DOI: 10.4274/tjo.galenos.2021.93384
Turk J Ophthalmol 2021;51:393-397

Case Report

Palytoxin-Related Keratoconjunctivitis Assessed by High-Resolution Anterior Segment Optical Coherence Tomography

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Abstract

Palytoxin (PTX) is produced by corals such as zoanthid corals. Here we present a case of bilateral PTX-induced keratoconjunctivitis. A 63-year-old man presented to the emergency department with symptoms of red eye, purulent discharge, and foreign body sensation in both eyes. On slit lamp examination, epithelial defects in both eyes with a ring-shaped corneal stromal infiltrate in the right eye and a marginal stromal infiltrate in the left eye were noted. High-resolution anterior segment optical coherence tomography (HR-AS-OCT) showed stromal hyperreflectivity and Descemet folds. Bacterial, fungal, and amoebic cultures were taken. Empirical treatment with topical dexamethasone as well as antibiotics and systemic doxycycline was started. The next day the patient stated that he had been handling zoanthid coral without gloves and had rubbed his eyes afterward. Bilateral PTX-induced keratoconjunctivitis was diagnosed. His eyes were irrigated abundantly with saline solution, and umbilical cord serum eye drops were added to the treatment. Treatment was tapered according to improvement of the corneal infiltrates and epithelial defects. After four months, the stromal infiltrates were resolved but corneal scars persisted in both eyes. HR-AS-OCT showed anterior stromal hyperreflectivity corresponding to corneal leucomas. PTX can cause ocular adverse effects such as keratolysis and corneal inflammation, and in some cases can lead to corneal perforation. It can also produce systemic adverse effects, hence the importance of the preventive measures when handling corals that can produce this toxin.
Keywords: Palytoxin, zoanthid, toxic keratoconjunctivitis, umbilical cord serum eye drops, high-resolution anterior segment optical coherence tomography

Introduction

Palytoxin (PTX) is a deadly marine toxin produced by many species of *Palythoa* coral. This coral, in the order Zoantharia, is commonly found in domestic aquariums due to its fast growth and low maintenance requirements.[1]

Ocular exposure to PTX can lead to surface toxicity. A wide variety of presentations have been reported in literature, from superficial punctate epitheliopathy to corneal perforation as a result of corneal melt. This exposure can be from direct contact with the coral, contact with contaminated water, or by rubbing the eyes with a toxin-contaminated hand after handling zoanthid coral. Management is based on recommendations according to the severity of the case; a surgical intervention such as a corneal transplant may be necessary in cases of ulceration that result in corneal perforation.[2,3,4,5,6,7]

We report a case of bilateral PTX-induced chemical keratoconjunctivitis, assessed by high-resolution anterior

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Received: 08.03.2021 **Accepted:** 20.08.2021

Cite this article as: Marti MB, Aragon-Roca D, Trejo-Velasco F, Garrido-Marin M, Oliveres J, Nalda SM. Palytoxin-Related Keratoconjunctivitis Assessed by High-Resolution Anterior Segment Optical Coherence Tomography. Turk J Ophthalmol 2021;51:393-397

segment ocular coherence tomography in which umbilical cord blood serum (UCBS) eye drops were added as a complementary treatment.

Case Report

A 63-year-old man with no ophthalmologic history presented with a 3-day history of bilateral foreign body sensation, red eye, and purulent discharge. On examination, the visual acuity (VA) was 20/200 in the right eye (OD) and 20/100 in the left eye (OS). Slit-lamp examination showed intense conjunctival hyperemia and follicular tarsal reaction in both eyes (OU). A 7x5-mm central corneal epithelial defect associated with a ring-shaped corneal stromal infiltrate was noted in the OD (Figure 1A, B). There was a grade 2+ anterior chamber reaction. The OS presented a 2x4-mm corneal epithelial defect and an inferior marginal infiltrate (Figure 1C). A grade 1+ anterior chamber inflammation was observed. Corneal edema and Descemet's membrane folds were present in OU. There was no limbal ischemia and no foreign bodies were noted in either eye. Intraocular pressure and fundus examination were unremarkable in OU. High-resolution anterior segment optical coherence tomography (HR-AS-OCT) was performed in OU. Hyperreflectivity in the corneal stroma and Descemet's membrane folds were observed with no thinning of the corneal stroma (Figure 1D, E).

Cultures for bacteria, fungi, and *Acanthamoeba* were performed and empirical therapy was initiated with fortified topical antibiotics (vancomycin 50 mg/mL and ceftazidime 50 mg/mL) every hour, combined dexamethasone and chloramphenicol 0.5/10 mg/mL ointment once a day, as well as oral doxycycline 100 mg twice a day.

The next day, the patient's VA was unchanged. On examination, the conjunctival hyperemia persisted, while the corneal epithelial defect size and the circumferential infiltrate (OD) and marginal infiltrate (OS) were stable.

The patient reported that 6 days before presentation, he had removed a zoanthid coral from a rock in a domestic aquarium without wearing gloves and rubbed his eyes afterwards. He did not present systemic symptoms. The patient was diagnosed with PTX-induced keratoconjunctivitis based on clinical history. The toxin was not isolated. The patient's eyes were irrigated with saline solution in order to remove any remaining toxin from the ocular surface. Topical treatment with dexamethasone drops every 3 hours was started, fortified antibiotic drops were reduced to 4 times a day, and UCBS eye drops every 2 hours were added, and ascorbic acid 100 mg daily was added to his doxycycline systemic treatment.

Over the following days, slit-lamp examination revealed improvement of the corneal epithelial defects, especially in his OS, and the infiltrate density decreased (Figure 2A-D). HR-AS-OCT showed persistent hyperreflectivity in the corneal stroma and Descemet's membrane folds (Figure 2E, F).

Fortified antibiotics were replaced with moxifloxacin 5 mg/mL 3 times a day and a therapeutic contact lens was applied in the OD. Culture results were negative.

One week later, his VA was 20/200 in the OD and 20/40 in the OS. The epithelial defect in the OD was smaller and the infiltrate density had decreased. The epithelial defect

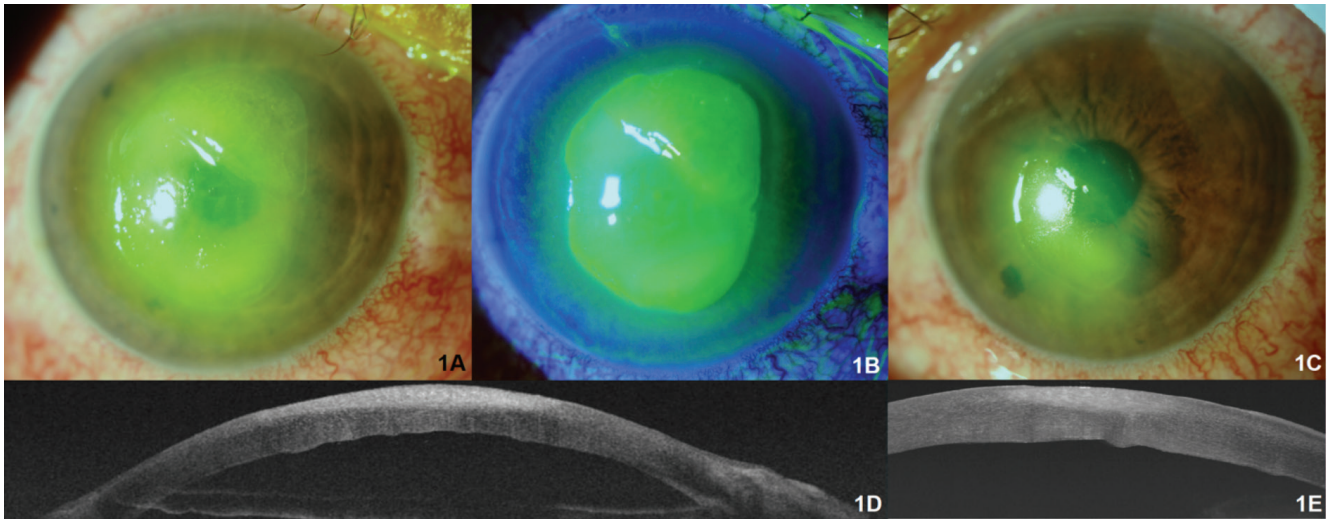

Figure 1. Slit-lamp photography and high-resolution anterior segment optical coherence tomography (HR-AS-OCT) before starting treatment. Slit-lamp photography of the right eye (OD) showed a ring-shaped stromal corneal infiltrate (A) and a 7x5-mm central corneal epithelial defect (stained with topical fluorescein, B). Slit-lamp photography of the left eye (OS) showed inferior marginal corneal infiltrate (C). HR-AS-OCT revealed Descemet's membrane folds and areas of strong hyperreflectivity with irregular and poorly defined borders corresponding to the corneal infiltrate in the anterior half of the corneal stroma in the OD (D) and the superficial third of the corneal stroma in the OS (E)

was healed in the OS, although corneal haze remained in the area where the infiltrate had been. Topical dexamethasone was tapered over 4 months; moxifloxacin was discontinued in OU and the UCBS eye drops were stopped when the epithelial defects were resolved.

At examination 4 months later, best-corrected visual acuity was 20/40 in the OD and 20/32 in the OS. Slit-lamp examination showed persistent corneal scarring in OU; we noted a ring-shaped anterior stromal scar in the OD and faint nasal anterior stromal leucoma in the OS (Figure 3A, B). Corneal topography demonstrated a non-uniform corneal steepening corresponding to irregular astigmatism in OU (Figure 3C, D). On HR-AS-OCT, a subepithelial area of increased reflectivity was observed in OU where the corneal scar was located (Figure 3E, F).

Discussion

Some corals, such as *Palythoa* in the order Zontharia, can release a toxin called PTX. It is a lethal toxin whose toxicity is mainly due to its profound vasoconstrictive effect and the release of norepinephrine by sympathetic nerve terminals. The toxin is also known to act on the sodium-potassium ATPase pump, converting it into a non-specific ion channel and causing intracellular calcium accumulation and cellular death. Moreover, it has been suggested that the signaling pathway triggered by PTX leads to actin filament system distortion.[1]

Exposure to PTX can be dermal (by direct contact with a coral or by contacting contaminated aquarium water), inhalational (usually while cleaning or eradicating the coral from home aquariums), or oral. This can lead to a systemic intoxication, manifesting with systemic symptoms such as dyspnea, rhabdomyolysis, and renal failure.[4,8,9]

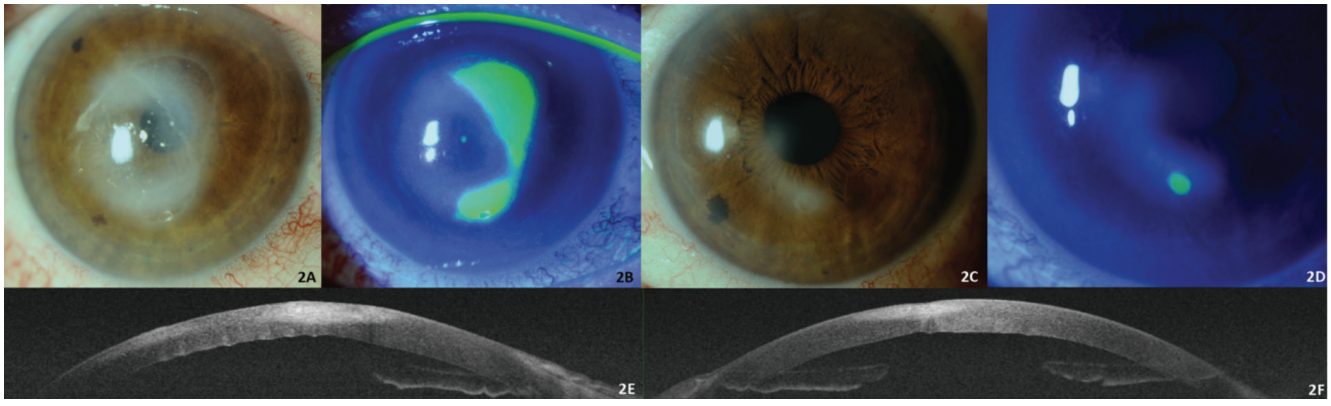

Figure 2. Slit-lamp photography and high-resolution anterior segment optical coherence tomography (HR-AS-OCT) on day 5 of treatment. Slit-lamp photography in the right eye (OD) showed the ring-shaped stromal corneal infiltrate (A) and the corneal epithelial defect with topical fluorescein staining (B). Slit-lamp photography in the left eye (OS) showed inferior marginal corneal infiltrate (C) and corneal epithelial defect with topical fluorescein staining (D). HR-AS-OCT revealed areas of hyperreflectivity in the anterior corneal stroma with more defined borders and Descemet's membrane folds in the OD (E) and OS (F)

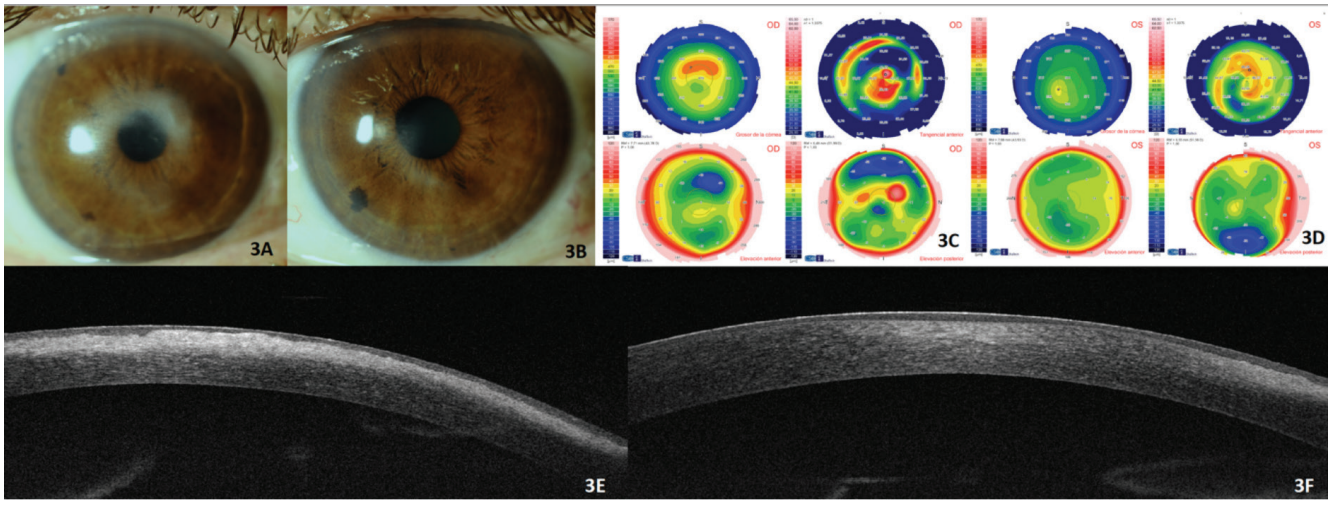

Figure 3. Slit-lamp photography, high-resolution anterior segment optical coherence tomography (HR-AS-OCT), and corneal topography at 4 months. Slit-lamp photography showed a ring-shaped stromal corneal leucoma in the right eye (OD, A) and nasal corneal scarring in the left eye (OS, B). Corneal topography in the OD and OS revealed irregular astigmatism (C, D) and HR-AS-OCT demonstrated thinner subepithelial hyperreflectivity with defined borders corresponding to the corneal scar (E, F)

Some cases of PTX ocular toxicity have been reported in the literature. The symptoms described are non-specific and include foreign body sensation, red eye, ocular pain, and decreased visual acuity. The most common ocular signs described are conjunctival hyperemia, circumferential corneal inflammatory infiltrate, and Descemet's membrane folds. Other ocular manifestations observed are conjunctival and limbal ischemia, punctate bulbar and tarsal conjunctival hemorrhages, superficial corneal punctate epitheliopathy, corneal erosions, corneal infiltrates, corneal melting and perforation, and anterior chamber reaction.[2,3,4,5,6]

Ocular exposure to PTX can occur by direct contact with the coral, contact with contaminated water, or rubbing the eyes after handing coral without gloves. In the presented case, the patient rubbed his eyes after manipulating zoanthids without using gloves.

Direct cellular toxicity of PTX and concomitant cytokine and protease activity causes keratocyte death and the degradation of collagen and proteoglycans. The subsequent inflammatory response can lead to epithelial defects, corneal melting, nerve damage, and corneal infiltrates. Disruption of the actin pathway slows the natural therapeutic process, interrupting the cell phenotype change from keratinocyte to myofibroblast.[2,5,6]

There are a limited number of case reports in the literature, so there is no defined treatment protocol. It has been reported that initial therapy should include eliminating the toxin by rinsing the eyes, with each eye irrigated individually. Treatment with topical corticosteroids is highly recommended in the early stages, together with prophylactic antibiotic therapy. Furthermore, it is also important to perform bacterial, fungal, and amoebic cultures. Artificial tears and autologous serum or UCBS eye drops should be added to the treatment. In our case, we did not use autologous serum because it takes 2 weeks to prepare in our center, but instead opted for UCBS eye drops, which can be obtained immediately as the patient needed. The use of oral corticosteroids, oral doxycycline, or ascorbic acid can be useful in cases with significant inflammation to reduce keratolysis and complications. In cases of persistent epithelial defects, the use of a therapeutic contact lens, amniotic membrane transplant, or tarsorrhaphy can be considered. Corneal transplant may be performed in cases of corneal perforation.[2,3,4,5]

PTX keratoconjunctivitis is a clinical diagnosis, based on a clinical examination, negative cultures for an infectious cause, and a temporal relation to toxin exposure.[2] Even so, the differential diagnosis from bacterial keratitis is very important. The differential diagnosis must also include other entities such topical nonsteroidal anti-inflammatory drugs (NSAID) toxic keratolysis, ophthalmia nodosa from mechanical irritants, and keratoconjunctivitis due to other toxic exposures, for example plant debris such as *Epipremnum aureum*.[2,7,10]

An early diagnosis is crucial to determine appropriate treatment and help avoid complications that involve permanent visual defects such as eye perforation, limbal stem cell failure, or extensive corneal scars.

In the presented case, we observed severe involvement in the OD and moderate involvement in the OS that had relatively good outcomes without the need for surgical intervention. Assessment with HR-AS-OCT allowed us to monitor corneal thickness to detect corneal thinning that would lead to a risk of corneal perforation and therefore more aggressive therapeutic management. It also let us analyze the depth of the corneal infiltrate and the leukoma. Unlike other reported cases, UCBS eye drops were added to the topical treatment and were found to facilitate healing of the corneal epithelial defects and reduce symptoms. Moreover, this case, as well as other cases reported in literature, shows the importance of taking a detailed clinical history and careful clinical assessment to diagnose this entity given the potential ocular and systemic complications related to PTX. In addition, it is important to know the effect of the toxin and how to prevent exposure by using protective equipment (goggles, gloves, face shield, air mask with activated charcoal filters) when handling zoanthids.

Ethics

Informed Consent: Obtained.

Peer-review: Externally peer reviewed.

Authorship Contributions

Surgical and Medical Practices: M.B.M., S.M-N., J.O., D.A-R, F.T-V., Concept: M.B.M., S.M-N., Design: M.B.M., S.M-N., Data Collection or Processing: M.B.M., M.G-M., Analysis or Interpretation: M.B.M., S.M-N., J.O., Literature Search: M.B.M., D.A-R., F.T-V., Writing: M.B.M., D.A-R., M.G-M.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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