Hyperkeratotic skin conditions in New World camelids

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INTRODUCTION

Hyperkeratotic skin conditions in New World camelids include chronic mite infestation, zinc-responsive dermatosis, ichthyosis, and idiopathic necrolytic neutrophilic hyperkeratosis (INNH, also known as "munge"). Although these disorders are relatively uncommon, clinical signs may be severe and aesthetics may negatively impact the value of animals used for production. Hyperkeratotic lesions are typically alopecic with varying degrees of skin thickness. Pruritis is not usually a characteristic of hyperkeratotic skin disorders, with the exception of sarcoptic and psoroptic mite infestation. Biopsy is an important diagnostic modality, and treatment depends on etiology; therapy may include steroids, antimicrobials, zinc supplementation, and/or antiparasitic treatment. Although studies investigating the prevalence of skin disorders in New World camelids are limited, a recent retrospective analysis of 68 alpacas with skin disorders found that 10% of animals demonstrated mite infestation, 8% had zinc-responsive dermatosis, and 4.5% had ichthyosis.[1] Diagnosis of INNH was not definitively made in these cases as the disease was thought to be secondary to several other skin disorders. In a separate study, the most common hyperkeratotic disease reported in New World camelids from the United Kingdom was zinc-responsive dermatosis which was diagnosed in 35% of animals with skin lesions, followed by mite infestation in 29% of animals; INNH and ichthyosis were not diagnosed in this report.[2]

MITE INFESTATION

New World camelids are exposed to and affected by several ectoparasites, the most common of which are mites. They are susceptible to sarcoptic, psoroptic, and chorioptic mange, and can be simultaneously infested with all three.[3] However, chorioptic mange appears to be the most common mite infestation.[4]

Chorioptic mange

The most common mite infestation of New World camelids is *Chorioptes bovis*, and is recognized in many countries including the United States. Unlike other types of mange, pruritis is generally absent or mild. Animals may appear clinically normal despite heavy parasite infestation, while animals with few mites may develop severe lesions. Early in the course of infestation, lesions are typically found on the ventral abdomen, perineum, ventral tail and medial thighs, and may progress to include the axillae, face, pinnae, distal limbs and interdigital spaces.[5-8] Alopecia, scaling and crusting lesions often progress to include lichenified, thickened skin. Like psoroptic mange, chorioptic mange does not constitute a zoonotic risk.

Sarcoptic mange

Sarcoptic mange is caused by *Sarcoptes scabiei* var. *auchinae*, and has been reported in many countries in South America, Europe and New Zealand.[3,9-11] The disease is thought to be rare in the United States because of routine use of ivermectin.[8,12,13] Sarcoptic mange is a significant cause of weight loss and fiber loss. In some populations, sarcoptic mange can be found in 40% of animals and can be responsible for up to 95% of monetary losses secondary to ectoparasite infestation.[9] Affected animals present with pruritis and alopecia.[1,10,11] Early lesions most commonly affect the ventral abdomen, axillae and groin, and may extend to the medial thighs, extremities, feet and face. Initially, the infested skin is erythematous with yellow to grey crusts, but with time the skin becomes thickened, lichenified and hyperpigmented. Secondary bacterial infection may occur and lead to further morbidity. Importantly, sarcoptic mange in New World camelids is a potential zoonosis.[7,8,10]

Psoroptic mange

Psoroptic mange in New World camelids is caused by a mite that has not been specifically named, so is referred to as *Psoroptes sp*. [1,7] Skin lesions predominantly affect the head, face and pinnae, with less common

sites including the shoulders, dorsum, and perineum.[2,3,7,8,14,15] If the ear canals are affected, the animal may present with ear twitching, head shaking, and head tilt. Like with sarcoptic mange, pruritis and alopecia are often observed and are associated with papules and crusts early in infestation; chronic disease is associated with thickened skin. Purulent discharge from the ears may indicate secondary bacterial infection. Psoroptic mange is not considered zoonotic.

Diagnosis

Diagnosis of mange is confirmed by the presence of mites in skin scrapings; however, the absence of visible mites does not rule out disease.[7,8] In a study evaluating the prevalence of *C. bovis* infestation in a herd of alpacas in the United Kingdom, skin scrapings were positive in 55% of clinically normal animals that had direct contact with animals bearing skin lesions, while only 28% of animals with skin lesions were positive for mites.[4] Chorioptic mites are most readily recovered by scraping the interdigital spaces of the forefeet.[4,5] Biopsy can be helpful in supporting the diagnosis of mange, with histopathology often revealing eosinophilic interstitial dermatitis, marked parakeratotic hyperkeratosis, and mites within surface crusts.[1,11] In addition to these histology findings, eosiniophilic epidermal microabscesses and pustules have been described in New World camelids with chorioptic mange.[16] Eosinophilia may be present with heavy mite infestation but normal peripheral eosinophil counts do not rule out disease.

Treatment

Avermectins in different formulations have been shown to be effective in treating mange in cattle,[17,18] sheep,[19,20] pigs,[21,22] and dogs.[23] Although its use is considered off-label, ivermectin at a dose of 0.2 - 0.4 mg/kg every 1 – 2 weeks subcutaneously for 2 – 4 injections is considered an effective means to treat mange in New World camelids; however, treatment failures with ivermectin, doramectin, and eprinomectin have been reported.[7,10,24] Topical amitraz administration has been shown to resolve clinical signs of sarcoptic mange for at least 10 months in infested alpacas that did not respond to avermectin treatment.[10] There is evidence that chorioptic mange may be more difficult to clear than sarcoptic or psoroptic mange. In one study evaluating treatment in a herd with simultaneous infestation with *Sarcoptes sp*., *Psoroptes sp*. and *Chorioptes sp*., ivermectin (1%) was effective in eliminating *Sarcoptes sp*. and *Psoroptes sp*. after subcutaneous administration of 0.2 mg/kg on day 0 and day 10; however, additional treatment with 50 µg/kg ivermectin as a pour-on on day 24 and day 34 was required to eliminate *Chorioptes sp*.[3] This is consistent with previous findings.[14,25,26] Topical administration of eprinomectin at a dose of 0.5 mg/kg weekly for four weeks was found to be highly effective at reducing *Chorioptic sp*. mite numbers in a herd of alpacas, but failed to completely eradicate them.[5] Similarly, the same dose of eprinomectin applied topically weekly for 10 weeks failed to eradicate chorioptic mange in a herd of llamas and alpacas.[6] The use of organophosphate dips to control mite infestation is not recommended for New World camelids as it is for small ruminants, as dipping can be stressful for the animals and there is no safety information available. Movement of animals to clean pasture following treatment and disinfection of fomites may aid in successful eradication; however, mites can survive in the environment for up to 2 months, making reinfestation possible.[27]

ZINC-RESPONSIVE DERMATOSIS

Zinc-responsive dermatosis may be due to a true zinc deficiency or a keratinizing disorder that is responsive to high dosages of zinc supplementation; thus, the disorder has also been termed "idiopathic hyperkeratosis." Lesions in affected animals consist of thickened skin with tightly adhering crusts that are found most commonly on hairless areas of the body (ventral abdomen, axilla, medial thighs, and inguinal area) but can also occur on the face, pinnae and neck.[1] Colored fleeced New World camelids appear to be more susceptible than white fleeced New World camelids, and young animals (1 - 2 years of age) are more frequently affected.[13,28] A herd of 48 llamas and alpacas were evaluated for nutritional status and skin lesions, 25% of

which were found to have lesions consistent with zinc-responsive dermatosis despite being fed grass hay and commercial camelid supplemental feed. [28] The grass hay and camelid feed contained 15.8 and 51.3 mg/kg zinc, respectively. Mean serum zinc concentrations were 0.17 μg/ml for all alpacas in the herd, and 0.22 μg/ml for all llamas in the herd. The proposed reference range for serum zinc concentrations for llamas is 0.30 – 0.50 μg/ml.[29] There was no significant difference in serum zinc concentrations between New World camelids with skin lesions and those without. In this particular study, only females were affected, but reports in males have also been documented.[7,12] The authors of this study made the following conclusions: 1) skin lesions are most likely to occur in young breeding females when the mineral content of feed is low; 2) dark fleeced animals are more affected because dark fleeces contains higher levels of zinc and copper than white fleeces and exert higher demands on mineral metabolism; and 3) serum zinc concentrations may not reflect total body zinc levels, but affected animals may demonstrate low serum zinc concentrations. It is important to note that zinc-responsive dermatosis often affects only one individual in a herd, even when all animals are fed the same diet.[1]

Diagnosis

Biopsy is an important component of diagnosis. Histologic changes in affected New World camelids demonstrates epidermal and follicular orthokeratotic hyperkeratosis with mild to moderate perivascular dermatitis containing lymphocytes, macrophages, plasma cells and occasional eosinophils.[7,8,12,28] This is different than the typical parakeratotic hyperkeratosis reported in sheep,[30,31] goats,[32,33] cattle,[34] swine[35] and dogs[36] with zinc deficiency. Serum zinc concentrations should be tested, even though normal levels do not rule out zinc-responsive dermatosis. Blood samples for serum zinc analysis should be placed into plastic tubes with no anticoagulant using a plastic syringe that does not contain rubber. Rubber in tube stoppers may contain zinc that may falsely elevate levels. Also, erythrocyte lysis can release zinc into the serum.[7] Finally, diagnosis may be aided by response to treatment.

Treatment

It is recommended that affected New World camelids receive 1 - 2 g zinc sulfate or 2 - 4 g zinc methionine once daily by mouth for several weeks. Although improvement is often seen in 30 - 90 days, lesions may not resolve for up to 12 months after the start of zinc supplementation.[1,7,8,28]

ICHTHYOSIS

Ichthyosis is a congenital disorder characterized by focal or diffuse hyperkeratosis and scaling, and has been described in humans, dogs, cattle, pigs, mice and New World camelids.[37-42] The disease is caused by defects in terminal differentiation of keratinocytes and desquamation, which occur in the upper layer of the epidermis. The result of defective desquamation is increased cohesion of keratinocytes. In humans, there are several clinical forms of ichthyosis including lamellar ichthyosis (LI), which is an autosomal recessive disease considered to be the form most similar to that in animals. Lamellar ichthyosis is a severe nonepidermolytic form of disease, and has been described in golden retriever and Jack Russell terrier dogs, as well as Chianina cattle.[40,42-45] In humans, approximately 40 genes are involved in ichthyosis, mutations of which can lead to the lamellar form. Mutations within the transglutaminase 1 (*TGM1*) gene have been shown to decrease or inhibit transglutaminase activity, which results in the LI phenotype in humans and dogs.[39,46-48] Recently, an indel mutation in the *PNPLA1* gene was found to be highly associated with LI in humans and golden retriever dogs.[49] Both genes (*TGM1* and *PNPLA1*) are important in formation of the epidermal lipid envelope.[49,50] A less common form of ichthyosis in humans and cattle is ichthyosis fetalis (harlequin ichthyosis), which is the most severe form of congenital ichthyosis and is characterized by diffuse, large, diamond-shaped or plate-like scales.[44,51] Because of cracked skin in locations where normal skin would fold, bacterial dermatitis can lead to fatal infection. In New World camelids affected with ichthyosis, lesions resemble those of LI. A genetic cause has yet to be elucidated, but it is reasonable to expect that a *TGM1* mutation is associated with disease.

Diagnosis

Diagnosis of ichthyosis in New World camelids relies on age, clinical signs, and biopsy. Lesions are present at birth or shortly thereafter.[1,37] Focal or diffuse nonpruritic, nonpainful hyperkeratotic plaques are typically observed. Histologic changes include prominent laminated orthokeratotic hyperkeratosis of the epidermis and infundibula of hair follicles with minimal epidermal hyperplasia.[1,37,38] This is similar to histology of affected dogs, cattle and humans.[39,42,44,46] The absence of inflammatory cells helps distinguish ichthyosis from zinc-responsive dermatosis.

Treatment

Treatment is not typically attempted in these animals, as most are otherwise healthy. In humans with ichthyosis, oral retinoids such as isotretinoin (Vitamin A derivative) have greatly improved quality of life and may be a candidate treatment for animals with the disease pending further research.

IDIOPATHIC NECROLYTIC NEUTROPHILIC HYPERKERATOSIS (INNH)

Idiopathic necrolytic neutrophilic hyperkeratosis (INNH), also referred to as "munge," is a hyperkeratotic disorder that affects alpacas and llamas. Two general forms of INNH are recognized. Focal INNH affects the perinasal and perioral regions with some extension to the periocular and periaural areas. Thick crusts may obstruct the nostrils in severe cases. Diffuse INNH is typically seen in llamas that are 1 - 2 years of age.[7] This condition is poorly understood and is likely a cutaneous reaction in the skin of New World camelids that is caused by host, environmental and pathogen factors. Disorders that may initiate the development of INNH include bacterial folliculitis, dermatophilosis, dermatophytosis, mite infestation, fly bites, viral papillomas/fibropapillomas, contact dermatitis, and zinc-responsive dermatosis.[1,7]

Diagnosis

Histology often reveals parakeratotic and orthokeratotic hyperkeratosis with a seropurulent, palisading crust associated with epidermal hyperplasia, degenerate nuclear and hyperkeratotic debris, epidermal edema and keratinocyte necrosis. Secondary bacterial dermatitis with neutrophils may also be observed.[8,12] A positive bacterial culture and antimicrobial susceptibility of the skin lesion may guide appropriate therapy. Serum zinc concentration may reveal deficiency that can be addressed with zinc supplementation.

Treatment

Because the etiology of INNH is unknown and predisposing factors are likely multifactorial, treatment often consists of "the kitchen sink." Cases have been reported to respond to topical and/or systemic antimicrobials, topical and/or systemic corticosteroids, oral zinc supplementation, or to spontaneously regress.[1,7,8] A popular treatment that is reported to be effective anecdotally includes a mixture of gentamicin, ivermectin, dimethyl sulfoxide and mineral oil.[1]

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