Zinc-responsive dermatosis

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Categories : Companion animal, Vets

Date : August 29, 2016

Zinc is an essential mineral involved in many aspects of body metabolism, including carbohydrate, lipid, protein and nucleic acid metabolism, regulation of keratinisation, maintenance of normal reproductive function, wound healing, normal immune system function, and senses of smell and taste.

Zinc is a component of more than 70 metalloenzymes and is found in muscle, bone, teeth, reproductive organs, liver, spleen and hair. Most zinc is acquired from diet and a continuous supply is needed as readily available stores from other sites are limited.

Figure 1. Periocular alopecia, crusting and scaling in a Siberian husky with zinc-responsive dermatosis.

Zinc can also be absorbed via the skin, which contains 20% of the total body stores. Young growing animals and reproducing adults need higher levels. Zinc is excreted in urine and faeces, with the latter being the major source of loss.

As zinc is important for various functions, it is logical a deficiency will result in disease. However, clinical signs vary depending on the species and deficiency severity. A reduced appetite is often seen and thought to result from the decreased senses of taste and smell. Other signs include stunted growth, decreased reproductive function, poor wound healing and skin disease[1].

Skin diseases due to zinc deficiency have been reported in species including dogs, cats, sheep, goats, pigs, cows, red wolves (*Canis rufus*), rats and humans[2-9]. The classic example of zinc-responsive dermatosis (ZRD) is parakeratosis of young growing pigs. Signs are usually limited to the skin and consist of thick, crusted lesions around the eyes, ears, nose and pressure points.

In humans, an inherited zinc deficiency syndrome, called acrodermatitis enteropathica, has been shown to involve abnormal zinc transport mechanisms at the apical surface of enterocytes[9]. It results in various systemic and cutaneous clinical signs that respond well to zinc supplementation. Lethal trait A46 in cattle is a similar inherited zinc deficiency syndrome that usually responds to zinc supplementation[6].

Clinical syndromes

ZRD is an uncommon disease in dogs, but two syndromes are well recognised. Syndrome I classically occurs in northern breeds, such as the Siberian husky, Alaskan malamute and Samoyed, although it has been reported in other breeds[10, 11]. No sex predilection exists and age of onset is variable, with a study reporting an age range of 2 months to 11 years[2]. Syndrome I develops despite a balanced diet and is thought to be associated with defective intestinal absorption of zinc.

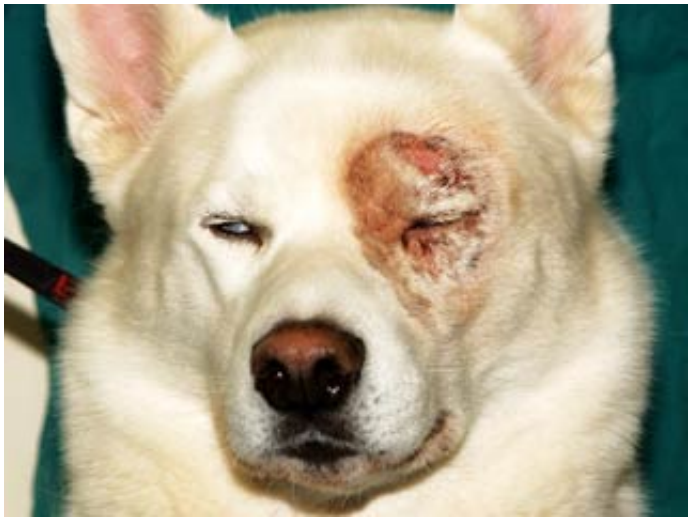

Figure 2. Severe asymmetric periocular erythema, alopecia and crusting in a dog with zinc-responsive dermatosis. Image: Peri Lau-Gillard.

Skin lesions tend to develop from September to January – consisting of crusting and scaling, alopecia and erythema – and usually develop around the mucocutaneous junctions (**Figures 1, 2 and 3**). Sites include the periocular, perioral, perigenital and perianal areas, along with the nasal planum. In addition, lesions of crusting and scaling often affect sites of wear and trauma, such as the footpads, limbs and muzzle.

Lesions are often symmetrical, but asymmetry does not preclude the diagnosis. Pruritus is variably present, with 16 of 41 dogs affected in one case series[2]. Affected dogs are also prone to secondary microbial infections and often develop a dull and lacklustre coat (**Figure 4**).

Syndrome II is seen most commonly in young, rapidly growing large-breed puppies. It occurs due to the feeding of diets either deficient in zinc, high in plant phytates (which interfere with zinc absorption) or high in minerals such as calcium (which chelates zinc in the food and decreases absorption). High levels of iron in the diet can also interfere with zinc absorption. The severity of clinical signs is variable, but lesions generally resemble those of syndrome I.

Another syndrome of note is lethal acrodermatitis – an autosomal recessive disorder of bull terriers that shares clinical and pathological features with acrodermatitis enteropathica in humans. Although the pathogenesis is not fully understood, defects in zinc and copper metabolism at the cellular level are suspected[12].

Clinical signs are apparent by six to eight weeks of age and include diarrhoea, growth retardation, abnormal behaviour (aggression) and difficulty eating due to a high-arched hard palate. Dogs are also immunocompromised and develop respiratory infections and nasal discharge. Feet are splayed and crusting, and scaling develops on footpads. Similar lesions develop around the mucocutaneous junctions and secondary bacterial infections are common. Unlike acrodermatitis enteropathica in humans, which usually has a good prognosis, affected dogs do not respond to zinc supplementation and usually die of bronchopneumonia by one year of age.

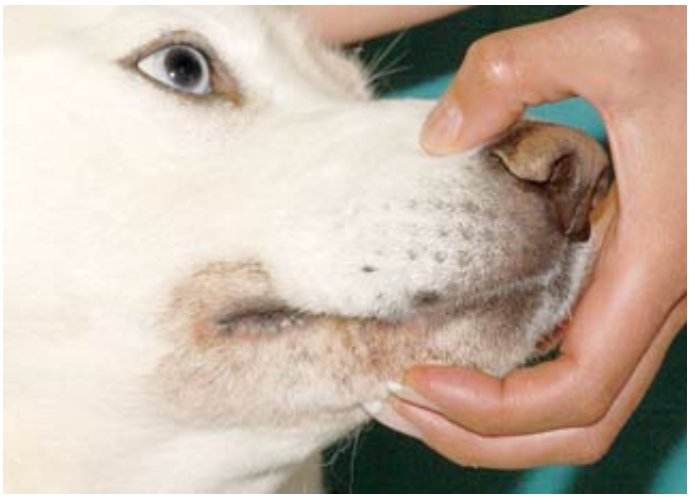

Figure 3. Perioral alopecia, erythema and crusting in a dog with ZRD. Image: Peri Lau-Gillard.

A further presentation of severe ZRD was described in a litter of pharoah hounds[11].These dogs developed similar clinical signs to acrodermatitis of bull terriers, but did respond to IV zinc supplementation. The authors concluded this presentation might, therefore, be a closer match to acrodermatitis enteropathica in humans.

Diagnosis

Important differential diagnoses include dermatophytosis, demodicosis, pemphigus foliaceus, superficial necrolytic dermatitis, generic dog food dermatosis, mucocutaneous pyoderma and systemic lupus erythematosus. A thorough diagnostic work-up for these diseases should be conducted if the history and clinical signs are suggestive.

Diagnosis of ZRD relies on compatible history, signalment and clinical signs, and is supported by histopathology of skin biopsy specimens. A response to zinc supplementation or dietary correction ultimately confirms the diagnosis.

The principal histopathological feature is parakeratosis and this was present in all 41 dogs in a case series[2]. Parakeratosis extending into hyperplastic follicular infundibula is a characteristic feature of the disease[13]. Cases will also often show acanthosis of the epidermis and mixed perivascular, diffuse and/or perifollicular inflammation in the dermis.

Serum and hair zinc levels have been shown to be reduced in dogs with zinc-responsive dermatosis[14].However, as zinc levels in deficient dogs can overlap with those of unaffected dogs, many clinicians feel these measurements are unhelpful. In addition, spurious values can be produced by haemolysis and from zinc contamination from glass tubes and rubber stoppers.

Treatment

Dogs with syndrome I usually show a complete resolution of clinical signs with zinc supplementation. In a retrospective study, 88% of dogs experienced resolution 3 to 210 days after initiating therapy[15]. Oral zinc supplementation is the treatment of choice in dogs and a variety of formulations are available.

No studies exist directly comparing the commonly used formulations in dogs (zinc sulphate, zinc methionine and zinc gluconate). However, in the two largest retrospective studies, no difference occurred in response rates, effective doses and recurrence of lesions between different formulations[2,15].

An initial oral dosage of 1mg/kg of elemental zinc per 24 hours is the usual recommended starting dose[1].This is given for four to six weeks to determine the response to treatment. If the response is poor, the dose may be increased by 50% per month until a response is produced[1]. Some dogs showing a poor response may respond better to another zinc formulation[2]. Vomiting is the most common adverse effect of zinc supplementation and occurred in 5 out of 17 dogs in a study[15].

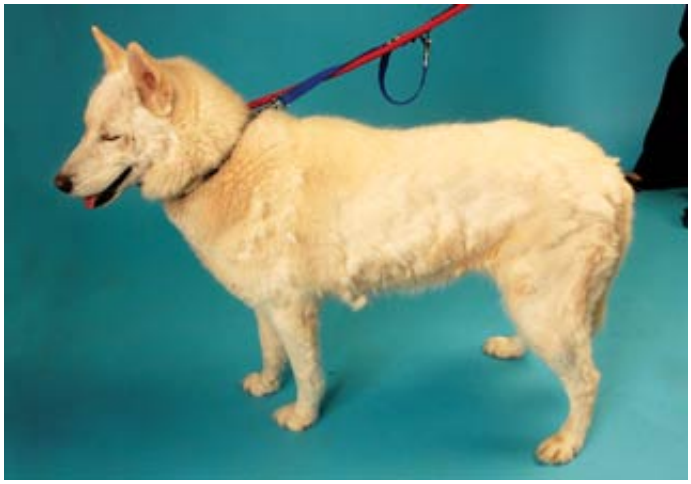

Figure 4. A dull and lacklustre coat in a dog with zinc-responsive dermatosis.

Zinc sulphate is the most commonly used formulation. Tablets should be crushed and mixed with food to increase absorption and decrease gastric irritation. Zinc methionine and zinc gluconate are reported to cause less gastric irritation.

Other therapeutic options include the addition of essential fatty acids, which act to increase zinc absorption from the gastrointestinal tract, and/or systemic glucocorticoids. The beneficial effects of glucocorticoids may result from their anti-inflammatory effects on the skin or their ability to increase gastrointestinal zinc absorption. Anti-inflammatory doses are normally recommended.

Some refractory cases benefit from IV administration of zinc[11]. Sterile zinc sulphate at 10mg/kg to 15mg/kg can be given weekly for four weeks and then every one to six months thereafter for maintenance[1]. This is expensive and cardiac arrhythmias can occur if injections are given too fast. Whichever formulation is used, most cases of syndrome I ZRD require life-long supplementation. In syndrome II, affected puppies usually respond to dietary correction alone, although supplementation can be considered to hasten resolution.

Conclusion

Zinc is involved in many aspects of body metabolism. ZRD is an uncommon disease in dogs resulting from a familial defect in zinc absorption/metabolism or feeding an inappropriate diet.

The prognosis should be good for both syndromes, but life-long supplementation is usually required for the familial form. Lethal acrodermatitis of bull terriers shares some clinical and pathological features with ZRD; however, it is a more severe disease with a poor prognosis.

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