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CASE REPORT

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Medical management and resolution of perinatal bilateral exophthalmia and secondary corneal ulcers in an Antillean manatee (*Trichechus manatus manatus*) neonate from Puerto Rico

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Abstract

Objective: To present a novel case of perinatal bilateral exophthalmos and corneal ulcers in a neonate Antillean manatee and describe the medical treatment that led to the resolution of the observed clinical signs and vision restoration.

Animal studied: A manatee stranded alone in Puerto Rico on July 5, 2020.

Results: The manatee was found in critical condition with pronounced exophthalmos, lagophthalmos, and corneal opacification of both eyes (OU). Vision impairment was evident due to the lack of ocular menace reflex and bumping into the tank's walls. Biomicroscopy revealed conjunctival hyperemia and chemosis, limited third eyelid movement, but had viscous tears present OU. Dense, full-thickness, white to cream-colored cellular infiltrates affected 70% of the cornea with peripheral active vascularization OU. Rubeosis iridis was also present OU. Treatment consisted of supportive medical management, including nutritional support and topical treatment for ulcerative keratitis. Resolution of the corneal ulcers and functional vision were achieved after 6 weeks of therapy. Currently, bilateral, mild, intermittent exophthalmos is observed with no adverse clinical signs, and the calf is in good health.

Conclusions: The extent of bilateral corneal disease on a neonatal calf may be a result of an intrauterine infection or possible trauma at or right after birth. While the latter may have led to exophthalmia and consequent corneal disease, the exact cause could not be determined. Supportive therapy and medical management of infectious keratitis were successful and led to vision recovery. This is the first report of ocular pathology in a neonatal manatee.

KEYWORDS
Antillean manatee, bilateral exophthalmia, corneal ulcers, infectious keratitis, perinatal, *Trichechus manatus*

1 | INTRODUCTION

The most common Antillean manatee (*Trichechus manatus manatus*) live strandings in Puerto Rico are either maternally dependent abandoned calves or orphaned neonates.[1–3] Between 1 and 4 calves per year are found under these circumstances and presented for rehabilitation at the Caribbean Manatee Conservation Center and released once they reach appropriate age (>2 years of age) and weight (>250 kg), and are cleared medically.[3] Most neonatal manatee cases involve gastrointestinal complications with very few traumatic injuries from watercraft collisions or stochastic events (hurricanes and heavy wave action).[1,2] We present a novel case of bilateral exophthalmos and corneal ulcers in a perinatal Antillean manatee.

2 | CASE DESCRIPTION

A male, perinatal, Antillean manatee calf, weighing 28.7 kg and measuring 120.6 cm in length, was stranded alone on July 5, 2020, off Punta Figuras in Arroyo, Puerto Rico. The orphaned manatee was rescued and transported for veterinary assessment and rehabilitation. Upon initial examination, he was found to be in critical condition with alterations of vital signs, including tachycardia (108–120 bpm) and tachypnea (6–16 breaths/5 min). A body score of 3–4 out of a total of 5,[4] with an estimated 5% dehydration based on elasticity and wrinkling of skin and bloodwork. Mucous membranes appeared highly congested with a capillary refill time of 0 s. The manatee calf also exhibited pronounced bilateral exophthalmia and corneal opacification (Figure 1A, B).

The manatee appeared to have vision impairment due to a lack of ocular menace response, which is commonly present in non-affected manatee neonates and bumping into the tank's walls. The ophthalmologic examination included biomicroscopy (Figure 2), photograph evaluation, and corneal cytology. Exophthalmos (Figure 1A) and lagophthalmos were observed; however, the palpebral reflex was present and resulted in complete eyelid closure when stimulated. Biomicroscopy revealed conjunctival hyperemia and chemosis, but tear presence and viscosity appeared adequate in both eyes (OU). Third eyelid movement was limited OU. Dense, full-thickness, white to cream-colored cellular infiltrates affected approximately 70% of the axial cornea with significant axial stromal loss and ventral keratomalacia bilaterally (Figure 1B). The peripheral cornea was vascularized, and rubeosis iridis was present OU. Corneal disease precluded further evaluation of the anterior and posterior chambers. Corneal cytology revealed degenerated neutrophils and numerous bacteria, predominantly rods; unfortunately, samples for culture and sensitivity were not collected and submitted.

Treatment included hydration and nutritional support and topical medical management for ulcerative keratitis.

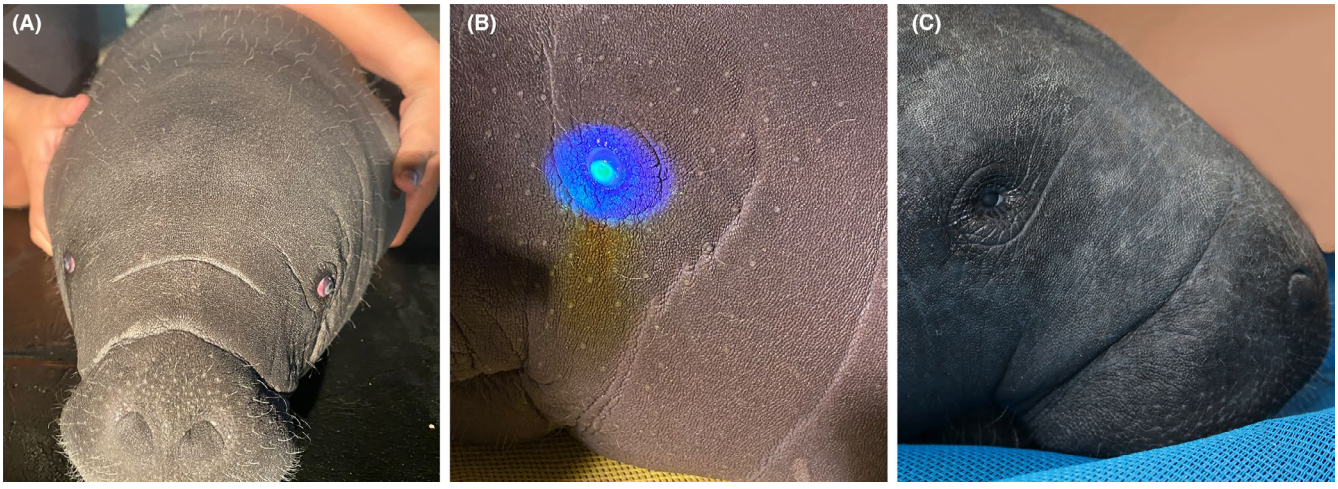

FIGURE 1 (A) Bilateral exophthalmos and corneal ulcers; (B) Fluorescein uptake, dense white to cream-colored corneal infiltrates, and corneal edema are evident over 70% of the corneal surface in a manatee calf upon patient admission; and (C) right eye of a clinically-healthy manatee patient depicting their enophthalmic nature and sphincter eyelid modification

Ophthalmic therapy was based on visual findings and corneal cytology. Treatment consisted of the following protocol: The patient was removed from the water and placed in a shaded area on a foam pad on the ground for every treatment lasting 15 minutes. The calf was treated 4 times a day for 4 weeks, then twice a day for 2 more weeks. Hypochlorous acid (MicrocynAH® Ophthalmic Gel, MannaPro Products, MO) was applied prior to additional ophthalmic medications. Topical antibiotics (moxifloxacin 0.5% ophthalmic solution, Alcon Laboratories, TX) were applied next, followed by allogeneic and autologous blood serum, Terramycin® ophthalmic ointment (Zoetis, Kalamazoo, MI), and a hypertonic ointment (Sodium Chloride 5% ophthalmic ointment, Walgreen Co., IL). Two to five minutes were allowed between medications for absorption. Nutritional support with a milk replacement formula used by other manatee facilities (EleCare infant formula [Abbott, OH], PROSource Protein formula [Medtrition, PA], sunflower lecithin powder [NOW, IL], coconut oil [Kirkland, WA], macadamia nut oil [Carlyle Nutritionals, NY], red palm oil [Omni, TX]) was administered in the water. This was supplemented with 1 mL of flaxseed oil as a good source of Omega-3 fatty acids,[5] Vitamin A (2400 mcg SID PO), and Ocuvite eye vitamins (1 softgel SID PO, Bausch + Lomb, NJ; C, E, zinc, copper, lutein, zeaxanthin, and Omega-3 fatty acids) were added to decrease oxidative stress and aid in the healing process.[6,7]

FIGURE 2 Examination with an ophthalmic portable slit lamp microscope on a manatee with exophthalmia and corneal ulcers

Water quality parameter monitoring[8] included pH ($\bar{x}$ 7.4 ± 0.46), total chlorine ($\bar{x}$ 0.86 ± 0.42 ppm), free chlorine ($\bar{x}$ 0.55 ± 0.31 ppm), turbidity ($\bar{x}$ 5.6 ± 4.5 FAU), salinity ($\bar{x}$ 7.0 ± 7.2 ppt), and water temperature ($\bar{x}$ 29.2 ± 0.79°C) tested daily, while ammonia nitrogen tests ($\bar{x}$ 0.0 ± 0.0 ppm) were tested twice a week, and coliform bacteria counts ($\bar{x}$ 22.9 ± 13.6 MPN) were performed weekly (Table 1). To maintain coliform bacteria counts under 1000 MPN per 100 mL, hypochlorite calcium was added daily as an oxidant agent to the rehabilitation tank with a total chlorine concentration up to 1.0 ppm.[9] Tank water was changed weekly, using well water supplemented with agricultural seawater salt (Cabo Rojo Enterprises & Empresas Padilla Salt Import, Cabo Rojo, PR) to about 7.0 ppt to decrease the potential for secondary corneal edema from freshwater. This also kept ammonia levels at 0 ppm and reduced secondary, irritating oxidant compounds such as chloramines.

Corneal vascularization quickly migrated towards the corneal defect within the first two weeks of treatment, and corneal infiltrates diminished rapidly. Corneal opacity diminished within 1-month post-initiation of therapy, and resolution of the corneal ulcers and vision recovery were achieved after 6 weeks of therapy (Figure 3). At present, both corneas are intact and clear, and though bilateral, mild, intermittent exophthalmos is observed, the calf's overall health appears to be normal.

TABLE 1 Water quality parameters monitored in the manatee's rehabilitation tank, and the incidence of water testing to ensure that parameters were maintained within the normal range

Water quality parameters	Rehabilitation tank parameters	Normal range[8,9]	Frequency of testing
Temperature (°C)	$\bar{x}$ 29.2 ± 0.79	25–32	Daily
pH	$\bar{x}$ 7.4 ± 0.46	7.0–8.5	Daily
Salinity (ppt)	$\bar{x}$ 7.0 ± 7.2	0–35	Daily
Turbidity (FAU)	$\bar{x}$ 5.6 ± 4.5	0–10	Daily
Total chlorine (ppm)	$\bar{x}$ 0.86 ± 0.42	0.2–1.0	Daily
Free chlorine (ppm)	$\bar{x}$ 0.55 ± 0.31	0.2–1.0	Daily
Ammonia nitrogen (ppm)	$\bar{x}$ 0.0 ± 0.0	0–0.1	Twice per week
Coliform bacteria count (MPN)	$\bar{x}$ 22.9 ± 13.6	0–1000	Weekly

Abbreviations: °C, degrees Celsius; ppt, parts per thousand; FAU, Formazin Attenuation Unit; ppm, parts per million; MPN, Most Probable Number.

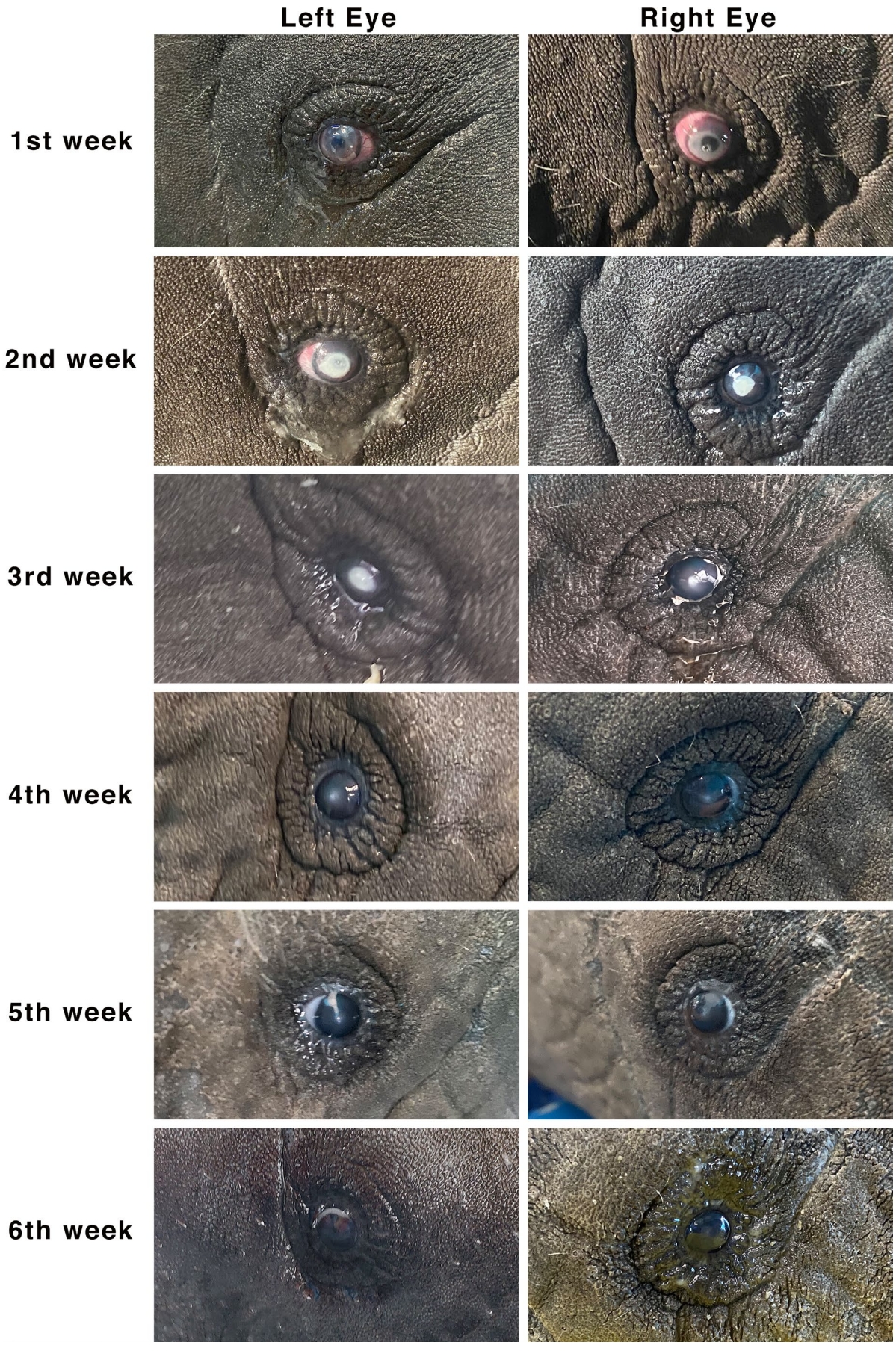

FIGURE 3 Evolution of the exophthalmia and corneal ulcers throughout the medical treatment process

3 | DISCUSSION

Ocular pathologies in manatees have not been well documented in the literature, mainly due to the difficulty of performing ophthalmologic examinations in this fully aquatic species, but also because few animals are under human care and their eye health is poorly monitored. In addition, evaluation is difficult due to the lack of access to the eyes, given their enophthalmic nature, sphincter eyelid modification, and natural protection response of the eyes when out of the water (Figure 1C).[10] The incidence of corneal ulcers in manatees is very low due to their ocular anatomy, protective eyelids, and the lack of academically sharing cases from facilities (authors' personal experience). This patient's clinical presentation of exophthalmos allowed for multiple follow-up ophthalmologic evaluations (Figure 2) and reassessment via digital photography, which allowed for optimal evaluation of treatment response.

In our experience, rehabilitating stranded manatees ($n > 115$) including calves, juvenile, and adult manatees in Puerto Rico, Colombia, Dominican Republic, Guyana, Panamá, Perú, and Venezuela, has included severe trauma caused by boats or jet-skis, or during stochastic meteorological events; however, we have not been presented with a case of exophthalmos and/or corneal ulceration. The extent of exophthalmia and corneal ulceration OU suggests that the calf suffered from an intrauterine infection or trauma during or after birth, leading to exophthalmia and secondary ulceration. Both possibilities should be considered given that the animal's age was estimated to be 1–5 days old due to its size, presence of umbilical cord sheath, meconium, and fetal folds of the manatee's fluke.[11]

Intrauterine and neonatal infections, particularly viruses and protozoa infections,[12] have been implicated as the main underlying cause of exophthalmia in children,[13–15] mammals,[16–18] reptiles,[19] and fish.[20,21] Seroprevalence test for leptospirosis and toxoplasmosis and thyroid disease based on serum T3 and T4 were tested as they can have clinical manifestations leading to somewhat similar ocular pathology to the condition of this patient.[12,22] However, these potential causes were ruled out as seroprevalence for leptospirosis and toxoplasmosis were negative, and T3 and T4 values were within normal ranges.[23]

It is suspected that the exophthalmia could have resulted from a difficult birth, trauma that led to orbital inflammation. The calf could have developed secondary infections from exposure to infected vaginal secretions as it passes through the birth canal, exposing the ocular surface, skin, hair, and umbilical cord.[12,22] Manatees under normal conditions are enophthalmic, with the *musculi palpebrae* and the extraocular muscles controlling the opening and closing of the palpebral fissure.[24] Lagophthalmos may occur due to excessive retrobulbar inflammation that prevents the globe from returning to its normal position.[25] With exophthalmia and lagophthalmos, the globe is predisposed to ulcerative keratitis with secondary infection, especially due to the environment in which manatees live.[25]

Corneal ulcers are associated with keratopathies in aquatic mammals with secondary opportunistic infections associated with varying degrees of corneal edema and cellular infiltrates.[26,27] Ocular treatments administered to aquatic mammals are often targeted to address the most common environmental pathogens, including coliforms, *Pseudomonas* spp., and fungal organisms.[7] The treatment implemented in this case was adapted from the literature based on the clinical appearance and cytology results, since culture and sensitivity were not obtained.

We attribute the success of this manatee's ocular resolution to the implementation of an integrated complementary therapy in which pathology is addressed locally, medically, nutritionally, and environmentally. Hypochlorous acid cleaning 2–4 times a day during treatment possibly allowed the reduction of corneal bacteria through peroxidation and halogenation of proteins and lipids.[28] A combination of antibiotics with anti-proteolytic medications reduced bacterial infiltrates and keratomalacia. Topical and systemic quinolones are frequently used antibiotics as they may be highly effective against gram-negative organisms, including *Pseudomonas* spp., which causes aggressive corneal malacia.[7] Moxifloxacin decreased bacterial proliferation through its bactericidal action and good corneal penetration. Topical oxytetracycline and topical and oral doxycycline are used to exert antibiotic, protease inhibitory, and immunomodulatory properties at the tear film level.[29-31] Oxytetracycline (Terramycin®) contributed to decreasing stromal loss and promoting corneal regeneration by inhibiting matrix metalloproteinase-9, immunomodulation, and enhanced epithelial migration.[29] The use of autologous serum contributed to the regeneration process of the extensive and deep corneal ulcers due to the presence of alpha-macroglobulin. Hyperosmotic (5%) sodium chloride ointment (Muro 128® and others) reduced corneal edema and is recommended if corneal edema is marked, further decreasing already impaired epithelial adhesion.[32] This manatee calf was originally suspected to have a fungal infection based on the appearance of the cellular infiltrates. However, due to the rapid improvement with the use of topical antibiotics and the lack of cytological evidence of fungal organisms, antifungal therapy was not initiated.

Nutritional management included vitamins, fatty acids, and minerals in the manatee's daily milk formula, which served as adjuncts to reduce oxidative stress. These nutritional supplements may decrease the chronicity of the case, as described in keratopathies, keratoconjunctivitis, and corneal ulcers in cetaceans and pinnipeds.[5–7] The use

of Omega-3 fatty acids was implemented to take advantage of its anti-inflammatory effects, reduce hyperosmotic stress in the epithelium of the ocular surface, and improve the production of the tear film, which contains substances that protect and nourish the corneal surface.[5] The use of these antioxidant agents may help to protect the corneal surface from chronic exposure to UV rays, exogenous factors in water, and the environment, which continuously create free radicals on the corneal surface, including the precorneal tear film.[7] The dietary supplementation of antioxidants may also reduce oxidative stress in the conjunctiva and cornea, while improving stabilization in tear secretion and control of the production of matrix metalloproteinase enzymes associated with delays in the ocular healing processes.[6,33] In addition, as swelling and exophthalmia decreased, lagophthalmos resolved, favoring the healing process.

Environmental management was also a crucial contribution in the ocular resolution of this manatee, as the individual was kept in a rehabilitation tank controlling water quality, temperature, and a salinity closer to normal saline, which should help reduce potential edema. In addition, the tank's wall and bottom were of warm colors (sage green walls and sand-colored bottom), colors known to be capable of absorbing UV rays.[7,27,34] Complete shade was provided to minimize further penetration of UV radiation from natural sunlight.

The manatee calf's eyes recovered relatively quickly, considering that infectious ulcerative keratitis in domestic mammals and other aquatic mammals may take weeks to months for a full recovery.[7,35] Another possible contributing factor that favored this patient's recovery was the constant production of the mucin-rich tear film, which has glycoproteins, lecithin, and components responsible for nourishing and protecting the cornea of the manatee.[33,36] The well-vascularized cornea that the manatees possesses is a beneficial evolutionary mechanism, a condition that in other mammals would be considered pathological.[10,37]

Corneal disease is rare in manatees due to their protective ocular anatomy. Corneal ulcers, in this case, likely developed due to an intrauterine infection or secondary to exophthalmia. Despite the severe ocular disease, comprehensive therapy played an essential role in the disease resolution and vision recovery.

4 | CONCLUSION

This is the first report of the treatment management of exophthalmia and keratopathy in a neonatal manatee. It documents the resolution of exophthalmia and severe bacterial keratitis suspected to be due to an intrauterine infection or trauma at or right after birth. While trauma during or right after birth could have led to exophthalmia and consequent corneal disease, the exact cause of exophthalmia could not be determined. Medical, nutritional, and antioxidant use and environmental management may all have played a synergistic role in the treatment success of this neonatal manatee calf.

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CONFLICTS OF INTEREST

None of the authors have any commercial or financial conflict of interest to declare.

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