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CASE REPORT

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Acremonium and trichosporon fungal keratoconjunctivitis in a Leopard Gecko (*Eublepharis macularius*)

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Abstract

A 6-year-old male leopard gecko (*Eublepharis macularius*) was presented with a 2-year history of recurrent dysecdysis involving the ocular surface of both eyes. Ophthalmic examination revealed ocular surface desiccation and multifocal superficial ulcerative keratitis with patchy remnants of retained shed. Other abnormalities included stomatitis and mandibular and maxillary osteomyelitis. Topical and systemic antibiotic therapy, oral vitamin A, and improved husbandry conditions resolved the stomatitis and osteomyelitis but did not improve the ocular surface. Corneal cytology collected with a cytobrush revealed branching hyphae and budding yeast consistent with fungal keratitis. Fungal culture grew *Acremonium* sp. and *Trichosporon* sp. The addition of topical antifungal therapy improved the ocular surface health, but the patient was euthanized 7 weeks after initial presentation for persistent vomiting and dyspnea. Necropsy was declined. This case describes the first case of fungal keratitis caused by *Acremonium* sp. and *Trichosporon* sp. in a reptile.

KEYWORDS

corneal ulceration, dysecdysis, fungicidal, hypovitaminosis A, keratitis, reptile

1 | INTRODUCTION

This case report describes the progression of fungal keratoconjunctivitis caused by *Acremonium* sp. and *Trichosporon* sp. in a 6-year-old male leopard gecko (*Eublepharis macularius*) that was co-managed by the Companion Animal Pet Exotic and Comparative Ophthalmology services at the University of California, Davis School of Veterinary Medicine.

The patient was first presented to the primary care veterinarian in May 2016 for a hyporexia, a purulent ocular discharge OS, and a 0.5 mm superficial corneal defect OD suspected to be related to dysecdysis, all of which resolved while being treated with meloxicam (Ostilox, VetOne) 0.15 mg/kg *per os* (PO) q24h for 7 days and Gentocin (Merck Animal Health) OU q12h for 14 days.

The following year, in May of 2017, a similar occurrence of dysecdysis was reported, which involved both palpebrae and conjunctiva OU. Stomatitis was also diagnosed. Manual removal of the shed was attempted 5 times over the next several months, and the patient was treated with

varying courses of topical gentamicin sulfate 0.3% ophthalmic solution (Bausch+Lomb) OU q12, Ofloxacin 0.3% ophthalmic solution (Bausch+Lomb) OU q12, GenTeal (Novartis Pharmaceuticals) OU q12-24h, Ceftazadime (Tazicef, Hospira) 30 mg/kg IM every 3-4 days for 2 weeks, Enrofloxacin (Bayer Healthcare LLC) 10 mg/kg PO q24h for 10 days, and twice weekly soaking. Additionally, the patient was transitioned to a coconut husk and sand substrate, with humidity kept constant between 60%-70% and temperature between 70-90°F. A UVB lamp was available at all times. Moss was made available in certain areas of the enclosure to further increase in humidity. Stomatitis resolved but the purulent ocular discharge was largely refractory.

The patient was initially presented to the UC Davis Veterinary Medical Teaching Hospital in November 2017 for evaluation of visual deficits and purulent discharge OU, along with lethargy and hyporexia. The patient had been receiving topical proparacaine hydrochloride 0.5% solution (Bausch & Lomb) for one week prior to presentation, topical Gentocin OU q12h, GenTeal OU q12-24h, and ceftazadime for 2 weeks (30 mg/kg IM every 3-4 days). Diet consisted of Carnivore Care and wax worms dusted with calcium and another unknown supplement. General physical examination revealed evidence of stomatitis and dermatitis of the right commissure of the mouth as well as ulceration of the rostral right maxilla and mandible. There was dysecdysis involving toes and head including the superior and inferior palpebrae of both eyes. The distal aspect of the tail was missing. Body condition was appropriate, and the remainder of the physical examination was unremarkable. Radiographs were performed at presentation, which revealed maxillary and mandibular osteomyelitis suspected to be secondary to stomatitis.

At the same visit, the initial ophthalmic examination revealed marked blepharospasm and enophthalmos OU, with a positive dazzle reflex OU. There was an evidence of dysecdysis of the head extending into the medial canthus OD and lateral canthus OS (Figure 1A,B). The corneal surface OU was covered by a moderately opaque pre-corneal membrane suspected to be retained shed that prevented intraocular evaluation. After the initial examination, the ocular changes were all attributed to dysecdysis related to husbandry. The patient was hospitalized for 4 days and was started on ofloxacin OU q12h, meloxicam 0.2 mg/kg PO q24h, enrofloxacin 5 mg/kg PO q24h, and I-Drop Vet Plus (I-Med Pharma Incz) administered topically through a 24 g intravenous catheter OU q1-2hr for the first day and then q2-3hr for 4 days. All previously prescribed medications were discontinued. The patient also received soaking bathes twice daily. Manual debridement of the corneal surface with a cotton-tipped applicator (CTA) was performed twice over a 4-day period. An appropriate nutritional plan was maintained by syringe feeding a mixture of Carnivore/Omnivore Care (Emeraid) q12h.

Recheck ophthalmic examination after 4 days revealed increased comfort with decreased blepharospasm OU. The pre-corneal membranes were largely absent with only small multifocal regions of retained shed still adhered to the corneas, OS being more affected than OD. The patient had a lackluster appearance to the tear film of both eyes, as well as mild diffuse corneal edema and diffuse superficial corneal vascularization OU. A 1 × 2 mm superficial corneal ulcer was present in the temporal paraxial cornea OD. Both anterior chambers were formed, and no other abnormalities were detected. Despite an improvement in corneal health, vitamin A deficiency was considered to be a possible contributing factor, and he was given vitamin A (Vitamin A 8000 IU gel capsule, NatureMade) 800IU PO once. Bathing was continued twice daily, as well as I-Drop Vet Plus OU q8-12h, Ofloxacin 0.3% ophthalmic solution OU q8h, and meloxicam

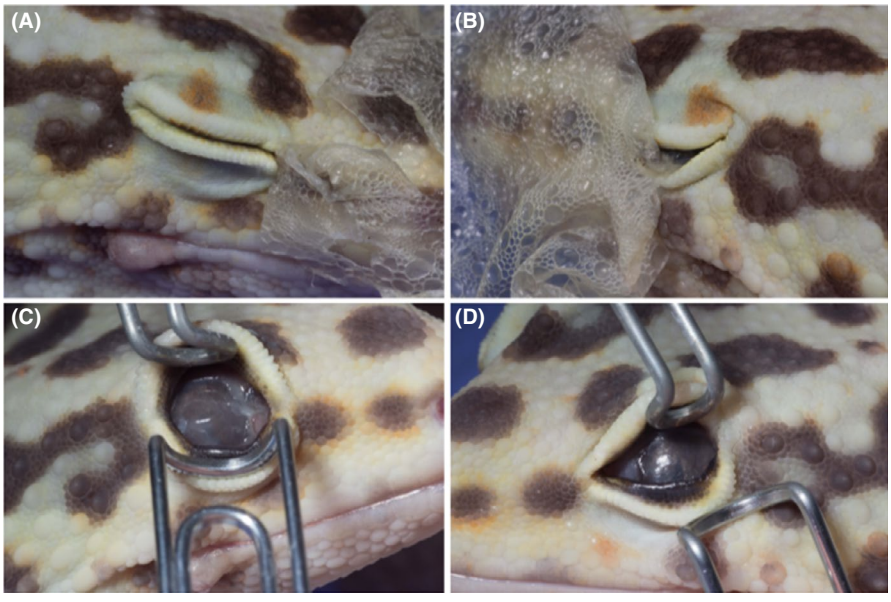

FIGURE 1 Initial presentation to the University of California, Davis Veterinary Medical Teaching Hospital. (A,B) Photographs showing dysecdysis extending from the head into the medial canthus (OD - A) and lateral canthus (OS - B). (C,D) A moderately opaque pre-corneal membrane was visible OU and was suspected to be retained shed. The membrane limited evaluation of internal ocular structures

0.2 mg/kg PO q24h. Diclofenac sodium 0.1% ophthalmic solution (Alcon Laboratories Inc) was started OS q12h. It was recommended to discontinue manual removal of the adhered corneal shed to reduce the risk of ulcer development or worsening of the existing ulcer OD.

By day 14 post-initial presentation, his overall condition had worsened from previous examinations. Blepharospasm was increased OU and remained enophthalmic, and he had mucoid discharge, moderate conjunctival hyperemia, and moderate chemosis with an irregular, nodular conjunctival surface. The corneal surface appeared moderately dry with multifocal areas of superficial punctate fluorescein stain uptake, and opacification was increased (mild edema and moderate diffuse fibrosis) and not permitting investigation beyond the cornea (Figure 2A). Redundant epithelium was evident over the corneal surface with accumulation of free epithelium in the conjunctival fornices. Corneal cytology collected with a cytobrush revealed branching hyphae and budding yeast, diagnostic for fungal keratitis (Figure 2B,C). A conjunctival scrape was performed with the blunt end of a scalpel blade in order to obtain a sample for fungal culture. Initial empirical therapy consisted of miconazole 2% vaginal cream OU q6-8h and itraconazole (Sporonox, Janssen Pharmaceutica) 5 mg/kg PO q24h. Vitamin A 800IU PO was again given once. Diclofenac was discontinued, while the remainder of the treatment protocol was unchanged.

Over the next 2 weeks, the patient stopped eating mealworms and only accepted food when fed with a syringe. Compared with initial presentation, he had a 3 g decrease in body weight and his body condition score declined to 4/9 with decreased fat storage in the tail. General physical examination showed no active stomatitis and only mild swelling in the region of the right commissure of the mouth. Ophthalmic examination was unchanged. Fungal culture results confirmed the presence of *Trichosporon* sp. and *Acremonium* sp.; however, the owner declined sensitivity testing. Topical washes with dilute betadine solution (1:50 dilution with sterile saline) q12h OU, followed by topical voriconazole 1% (Pfizer Inc) reconstituted to 20 mg/mL in sterile water q12h OU, and amphotericin B (X-Gen Pharmaceuticals) reconstituted to 5 mg/mL in sterile water q12h OU were initiated, and I-Drop Vet Plus q12h OU was continued. Ofloxacin, miconazole, enrofloxacin, itraconazole, and vitamin A were discontinued due to a lack of improvement and a patient stress related to the administration of the medications.

Three weeks later (7 weeks after initial presentation to UC Davis), the patient presented to his primary care veterinarian for declining condition with cessation of normal grooming behavior, worsening hyporexia and weight loss, vomiting, and dyspnea. Amphotericin B had been discontinued by the owner. Physical examination revealed a 12% weight loss since last visit (56 g from 64 g), an oral ulceration in the region of the hard palate, an increased respiratory effort and an open mouth breathing, and a dull mentation. Thoracic radiographs showed a mild caudal interstitial pattern. Ophthalmic examination showed mild improvement in the conjunctival hyperemia and chemosis, and corneal blood vessels were becoming hypoperfused. Repeat corneal cytology revealed ghost fungal organisms and extracellular cocci/coccobacilli arranged in chains, consistent with resolving fungal keratitis yet persistent *Streptococcus* sp. bacterial keratitis. The patient was prescribed ofloxacin OU q12, Tramadol 5-10 mg/kg PO q24, and enrofloxacin PO at an unknown dose. The vomiting resolved, but returned 4 days following discharge. Unfortunately, the patient was found dead five days later before further diagnostics and treatment could be pursued, and necropsy was declined.

2 | DISCUSSION

Here, we present a novel case of fungal keratoconjunctivitis in a leopard gecko (*Eublepharis macularius*) caused by *Trichosporon* sp. and *Acremonium* sp. Ophthalmic disease is among the most common findings in leopard geckos presented to tertiary referral hospitals, with the corneal being the

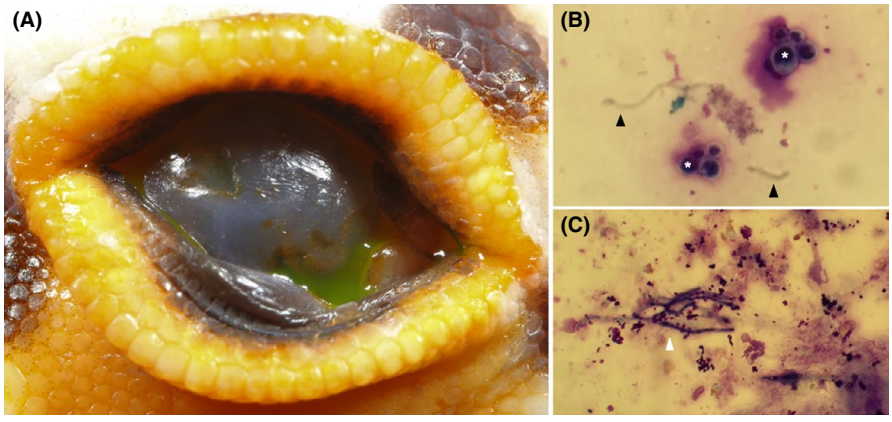

FIGURE 2 Day 14 after initial presentation. (A) View of OD showing a moderately desiccated corneal surface with multifocal areas of superficial punctate fluorescein stain uptake, mild edema, and moderate diffuse fibrosis that limited evaluation of internal ocular structures. Patches of redundant epithelium is visible over the corneal surface. (B,C) Corneal cytology collected with a cytobrush showing branching hyphae (arrowhead) and budding yeast (asterisk), confirmed fungal keratitis

most commonly affected ocular structure. Husbandry also plays a key role in prevention and treatment of ocular surface diseases in geckos.[1,2]

Other than horses, fungal keratitis is uncommon in most species, including humans.[3-5] The increased prevalence of fungal keratitis in horses is thought to be due to increased environmental exposure, increased corneal surface area, immunologic tear film deficiencies, and/or ocular conformation, all of which may increase the risk of corneal ulceration and colonization by obligate commensal organisms including fungi.[6,7] In other species, fungal keratitis is typically related to systemic illness or penetrating (eg, plant material) corneal injury, leading to established infection.[3] There are only a few documented cases of fungal keratitis in reptiles (see Table 1).

Among reptiles, the commensal fungal population of the ocular surface has only been reported in turtles and tortoises and is currently unknown for *Eublepharis macularius*.[8] *Trichosporon* sp. (yeast) and *Acremonium* sp. (saprophyte) are both ubiquitous in the environment and are uncommon causes of fungal keratitis in both human and veterinary patients.[5] They are known normal ocular surface flora of some veterinary species (eg, cows,[9] donkeys,[10] and horses[7]), as well as normal inhabitants of the skin surface of some squamates.[11]

In general, fungal organisms cannot invade the corneal stroma through an intact corneal epithelium, and thus, fungal keratitis is mostly an opportunistic infection.[3] Risk factors for fungal keratitis include tear film deficiencies, dysbiosis of the ocular surface from use of topical antibiotics and/or steroids, presence of fungal organisms on the ocular surface, penetrating corneal trauma, pre-existing corneal disease, and systemic disease.[3,5-7,12,13] Chronic dysecdysis, a common cause of ocular surface disease in geckos and snakes, was the likely inciting cause of fungal keratoconjunctivitis in the present case. Additional risk factors exhibited by our patient included poor quality tear film, chronic use of topical antibiotics, and possibly self-trauma following dysecdysis.

Both systemic and ocular treatments were unsuccessful at resolving either the corneal ulceration or infection in the present case. At initial presentation, the patient had been receiving topical proparacaine hydrochloride 0.5%, which may have delayed epithelialization due to epithelial toxicity.[14] *Acremonium* sp. has been shown to be most sensitive to topical treatment with amphotericin B and voriconazole.[12,15,16] A case of *Trichosporon* sp. fungal keratitis in a human was successfully treated with topical amphotericin B and oral ketoconazole.[5] Topical betadine has been successfully used in the treatment of equine keratomycosis and was instituted here for the same purpose.[17] Ofloxacin was instituted to address the *Streptococcus* sp. that was cultured (no sensitivity information is available), and Amphotericin B, Voriconazole, and dilute betadine were all instituted as an attempt to clear the fungal infection. Unfortunately, the patient died, and we were unable to obtain the eyes for histopathology and to assess the efficacy of topical therapies on the chronic keratitis. In addition, we were unable to complete any underlying systemic disease predisposing the patient to developing fungal keratitis.

Enteral vitamin A supplementation was started as it has been linked with epithelial squamous metaplasia, which can affect any epithelial surface including that of the conjunctiva.[1,2] Hypovitaminosis A is typically due to insufficient diet, and treatment consists of enteral supplementation.[2] Stomatitis has similarly been linked with hypovitaminosis A.[2] Following a 2-week course, no improvement in clinical signs were noted and the patient continued to decline. Many reptiles are unable to convert beta carotene or other precursors to vitamin A.[18] There is debate over the ability of leopard geckos to convert beta carotene to vitamin A and specific dosage recommendations of vitamin A in this species do not exist, thus a higher dosing regimen may have been more effective.[1]

Based on our findings, fungal etiologies should be considered for future cases of keratoconjunctivitis in leopard

TABLE 1 Documented cases of ocular disease caused by fungi in reptiles

Species	Scientific Name	Diagnosis	Fungal Organism(s)	References
Fat Tailed Gecko	*Hemitheconyx caudicinctus*	Keratitis	N/A	Reavill et al[19]
Bibron's gecko	*Pachydactylus bibronii*	Keratitis → Panophthalmitis	N/A	Reavill et al[19]
Galapagos tortoise	*Geochelone nigra*	Retrobulbar abscess	Phaeohyphomycosis	Manharth et al[20]
Gopher tortoise	*Gopherus polyphemus*	Keratitis	*Culvaria* spp., *Aspergillus* spp.	Myers et al[21]
Green Sea Turtle	*Chelonia mydas*	Traumatic blepharitis	N/A	Millichamp et al[22]
King Snake	*Lampropeltis* sp.	Spectacular infection	*Penicillium* sp.	Millichamp et al[22]
Massasauga	*Sistrurus catenatus*	Fungal granuloma of brain and extraocular structures	N/A	Millichamp et al[22]
Rainbow Boa	*Epicrates cenchria maurus*	Endophthalmitis OU	*Fusarium oxysporum*	Zwart et al[23]
Reticulated python	*Python reticulatus*	Keratitis → endophthalmitis	N/A	Collette and Curry[24]
Water Snake	*Nerodia* sp.	Spectacular infection	N/A	Millichamp et al[22]

geckos, particularly with ocular surface disease that is unresponsive to antibiotic therapy. Early fungal culture and sensitivity are recommended to obtain a diagnosis and guide therapy. Additionally, reports of the fungal genera identified in the present case are scarce in the veterinary and human literature, and further supports the need to perform cytology and culture, both bacterial and fungal, in cases of a chronic ocular surface disease in geckos.

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