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Case Report

Palytoxin Exposure Causing Prolonged Conjunctivitis and Episcleritis without Corneal Involvement

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Abstract

Palytoxin and its derivatives are marine biotoxins with potentially serious sequelae, including blindness, respiratory failure, and death. We present a case of ocular exposure in a 35-year-old Caucasian male causing prolonged unilateral conjunctivitis and episcleritis without corneal involvement. He presented with right eye pain, redness and decreased vision after handling Zoanthid coral. Examination of the affected eye revealed best corrected visual acuity of 6/9**,** diffusely injected conjunctiva, a clear cornea, quiet anterior chamber and unremarkable fundus. To our knowledge this is the first case of ocular exposure to palytoxin without corneal involvement. Following management with topical prednisolone acetate/phenylephrine HCL, intensive carboxymethylcellulose, olopatadine, and prophylactic chloramphenicol, and oral ibuprofen, symptoms gradually resolved over 7 weeks with final vision returning to 6/4. Education and eye protection is encouraged when handling coral.

Keywords: Episcleritis, Conjunctivitis, Keratitis, Ocular inflammation, Palytoxin, Palythoa, Zoanthid Coral

Introduction

Palytoxin was first isolated in 1971 from soft coral *Palythoa toxica* [1], and has since been identified in zoanthid coral, molluscs, crabs, and fish [2]. Palytoxin is produced by marine dinoflagellate *Ostreopsis* spp and likely reaches high levels in marine animals through biomagnification [3]. The most well studied mechanism of palytoxin includes its conversion of gated Na/K+ pumps into nonselective pores, causing unregulated flux of ions, loss of sodium gradients, and membrane depolarisation [4]. Palytoxin also disrupts actin filament function [5]. These mechanisms are thought to potentiate palytoxin's downstream effects of vasoconstriction, muscle contraction, and neurotransmitter release in vascular, muscular and nervous tissues, and may also potentiate cell death [6].

Palytoxin is a potent marine toxin, requiring estimated doses of 4mg to cause lethality in humans [7]. Clinical features of palytoxin poisoning include vomiting, dysgeusias, rhabdomyolysis, and ventricular fibrillation [8]. Two cases of death thought to occur through cardiac arrest and renal failure are reported following ingestion of contaminated seafood [9,10]. Palytoxin may also become aerosolised through evaporation and during algal blooms, resulting in local irritation from inhalation and respiratory failure [11].

Ocular exposure to palytoxin is rare. Aquarium water filtered through activated charcoal reduces palytoxin levels by 99.4% [12], and ocular exposure occurs after handling coral above water, by auto-contamination or direct ocular contact with water jets siphoned by coral [13-16].

Case Study

A healthy 35-year-old male was stacking boxes of coral (*Zoanthus spp*, Figure 1) on his boat when his right eye suffered a jet of water directed by the coral. He experienced immediate pain and irrigated his eye immediately with saltwater. He was not wearing any protective eyewear. The next day he presented with worsening right eye pain and conjunctivitis (Figure 2, top). His left eye was unaffected. Further irrigation was undertaken and treatment instigated with prophylactic chloramphenicol 0.5% drops four times a day, intensive carboxymethylcellulose lubricants, and oral opioid analgesia.

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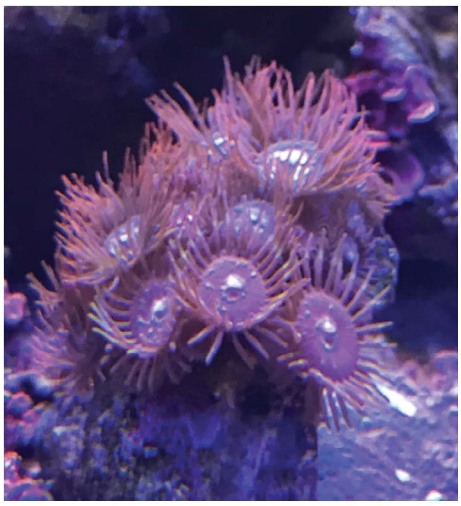

Figure 1: Zoanthus spp coral. The patient was moving boxes of the pictured coral when it siphoned a jet of water into his right eye. Members of the Zoanthus family sold in the aquarium trade can contain detectable levels of palytoxin.

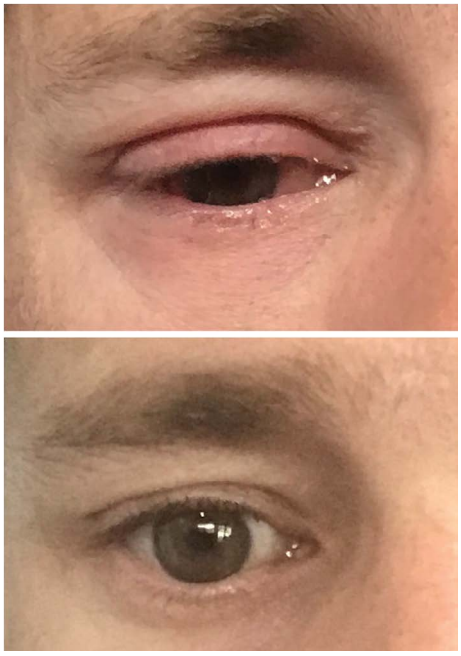

Figure 2: Case photo (top) Day 1 after palytoxin exposure and (bottom) 7 weeks after exposure.

Five days after initial exposure, he represented for ophthalmology review with deteriorating right eye symptoms including severe pain, photophobia and decreased vision. His best corrected visual acuity (BCVA) was 6/9 in the right eye and 6/6 in the unaffected left eye. Intraocular pressures were normal. Aside from a grossly injected conjunctiva of the right eye (which blanched with 10% phenylephrine), the examination was unremarkable. Unlike previous reports of palytoxin-related keratoconjunctivitis, there was no corneal involvement and no anterior chamber reaction present. A diagnosis of conjunctivitis associated with episcleritis was made.

He was commenced on prednisolone acetate/phenylephrine HCL 1%/0.12% every 2 hours, oral ibuprofen 400mg three times a day, and encouraged to use lubricants liberally. On subsequent review two weeks later his BCVA had improved to 6/4 bilaterally, however he had ongoing episcleritis. Topical olopatadine 0.1% twice a day and ketorolac 0.5% four times a day were introduced to good effect. The steroid was slowly tapered over two weeks with complete resolution of his episcleritis 7 weeks after exposure (Figure 2, bottom).

Literature Review

A English language Medline search using MESH terms "Palytoxin" and "Eye"; "Palytoxin" and "Ophthalmology"; "coral" and "eye"; "coral" and "ophthalmology"; "coral" and "keratitis"; "coral" and "keratoconjunctivitis"; returned 4 papers totalling 11 cases of ocular exposure (two females and 9 males, 31 to 71 years old) with 8 full case histories. Due to the unavailability of palytoxin testing in humans, all exposures were presumed based on the temporal relationship between coral handling and occurrence of symptoms. Incidence of ocular palytoxin exposure is likely higher than that in published literature, as many self-reported cases of exposure on aquarium enthusiast websites did not seek medical attention.

Exposure occurred while patients were handling or fragmenting coral above water, through self-inoculation by rubbing the eye(s), or after coral directed water jets into patients' eye(s). In all cases protective eyewear was not worn. Patients complained of isolated ocular symptoms including immediate burning pain in the affected eye(s), photophobia, and blurry vision. One case also presented with nausea, shivering, and palpitations after coral squirted into his eye [15] possibly due to ingestion of contaminated tears following lacrimal drainage. Self-irrigation prior to presentation was common.

Examination revealed decreased visual acuity, injected conjunctiva, and normal intraocular pressures. Anterior chamber reaction was variable, however four cases that presented with – or subsequently developed–anterior chamber inflammation were associated with poorer visual outcomes [13-15]. This suggests an inflammatory component of the disease.

The most devastating injury after palytoxin exposure is reported in the cornea, with clear progression of severity [13-16]. Mild changes included reversible superficial punctate epitheliopathy, while progression or concurrent presentation with corneal ulceration led to permanent sequelae, including circumferential corneal scarring, melt, or perforation. In total six patients required surgical intervention including amniotic membrane grafts (AMG), penetrating keratoplasty (PKP), both AMG and PKP, anterior lamellar patch grafting with AMG, or lateral tarsorrhaphy [13-15]. Three patients required rigid contact lenses [13] or scleral lenses [15] to improve their vision. The incidence of visually significant corneal scarring is high following palytoxin exposure with only three of eleven patients regaining 6/6 vision. Corneal histology has demonstrated epithelial disruption and bulla formation, stromal keratolysis, and endothelial cell attenuation [13]. This pattern of disease progression raises the possibility of limbal stem cell damage from palytoxin.

Patients were treated with a combination of prophylactic antibiotic drops, oral and topical steroids, lubricants, and oral anti-

inflammatories. In cases where steroid treatment was delayed, patients only improved when steroids were commenced [13-16]. Improvement in all cases was slow, and tapering of steroids took between 2 to 12 weeks until resolution of symptoms.

Discussion

There is no widely available commercial test for palytoxin in humans. Several members of the zoanthid family sold in the aquarium trade have been demonstrated to contain palytoxin [17], and the temporal nature of symptoms following exposure has been used to evidence a causal relationship. As the popularity of aquarium keeping continues to rise, public health education regarding proper decontamination of tanks with activated charcoal, working in well-ventilated areas, and safe handling practices-such as wearing protective goggles and gloves-helps to minimise severity of exposure. Immediate irrigation is recommended following exposure.

The full pathophysiology of palytoxin damage to the eye remains unknown. The cornea may be particularly susceptible as Na/K+ pumps maintain stromal deturgescence via the corneal endothelium acting against sodium gradients, and dysregulation of this process may lead to corneal swelling and bulla formation. Adequate tear film production depends upon the action of Na/K+ against sodium gradients, and poor quality tear films may exacerbate corneal injury. Palytoxin disruption of actin filament systems may also impair migration of endothelial and limbal stem cells during corneal repair and explain the prolonged healing process.

Minute doses of palytoxin can cause significant pathology. Rabbits exposed to ocular doses of 0.04μg/kg palytoxin developed severe inflammation, corneal ulceration and formation of anterior synechiae [18]. Duration of corneal contact also affected outcome due to the stability of palytoxin in the neutral tear film [8]. In animal studies, delayed irrigation from one minute to five minutes post exposure increased incidence of corneal scarring [18]. We believe our case is the only published report of ocular palytoxin exposure causing conjunctivitis and episcleritis without corneal involvement. The good visual outcome in this case may be attributed to immediate self-irrigation following exposure and lack of corneal involvement.

The mainstay of medical treatment remains early and aggressive topical steroids-recommended up to 6 times a day by some authors [13]. This may dampen the inflammatory component of disease and prevent progression of corneal disease. Topical steroids may also provide symptomatic relief, as the symptoms in our case and two others were only controlled following an aggressive regimen of topical steroids. Weaning of the steroid may require weeks before the resolution of symptoms.

Conclusion

Timely ophthalmology review, immediate irrigation and early treatment with steroids must be initiated to improve patient outcomes. Ocular antihistamines and anti-inflammatories may be used to improve persistent irritant symptoms. Further research needs to be performed to see if activated charcoal has any role in decontamination following palytoxin ingestion, and appropriate education should be given to anyone handling coral, including wearing appropriate protective eyewear along with working in adequately ventilated areas to limit palytoxin exposure.

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