

## Acute bullous keratopathy in a domestic shorthair

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**Abstract** – A 14-year-old cat was presented for corneal rupture of the right eye and bulla formation of the left cornea. It was diagnosed with acute bullous keratopathy, based on clinical and histopathologic examination. This is a rare condition of unknown origin in cats; it was treated successfully with bilateral conjunctival pedicle grafts.

**Résumé** – **Kératite bulleuse aiguë chez un poil court domestique.** Un chat âgé de 14 ans a été présenté pour une déchirure de la cornée de l'œil droit et une formation vésiculaire dans la cornée gauche. En se basant sur l'examen clinique et histopathologique, un diagnostic de kératite bulleuse aiguë a été posé. Chez le chat, il s'agit d'une condition rare d'origine inconnue; le traitement bilatéral par greffons conjonctivaux pédiculés a été réussi.

(Traduit par Docteur André Blouin)

Can Vet J 2008;49:187–189

**A** 14-year-old, castrated male, domestic shorthair was referred to the Ophthalmology Department at the Western College of Veterinary Medicine, with pain portrayed by right blepharospasm and epiphora. He had been seen 2 d prior to presentation by his referring veterinarian, who had diagnosed corneal dystrophy. Two months earlier, the cat had been treated for bilateral epiphora, which had resolved within 8 d, with a topical triple antibiotic ointment (Bacitracin, neomycin, polymixin and Bacitracin, neomycin, polymixin, hydrocortisone ointments; Vetcom, Upton, Quebec).

Examination revealed a right paracentral corneal ulcer, 10 mm × 7 mm, miosis, a flat anterior chamber, and 2+ aqueous flare (Figure 1a). There was a left paracentral edematous bulla, approximately 7 mm in diameter (Figure 1b). Bilateral conjunctivitis was also present. Results from a neuro-ophthalmic examination were normal. Schirmer tear tests (Schirmer Tear Test Strips; Alcon Canada, Mississauga, Ontario) were 20 and 10 mm/min in the right and left eye, respectively. Intraocular pressures, estimated with a tonometer (Tonover; Tiolat, Helsinki, Finland), were 2 and 14 mmHg in the right and left eyes, respectively. The right eye stained positively with fluorescein (Fluoret; Chauvin Pharmaceuticals, Romford, Essex, UK). The pupils were dilated with 1 drop tropicamide in each eye (OU) (Mydriacyl; Alcon Canada, Mississauga, Ontario); no abnormalities were detected in either fundus, using an indirect ophthalmoscope (Heine Omega 200; Heine Instruments Canada, Kitchener, Ontario). No abnormalities were detected in either fundus.

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The diagnosis was acute bullous keratopathy and uveitis. Surgical keratectomies and bilateral conjunctival pedicle grafts were recommended.

A complete blood (cell) count (CBC) (Cell-dyn 3500R; Abbott Diagnostics, Santa Clara, California, USA), a serum chemical profile (Hitachi 912 Automatic; Boehringer Mannheim, Division of Hoffman-LaRoche, Laval, Quebec), a serum thyroxine (T<sub>4</sub>) (Immulite; Diagnostic Products, Los Angeles, California, USA), and a urinalysis were performed. The CBC, serum chemical, urinalysis, and resting T<sub>4</sub> values were within normal reference ranges.

The cat was premedicated with acepromazine (Atravet; Ayerst Veterinary Laboratories, Guelph, Ontario), 0.1 mg/kg bodyweight (BW), IM, and hydromorphone (Hydromorphone; Sabex 2002, Boucherville, Quebec), 0.1 mg/kg BW, IM. General anesthesia was induced with propofol (Rapinover; Schering-Plough Animal Health, Pointe-Claire, Quebec), 30 mg, IV, and maintained with inhalational isoflurane (Aerrane; Baxter Corporation, Mississauga, Ontario). The cat was placed in dorsal recumbency, and put on a ventilator. Atracurium besylate (Atracurium besylate; Sandoz Canada, Boucherville, Quebec), 0.2 mg/kg BW, IV, was administered, and a nerve stimulator was used to test for returning nerve impulses. Additional atracurium, 0.1 mg/kg BW, IV, was given to maintain paralysis and a central eye position throughout the surgical procedure. Cefazolin (Novopharm, Toronto, Ontario), 22 mg/kg BW, IV, was administered intra-operatively. For pain control, hydromorphone, 0.05 mg/kg BW, IV, was given intra-operatively and q6h post-operatively for 2 doses.

Swabs for anaerobic and aerobic culture, taken at surgery, were submitted for Gram staining and culture. A stay suture of 5-0 monofilament nylon (Monosof; United States Surgical, Norwalk, Connecticut, USA) was placed in the ventromedial episclera of the left eye. A conjunctival pedicle graft was harvested from the dorsolateral bulbar conjunctiva. A keratectomy



**Figure 1a.** Right eye on presentation. The eye has been stained using fluorescein. Note the wrinkled appearance of the flattened anterior chamber of the ruptured corneal center.

was performed by using a 6400 beaver blade (Becton Dickinson, Franklin Lakes, New Jersey, USA) to remove the corneal bulla. The keratectomized specimen was submitted in 10% formalin for light microscopic examination. The anterior chamber of the perforated right eye was maintained by intracameral injections of a viscoelastic substance (Ivisc; I-MED Pharma, Montreal, Quebec). The conjunctival graft was sutured onto the corneal defect with 9-0 polyglactin 910 (Vicryl; Ethicon, Johnson and Johnson Medical Products, Markham, Ontario) in a simple interrupted pattern. A temporary tarsorrhaphy was placed at the lateral canthus by using 5.0 monofilament nylon (5-0 Monosof United States Surgical). The procedure was repeated for the right eye. The cat recovered and was discharged the following day. Postoperative medical therapy included topical ciprofloxacin (Apo-Ciproflox 0.3% w/v; Apotex, Toronto, Ontario), 1 drop, OU, q6h, to prevent infection; topical diclofenac sodium (Voltaren 0.1%; Novartis Pharmaceutical Canada, Mississauga, Ontario), 1 drop, OU, q6h to reduce anterior uveitis secondary to corneal surgery; topical atropine (Isopto Atropine 1%; Alcon Canada), 1 drop, OU, q12h, to achieve mydriasis and cycloplegia; and tear replacement gel (Tear-Gel; Novartis Pharmaceuticals Canada), 1 drop, OU, q6h to maintain corneal moisture until reexamination.

No visible organisms were noted under direct examination, and all cultures were negative. Light microscopy revealed hyperplastic corneal epithelium, corneal edema, and corneal ulceration. The corneal epithelial basement membrane was thickened and less clearly defined.

On recheck 5 d postsurgery, the temporary tarsorrhaphy sutures were removed. Results of a neuro-ophthalmic examination were normal, although both pupils were dilated due to the atropine drops. Schirmer tear tests were found to be 25 mm/min bilaterally. Intraocular pressures estimated with a tonometer (as previously cited) were found to be 1 mmHg bilaterally. Both eyes were found to be fluorescein positive at the suture sites only. Both conjunctival grafts appeared viable, and there was a small amount of limbal vascularization. The anterior chamber of the right eye had regained its normal depth, and a trace amount of aqueous flare was present bilaterally. A Sidel test, which is used to assess for presence of aqueous humor leakage, was negative.



**Figure 1b.** Left eye on presentation. The eye has been stained using fluorescein. Note focal region of corneal edema.

Ciloxan drops were continued, OU, q6h. Voltaren drops were to be given, OU, q6h for 1 wk, then, OU, q12h for 2 wk. Tear-Gel and atropine drops were discontinued.

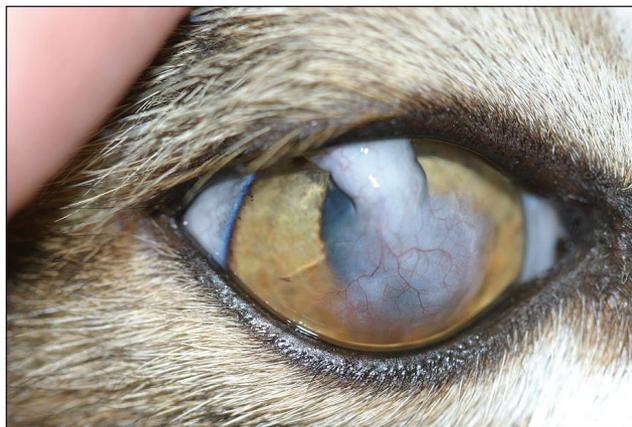
On recheck 3 wk postsurgery, results from a neuro-ophthalmic examination were normal. Schirmer tear test was 10 and 11 mm/min in the right and left eyes, respectively. Intraocular pressure was estimated with a tonometer and found to be 4 mmHg bilaterally. Both eyes were fluorescein-negative, and the conjunctival grafts were healing well. Ciloxan drops were to be continued, OU, q6h for 1 wk, then discontinued. Voltaren drops were to be continued, OU, q12h for 1 more wk, then discontinued.

On recheck 4 mo postsurgery, results from the neuro-ophthalmic examination were normal. Schirmer tear tests were 11 and 10 mm/min in the right and left eyes, respectively. Intraocular pressures were estimated with a tonometer and were 8 and 20 mmHg in the right and left eyes, respectively. Both eyes were fluorescein-negative. The conjunctival grafts were well incorporated into the cornea (Figures 2a and 2b). A recheck was recommended in 1 y.

Acute bullous keratopathy is an uncommon rapidly progressive corneal disease, which is usually seen in young adult cats (1). The condition is manifested with edema (bulla) (1,2), which can range from a few millimeters in diameter to the complete cornea (3). Several small vesicles may coalesce to form a larger bulla (4). This condition is usually bilateral, but initially it may appear unilateral (5). The diagnosis is made on the basis of clinical presentation and ophthalmologic examination, although the condition must be differentiated from septic ulcers with collagenolysis.

Light microscopic examination confirms the diagnosis by revealing marked edema separating the collagen fibrils of the corneal stroma. Inflammatory cells are inconsistently present; when present, they are usually scant and occasional polymorphonuclear cells will be noted within the stroma (3). No abnormalities are seen in Descemet's membrane or the endothelium on light microscopy (5). The cornea surrounding the lesions appears normal.

The etiology and pathogenesis of feline bullous keratopathy is unknown. In published reports, tests for feline immunodeficiency virus, feline leukemia virus, feline infectious peritonitis virus, feline herpesvirus, aerobic bacteria, *Mycoplasma* spp.,



**Figure 2a.** Right eye 4 mo post-surgery. Conjunctival grafts are healed and well incorporated into the cornea.

*Chlamydia* spp., and fungi were negative (5). Microbial cultures were negative and organisms were not detected on cytologic examination (1). There are several theories as to how this condition develops in cats. The 1st is that it may be an inherited stromal dystrophy, as has been reported in the Manx cat (3,5,6). Ultrastructural examination indicates severe stromal edema, as well as abnormalities in Descemet's membrane. However, abnormalities are not detected in the endothelium (6). In contrast to cats with bullous keratopathy, the entire cornea eventually becomes involved and the corneal lesions are usually progressive over a period of several years (5). The 2nd theory is that the bullae are caused by a localized breakdown in the ultrastructure of the collagen fibers through an enzymatic degradative process (5). This results in a breakdown of the collagen fibers, causing a lack of structural support, as well as breakdown of the ground substance, whose function is to help imbibe fluid within the stroma. A 3rd theory is that an underlying condition, such as pre-existing uveitis, may cause bullae formation, as the inflammatory process taking place in the anterior chamber may disrupt the ability of the corneal endothelium to draw fluid from the corneal stroma. However, there is no histological evidence of inflammation in any of the reported cases of acute bullous keratopathy. The relationship between uveal disease and the corneal changes remains unclear. Finally, in cats that develop bullous keratopathy, there is anecdotal evidence of prior treatment with topical or systemic dexamethasone (1). However, there is no evidence that this predisposes the cornea to develop this condition, and several cases of bullous keratopathy have been published that have not received steroids (5).

Similar conditions occur in dogs (2,7) and humans (8,9); however, the clinical presentations, histopathology, and etiologies vary from the condition in cats. In dogs, formation of multiple small superficial corneal bullae occurs as a complication of severe corneal edema usually seen in chronic cases of endothelial dystrophy (2,7). In humans, the condition of keratoconus is a noninflammatory corneal thinning disorder that usually involves a focal area of the cornea, much like feline bullous keratopathy (8). However, keratoconus is usually more chronic in nature. Occasionally, there have been incidents of edema (known as acute hydrops) and rupture seen after long-standing cases (8,9). The light microscopic findings in human keratoconus differ from those of feline bullous



**Figure 2b.** Left eye 4 mo post-surgery.

keratopathy. In keratoconus, ferritin deposits are often present, and breaks in both the Bowman's and Descemet's membranes are seen (9). The edema seen in acute hydrops is the result of these breaks in Descemet's membrane, which has not been documented with feline bullous keratopathy. The etiology of keratoconus is also unknown, but theories have been proposed, including genetic mutations (it is suspected to be an autosomal dominant trait), eye-rubbing, atopy, Down's syndrome, and systemic collagen disease such as Ehler-Danlos syndrome (8,9).

Treatment of feline bullous keratopathy consists of procedures that provide pressure or structural support to the bulla (3). The most common treatment is a combination of a keratectomy, conjunctival flap, and temporary tarsorrhaphy (3). If these surgical procedures are not an option for owners, a long-term 3rd eyelid flap may be successful (1). The use of topical antibiotics, mydriatics, and analgesics are indicated (1,3,4). Bullae may recur in the same spot as previous bullae or in new locations within the cornea (2). Some bullae resolve without treatment. The prognosis for bullous keratopathy with surgical treatment is good (4).

## Acknowledgments

The author thanks Drs. Lynne Sandmeyer and Bruce Grahn of the Western College of Veterinary Medicine Ophthalmology Department for their support and assistance. CVJ

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