Ecological problems of primary and secondary keratopathies

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Abstract. Among the large number of eye diseases in horses, the largest percentage is occupied by keratopathies, accompanied by damage to one or more layers of the cornea. Keratopathies are multifactorial diseases that occur in one case with traumatization of the cornea and further development of the disease – primary, in the other case with the accumulation of toxins, antigens, and under – oxidized products in the tear fluid-secondary. The absence in the modern literature of the hypothesis of the pathogenesis of keratopathies, summarizing the data accumulated to date, makes it difficult to develop further promising directions in the study of these complex diseases.

1. Relevance

Among the large number of eye diseases in horses, the largest percentage is occupied by keratopathies, accompanied by damage to one or more layers of the cornea. Our previous studies allowed us to present a classification of keratopathies on the example of primary and secondary ulcerative keratitis, based on the state of the physiological barriers of the eyeball. At the same time, such diseases of the cornea as keratolysis, corneal abscess, microabscesses, non-ulcerative keratouveitis, marginal vascular keratitis, bullous keratopathy require further study. The polyetiolo gy of keratopathies, the role of systemic mechanisms and the impact of the external environment (improper operation and feeding) in the development and course of keratopathies determine the complex nature and complexity of the problem. The latter is directly related to the lack of knowledge of predisposing triggering factors and mechanisms in the development of keratopathies. Despite the high frequency of this pathology in horses, the spread, risk factors for the occurrence and development of complications associated with the formation of anterior synechiae, subatrophy, hemorrhagic uveitis in the early period of the disease and the development of chronic inflammation, the occurrence of sluggish forms of inflammation that are torpid to the treatment carried out, have not been determined. In the pathogenesis of primary and secondary keratopathies in horses, the role of the state of the physiological barriers of the eyeball, which determine the form of the course of the disease, the mechanisms of reparative regeneration, and also reflect the role of biochemical reactions, has not been determined.

Primary keratopathies occur under the influence of various traumatic factors, the course of such diseases is usually acute, in some cases it is complicated by the development of a corneal abscess or keratolysis. In the case of an injury to the anterior segment of the eye, the defect of the corneal tissue is seeded with microorganisms located in the conjunctival cavity in horses, which also contributes to the progression of the disease and the development of complications [1, 2].
Secondary keratopathies are induced by spontaneous destruction of the endothelial-epithelial barrier or occur against the background of chronic hypoxia of the corneal tissues. The course of secondary keratopathies was either subacute or chronic. In the study of horses with secondary keratopathies, the presence of systemic concomitant diseases of infectious and non-infectious etiology, recurrent conjunctivitis, an increase in the antioxidant activity of the tear by 15 times compared to the norm was established, which suggests the presence of oxidative stress as the main mechanism triggering the pathological process. With such keratopathies, microflora does not segregate the area of inflammation, but at the same time, microorganisms that are normally located in the conjunctival cavity contributed to the development of the pathological process [3,4,5].

Based on our own clinical, ophthalmic, hematological, microbiological, cytological, chemiluminescent studies conducted in various forms of keratopathies: the primary form (primary ulcerative keratitis, keratolysis, corneal abscess) and the secondary form (secondary corneal ulcer, non-ulcerative keratouveitis, bullous keratopathy, marginal vascular keratitis), as well as recent literature data, the concept of the pathogenesis of inflammatory and degenerative diseases is presented corneas in horses.

2. Materials and research methods

The material for the study was horses with various clinical forms of keratopathies in the number of 188 heads, of which 99 horses (52%) were affected by primary keratopathies, and 89 horses (48%) were affected by secondary keratopathies. The horses were kept in private stables in Moscow and the Moscow region, and had similar feeding and maintenance conditions. Research methods: clinical, ophthalmic, hematological, microbiological, cytological, chemiluminescent.

For the study of the eyeball, a Heine frontal magnifier, a Schwabe slit lamp, a Heine ophthalmoscope, an iCare Tonovet tonometer, a set of vital dyes (sodium fluorescein, lissamine green and Bengal pink), mydriatics for the study of the lens, vitreous body and fundus (tropicamide 1.0%) - if the transparency of the cornea allowed; functional tests were performed: the Schirmer test and the Norn test, for analgesia the eyes used the drug alkaine, and also manually assessed the soreness of the eyeball.

The pupils' response to light, their shape, the surface of the eyelids, their integrity, the presence of blepharospasm, the position of the eyelashes, the color of the conjunctiva, the presence of effusions from the conjunctival cavity, their nature and number were evaluated using a frontal magnifier.

Using slit biomicroscopy, changes in the cornea were detected: a violation of its transparency, the presence of infiltrate, pigment or pus in its tissue, loss of specularity and moisture, the direction of growth, the number and length of vessels, the presence of corneal tissue defects, the depth of the anterior chamber, the presence of content in it, its quantity and nature, the surface of the iris was examined, its color, uniformity of structure, the presence of cluster bodies and synechiae were determined.

The aim of the study is to present the concept of the pathogenesis of primary and secondary keratopathies in horses.

3. Research results and their discussion

Primary keratopathies occur in the presence of primary exogenous exposure. There is a violation of the integrity of the multilayered flat, the death and loosening of the collagen fibers of the stroma, the secondary destruction of collagen and keratocytes due to the multiplication of microflora, the secretion of enzymes of the conjunctiva, lacrimal fluid and cornea, and the release of inflammatory mediators. The path of the development of an inflammatory reaction of the anterior segment of the eye, in the direction of tolerance (areactivity – a simple corneal ulcer), or an immunopathological response with the development of keratolysis or abscess, depends on many factors: first of all, on the primary trigger factor, the nature of the microflora and enzymes in the conjunctival cavity, the number of destroyed collagen fibers, the reparative capabilities of the epithelium and timely veterinary care.

Secondary keratopathies depend on many factors: the primary trigger mechanism (the general state of the animal's body), the age of the animal, the presence of stress, improper operation, feeding,
infectious diseases and reduced immunity, etc., and as a result, the degree of inflammation of the corneal tissue.

With the above-mentioned clinical risk factors for the occurrence and development of keratopathies, the most favorable conditions are created for inhibiting the reparative regeneration of the cornea.

Vascular reactions in non-ulcer keratouveitis and marginal vascular keratitis occur in the absence of damage to the epithelium and stroma, as a result of the accumulation of antigens, toxins, and under-oxidized products in various layers of the stroma. The liquid part of the blood and proteins leaves the vascular bed due to an increase in vascular permeability. Chemotaxis of polymorphonuclear leukocytes and their infiltration into the cornea occurs due to the production of leukotrienes. Infiltration of polymorphonuclear leukocytes into the cornea may increase tissue damage resulting from the release of lysosomal enzymes.

The formation of reactive oxygenase metabolites, such as superoxide dismutase, under the influence of infiltrated polymorphonuclear leukocytes can lead to further inflammatory cell infiltration.

Despite the multifactorial nature of keratopathies, oxidative stress plays a significant role in the pathogenesis. Our studies have shown that in primary keratopathies there is an increase in the antioxidant activity of the tear fluid by three times, and in secondary keratopathies by fifteen times. Spontaneous degeneration of the endothelium and impregnation of the stroma with intraocular fluid in bullous keratopathy occurs with the direct participation of oxidative stress: endothelial ischemia and degeneration occur.

The previously stated assumption about the immune nature of inflammation in the cornea is confirmed by the results of works performed using chemiluminescent and spectrophotometric studies [1,6,7]. The authors found that the development of corneal erosions and ulcers is accompanied by multidirectional changes in the content of the main proteins of the tear film. The results of the proteomic analysis of the tear suggest the possibility of using the proteins serotransferrin, serum albumin and annexin A1 as markers of the studied ophthalmic complication.

Figure 1. Scheme of pathogenesis of primary keratopathies.
4. Conclusion

Thus, the concept of the pathogenesis of keratopathies in horses is based on the following mechanisms:

- the induction of the inflammatory process by exogenous factors that contribute to the violation of the integrity of the cornea, and depending on the nature of the injury and the degree of contamination of the traumatic object, the immunoresistance of the conjunctival cavity and the involvement of enzymes in the pathological process, the development of primary corneal ulcer, corneal abscess or keratolysis;
- the induction of the inflammatory process by endogenous factors, such as a decrease in the function of the physiological barriers of the anterior segment of the eye and a violation of the metabolic processes in the cornea, which contributes to the occurrence of secondary corneal ulcers, marginal vascular keratitis, non-ulcerative keratouveitis and bullous keratopathy, the development of these diseases are factors that contribute to the immunosuppressive state of the horse's body (transportation, vaccination, the presence of concomitant diseases, intensive training) and the progression of secondary keratopathies.

The concept of pathogenesis does not claim to be a complete, comprehensive explanation of all aspects of this complex disease. However, at the present stage, it allows us to approach the development of more effective methods of diagnosis, treatment and prevention from a pathogenetic perspective and to outline promising ways to further study this problem.

References

[1] Sandmeyer L S, Bauer B S and Grahn B H 2014 Diagnostic ophthalmology Can Vet J. Jan 55(1) 1263-4
[2] Brooks E D 2002 Equine Ophthalmology Gainesville FL 32610
[3] Zernii E Y, Baksheeva V E, Yani E V, Philippov P P and Senin I I 2017 Therapeutic Proteins for Treatment of Corneal Epithelial Defects Curr Med Chem. 8 doi:10.2174/0929867324666 170609080920
[4] Goncharova A V and Sotnikova L F 2020 Clinical and ophthalmic assessment of reparative regeneration of the cornea in ulcerative keratitis in horses Bul. of the Altai State Agrarian Univ.
12(194) 65-70

[5] Matthews A and Gilger B C 2009 Equine immune-mediated keratopathies Vet Ophthalmol. 1 10-6

[6] Göncü T, Akal A, Adıbelli F M, Çakmak S, Sezen H and Yılmaz Ö F 2015 Tear Film and Serum Prolidase Activity and Oxidative Stress in Patients With Keratoconus Cornea 34(9) 1019-23 doi:10.1097/ICO.0000000000000510

[7] Uchino Y, Kawakita T, Miyazawa M, Ishii T, Onouchi H, Yasuda K, Ogawa Y, Shimmura S, Ishii N, and Tsubota K 2015 Correction: Oxidative stress induced inflammation initiates functional decline of tear production PLoS One 10(5) doi:10.1371/journal.pone.0127720