Caprine Infectious Keratoconjunctivitis:

A Case Report

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INTRODUCTION

Infectious keratoconjunctivitis, also known as pinkeye or contagious ophthalmia, is a contagious bacterial disease of the eye.[6] Pinkeye is the inflammation of the inside of the tissue lining the eyelid, the conjunctiva, and the cornea in one or both eyes. Ultimately, this can lead to ulceration which produces pain, and may worsen leading to temporary or permanent blindness.[2,6] In goats, pinkeye is primarily caused by the microorganisms *Mycoplasma conjunctivae* and *Chlamydia percorum*.[4] These will be the etiological agents of focus in this case report. Other aerobic bacteria that could lead to this condition in goats include *Pseudomonas sp*., *Staphylococcus aureus*, *Branhamella* spp., and in cattle and sheep, *Listeria monocytogenes*.[9] Less common causes of caprine infections keratoconjunctivitis may include parasites, infectious bovine rhinotracheitis, as well as non-infectious causes such as trauma. While the most common cause of pinkeye in cattle is *Moxarella bovis*[4], this is not the main causative agent in sheep and goats with the same clinical signs. [9] There have been some reported cases in the state of Mississippi of Caprine herpesviris 1, (CpHV-1), as a cause of keratoconjunctivitis, however these cases are not well documented.[12]

Due to the potentially multi-etiological nature of ocular disease in goats and other livestock, pinkeye is of major economic significance to livestock producers through decreased weight gain (failure to thrive), decreased milk production, and treatment costs. [2,13]

HISTORY AND PRESENTATION

Mycoplasma conjunctivae

Mycoplasmas belong to the class *Mollicutes,* and are largely host-specific. Mycoplasmas differ from bacteria in that they lack a cell wall, and only have a cell membrane. They are the smallest genomes of any free-living organism, and have surface cell proteins that are vital to the survival in the host. Because most are primarily extracellular pathogens, the surface proteins are thought to play very important roles in their adherence to host cells.[11,9] Due to these characteristics, mycoplasma-associated disease often "waxes and wanes" due to the ability of mycoplasmas to trick the immune system into thinking that they are commensal organisms within the body.[11]

There is strong evidence that *Mycoplasma conjunctivae* is a major causal agent of keratoconjunctivitis in goats.[6] It has frequently been isolated from epidemics of keratoconjunctivits, respiratory disease, and arthritis in goats and sheep. Although *M. conjunctivae* is suspected to play a part of many mycoplasma-associated syndromes, it can also be a primary entity in itself.[11] *M. conjunctivae* was the most common microorganism isolated from the eyes of goats showing signs of keratoconjunctivitis, and has been successfully reproduced experimentally via subconjunctival injection. The disease spreads rapidly during natural infection, and once in a herd, the disease is likely to recur following stressful events. Transmission is greatest when herds are gathered together in tight, dusty quarters during winter months, exposed to extremely bright sunlight, and long grass in their pastures.[6,11]

Chlamydophila percorum

Two species of the genus *Chlamydophila* cause diseases in small ruminants. *C. abortus* and *C. percorum* are members of the order *Chlamydiales* and are obligate, intracellular bacteria that depend on the host cell for energy. *C. percorum* is commonly isolated from the digestive tract of ruminants, and is recognized as a cause of conjunctivitis, arthritis, and inapparent infections in sheep and goats.[8]

Strains of *C. percorum* are recognized as important causes of keratoconjunctivitis in small ruminants.[8] Pneumonia is also a reported sequelae, but their role as a primary respiratory pathogen is very uncertain.[8] Risk factors associated with *C. percorum* outbreaks show the highest prevalence of disease occurs in the summer months when conditions are dry, dusty, and the fly population is heavy. [9] *C. percorum* commonly inhabits the gastrointestinal and reproductive tracts, with fecal shedding and infection occurring as young as 3 months in sheep and goats. Transmission of *C. percorum* is believed to be through the fecal-oral route via the ingestion or inhalation of infective *Chlamydia* in secretions from infected animals.[13]

Together, *Chlamydophila percorum* and *Mycoplasma conjunctivae* are considered the most important primary causes of infectious keratoconjunctivitis in sheep and goats.[8] Animals infected with both agents are usually introduced to the flock as apparently healthy goats, with either mild or inapparent infection. However, the stress of recent transport, introduction to a new herd, or change in feed and housing can precipitate the appearance of clinical signs of the disease in the infected animals. Direct contact is the most important method of transmission between animals, and disease is most common in situations in which the animals are closely confined. Morbidity rates are as high as 90% in feedlot lambs and kids. The disease is usually acute and spreads rapidly. In all species, the young animals are affected most frequently, but animals of all ages are susceptible.[3, 8, 9]

CLINICAL SIGNS

Initially, goats presenting with keratoconjunctivits typically present with hyperemia of the vessels of the conjunctiva and sclera.[8] One or both eyes may be affected.[3] Early on in the disease, there will be signs of photophobia, blepharospasm, and epiphora.[3] As the disease progresses, the ocular discharge may become more mucopurulent.[3] Conjunctivitis, with varying degrees of keratitis is usually present.[3] If left untreated, chemosis, corneal neovascularization, and varying degrees of corneal opacity and ulceration can occur. [3,13] In sheep and goats, concurrent polyarthritis, (if associated with *C. percorum*), and respiratory infections, (if *M. conjunctivae* associated), may be present in the affected animals.[1, 3, 8, 11] Both organisms are contagious, which makes this a herd problem. Angora goats may be more severely affected than dairy breeds, and older goats may be more severely affected, especially following previous exposure.[6]

DIAGNOSTIC APPROACH AND CONSIDERATIONS

The diagnostic approach for infectious keratoconjunctivitis can be presumptively based on the ocular signs and concurrent systemic disease.[3] It is an important first step to distinguish that the lesions observed are not due to any foreign bodies in the eye or parasites.[3] Additionally, the diagnosis can sometimes be made based on herd health history, the observed clinical signs, and the pathological findings.[13] However, in an effort to determine the causative agent behind the clinical signs, further diagnostics are warranted.

A range of traditional methods have been employed to identify *Chlamydophila percorum* infections in livestock.[13] Identification can be made by fluorescent antibody staining of exfoliated cells in conjunctival scrapings after topical anesthesia, or by isolation of *C. percorum* in cell culture or embryonated eggs.[8, 9] However, isolation in embryonated eggs is very time consuming, and the isolation of *C. percorum* in cell culture is more difficult than other Chlamydia species. The exfoliated cells of the conjunctiva can be fixed in methanol and stained with Giemsa stain and examined for chlamydia inclusions. However, immunofluorescent antibody staining is the preferable method of diagnosis.[6,8,9] This is because chlamydial organisms can easily be confused with melanin granules.[8] There are currently enzyme-linked immunosorbent assay, (ELISA), kits available that are used for the identification of *C. trachomatis*, but have not been evaluated for the effectiveness in identification of *C. percorum.*[8]

Polymerase chain reaction, (PCR), is also an available technique for identifying *C. percorum*, however, similarly to the use of PCR to diagnose *C. abortus*, there are high incidents of false-negatives due to inhibitors in the samples.[8] Serology, based on the use of compliment fixations tests (CFT), are routinely used by veterinary diagnostic laboratories to identify *C. percorum* strains. This method of testing detects serum antibodies to the lipopolysaccharide that is common to all chlamydial species. This method is more economical to the livestock producers, and it is technically simple, however it is suspected that this method is contributing to the misdiagnosis and possible under-reporting of *C. percorum* infections.[13] CFT lacks sensitivity and specificity due to its likely cross-reactivity between different species of chlamydia.

Similar techniques are used to obtain samples to diagnose *Mycoplasma conjunctivae.*[6] Exfoliative cytology from the palpebral conjunctiva from early clinical cases can also be Giemsa-stained as smears or explored using immunofluorescent staining similar to that used in chlamydial sample identification. Samples can also be submitted for cultural identification with paired serum samples.[9] The most commonly used diagnostic technique for mycoplasmas has been culture. However, because of the unique nutrient requirements of mycoplasmas, this technique requires special growth medias and laboratory expertise, which are not commonly successful. [11] These specific requirements cause poor sensitivity in routine mycoplasma cultures. In addition, cultures are time consuming.[11] The immunofluorescence test and growth inhibition tests use anti-sera against whole mycoplasmas or cell membranes. These tests have very high specificity and are good methods to detect between species of mycoplasma. Monoclonal antibodies have been used in ELISA, antigen-capture ELISA, and immunohistochemistry to increase sensitivity and specificity.[11] PCR has been shown effective in detecting *M.*

conjunctivae, and may serve as a better technique in the future than the currently utilized cultures.[9]

The actual determination of the etiological agent responsible for the outbreak of infectious keratoconjunctivitis currently has limited significance to the approach to controlling the disease. The efforts currently employed for identification are largely academic.[9]

TREATMENT AND MANAGEMENT OPTIONS

Consideration of the herd, its housing, and size of pasture should be made before commencing with treatment efforts.[9] Repeated treatments of goats pastured under extensive grazing are impractical and spontaneous recovery will occur within weeks. Consequently, in extensive grazing conditions, a decision to not impart any treatments of the disease is often made.[9] A single intramuscular injection of long-acting tetracycline at 20mg/kg can be used prophylactically in the unaffected members of the herd.[6] In the clinically ill members of the herd, this treatment halts further development of clinical conjunctivitis.[9] This treatment option should be considered in any herds with high morbidity.[8] Rapid recovery should be seen in animals that are affected with keratoconjunctivitis produced by *M. conjunctivae* with this treatment alone.[9] In an extra-label drug use (ELDU), capacity, daily feeding of 150-200mg of tetracycline per head to kids reduces the incidence and severity of disease. However, the use of a tetracycline in feed would require a veterinary feed directive, (VFD) prior to administration. Tylosin, a macrolide and another ELDU option, administered as an intramuscular injection has also produced good results.[8] In cases where systemic administration of medications is undesirable due to milk-contamination, tetracycline-containing powders, drops, and ointments can provide satisfactory results.[8] In these cases, topical tetracycline ointments, such as Terramycin, oxytetracycline/ Polymyxin B, or erythromycin, 3-4 times daily for 5-6 days, are generally effective, especially if used in conjunction with long-acting tetracycline injections and started early in the course of the disease.[3,4,6] Subconjunctival injections can be used additionally to achieve a high concentration of the antibiotic locally.[6] Animals with severe secondary uveitis which is particularly painful may benefit from topical ophthalmic application of 1% atropine ointment 1-3 times daily. This will prevent ciliary body spasms and reduce the likelihood of posterior synechia formation that occurs with miosis. Because of mydriasis caused by atropine, treated animals should be provided shade.[3] Systemic NSAID administration of banamine or meloxicam may be utilized for treatment of the pain associated with the clinical signs of the disease. When the infected eye is extremely painful, topical anesthesia can also be utilized in the eye with the use of 0.5% proparacaine, and an auriculopalpebral nerve block can be used in very fractious animals to administer some treatments.[3,6]

Preventative measures and close management of clinically ill animals has been shown to be a major factor of decreasing the morbidity of the rest of the herd. Always wearing gloves while treating the sick animals, and performing treatments and feedings to the sick animals after attending to the healthy ones are simple steps that can be taken to decrease transmission rates.[4] Severely affected animals should be separated from the rest of the herd, and should be penned in dark surroundings with easy access to clear drinking water and high quality feed.[4,6] Because the clinically affected animals may be partially blinded by the disease, it may be difficult for them to find their food sources and water, so they should be kept in a relatively small space.[4]

In nearly all peer-reviewed research and published case reports, it is commonly accepted that the highest risk factor for seeing signs of clinical disease is placing inapparent carriers of the causative agents for infectious keratoconjunctivitis into a new herd without proper protocol. This replacement of animals from outside sources, the lack of separate pens when newly introduced, and the stress of transport have all been shown to precipitate the condition in the goat.[13, 2] Other predisposing factors for animals showing signs of disease are exposure to very bright sunlight, a dusty environment, and poor hygiene condition on the farm.[2]

Overall, good management practices are of paramount importance to reduce or prevent the spread of infection in all livestock, not just goat herds. Always purchasing animals from clean grounds, minimizing transportation stress, preventing stress when managing the heard, quarantining newly purchased animals, and separating sick animals from the herd into small enclosures, using appropriate PPE, (gloves, protective clothing), and disinfecting between animals when possible are all effective steps to take to prevent the spread of disease. [3,4]

EXPECTED OUTCOME AND PROGNOSIS

In most uncomplicated cases, this disease is self-limiting. The eyes can return to normal in 2 to 3 weeks.[12] The signs of conjunctivitis and corneal ulcers can cause significant pain, and usually warrant pain control and more extensive treatment, but these conditions have been seen to subside by the fifth day of treatment.[2] Therefore, the prognosis for recovery from this disease is considered good since the affected animals have shown positive response to treatments given.[2,9]

CONCLUSION

Complete eradication of this disease is not currently attempted, and antimicrobial treatment also raises the potential issues of inducing latency, rather than eliminating the infection.[9,13] This could explain why some producers report a relapse in clinical signs in their livestock 3 to 6 weeks after treatment, or reports of chronic persistent infections in livestock.[13] Studies have shown that short-term antimicrobial treatment initially reduced DNA-loads of chlamydial causative agents, but then animals later relapsed to pre-treatment levels after completion the antimicrobial therapy.[13]

Development of vaccines that might provide protection of small ruminants from an early age would offer a more attractive approach to infection control, compared with the use of antimicrobial drugs.[13] Moving forward, some of the key research priorities surrounding infectious keratoconjunctivitis may include a requirement for in depth economic analysis, increased global surveillance in other livestock industries, better diagnostic testing, and experimental infection studies involving the most common pathogens precipitating this disease.[2,11,13] Engaging veterinarians from clinical practice, academia, and industry in research is essential for the development of a practical and integrated management program for prevention, treatment, and control of infectious keratoconjunctivits in livestock.[13]

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