Alpha2EQ® for the Management of Equine Recurrent Uveitis

Introduction

Equine recurrent uveitis (ERU) is a disease of the eye characterized by inflammation of the uveal tract, and may involve the iris, the ciliary body or the choroid either individually or in combination.[1] The disease can present with a wide range of clinical signs of varying intensity, including photophobia, blepharospasm, corneal edema, and aqueous flare.[1] Equine recurrent uveitis is generally considered to be an autoimmune disease that is the most common cause of blindness in horses worldwide.[2,3] Prevalence rates for ERU are 2-25% in the United States and 8-10% in Europe.[3] Equine recurrent uveitis demonstrates similarities to autoimmune uveitis in humans in terms of the relapsing– remitting course, the clinical signs and the pathology.[2]

Etiology and Management

Leptospirosis is often suggested as the principal initiator of ERU.[3] The disease is, however, multifaceted and the exact mechanism of induction of uveitis and the pathogenesis of how the *Leptospirosis* is associated with the recurrences is not completely understood.[1] Other infectious and noninfectious etiologies, including past ocular trauma, may also trigger ERU.[3] It is also suspected that environmental influences and genetics play a role in the development of ERU.[3] While any breed of horse can be affected, breeds that are overrepresented include Appaloosas, draft breeds, and Warmbloods.[1,3]

The general treatment goals for ERU include management of the intraocular inflammation and associated pain, and preservation of vision.[1] Medical management of ERU consists of topical and systemic medication(s), including non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, and mydriatics to suppress and control inflammation and manage the associated pain.[1,3] Addition of intravitreal injections with rapamycin or gentamicin or suprachoroidal triamcinolone injections, and/or surgical options may be required if medical management alone is not providing adequate control of the disease.[1,3]

Alpha-2 Macroglobulin

Alpha-2 macroglobulin (A2M) is a glycoprotein, part of the innate immune system evolutionarily conserved across all vertebrate species, with a unique, multi-modal mechanism of action.[4] Through a combination of non-specific protease inhibition, the ability to specifically bind pro-inflammatory cytokines, and a favorable gene regulatory profile, the molecule acts as a naturally occurring anti-inflammatory.[4] Based on the anti-inflammatory activity of A2M, and the ability to inhibit proteases, including collagenases[4], the molecule was considered as a potential new addition to the available means of managing equine recurrent uveitis.

Protocol for Managing Equine Recurrent Uveitis

The protocol for managing ERU begins with processing blood from the horse diagnosed with ERU. Using an Alpha2EQ® EQ30 system from Astaria Global according to manufacturer's recommendations will yield more than 30 mL of plasma with no cells, no cytokines, and functionally isolated, functional alpha-2 macroglobulin. The plasma "product" is drawn into syringes in 2.0 mL aliquots. All the syringes but the syringe used for the initial round of applications should be placed in a freezer for future use. The eye is medicated with 0.5 mL applied topically to the affected eye q12hr. Systemic NSAIDs were administered

as needed for the first two (2) weeks. The Alpha2EQ® should continue for 30 consecutive days. Each syringe provides enough Alpha2EQ® for four (4) applications and any remaining should be stored in the refrigerator until it is used.

This protocol has been used on 12 horses to date. As of this writing all 12 horses have responded positively to this regimen, with no adverse events reported. The first horse managed with Alpha2EQ® was started on the protocol over two (2) years ago and has not received any subsequent medications and has not experienced a recrudescence of clinical ERU since that time. Photographs of this horse's eye at the time of diagnosis, at 6 weeks, and at 3 months are in Figure 1A-C below.

Summary

Equine recurrent uveitis can be difficult to manage and combination therapy using multiple treatment modalities is often required. As with many multifaceted disease processes there is often no single method that will benefit all cases, having many options available for clinical use can be of great value. Alpha-2 macroglobulin, isolated in a functional form with the Alpha2EQ® system, may provide an additional, non-invasive, non-pharmaceutical means of managing this devasting equine ophthalmic disease. These results are preliminary, and further studies will be needed to confirm the usefulness of Alpha2EQ® derived A2M for managing ERU.

Acknowledgement

Thank you to Dr. Wim Malisart for developing the protocol for managing horses with ERU with Alpha2EQ® and for sharing the included photographs of the horse's eye.

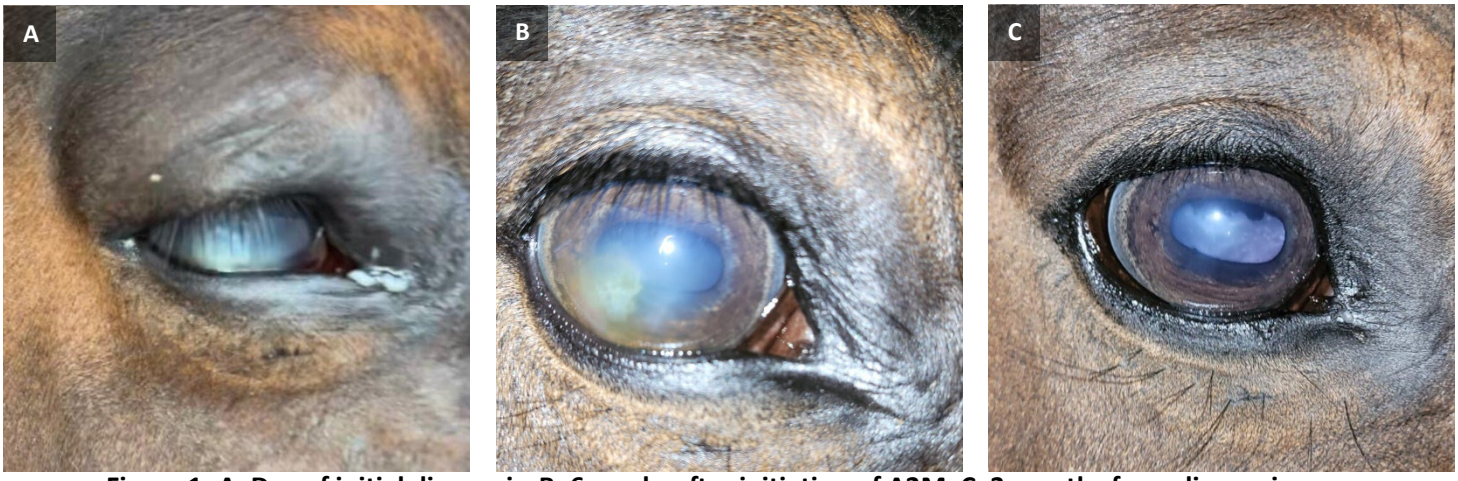

Figure 1- A. Day of initial diagnosis, B. 6 weeks after initiation of A2M, C. 3 months from diagnosis

References

1. Fischer B, Brehm W, Reese S, et al. Equine recurrent uveitis- a review. Equine Vet Educ 2023;35:254-264.
2. Degroote R and Deeg C. Immunological insights in equine recurrent uveitis. Front Immunol 2021;11:609855. doi: 10.3389/fimmu.2020.609855.
3. Allbaugh R. Equine recurrent uveitis: a review of clinical assessment and management. Equine Vet Educ 2017;29:279-288.
4. Vandooren J and Itoh Y. Alpha-2-macroglobulin in inflammation, immunity, and infections. Front Immunol 2021;12:803244. doi: 10.3389/fimmu.2021.803244.