Prissy's Peculiar Plight

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Introduction:

Dystrophic epidermolysis bullosa in goats is a rare mechanobullous disease that results in cutaneous blister and ulcer formation following minimal trauma. An autosomal recessive mutation of the gene responsible for synthesis of collagen VII has been identified as the cause of this disease. Signs typically occur soon after birth and may range from mild blistering to severe ulcerations. The only definitive treatment identified for dystrophic epidermolysis bullosa in other species is gene therapy. Most cases are managed symptomatically with supportive care and routine physical examinations.

History and Presentation

Prissy is a 3-week-old Kiko doe that presented to Mississippi State University College of Veterinary Medicine Food Animal Medicine service on March 21, 2019 for swelling and blepharospasm of the right eye. Upon presentation, she weighed 7.1 kilograms with a temperature of 103.4 degrees Fahrenheit, heart rate of 156 beats per minute, and respiratory rate of 24 breaths per minute. Her owner noticed an abrasion ventral to the right eye two days prior to presentation that worsened until she was unable to open her palpebra. During the physical exam, severe interdigital phlegmon (foot root) was noted in the interdigital space of all four feet and appeared to be causing sloughing of the lateral dewclaws of the hind limbs. Prissy was administered BNP ophthalmic ointment OD q8h and long-acting oxytetracycline (20 mg/kg) and was discharged with instructions to monitor and recheck on March 27, 2019. At recheck, the corneal ulcer was healed with no remaining fluorescein stain uptake. The areas of foot rot on all feet were also improving; however, the owner noted superficial crusts distributed on the concave surfaces of the pinna, bilaterally along the neck, and on the ventral and dorsal aspects of the pelvic region. No evidence of ulceration or infection was associated with the crusts. Sloughing of

the wall of the left horn and ectoparasites (*Linognathus africanus*) were also observed. The feet were cleaned with chlorhexidine solution and topical 5% permethrin and 5% piperonyl butoxide insecticide was applied for treatment of the lice. The sloughing horn wall was removed.

On April 4, 2019, Prissy again presented to MSU CVM for a two-week history of non-weight bearing lameness of the right hindlimb. Additionally, she was lethargic and withdrawn from the remainder of the herd, but continued to nurse and eat adequately. At presentation, Prissy was quiet with a weight of 8.6 kilograms, temperature of 104.9 degrees Fahrenheit, heart rate of 198 beats per minute, and a respiratory rate of 48 breaths per minute. She was dull and exhibiting bruxism continuously. Erythematous lesions were noted on the concave surfaces of the pinna bilaterally as well as multifocal to coalescing ulcerative areas in the mucosa of the oral cavity. Scabs, epidermal scaling, and crusts were observed along most of her body, including the ears. The previously treated lice infestation was also still present but improved. While much of the foot rot had healed, the medial hoof wall capsule of Prissy's right hind foot had sloughed with heat and swelling present. Due to the extent of Prissy's condition, she was hospitalized and underwent further diagnostics and treatment.

Diagnostic Approach

On April 4, 2019, Prissy's right hind foot was soaked in chlorohexidine solution and bandaged to protect the medial aspect where the hoof capsule had sloughed. Florfenicol was administered subcutaneously (40 mg/kg) to prevent an ascending infection. Skin punch biopsies were taken from the right shoulder, left lateral abdomen, and chest ensuring involvement of healthy and diseased epidermis. The biopsies were submitted for histopathology in attempt to identify the cause of the widespread skin wounds.

Pathophysiology

Epidermolysis bullosa (EB) is a group of skin diseases that are distinguished by the location of their defect within the epidermis and whether the disease is inherited or acquired. This group of diseases has been recognized in several mammalian species including man, sheep, cattle, horses, dogs, cats, rats, and mice. The unifying characteristic of this group is the formation of oral and cutaneous blisters, ulcers, and erosions following even minimal mechanical trauma due to extreme epidermal fragility. Due to this unique feature, all subtypes of EB are known as mechanobullous diseases where bullae form due to structural defects in the basement membrane zone, the area between the epidermis and dermis. Epidermolysis bullosa can be either acquired or inherited and is divided into three broad categories based on the level of ultrastructural tissue separation. Epidermolysis Bullosa Simplex (EBS) is the most superficial disease with clefts occurring in the keratinocytes of the epidermis. Junctional Epidermolysis Bullosa (JEB) is characterized by defects within the lamina lucida and is more severe than EBS. Dystrophic Epidermolysis Bullosa (DEB) is the most clinically severe of these diseases and occurs in the deeper portion of the dermoepidermal junction below the lamina lucida. Dystrophic epidermolysis bullosa in animals has only been reported to be inherited through an autosomal recessive mutation in the COL7A1 gene that is responsible for expression of type VII collagen. This mutation causes qualitative and quantitative changes in the anchoring fibrils which are responsible for maintaining the adherence of the epidermis to the dermis.

In goats with DEB, clinical signs typically appear between time of birth and three months of age. Kids may be born apparently normal, but when slight shearing pressure is applied to the skin the epidermis is easily loosened from the underlying dermis. This characteristic is known as Nikolsky’s sign and is present in many blistering diseases. As the animal ages, erosions and

crusts begin to form on the pinna, ventral thorax and abdomen, and around the carpus and tarsus. The coronary bands of the hooves may become erythematous with eventual exungulation, or detachment of the hoof wall. Most of the lesions tend to heal spontaneously by scarring which is not seen in other forms of EB and often disrupts the anatomical function of the tissue. Erosions and ulcers may form in the oral mucosa making it difficult for kids to nurse or eat leading to possible malnutrition and growth retardation. On post-mortem examination of several affected goats, mucosal ulceration was noted to extend from the lips through the soft and hard palate, and down into the esophagus. Histological examination of the lesions showed separation of the epidermis and dermis with the basement membrane on the roof of intact blisters that were often filled with eosinophilic fluid with occasional cellular debris and neutrophils. No cytolysis of epithelial cells was noted. When viewed under a scanning electron microscope, the anchoring fibrils, composed of type VII collagen, were rare and rudimentary even in skin with no apparent lesions.

The three skin biopsies taken from Prissy were evaluated. Each section showed hyperplastic epidermis that was multifocally covered by increased amounts of laminated anuclear keratin, known as orthokeratotic hyperkeratosis. In some sections, the keratin was expanded by eosinophilic serocellular debris. The epidermis was lifted off the dermis forming multifocal subepidermal clefts. Within these clefts, irregular frayed collagen and stretched basal epithelial cells were seen. Some areas of the dermoepidermal junction were noted to be expanded by clear vacuoles of varying sizes. There was an increase in number of plasma cells seen scattered throughout the dermis as well as prominent blood vessels. The histologic features seen in Prissy's biopsies combined with her clinical signs makes dystrophic epidermolysis bullosa a likely diagnosis.

Treatment and Management

The only corrective treatment known for inherited DEB is gene therapy, which is being studied in colonies of golden retrievers and German shorthaired pointers for use in human EB. While gene therapy appears to have great potential, it is not yet available for animals other than humans. Other treatments attempted in dogs with EB include human immunoglobulin, glucocorticoids, azathioprine, colchicine, and modified epidermal autographs. Dosages and success rates are unclear due to little data available on individual treatments. Supportive therapy for DEB involves minimizing trauma, managing pain associated with lesions, and use of antimicrobials as needed to manage secondary infections. Periodic physical exams should be used to monitor clinical improvement.

Prissy's sloughed hooves were managed with bandage changes and administration of florfenicol to prevent the development of a secondary infection. Eprinomectin (500 mcg/kg) was applied topically for treatment of the persistent lice infestation. Dexamethasone (0.15 mg/kg) was administered intramuscularly every other day during hospitalization for a total of six treatments. Prissy was discharged on April 16, 2019, day 13 of hospitalization, with instructions for administering a tapering dose of dexamethasone every other day for two weeks and then every three days for one week. Her owner was instructed to change her bandage on the right hind hoof every three days until healed and keep her in a clean and confined area to help prevent infection and decrease trauma. Due to the hereditary component of the disease, Prissy's owner was advised not breed her and consider performing an ovariectomy in the future.

Case Outcome

Prissy returned to MSU CVM on April 30, 2019 for a recheck appointment. Her owner felt she was doing better overall, and her vital parameters were within normal limits. Upon

physical examination, new oral and cutaneous ulcerations were noted with continued skin crusts and scaling. Her hooves were under run and several claws were beginning to slough. A new corneal ulcer was noted in the left eye that was treated with BNP ophthalmic ointment for one week. Dexamethasone was again sent home with the owner to be administered every other day for one week and then every three days for four weeks. Due to the intensive supportive care and unique needs of Prissy and her disease, she was donated to MSU CVM and subsequently adopted.

Approximately two weeks after adoption, Prissy was diagnosed with pneumonia and recovered uneventfully. She was adequately dewormed to manage the high parasite burden that was likely worsened by long-term steroid administration. Prissy now lives primarily indoors with access to a grazing lot and plenty of opportunity to be a normal goat kid. Her owner reports that her horns and hooves have grown back well, and she has had minimal recurrences of clinical signs related to her disease since her change in lifestyle. She is being monitored closely for new cutaneous and oral ulcerations and her daily care is adjusted as needed to decrease the chance for trauma to occur. While there is still no definitive treatment for Prissy, the supportive care she is receiving has greatly improved her quality of life.

References

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