Aerosolized palytoxin toxicity during home marine aquarium maintenance

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ABSTRACT
Decorative coral species capable of producing palytoxin (PTX) frequently adorn marine aquariaums. PTX is an ultra-potent toxin with significant morbidity and mortality. Toxicity from PTX results in a spectrum of symptoms depending on route of exposure. We report the case of a 30-year-old man who accidentally aerosolized PTX while cleaning his saltwater fish tank, resulting in precipitous respiratory distress.

KEYWORDS
Palytoxin; coral; marine; fish tank; inhalational exposure; toxin; respiratory distress; sodium–potassium pump

Introduction
An estimated 700,000 households in the United States feature a saltwater aquarium [1]. Enthusiasts often decorate these with colorful exotic animals, including coral. Zoanthid corals are colonizing animals of the phylum Cnidaria, thus phylogenetically related to venomous species of jellyfish such as the box jellyfish. Some zoanthids are capable of synthesizing or bioaccumulating a heat stable, ultra-potent toxin which the animal releases under duress. We present a case of inhalational exposure to aerosolized palytoxin (PTX) from zoanthid coral.

Case
A 30-year-old man without pertinent past medical history presented to the Emergency Department (ED) with complaints of rigors, fever (home temperature of 102°F), dyspnea, pharyngitis, emesis, myalgias, and headache. His symptoms started within an hour of inhaling steam released while eradicating overgrown Zoantharia from a rock in his saltwater fish tank (Figure 1) by dousing it with boiling water. His partner who was in a separate room developed similar, milder symptoms.

Upon arrival to the ED he was tachycardic (140 bpm), tachypneic (30 rpm), and hypoxemic (pulse oximetry 90% on room air). His blood pressure was 135/89 mmHg and temperature 99.2°F (oral) after self-administration of 500 mg acetaminophen orally prior to arrival. He exhibited sub-costal retractions, wheezing, accessory muscle use, and appeared ill. His ECG showed sinus tachycardia with appropriate electrical intervals and no changes consistent with pharmacologic cardioactive steroid effects. His chest X-ray showed a small right basilar infiltrate (Figure 2).

He received supplemental oxygen, intravenous crystalloids, corticosteroids, and nebulized albuterol with ipratropium. After poor initial response to these interventions he also received magnesium sulfate. Laboratory results showed initial mild leukocytosis of 11.21 k/μL, normal creatine phosphokinase of 149 IU/L, elevated lactate of 3.0 mmol/L, and initial elevated procalcitonin of 0.35 ng/mL which increased to 2.59 ng/mL over an 8-h interval. Influenza and respiratory syncytial virus PCR were negative. The patient received empiric, broad spectrum antibiotics, yet blood cultures remained negative. During the patient’s course in the ED, his blood pressure decreased to 104/54 mmHg and he required additional IV fluids, inhaled β2-agonists, and oxygen by non-rebreather mask.

Based on the history and presentation, the treating clinician suspected PTX toxicity but elected to empirically treat bacterial pneumonia. The consulting toxicologist recommended supportive therapy. The patient improved as an inpatient over the subsequent day. Outpatient therapy included systemic corticosteroids and inhaled β2-agonist therapy.

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Discussion

PTX is a highly complex non-protein compound first isolated in 1971 from *Palythoa toxica*, an anemone of the phylum *Cnidarian*, order *Zoantharia*. Several species of the dinoflagellate genus *Ostreopsis* are also capable of producing PTX. Consumption of coral or dinoflagellates facilitates bioaccumulation in predatory marine animals, including fish and crabs. Multiple analogues to PTX exist, including homopalytoxin, bishomopalytoxin, neopalytoxin, deoxypalytoxin, and 42-OH palytoxin [2].

The molecular target of PTX and its analogues is the $\text{Na}^{+},\text{K}^{+}$-ATPase [3]. This ubiquitous ion pump maintains normal electrochemical equilibria required for the function of multiple excitable tissues including the nervous system, cardiac conduction system, and contractile apparatus of myocytes. Binding of PTX to $\text{Na}^{+},\text{K}^{+}$-ATPase occurs near the ouabain binding site and exerts a similar inhibitory effect [3]. Unlike ouabain, PTX leads to arrest of the $\text{Na}^{+},\text{K}^{+}$-ATPase in a conformational position that allows free flux of single-charge cations across the cellular membrane, thus effectively converting it into a non-selective cation channel [4].

Toxicity occurs by various routes: ingestion of seafood containing PTX, dermal absorption after contact with *P. toxica*, or inhalation of aerosolized PTX during cleaning of aquaria or inhalation of sea spray during *Ostreopsis* bloom. Ocular exposure to PTX may occur with inhalation or direct inoculation.

Ingestion of seafood containing PTX is often associated with metallic taste and leads to rapid development of symptoms over minutes to hours. Gastrointestinal distress and paresthesias are commonly described in the early course. Myalgias herald the beginning of rhabdomyolysis with associated laboratory abnormalities. Seizures and cardiotoxicity caused death in three patients with laboratory-proven PTX ingestions [5,6].

Topical absorption with subsequent systemic toxicity may occur in swimmers or divers who touch PTX-producing coral, or individuals handling these animals during maintenance work of aquaria. Clinically significant absorption of PTX occurs with minimal dermal injury, as was the case with a 32-year-old man who developed cardiotoxicity after sustaining a 5 mm cut [7]. Visible dermal injury is not necessary for systemic toxicity to occur. A 25-year-old woman developed a metallic taste, paresthesia, diffuse urticaria, and perioral edema after touching *Zoantharia* coral with her bare hands without sustaining visible injury [8]. A special case of topical exposure is ocular contact. During rapid closing (a protective reflex), a zoanthid sprayed water into the eye of a 63-year-old man, leading to corneal ulceration requiring in situ amniotic membrane transplantation. In addition, he
developed myoglobinuria and mild rhabdomyolysis [9]. A similar case resulted in keratitis and persistent corneal scarring in a 45-year-old woman [10]. In a series of seven patients, four developed corneal melt, at times with perforation [11]. Other patients experienced full recovery [12].

Inhalational exposure to PTX occurs from two distinct sources: *Osteropsis* algal blooms and *Zoantharia* corals from coastal environments or aquarium, respectively. During a dinoflagellate bloom in Genoa, Italy, beachgoers were exposed to ocean spray containing *Ostreopsis*. Over a period of ten days, 209 patients presented to local hospitals with respiratory complaints, over half were febrile on presentation [13]. Alternatively, inhalational exposure occurs after aerosolizing PTX during aquarium maintenance. *Zoantharia* coral can overgrow a saltwater tank, and thus are often killed by pouring boiling water over the affected aquarium rock. The stress-response of the dying animal liberates PTX, which is heat stable and aerosolized with the steam.

PTX depolarizes bronchial smooth muscle and results in calcium influx [14]. Thus, patients develop bronchospasm within minutes to hours of exposure. Pneumonitis occurs in the majority of patients with associated fever, leukocytosis, and patchy infiltrates on high resolution computed tomography pulmonary imaging [15]. Patients can progress to acute respiratory distress syndrome (ARDS) with subsequent respiratory failure [16]. The proximity of the exposure correlates to the severity of the symptoms [17], but toxicity can affect individuals in different rooms or floors of a dwelling [18]. The partner of our patient was in the adjacent room and developed only mild respiratory symptoms. A review of the Pubmed-indexed literature revealed 17 cases of respiratory symptoms due to PTX inhalation [15–19]. There were no fatalities. Unlike other routes of exposure, clinically significant rhabdomyolysis has not been reported when inhalation was the primary route of exposure.

Inhalational exposure to PTX results in bronchospasm as well as airway inflammation. Inhaled β-receptor agonists and systemic corticosteroids appear to have some treatment benefit [15], but data from rigorous trials establishing efficacy are not available. The benefit of antihistamines is unknown. The membrane-stabilizing and sedating properties of members of this drug class may theoretically complicate the clinical course of patients with severe PTX toxicity, and PTX toxicity is not primarily histamine-mediated.

Laboratory confirmation of PTX utilizes a variety of assays. Enzyme-linked aptamers (horseradish peroxidase) [20], spectrophotometric hemolytic assays [21], liquid chromatography with mass spectrometry [22], and cytometry-based immunoassays [23] can detect PTX in either food scraps or collected coral specimens. No PTX confirmation from human body fluids is reported [24]. Laboratory testing for PTX was not performed in the case presented here, and is not available in time to support clinical decision making. The patient’s presentation satisfies criteria for clinical diagnosis of PTX toxicity [2], and he was treated accordingly. Apart from medical toxicologists, most physicians are likely not familiar with this unique toxicity, and consultation with the local poison center is encouraged.

**Disclosure statement**

The authors report no conflict of interest.

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