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Case report

A CASE REPORT OF ACUTE BILATERAL BULLOUS KERATOPATHY IN A SEPTIC CALF

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Summary

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Bullous keratopathy occurs in dogs, cats and humans, and it is diagnosed by clinical and ophthalmic presentation. A 20 days old septic calf developed an acute bilateral ocular abnormality, with mild ocular discharge and corneal opacity. Slit-lamp biomicroscopy showed a severe central cornea oedema with a subepithelial bulla. The clinical diagnosis was bilateral bullous keratopathy; it was treated with glucose 35% ointment. After 2 weeks, corneal bullas were reabsorbed, and mild focal areas of corneal oedema were present bilaterally. Three weeks after discharging, the calf was hospitalised again for severe dyspnea, recumbency and depression and was euthanised due to worsening of clinical conditions. A necropsy was performed. Clinical signs, ophthalmic examination and histopathologic findings were suggestive of bullous keratopathy. Bullous keratopathy might be rare but due to the importance of predisposing diseases (i.e. septicaemia), early diagnosis and proper therapy could be useful to reduce farmers' economic losses.

Key words: bullous keratopathy, calf, ophthalmology, septicaemia

Bullous keratopathy (BK) occurs in dogs (Michau *et al.*, 2003), cats (Patullo, 2008) and humans (Dawson & Edelhouser, 2010). It is caused by oedema of the cornea, resulting from failure of the endothelium to maintain the normally dehydrated state of the corneal stromal layer. Most frequently, it is due to Fuchs corneal endothelial dystrophy or corneal endothelial trauma. Another frequent cause of BK is corneal endothelial trauma, which can occur during intraocular surgery or after placement of a poorly designed or malpositioned intraocular lens implant (Zemba & Camburu, 2017). Diagnosis is posed by clinical presentation and ophthalmologic evaluation. The light microscopic examination shows marked oedema separating the collagen fibrils of the corneal stroma. Inflammatory cells, when present, are in small quantities and the cornea surrounding the lesions appears normal (Moore, 2005).

This paper reports a case of acute BK in a calf suffering from a concurrent septic systemic inflammatory response syndrome (SIRS). To the best of authors' knowledge, this is the first report concerning a bilateral acute BK in the bovine species.

Case details

A 20-day-old female Holstein calf was evaluated for an acute bilateral ocular opacity. The calf was hospitalised, and the owner's written consent was obtained for all the procedures.

The calf presented poor general condition, depression, inappetence, bilateral mucous-purulent nasal discharge, increased hearth rate (HR), increased respiratory rate (RR), decreased body temperature (BT), pale mucous membrane, cold extremities, increased lung sounds both on the left and the right side, and increased abdominal sounds especially in the right ventral abdomen. Diarrhoea was also present.

Blood samples for complete blood cell count, biochemical analysis, protein electrophoresis and blood culture were collected. Main abnormalities found were leukocytosis, neutrophilia plus presence of band neutrophils and regenerative anaemia, high plasma urea concentration with mildly increased creatinine, high total and direct bilirubin concentrations, high GGT, hypoglycaemia and increased plasma CK activity. Proteins electrophoresis showed low concentrations of total protein, albumin and γ-globulins. Blood culture was negative. According to the SIRS evaluation proposed by Trefz *et al.* (2016), the calf was scored as positive (4/4) based on the meeting of more than 2 SIRS criteria. Faecal sample was positive for *C. parvum*.

An ultrasonography (US) evaluation of the thorax, abdomen and umbilicus showed diffuse comet tails on both sides of the thorax, more severe in the cranioventral lung lobes. Abdominal and umbilical US were normal.

A diagnosis of SIRS of infectious origin was made and a systemic therapy including enrofloxacin (5 mg/kg SC q24h for 7 days) and flunixin meglumine (2.2 mg/kg IV q24h for 3 days) was immediately started.

After 4 days of systemic therapy, an acute bilateral ocular abnormality developed (Fig. 1A, B). Gross ocular examination showed a mild bilateral ocular discharge and a bilateral corneal opacity. Schirmer I tear test readings were over 20 mm/min in both eyes. Slit lamp biomicroscopy showed bilaterally a mild conjunctival hyperaemia and a severe oedema of the central cornea with a subepithelial bulla. The highly deformed profiles of both corneas did not allow obtaining reliable intraocular pressure readings *oculus uterque* (OU). The anterior chamber and the iris were partially evaluated from the peripheral cornea that was not involved by the lesion OU, and they appeared normal. The lens, the vitreous body, and the fundus of both eyes were not examined because of the opacity of corneas. Fluorescein stain test was negative OU. A clinical diagnosis of a bilateral BK was formulated. Differential diagnoses included infectious bovine rhinotracheitis (IBR), infectious bovine keratoconjunctivitis (IBK) due to *Morexella bovis*, septic keratitis and primary corneal endothelial dysfunction.

Concurrently with the systemic therapy, a topical treatment with glucose 35% ointment (Gel Oft 5 g) q8h was prescribed. The calf started to improve gradually. After two weeks of systemic therapy the calf showed no more signs of SIRS, the diarrhoea stopped and the auscultation of the lungs and of the abdomen was normal.

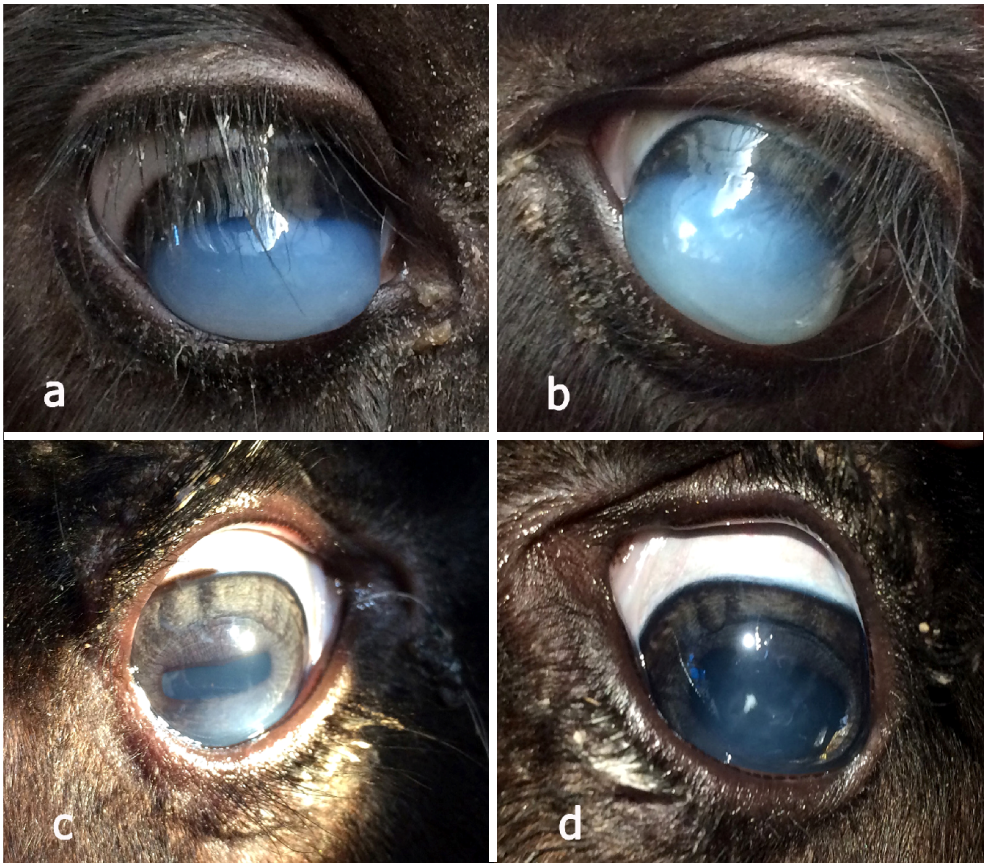

Fig. 1. A, B: Bilateral non-ulcerative bullous keratopathy in a 20-day-old female Holstein calf (right eye: A; left eye: B). Note the mild mucous ocular discharge and the central corneal oedema. The peripheral part of the cornea is free from the abnormality. **C, D:** Ocular appearance at the 2-week follow-up (right eye: C; left eye: D). It is possible to note a residual mild oedema in both corneas. No other ocular abnormalities are present.

The BK improved, and no other signs of ocular diseases were present. After 2 weeks from the initial diagnosis, corneal subephitelial bullas were completely reabsorbed, while focal areas of corneal stromal oedema were still present bilaterally (Fig. 1C, D). At that time, a complete ophthalmic examination was performed and since no other ocular abnormalities were found, the calf was discharged.

Three weeks after discharging, the calf was presented again for severe dyspnea. It was euthanised few hours after the admission due to the rapid and severe worsening of dyspnea. A complete post-mortem examination was performed. Fibrinous pleuritis with adherences between lung lobes, pericardium and thorax wall were observed. Interstitial oedema and multifocal abscesses involving primarily the right apical lobe, suggestive of a suppurative

pneumonia, were found. Stable whitish froth in the tracheobronchial tree, consistent with pulmonary oedema, was evident. Grossly, corneal opacity involving both eyes was noticed. Samples for histopathological examination including both globes were collected. Globes were fixed in Davidson's solution whereas other tissue samples were fixed in 10% neutral-buffered formalin. Then, the fixed tissues were routinely processed for histology and 5-µm thick sections were stained with haematoxylin and eosin (H/E).

Histologically, the right eye was normal with the exception of a multifocal disarrangement of corneal collagenous lamellae, interpreted as stromal oedema. The left eye presented subephitelial multifocal small bullae with separation of the epithelium from the basal membrane. At that level, the epithelial cells were thinned due to the compression (Fig. 2). The corneal endothelium was heterogeneously thickened. No inflammatory infiltrate was observed in both eyes, although neutrophil aggregates were detected in the lumen of some vessels, consistent with the septic state of the calf.

The conjunctiva and cornea are major sites for ophthalmic diseases with large economic impact in food-producing animals. Differential diagnoses for this case included IBR, IBK due to *Morexella bovis*, septic keratitis due to other bacteria and primary corneal endothelial dysfunction (Pearce & Moore, 2013). Both IBR and IBK have been ruled out in this case because of absence of ulcers and presence of a bullous oedema of the corneal structures that was not consistent with both conditions. Moreover, the presence of several signs of septicaemia can be related to a secondary infection rather than a primary involvement of the eye.

A primary corneal endothelial dysfunction may be less likely in this case because the calf largely improved after therapy. Generally, no improvement follows treatment in primary corneal endothelial dysfunction (Pearce & Moore, 2013). Septic keratitis due to bacteria other than *M. bovis* could not be com-

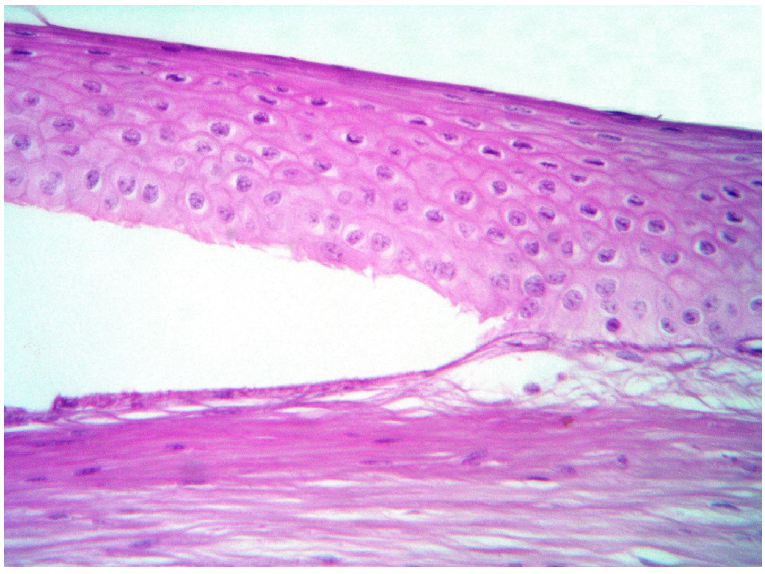

Fig. 2. Left eye cornea. Detachment and thinning of the epithelial layer from the basal membrane. H/E, 320×.

pletely ruled out in this case. There were no signs of corneal ulceration, thus a cultural swab aiming to isolate involved bacteria was not indicated. A more invasive procedure was refused from the owner. Eventually, a diagnosis of BK was considered the most likely.

BK occurs in dogs (Michau *et al.*, 2003) and humans (Dawson & Edelhouser, 2010) usually as a chronic condition. Based on the acute clinical presentation of this case, BK in calves might be more similar to what was reported in cats. In cats, BK represents an uncommon rapidly progressive corneal disease that can occur in less than 24 hours. It is characterised by the rapid formation of corneal oedema with large bullous lesions that are usually bilateral (Patullo, 2008). Our calf developed acute bilateral ocular opacity in almost 24 hours. At the ophthalmologic evaluation, the slit-lamp biomicroscopy showed a mild conjunctival hyperaemia and a severe edema of the central cornea with a subepithelial bulla. This clinical presentation is similar with the ophthalmological findings in cats in which a marked oedema splits the collagen fibrils of the corneal stroma (Moore, 2005). Moreover, the cornea surrounding the lesions appears normal, as already reported in cats (Moore, 2005).

Our histological findings reported alterations of both corneal stroma and endothelium. Thus, the bullae formation in our calf might be due to the same failure in maintaining the normally dehydrated state of the corneal stromal layer, leading to an oedema of the cornea, as already reported for other species (Michau *et al.*, 2003; Patullo, 2008; Zemba & Camburu, 2017).

Treatment of BK is usually surgical and expensive. Medical therapy is generally the first choice for food animals for economical reasons, thus antibiotic has been used in our case, as reported in other species (Michau *et al.*, 2003; Moore, 2005). Moreover, in order to reduce the corneal oedema, the calf has been treated with the glucose 35% ointment (Gel Oft 5 g).

In conclusion, to the best of our knowledge, this is the first report of an acute bilateral BK reported in a septic calf. BK might be rare but due to the importance of predisposing diseases such as septicaemia, this condition might cause economical damage if it would not be recognised or treated.

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