ACUTE BULLOUS KERATOPATHY IN CATS

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***Abstract**: Bullous Keratopathy, a severe edema of the corneal stroma and epithelium with a characteristic bulla formation on the corneal surface, is a rare opthalmological emergency in cats. Rapidly progressive and uncontrollable by medical means, this condition will result in corneal perforation hours after initial presentation if left unattended. Its pathophysiology and treatment options are reviewed in this article.*

Key words: acute, bullous, keratopathy, cat

QUERATOPATIA AMPOLLAR AGUDA DE LOS GATOS

***Resumen:** Queratopatia ampollar felina aguda define el edema corneal agudo severo con la formacion de una caracteristica ampolla subepithelial y es una rara emergencia oftalmologica en gatos. Es de progreso rapido y no responde satisfactoriamente a terapias medicas. Esta condicion resulta en perforacion corneal pocas horas despues de ser diagnosticada si es no es tratada de inmediato. Su patofisiologia y las opciones terapeuticas son discutidas en este articulo.*

Palabras clave: queratopatia ampullar, felina

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INTRODUCTION

Bullous keratopathy describes severe edema of the corneal stroma and epithelium with a characteristic bulla formation on the corneal surface. Corneal edema results from excessive accumulation of fluid within the corneal parenchyma. It has been established that corneal thickness is linearly related to its fluid content (2). Edema is a common sign of corneal disease and is typically caused by loss or dysfunction of the anterior or posterior epithelium (endothelium) (1, 3, 15). The etiology of acute bullous keratopathy has not yet been identified, but affected cats have several common characteristics: they are young adults (range 1.5 to 3 years); have no significant hematologic or serum chemistry abnormalities; and tend to be affected bilaterally. Recurrence after initially successful therapy is common. No sex or breed predisposition has been reported.

HISTOLOGICAL STRUCTURE OF THE CORNEA

The cornea forms the anterior segment of the fibrous tunic of the eye (6) and is sturdy and clear. To maintain these properties, this avascular collagenous tissue must remain metabolically active in a state of relative deturgescence (7). The cornea is composed of five layers; the outermost epithelium, then the subepithelial basement membrane, stroma, Decement's membrane, and endothelium (8). The corneal epithelium is a nonkeratinized stratified squamous, between 4 and 12 layers in thickness. The subepithelial basement membrane is predominantly formed by reticular fibers. The substantia propria or stroma accounts for 90 % of the total corneal thickness and is composed of some 100 lamellae in the cat. These layers are mainly collagen fibers arranged in a precise parallel fashion. Keratocytes are the predominant cell population and lay between the collagen fibers. The specific architecture of the stroma allows for 99 % of light permeability without scattering (8, 9). The Decement's membrane is the posterior limiting membrane that gives support to the corneal endothelium. It consists of tightly organized collagen fibers. Decement's membrane is constantly produced by the posterior epithelium so it grows thicker as the animal ages. The endothelium is the innermost layer of the cornea and consists of a single layer of flat, hexagonal cells. These cells interdigitate heavily and the high number of mitochondria and pinocytotic vesicles suggest a high metabolism (8) (figures 1a & b).

CORNEAL PHYSIOLOGY

The cornea is an extremely specialized tissue despite a relatively simple structure. The ultimate goal of the cornea is to remain transparent and to provide the major refractive function of the eye (9). To do so, about 10 % of the total corneal tissue must keep a very delicate water balance by working against the remaining 90% highly hydrophilic corneal stroma. This phenomenon depends on the continuous pumping out of interstitial fluids, a process that has been localized mainly in the posterior epithelium (9, 11). The ideal physiologic level of hydration in the human cornea is approximately 78 %. An increase or decrease from this ideal level can result in corneal opacity (9). This level is maintained by active pumping of ions (Na, K-ATPase pump) from the stroma to the aqueous humor (12-13). The endothelial cells are able to sustain this function and maintain corneal deturgescence and clarity even if their number is decreased by 80 % (7).

PHYSIOPATHOLOGY OF BULLOUS KERATOPATHY

The primary etiology of bullous keratopathy has not been elucidated, however, there is evidence that bullous keratopathy occurs when the pumping capability of the endothelial layer is overwhelmed. This allows water to passively diffuse across the endothelium from the aqueous humor to the corneal stroma. The passage occurs following a concentration gradient. The highly hydrophilic proteoglycans located in the substantia propria, their distribution within the stroma, and the ratio between the various proteoglycan (dermatan sulfate, keratan sulfate, etc [14]) will finally determine the water distribution (9). With chronic or severe edema, formation of subepithelial and intraepithelial fluids-filled pockets, referred to as bullae, may occur. The bullae accumulate beneath or within the corneal epithelium and may spontaneously rupture causing corneal erosion or ulceration (15). Bullae formation is associated with several primary keratopathies in both people and animals. In the cat, bullous keratopathy is also reported as a sole entity (1, 16). In these cats, a profound, rapidly progressive corneal edema follows soon after a small corneal bulla is identified. The edema worsens despite aggressive topical therapy (figures 2 & 3). Glover et al. (1) tried unsuccessfully to link this syndrome with viral (FIV, FeLV, FIP, Feline Hepes Virus), bacterial, and mycoplasmal infections.

TREATMENT

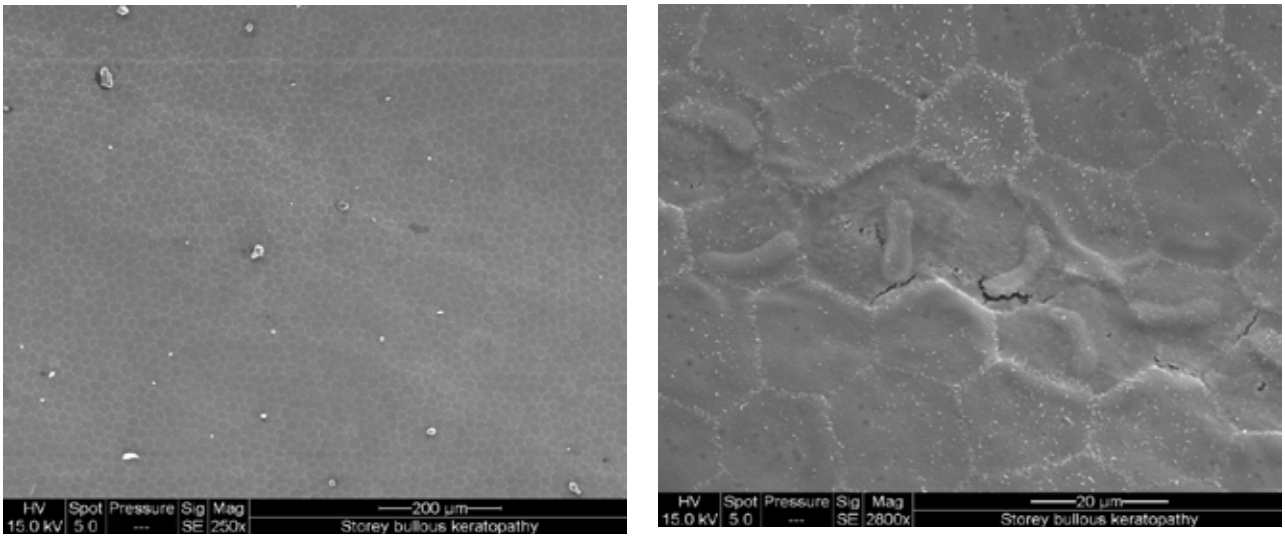
The treatment must be aggressive and timely to avoid corneal perforation. Several medical treatments have been proposed for people; however, it is crucial to realize that the presentation and origin of bullous keratopathy in humans is very different from the acute and rapidly progressive syndrome observed in the cat. In people bullous keratopathy is a chronic problem associated with intractable glaucoma and lens implantation which does not usually

progress to affect the entire surface of the cornea, but remains as a sole lesion. Similar behavior has it in the dog (17). Medical treatments such as topical hyperosmolar agents (5, 18, 19, 21) and chondroitin sulfate containing solutions (20) have been described, but their efficacy is poor and controversial. Surgical treatments appear more promising. The selection and execution of a surgical procedure depends on the animal's needs and the extent of the injury. The surgical procedures fall into two categories. The first category includes those procedures that aim to replace the deficient endothelium and/or epithelium and reestablish control of the water content in the stroma. Examples are penetrating keratoplasty (corneal transplant) (22) and fresh and frozen lamellar grafting (23). The second category includes techniques that provide a prompt vasculature supply for fluid drainage. Examples are conjuctival flaps (1, 16), and application of amniotic membrane (4, 24). The newest and most promising techniques, require further development, but aim to replace the endothelium by an in-vitro mass production and injection in the anterior chamber of endothelial stem cells (25, 26).

PROGNOSIS AND COMPLICATIONS

Bullous keratopathy in cats is uncommon, and the lack of understanding of its pathogenesis, and the sporadic reports in scientific literature make an assessment of its prognosis very difficult. Most reports cite bilaterally compromise at some point despite the size of the bulla or the extent of the consequent edema. The bulla recurred after

Figure 1 – Electron microscopy view of: a) the normal endothelium. *b)* Detailed view of intercellular junctions. Note the apoptotic cells in the center of the picture.
Figura 1. Fotomicrografia electronica de barrido. Epitelio corneal normal; a) Dertalle de las uniones intercelulares. Note las celulas apoptoticas en el centro de la figura.



Figures 2 & 3 – Severe edema corneal with corneal protrusion. Picture taken 12 hours after initial presentation of a 3 mm corneal ulcer. The patient was administered topical antiinflamatories every other hour. *Edema corneal severo con protrusion de cornea. La foto fue tomada 12 despues de la presentacion inicial de una ulcera de 3 mm de diametro. El paciente fue tratad con antiiflamatorios topicos aplicados cada dos horas.*

initial response to neovascularization techniques or quickly progressed with eye perforation. There are no reports of corneal allografting as a treatment of acute bullous keratopathy in the cat. Replacing the endothelium may reestablish the capability of the eye of controlling the water balance in the corneal stroma, the same principle that governs the endothelial cell replacement with stem cells. Further investigation is warrant.

CONCLUSION

Acute bullous keratopathy in cats is a rare condition; however its prompt identification is crucial in saving the eye. Aggressive surgical treatment must be pursued as soon as the condition is identified. Intensive medical treatment will fail and corneal perforation will follow few hours after the initial presentation of clinical signs. In our clinic, as well as in previous reports, an infectious component has not been linked to the problem.

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