A Sight for Sorre(l's) Eyes

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Class of 2022

Clinicopathologic Conference

December 3, 2021

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Introduction

"Moon Blindness" has been described as one of the first veterinary diseases ever documented. The validity of this argument is supported by the archaic laymen's term itself, originating in the 1600s, the term reflects the cyclic recurrence of the disease having been associated with the waxing and waning phases of the moon. The disease could also be connected to descriptions of equine blindness experienced by the ancient Egyptian horses of Giza (Smith Thomas, 2007).

Being that this disease pre-dates modern medicine, we expect the list of suspect causes to be long. From sewage irrigation, to bad feed (Smith Thomas, 2007) and yes, phases of the moon, there have been many proposed etiologies of Equine Recurrent Uveitis (ERU). What may be unexpected is, veterinary professionals have still not landed on a clear picture of the definitive cause of Equine Recurrent Uveitis. A multi-modal etiology is widely accepted with both auto-immune and infectious, namely Leptospirosis, as the primary contenders.

Whether you call it "Moon Blindness", "Periodic Ophthalmitis", "Iridocyclitis" or Equine Recurrent Uveitis the importance of this disease cannot be denied. ERU is the number one cause of blindness in the horse worldwide, affecting up to 25% of horses with 60% of those horses progressing to blindness (UC Davis Veterinary Medicine, 2020).

History and Presentation

Sorrel is an adult Quarter Horse mare in the Mississippi State, College of Veterinary Medicine: Theriogenology Service Teaching Herd. She was removed from the herd on 11/17/20 for routine palpation labs when purulent debris was noted around the eyes with hypopyon present bilaterally. The presence of blepharospasm was also identified. A menace response was present

in the left eye but was absent in the right. An injection of dexamethasone and ophthalmic atropine drops were administered to provide comfort until she could be assessed by the Ophthalmology service. During her ophthalmic exam on 11/18/20, conjunctivitis, corneal edema and aqueous flare were identified in addition to the previously noted hypopyon. Her right eye was noted to be the more severe of the two. However, clinical signs were present bilaterally.

Pathophysiology

Not to be confused with a single bout of uveitis in equine patients, the hallmark of Equine Recurrent Uveitis is its persistent (or recurrent) nature, having 2 or more episodes within 2 years with quiescence in between (Telle, 2019).

As previously highlighted, the exact cause of ERU is not well known. Associations have predominately been made between autoimmune causes and comorbid Leptospirosis exposure as well as certain breed predispositions. A multi-faceted etiology is widely accepted with the combination of both host and outside factors resulting in a perfect inflammatory storm.

The auto-immune component has been associated with the breakdown of the blood-ocular barrier in response to massive numbers of antigens, allowing CD4+ T Helper lymphocytes to access the normally-immunoprivileged eye (Gerding, et al. 2015). Epitope spreading, a concept described by Cornelia Deeg, et al, is when one immune-reactive autoantigen promotes an immune reaction to novel epitopes. This concept could provide an explanation for the recurrent nature of the disease.

A breed pre-disposition has been established between insidious ERU and Appaloosa horses, most directly correlated with their Leopard Complex Spotting coat which refers to a loss of pigment with age (Rockwell, et al). Appaloosas are 8 times more likely to develop ERU than

other horses and 62.5% of horses with ERU are Appaloosas (Rockwell, et al). A direct correlation has been made between horses with less pigment and increased risks of ERU (Telle, 2019) however, a molecular understanding of this process is not yet understood (Rockwell, et al).

Multiple studies have identified a link between ERU and Leptospirosis. Specifically, a study conducted in the Southeastern United States found that, "horses with ERU had a high prevalence of Leptospira infection based on PCR and MAT results from intraocular fluid compared to control horses," (Polle, Florence. et al). The most commonly isolated species are L. pomona and L. gryppotyphosa (Telle, 2019), with the latter being more prominent in Europe (Polle, Florence. Et al). The mechanism by which Leptospira compromises the blood-ocular barrier and provides disease recurrence is not well understood. However, Geibler et al, suggested the presence of a biofilm could play a role in the evasion of the immune system. Electron microscopy has demonstrated Leptospira surrounded by a granular material in the vitreous (Geibler et al.) and we know that Lepto has the ability to form biofilms in vitro (Evangelista, et al). It is therefore conceivable that the bacteria could utilize this method in the vitreous as well.

Regardless of the cause, inflammation of the uvea can be painful and frustrating with sequela that are not benign. Cataracts, corneal edema, corneal scarring, phthisis bulbi, glaucoma, retinal detachment and thus blindness are all potential sequela to ERU (Telle, 2019). Chorioretinal scarring, known as a "butterfly lesion" may also be observed with ERU (Telle, 2019). These sequalae may contribute to a reduced return-to-function for many of our equine patients, predisposing them to euthanasia or change of ownership.

Diagnostic Approach

During Sorrel's initial ophthalmic exam on 11/18/20, standing sedation was administered so that a complete ophthalmic exam could be performed. The Split Lamp revealed bilateral

aqueous flare with marked hypopyon and conjunctivitis. During corneal staining at a subsequent exam on 11/23 a small corneal ulcer was identified in the left eye.

A Leptospiral panel consisting of 8 serovars was submitted resulting in significantly high titers for 3 of the 8. Titers were elevated for serovars: autumnalis (800), bratislava (1600) and most notably Pomona (6400). Sorrel has no history of Lepto vaccination so it can be deduced that these values reflect exposure alone.

Treatment

Sorrel was treated with intravenous Banamine, every 12 hours at 1.1 mg/kg for 3 days, then decreased to every 24 hours for 9 days. She also received intraocular 1% Atropine HCL, every 24 hours for 12 days. Neomycin and Polymyxin B Sulfates, Bacitracin Zinc, and Hydrocortisone ophthalmic ointment was applied to both eyes 4-6 times daily until a corneal ulcer was identified in the left eye on 11/23/2020. Neomycin Polymyxin B Sulfates and Bacitracin Zinc ophthalmic ointment was then applied to the left eye 4-6 times per day while the Neomycin and Polymyxin B Sulfates, Bacitracin Zinc, and Hydrocortisone was continued on the right. On 11/30/2020, the ophthalmic ointments were decreased to twice daily. On 12/13/2020, Sorrel began receiving Neomycin Polymyxin B Sulfates and Bacitracin Zinc ophthalmic ointment bilaterally, every 24 hours. This regimen was maintained for 10 days. Sorrel received oral Doxycycline 10 mg/kg every 12 hours for 15 days beginning on 11/30/2020.

In February of the following year, Sorrel experienced an ERU flare-up in her left eye, during which she received 6 days of 1% Atropine HCL drops in the left eye, 3 days of intravenous Dexamethasone and 7 days of Neomycin and Polymyxin B Sulfates, Bacitracin Zinc, and Hydrocortisone ophthalmic ointment in both eyes.

On March 25th 2021, Sorrel received a 10 mg/ml intravitreal preservative-free Gentamicin injection in her right eye. On July 14th 2021, Sorrel received the subsequent 10 mg/ml preservative-free Gentamicin injection in her left eye. NeopolyDex ophthalmic ointment was applied daily until one month following Sorrel's second injection. She recovered uneventfully and has experienced no identified ERU flare-ups following her injections.

Case Outcome

On October 29th, 2021, Sorrel received a follow-up exam from the MS State Ophthalmology Service, approximately 7 months following Gentamicin injection of the right eye and 3 months following injection of the left. An abbreviated ophthalmic exam revealed resolution of signs and complete return to vision.

Conclusion

While Cyclosporine implants and Vitrectomies have been more widely studied, Gentamicin injections have shown promise, not only in Sorrel herself, but in the literature as well. Fischer et al, found that 88.1% of horses who received Gentamicin injections in their controlled study had the absence of inflammation at least 30 days post-op. Gentamicin injections currently cost approximately $200 per eye at institutions like MS State CVM, while vitrectomies run approximately $5000 and Cyclosporine implants can easily reach $1500. This makes the accessibility for ERU relief attainable for many more patients who may be limited by financial constraints. Gentamicin injections may also be the treatment of choice for ERU cases that do not achieve "quiescence" between flare-ups or for cases with poorer prognosis; less financial risk is required. The success of Sorrel's case is encouraging for horses plagued by ERU who come from more modest financial backgrounds or who may be unable to travel to specialty institutions. Per

Dr. Caroline Betbeze, Veterinary Ophthalmologist, intravitreal low-dose preservative-free Gentamicin injections can be performed by general practitioners who research the procedure. This opens up ERU relief to many patients who do not have the luxury of visiting a referral or specialty center. Equine Recurrent Uveitis is a disease that has withstood the test of time. It has plagued our patients for centuries and doesn't appear to be on its way out. Cases like Sorrel's are encouraging for not only for the animals suffering from this disease, but also the practitioners who are eager to provide relief.

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