Case Series: Inhaled Coral Vapor—Toxicity in a Tank

Payal Sud · Mark K. Su · Howard A. Greller ·
Nima Majlesi · Amit Gupta

Published online: 24 May 2013
© American College of Medical Toxicology 2013

Abstract

Introduction Palytoxin (PTX) is considered a severe marine toxin. Although rare, reports of human exposure from consumption of PTX have described significant morbidity and mortality. PTX is the suspected agent in Haff disease, in which rhabdomyolysis occurs within 24 h of eating contaminated fish such as buffalo fish. PTX is primarily present in soft corals or in dinoflagellates, and it can contaminate crustaceans and other fish as it bioaccumulates up the food chain. Only 23 cases have been reported in the USA, including two recent cases in New York City. Reports of inhalational exposure to PTX are uncommon.

Case Reports We describe a case series of six patients, including four adults and two children, with inhalational exposure to PTX aerosolized from *Palythoa* corals. Their symptoms included some degree of respiratory involvement, myalgias, paresthesias, low-grade fevers, and gastrointestinal symptoms. Fortunately, there were no serious outcomes and all patients survived without sequelae.

Discussion Although rare, exposure to palytoxin is not restricted to people visiting marine environments because of *Palythoa* coral in some home aquariums. Routes of exposure go beyond consumption of fish that feed on the coral and include dermal as well as inhalational exposure. Palytoxin exposure should be considered in the differential diagnosis of patients who own or work with fish tanks and present with symptoms that include respiratory complaints, myalgias, neuromuscular dysfunction, hemolysis, and cardiac toxicity. There is no known antidotal therapy and treatment should focus on meticulous supportive care.

P. Sud (✉) · M. K. Su · H. A. Greller
Department of Emergency Medicine—Toxicology,
North Shore University Hospital, 300 Community Drive,
Manhasset, New York, NY 11030, USA
e-mail: payalpotnis@gmail.com

N. Majlesi · A. Gupta
Department of Emergency Medicine—Toxicology,
Staten Island University Hospital, 475 Seaview Avenue,
Staten Island, New York, NY 10305, USA

Keywords Palytoxin · Marine · Envenomation · Coral

Introduction

Palytoxin (PTX) is a deadly marine toxin, second only to another marine dinoflagellate toxin, maitotoxin, in terms of potency [1, 2]. PTX has an intravenous LD₅₀ in mice of 0.15 mcg/kg [3], compared to tetrodotoxin, which has an intravenous LD₅₀ of 8.7 mcg/kg in mice. Thus, while tetrodotoxin is more commonly recognized as a dangerous marine toxin, it is only about 1/60th as potent a toxin as is PTX. Another common marine toxin is stonustoxin from stonefish, with an intravenous LD₅₀ of 17 mcg/kg [4].

Although rare, reports of human exposure from consumption of PTX have described significant morbidity and mortality. Symptoms after PTX exposure include: myalgias, weakness and neuromuscular dysfunction, wheezing or respiratory distress possibly due to muscular contraction, delayed hemolysis, and cardiac conduction abnormalities [5–7]. PTX is the suspected agent in Haff disease, in which rhabdomyolysis occurs within 24 h of eating contaminated fish such as buffalo fish. PTX is primarily present in soft corals or in dinoflagellates, and it can contaminate crustaceans and other fish as it bioaccumulates up the food chain [8]. Only 23 cases have been reported in the USA, including two recent cases in New York City [9].

Reports of inhalational exposure to PTX are uncommon [7, 10]. A case series of six patients with inhalational exposure to PTX aerosolized from *Palythoa* corals is described. Their symptoms included some degree of respiratory involvement, myalgias, low-grade fevers, and occasionally gastrointestinal symptoms. Fortunately, there were no serious outcomes, and all the patients survived without sequelae.

Case 1

A 32-year-old man without any past medical history presented to the emergency department (ED) complaining

of shortness of breath and chest tightness. Prior to arrival, he attempted to kill a presumptive *Palythoa* coral, which was decimating the other life in his saltwater aquarium. Without personal protective equipment, he transferred the coral to a sink and noticed that it secreted a mucous-like substance. He then doused the coral with boiling water. He noted that the liberated steam had a foul odor, and that his symptoms began shortly after inhalation of this steam.

Presenting vital signs included: a heart rate of 120 beats per minute, a blood pressure of 140/80 mmHg, afebrile, and a respiratory rate of 24 breaths per minute with an oxygen saturation of 100 % on room air. On physical examination, he was noted to have scattered wheezing in all lung fields. A 12-lead electrocardiogram showed sinus tachycardia at 126 beats per minute without any other abnormalities. A chest X-ray (CXR) showed no infiltrates or pneumothorax. Comprehensive metabolic panel and cardiac enzymes were all within normal limits. Complete blood count was significant for a measured white blood cell count of 21,000/mcl (normal range, 3,500–10,500/mcl) with a normal manual differential. The patient's symptoms improved with three doses of nebulized albuterol, although his chest tightness persisted. The patient was admitted for telemetry observation and was discharged after 24 h without any cardiac events, elevations in cardiac enzymes, or other sequelae.

Case 2

A 42-year-old man, a professional fish tank cleaner, presented to the ED with shortness of breath 6 h after cleaning a fish tank. He reported that he had poured boiling hot water over a presumptive *Palythoa* coral; steam was liberated and almost immediately he experienced shortness of breath. He also measured a temperature of 101 °F. He treated himself with over-the-counter oral *N*-acetylcysteine and vitamin C and prior to ED presentation.

In the ED, his temperature increased to 103 °F. He continued to complain of shortness of breath, although his lungs were clear to auscultation and his CXR did not show any abnormalities. Labs measured a leukocytosis of 16,000/mcl. He was administered nebulized albuterol with some relief, after which, he left against medical advice before any further work-up could be performed. He was discharged with prescriptions for albuterol and levofloxacin.

Case 3

A 51-year-old man with no known significant past medical history, the owner of the fish tank that was being cleaned by patient #2, was in close proximity to the fish tank when it was being cleaned and developed a dry cough shortly after

exposure. He presented to the ED 8 h later when his cough continued to worsen and he started experiencing chills, myalgias, and fatigue.

Upon arrival, he was externally decontaminated by showering. His vital signs were: temperature of 100.8 °F, heart rate of 93 bpm, blood pressure of 125/86 mmHg, and a room air oxygen saturation of 98 %. His dry cough continued to worsen in the ED, but his CXR was normal. He refused nebulized albuterol stating that the nebulizers “induce migraine headache.” He continued to have a dry cough, myalgias, and fatigue during his 3-day hospital stay.

His initial labs revealed a leukocytosis of 21,800/mcl, which peaked at 27,600/mcl on hospital day 2, with 87 % neutrophils. On hospital day 3, his white blood cell count decreased to 20,000/mcl. His lactate dehydrogenase (LDH) on admission was 292 U/L (normal range 135–225 U/L). His LDH normalized to 138 U/L by hospital day 3. His admission creatine phosphokinase (CPK) was 184 U/L (normal range 30–200 U/L) and continued to trend down to 77 U/L by hospital day 3.

Upon discharge, he was given a prescription for albuterol, which he did not fill. Two days post-discharge, he continued feel fatigued, although his cough had improved. He was offered follow-up with the Toxicology Faculty Practice, but has not done so.

Case 4

A 35-year-old woman with no past medical history, and the wife of patient #3, was also in close proximity to the fish tank and developed a dry cough shortly after exposure. She presented to the ED 8 h later when her cough continued to worsen and she started experiencing chills, myalgias, fatigue, and paresthesias in both upper extremities.

Upon arrival in the ED she, too, was externally decontaminated. Her vital signs included a temperature of 100.4 °F, heart rate of 93 bpm, blood pressure of 108/67 mmHg, and a room air oxygen saturation of 100 %. A CXR was performed, which was normal. In the ED, she developed nausea and had one episode of non-bilious and non-bloody emesis. During the course of her 3-day admission, she continued to experience myalgias, fatigue, and nausea and developed mild wheezing on hospital day 2. She felt relief with nebulized albuterol. She had no further episodes of paresthesias or vomiting during her hospital stay.

Initial laboratory studies revealed a white blood cell count of 10,700/mcl, which peaked at 16,400/mcl on hospital day 1 and by hospital day 3 had decreased to 12,100/mcl. Her LDH on admission was 193 U/L (normal range 135–225 U/L) and decreased to 123 U/L on hospital day 3. Her admission CPK was mildly elevated at 197 U/L (normal range 25–170 U/L) and trended down to 60 U/L by hospital day 3.

This patient was 2 months postpartum and was breast-feeding her child at the time. Due to the lack of data on the excretion of palytoxin in breast milk, she was advised to avoid breast-feeding during her hospital stay.

Upon discharge, she was given a prescription for albuterol, which she did not fill. Two days post-discharge, her fatigue and myalgias had improved and she had no further respiratory or gastrointestinal complaints. She was offered follow-up with the Toxicology Faculty Practice, but has not done so.

Case 5

A 3-year-old boy with no past medical history, the son of patients #3 and #4, was playing near the fish tank during the cleaning. He immediately developed a dry cough, had one episode of non-bilious, non-bloody emesis and became extremely fatigued. His fatigue continued to worsen and he presented to the ED along with his parents 8 h after the exposure.

Upon arrival, he underwent external decontamination. His vital signs included a temperature of 103.5 °F and a heart rate of 154 bpm (normal range 80–125 bpm). He was breathing at 34 bpm (normal age-appropriate range 22–30 bpm) and his room air saturation was 100 %. His EKG was normal for age. He continued to experience fatigue in the ED. A CXR was performed which was normal. His cough and fatigue resolved by hospital day 2.

Initial labs revealed a marked leukocytosis of 34,100/mcl (normal range 5,000–15,500/mcl). His white blood cell count peaked at 35,400/mcl on hospital day 2 and decreased to 24,800/UL by hospital day 3. His LDH on admission was elevated to 331 U/L (normal range 135–225 U/L). His LDH decreased to 253 U/L by hospital day 3. His CPK was initially normal at 78 U/L (normal range 30–200 U/L) and continued to trend down to 39 U/L by hospital day 3.

By the time he was discharged on hospital day 3, he was completely asymptomatic and no further fever. His fatigue had completely resolved and he continued to do well after discharge. He was offered follow-up with the Toxicology Faculty Practice, but has not done so.

Case 6

A 2-month-old girl with no past medical history, the daughter of patients #3 and #4, was the furthest away from the fish tank during the cleaning. She was asymptomatic but was brought in to the ED along with her parents and brother.

She underwent external decontamination. Her vital signs included a temperature of 100.1 °F and a heart rate of 156 bpm (normal range 100–160 bpm). She was breathing

at 40 bpm (normal range 30–60 bpm) and her room air saturation was 100 %. Her EKG was normal. She remained asymptomatic in the ED. A CXR was performed which was normal. She did not develop any symptoms throughout her 3-day hospital stay.

Her initial labs revealed a marked leukocytosis of 34,400/mcl (normal range 6,000–17,500/mcl). Her white blood cell count decreased to 8,700/mcl on hospital day 3, prior to discharge. Her LDH on admission was elevated at 507 U/L (normal range 135–225 U/L) and decreased to 285 U/L on hospital day 3. Her venous lactate measured 5 mmol/L (normal range 0.5–2.2 mmol/L) upon admission, which decreased to 1.4 mmol/L by the next day. CPK was initially 169 U/L (normal range 25–170 U/L) and peaked at 259 U/L on hospital day 2. It normalized to 115 U/L on hospital day 3. The patient also had an elevated initial creatine kinase MB isoenzyme (CKMB) of 7.82 ng/mL (normal <4.8 ng/mL) and an elevated CKMB relative index of 4.6 (normal range is 0–2.5). A transthoracic echocardiogram was performed which was normal.

The infant tolerated formula feedings throughout her hospitalization. Upon discharge, she remained well, except for some constipation that developed when she was switched back to breast milk. She was offered follow-up with the Toxicology Faculty Practice, but has not done so.

Discussion

Our case series reports the effect of inhalational exposure to presumptive PTX in six patients, four adults and two children. All adult patients developed respiratory symptoms including wheezing and shortness of breath after exposure. Two patients developed gastrointestinal symptoms, including nausea and vomiting. All the patients who had data available showed development of a low-grade fever and an increase in their white blood cell count and a minor elevation in creatine phosphokinase values during hospitalization. The white blood cell counts of the family of four peaked during hospitalization and decreased towards normal by discharge with supportive care. Similarly, their creatine phosphokinase increased during hospitalization and returned to normal by discharge with supportive care.

The majority of previous reports of PTX exposure have been secondary to the consumption of fish that bioaccumulate PTX by feeding on the dinoflagellate *Ostreopsis* species or on *Palythoa* species [6, 7, 10]. Some examples of these fish include the parrotfish (*Scarus ovifrons*), marine pufferfish (*Sphoeroides spengleri*), and filefish (*Altera scripta*). A previous case report describes a 55-year-old Japanese man who developed rhabdomyolysis and myocardial damage after ingestion of the raw meat and liver of a blue humphead parrotfish [11]. The presence of PTX was confirmed in the

tissues and liver of the remaining fish. The patient recovered fully after 4 weeks with an aggressive therapeutic regimen of gastric lavage, multiple days of activated charcoal, and forced diuresis with mannitol. It is unclear what effect, if any, these treatments had on the outcome. Another report describes a 35-year-old man presenting with severe muscle cramping which progressed to a “spinal seizure” and respiratory failure. The spinal seizure consisted of tonic contractions of all muscles and the severe muscle spasms resulted in elevations of the patient’s CPK. The patient had ingested a whole smoked mackerel (*Decapterus macrosoma*) including the viscera [12]. The patient recovered after 9 days. PTX was isolated from the same batch of fish that had been imported from the Philippines. Another report described a 40-year-old man who developed cardiopulmonary arrest and renal failure after ingestion of cowfish (*Lactoria diaphana*) that was contaminated with PTX [13].

There have been reports of PTX poisoning via dermal exposure as well. Hoffmann and colleagues provided the first such report in 2008 [14]. It described a 31-year-old man who experienced shivering, myalgias, digital paresthesias, speech disturbance, and syncope after handling zoanthids (a type of cnidarian found in coral reefs) in an aquarium. The patient was found to have small lacerations on the tips of his fingers. His symptoms persisted for 48 h and he recovered without sequelae. The zoanthid coral was analyzed and high concentrations of palytoxin were found in it (2–3 mg/g).

The largest suspected report of inhalational exposure to PTX was in 2007, where more than 200 patients developed respiratory symptoms after an *Ostreopsis ovata* algal bloom in Italy [15]. The most common symptom was fever, followed by sore throat, cough, and dyspnea. Ten percent of the population developed vomiting as well [15]. Another report of presumed inhalational PTX exposure to zoanthids in an aquarium is from 2006 in Virginia [6, 7]. The patient in this case developed respiratory symptoms after pouring boiling water over the zoanthid coral. Two weeks later, the patient was diagnosed with bronchial inflammation and bronchoconstriction by a pulmonologist. A similar case report of a family developing a fever after being exposed to steam from zoanthid corals was recently published [16]. Pouring hot water over the zoanthid coral may aerosolize the toxin and cause symptoms similar to those seen with algal blooms.

Most patients with PTX exposure develop elevations in their LDH and CPK, thus implicating PTX as the causative agent in Haff disease where rhabdomyolysis occurs after ingestion of contaminated fish. The mechanism of action by which PTX achieves this is complex and has been the focus of several in vitro and in vivo animal studies. Understanding the function of the Na^+/K^+ -ATPase allows insight into the PTX’s mechanism of action. There are two types of Na^+/K^+ -ATPase toxins: the cardiac glycosides such as digitalis and ouabain and PTX [17]. While the cardiac glycosides inhibit the action

of the Na^+/K^+ -ATPase, PTX turns the pump into a nonselective ion channel [17, 18] resulting in cell lysis.

Membrane-based exchange transporters, in general, have a cytoplasmic gate and an extracellular gate, and in order to function properly, the gates have to open one at a time. Ion channels, on the other hand, can have both cytoplasmic and extracellular gates open at the same time. With the Na^+/K^+ -ATPase, when intracellular Na^+ binds the pump, ATP is hydrolyzed and the cytoplasmic gate closes. This allows the extracellular gate to open and Na^+ exits while K^+ binds the extracellular side of the pump. Once K^+ binds the pump, the pump is dephosphorylated and the extracellular gate closes. This allows the cytoplasmic gate to open and K^+ can enter the cell [17, 19]. PTX binds at the ouabain site on the Na^+/K^+ -ATPase and opens both the cytoplasmic and the extracellular gates, “locking” them open. This converts the pump into a nonspecific cation channel in contrast to toxins such as tetrodotoxin, grayanotoxins, and aconitine, which open sodium channels, rather than the Na^+/K^+ -ATPase. Increasing cation conductance by PTX in erythrocytes results in cell lysis [20], which is one explanation for the elevation in LDH. PTX may cause similar breakdown of skeletal muscle myocytes, resulting in the observed elevations in CPK and LDH.

In vivo and in vitro animal studies have examined the potential implications of PTX exposure. One study, which evaluated the effects of PTX on the in vitro rabbit aorta, noted sustained contraction that was resistant to treatment with sodium nitroprusside [21]. This contraction appeared to be dependent on calcium, and there appeared to be a dose-dependent increase in calcium uptake in the presence of increasing PTX concentrations. As PTX converts the Na^+/K^+ -ATPase to a nonselective cation channel, increasing cation conductance leads to depolarization. Depolarization results in increased calcium conductance through voltage-dependent L-type Ca^{2+} channels as well as via the $\text{Na}^+/\text{Ca}^{2+}$ exchanger [22]. PTX has also been shown to open an H^+ conductive pathway with a resulting activation of Na^+/H^+ exchanger in bovine adrenal chromaffin cells [23]. This was shown to result in cardiac cellular acidification in embryonic chick ventricular cells [8]. Although not studied clinically, this could be a potential mechanism for the cardiotoxic effects of PTX. Lastly, it is believed that PTX may be able to increase influx of calcium independently of sodium-induced depolarization through mechanisms not yet defined. Most of the studies show a consistent depolarization and contraction effect in all end organs tested.

The mechanism by which our patients may have developed bronchospasm is interesting and novel to this toxin. PTX’s ability to cause smooth muscle contraction as described in the in vitro study on rabbit aorta [21] may have contributed to bronchospasm and resultant respiratory symptoms observed in our cases. The short duration of symptoms that our patients developed may have been secondary to a low dose of toxin inhaled or possibly due to the

route of exposure. Hypersensitivity to the coral due to repeated exposure is unlikely to be a cause of the symptoms because the symptoms were observed in the patients that did not have repeated exposure to the coral as well.

Limitations

In the cases described, it was not possible to perform high-pressure liquid chromatography or liquid chromatography with mass spectrometry to detect PTX in the serum or tissues of the patients. It was also not possible to obtain the original coral to detect PTX in the source as well. Thus, the diagnosis was made on recognition of the coral and by the symptoms present in the patients. However, it is possible that the symptoms experienced by the patients may have been due to the presence of other marine toxins in the coral, such as maitotoxin, brevetoxin, or a PTX analog such as homopalytoxin, bishomopalytoxin, neopalytoxin, depalytoxin, or 41-hydro-palytoxin. No chemicals were used to clean the aquariums, only hot water; thus, chemical exposure as the cause of the observed symptoms is unlikely.

Conclusion

Although rare, exposure to palytoxin is not restricted to people visiting marine environments because of *Palythoa* coral in some home aquariums. Routes of exposure go beyond consumption of fish that feed on the coral and include dermal as well as inhalational exposure. Palytoxin exposure should be considered in the differential diagnosis of patients who own or work with fish tanks and present with symptoms that include respiratory complaints, myalgias, neuromuscular dysfunction, hemolysis, and cardiac toxicity. There is no known antidotal therapy, and treatment should focus on meticulous supportive care.

Conflict of interest The authors have no conflicts of interest

References

- Nicolaou KC, Frederick MO, Aversa RJ (2008) The continuing saga of the marine polyether biotoxins. *Angew Chem Int Ed Engl* 47(38):7182–7225
- Deeds JR, Handy SM, White KD, Reimer JD (2011) Palytoxin found in *Palythoa* sp. zoanthids (Anthozoa, Hexacorallia) sold in the home aquarium trade. *PLOSone* 6(4):e18235
- Moore RE, Scheuer PJ (1971) Palytoxin: a new marine toxin from a coelenterate. *Science* 172:495–498
- Khoo HE (2002) Bioactive proteins from stonefish venom. *Clin Exp Pharmacol Physiol* 29:802–806
- Shinzato T, Furusu A, Nishino T, Abe K, Kanda T, Maeda T et al (2008) Cowfish (*Umisuzume*, *Lactoria diaphana*) poisoning with rhabdomyolysis. *Intern Med* 47:853–856
- Deeds JR, Schwartz MD (2010) Human risk associated with palytoxin exposure. *Toxicon* 56:150–162
- Tubaro A, Durano P, Del Favero G, Ansaldi F, Icardi G, Deeds JR et al (2011) Case definitions for human poisonings postulated to palytoxins exposure. *Toxicon* 57:478–495
- Frelin C, Vigne P, Breittmayer JP (1990) Palytoxin acidifies chick cardiac cells and activates the Na⁺/H⁺ antiporter. *FEBS Lett* 264(1):63–66
- Gounder P, Balter S (2011) Advisory #26, Haff disease: rhabdomyolysis associated with fish Consumption, NYC DOH and MH
- Tichadou L, Glaizal M, Armengaud A, Grossel H, Lemee R, Kantin R et al (2010) Health impact of unicellular algae of the *Ostreopsis* genus blooms in the Mediterranean Sea: experience of the French Mediterranean coast surveillance network from 2006 to 2009. *Clin Tox* 48(8):839–844
- Okana H, Masouka H, Kamel S, Seko T, Koyabu S, Tsuneoka K et al (1998) Rhabdomyolysis and myocardial damage induced by palytoxin, a toxin of blue humphead parrotfish. *Inter Med* 37(3):330–333
- Kodama AM, Hokama Y, Yasumoto T, Fukui M, Manea SJ, Sutherland N (1989) Clinical and laboratory findings implicating palytoxin as cause of ciguatera poisoning due to *Decapterus macrerosoma* (mackerel). *Toxicon* 27(9):1051–1053
- Shinzato T, Furusu A, Nishino T, Abe K, Kanda T, Maeda T et al (2008) Cowfish (*Umisuzume*, *Lactoria diaphana*) poisoning with rhabdomyolysis. *Inter Med* 47:853–856
- Hoffmann K, Hermanns-Clausen M, Buhl C, Buchler MW, Schemmer P, Mebs D et al (2008) A case of palytoxin poisoning due to contact with zoanthid corals through a skin injury. *Toxicon* 51:1535–1537
- Durando P, Ansaldi F, Oreste P, Moscatelli P, Marensi L, Grillo C, Collaborative Group for the Ligurian Syndromic Algal Surveillance et al (2007) *Ostreopsis ovata* and human health: epidemiological and clinical features of respiratory syndrome outbreaks from a two-year syndromic surveillance, 2005–06, in north-west Italy. *Euro Surveill* 12(23):pii=3212
- Snoeks L, Veenstra J (2012) Family with fever after cleaning a sea aquarium. *Ned Tijdschr Geneesk* 156(12):A4200
- Hilgemann DW (2003) From a pump to a pore: how palytoxin opens the gates. *PNAS* 100(2):386–388
- Artigas P, Gadsby DC (2003) Na⁺/K⁺-pump ligands modulate gating of palytoxin-induced ion channels. *PNAS* 100(2):501–505
- Hobbs AS, Albers RW, Froehlich JP (1980) Potassium-induced changes in phosphorylation and dephosphorylation of (Na⁺ + K⁺)-ATPase observed in the transient state. *J Biol Chem* 255(8):3395–3402
- Tosteson MT, Halperin JA, Kishi Y, Tosteson DC (1991) Palytoxin induces an increase in the cation conductance of red cells. *J Gen Physiol* 98(5):969–985
- Ito K, Karaki H, Urakawa N (1977) The mode of contractile action of palytoxin on vascular smooth muscle. *Eur J Pharm* 46:9–15
- Frelin C, Renterghem CV (1995) Palytoxin. Recent electrophysiological and pharmacological evidence for several mechanisms of action. *Gen Pharm* 26(1):33–37
- Yoshizumi M, Houchi H, Ishimura Y, Masuda Y, Morita K, Oka M (1991) Mechanism of palytoxin-induced Na⁺ influx into cultured bovine adrenal chromaffin cells: possible involvement of Na⁺/H⁺ exchange system. *Neurosci Lett* 130:103–106