitoxin and their significance in the study of excitation phenomena. *Pharmacol Rev* (1966), **18**: 997–1049
5. Miyazawa, K, and Noguchi, T Distribution and origin of tetrodotoxin. *J Toxicol Tox Rev* (2001), **20**: 11–33
6. Malpezzi, ELA, Freitas, JC de, and Rantin, FT Occurrence of toxins, other than paralysing type, in the skin of tetraodontiformes fish. *Toxicon* (1997), **35**: 57–65
7. Kodama, M, Sato, S, Ogata, T, Suzuki, Y, Kaneko, T, and Aida, K Tetrodotoxin secreting glands in the skin of puffer fishes. *Toxicon* (1986), **24**: 819–829
8. Phisalix M. *Animaux venimeux et venins*. Masson et Cie. 1922, Paris.
9. Nakashima, K, Arakawa, O, Taniyama, S, Nonaka, M, Takatani, T, Yamamori, K, Fuchi, Y, and Noguchi, T Occurrence of saxitoxins as a major toxin in the ovary of a marine puffer *Arothron firmamentum*. *Toxicon* (2004), **43**: 207–212
10. Evans, MH Mechanism of saxitoxin and tetrodotoxin poisoning. *Br Med Bull* (1969), **25**: 263–267
11. Tambyah, PA, Hui, KP, Gopalakrishnakone, P, Chin, NK, and Chan, TB Central-nervous-system effects of tetrodotoxin poisoning. *Lancet* (1994), **343**: 538–539
12. Benzer T. Tetrodotoxin. eMedicine Journal. www.emedicine.com/emerg/topic576.html.