Nutrition and skin diseases in veterinary medicine

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Abstract

Veterinarians are confronted with a variety of food and nutrition-related skin diseases, with cutaneous food adverse reaction the most common in small animal dermatology. In addition to canine atopic dermatitis, cutaneous food adverse reaction has been an area of interest for extensive research for the last decade. Nutritional deficiencies and toxicoses are rare these days due to commercially available high-quality diets; however, poorly stored diets, inadequate husbandry of exotic pets, or problems in a farm animal environment may result in zinc, vitamin A, vitamin C, and fatty acid, or copper deficiency. Inherited deficiencies due to abnormal zinc absorption through the gastrointestinal tract must be considered in Nordic breed dogs and goats.

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Introduction

Veterinary dermatologists are confronted with various food- and nutrition-related skin diseases. The most common one is cutaneous adverse food reaction (CAFR) in dogs and cats. Skin diseases caused by nutritional deficiencies or toxicoses are less common, but are seen in farm animals and exotic animals due to inappropriate husbandry. Hereditary nutritional deficiencies have been reported in Nordic breed dogs and goats. The clinical presentations among these diseases vary, and lesions such as alopecia, coat discoloration, seborrhea, hyperkeratosis, and pruritus may be seen. These diseases can affect many animals in a herd due to husbandry-related problems, or may affect a single animal, as seen with CAFR or inherited zinc-responsive dermatosis in Northern breed dogs.

Cutaneous food adverse reaction

Adverse food reactions are divided into two categories: immune-mediated and non-immune-mediated reactions. Although food hypersensitivity is believed to be immune-mediated, the reactions in most dogs are non-immune-mediated, which are referred to as food intolerance. Food idiosyncrasy, food toxicity, and food poisoning, anaphylactic food reaction, pharmacologic, and metabolic food reactions are all forms of food intolerance (Figure 1). Tolerance and exclusion of food allergens requires an intact gastrointestinal (GI) barrier, which is supported by four mechanisms within the GI wall:

1. integrity of the mucosal barrier provided by morphology and functionality of the enterocytes, presence of immunoglobulin (Ig) A, effective digestion, quality and composition of the food, and presence of inflammation;
2. immune response regulated by M cells in the Peyer patches;
3. elimination of formed immune complex through the mononuclear phagocytic system of the liver and the mesenteric lymph nodes;
CAFR, Cutaneous Adverse Food Reaction

Fig. 1  Classification of adverse food reaction. CAFR, Cutaneous adverse food reaction; Ig, immunoglobulin.

4. tolerance of antigens reaching the mucosa provided by the suppressor function of the gut associated lymphoid tissue (GALT).1,2

CAFR in dogs and cats caused by a hypersensitivity has been associated most commonly with a type I hypersensitivity reaction; however, type III and type IV hypersensitivity are possible immunologic mechanisms.3

Theoretically, any food has the potential to induce adverse reactions; but so far only a limited number of food ingredients have been identified in veterinary medicine. Many different food ingredients are used and are commonly combined in commercially available dog and cat foods, which makes the identification of a specific food allergen very difficult. Several studies determined that the most common foods responsible for causing CAFR are beef, dairy products, wheat, and to some degree lamb, soy, and fish in companion animals.4-11 Food additives, such as dyes and preservatives, are also a concern, but scientific evidence could be established only in two cats, so far.12,13 Adverse reactions to multiple food ingredients are not unusual and have been identified in 35% to 50% of food-allergic dogs and cats.14,15 Cross-reactivity among food allergens is another concern. The results of a recent study showed that bovine IgG was identified as a major allergen in cow’s milk and appeared to be a source of cross-reactivity with beef and probably lamb.16

CAFR is recognized as a potential cause of nonseasonal pruritic skin disease and occasional GI signs in dogs and cats. The exact prevalence of CAFR is not well established, but a few studies determined that the prevalence of CAFR in dogs with nonseasonal pruritus may range between 14% and 24%.5,17,18 Sex, breed, or age predilection could not be confirmed, but a higher risk for certain breeds, such as Boxers, West Highland White Terriers (Figure 2, A-D), retrievers, Cocker/Springer Spaniels, and others has been reported.5,6,14,18-20 CAFR can occur at any age, and most authors report an age range of as early as 4 months to 14 years,11 whereas other authors suggest that a contact time of 1 to 2 years is necessary to develop clinical symptoms.5,6,20

The typical clinical presentation of adverse food reactions in dogs is nonseasonal pruritus of variable intensity affecting face, ears, feet, axillae, inguinal, or perineum.5,6,14,20 CAFR often cannot be distinguished from canine atopic dermatitis, pyoderma, Malassezia dermatitis, and skin diseases caused by ectoparasites, such as sarcotic and demodectic mange and fleas.5,11 Dogs also commonly present with a combination of food adverse reaction, atopy, and flea bite hypersensitivity.5,15,19

Depending on severity and duration, the following skin lesions can be found: erythema, papules, excoriations, epidermal collarettes, seborrhea, and otitis.5,6,14,19,20 In severe, chronic cases, the skin becomes lichenified, accompanied with marked hyperpigmentation, seborrhea, alopecia, secondary superficial pyoderma, and Malassezia dermatitis (Figure 2 A-D). The most common presentation in cats is generalized or localized pruritus around the neck and face (Figure 3), miliary dermatitis, traumatic alopecia, eosinophilic plaques, granulomas, and indolent ulcers.4,5,20-22

Diagnosing a food adverse reaction in veterinary medicine can be very challenging and depends heavily on correct food selection, food trial duration, and owner education and compliance. Several attempts have been made to find a valuable method to diagnose CAFR, but the most effective diagnostic method in dogs and cats is still a strict elimination diet trial.7,17,23-29 Challenging the pet with its previous diet and a relapse of the clinical signs is considered necessary to confirm the CAFR. Because many owners are reluctant to challenge their pet with their previous diet, CAFR can also be identified by adding a single ingredient to the elimination diet for 1 to 2 weeks.7,20 If no relapse is observed, the ingredient is considered safe to give. It is very important during an elimination diet trial that no treats, table food, flavored heartworm and flea preventatives, or medication with gelatin capsules are fed to the animal.3,26 Although most dogs and cats respond within 3 to 4 weeks into a diet trial, improvement is sometimes not seen for 10 to 13 weeks.5,14,15,19,30

The three groups of elimination diets used in veterinary medicine are home-cooked diets, commercially available novel protein diets, and hydrolyzed protein diets. Home-cooked diets are considered superior due to the lack of additives and by-products but are difficult to balance nutritionally, especially for long-term management, and may be more time consuming to prepare, which may have a negative effect on owner compliance. Study results indicate that home-cooked diets may be more effective than commercially available equivalents.4,6,28,31

Commercially available novel protein diets are composed of a single protein that is not used in over-the-counter diets, and a carbohydrate source, such as potato and or oatmeal. Venison, duck, rabbit, and kangaroo are currently used as novel protein sources in commercial veterinary prescription diets.

Commercial hydrolyzed diets are considered real hypoallergenic diets and results from studies indicate that, for example, dogs sensitive to soy did not develop a reaction to hydrolyzed soy.23,32 In up to 50% of dogs with CAFR,
A partially hydrolyzed diet may worsen the clinical signs and so it must be concluded that hydrolyzed prescription diets may reduce but do not eliminate immunologic and clinical allergenicity. Despite these concerns, the use of hydrolyzed diets for the diagnosis of CAFR in dogs and cats became more popular, especially because diets containing hydrolyzed chicken liver, casein, or soy have become commercially available. An evaluation of the efficacy of these veterinary prescription diets reported a success rate of 60% to 75%. Concurrent complications, such as superficial pyoderma, Malassezia dermatitis, or bacterial or yeast otitis externa, often need to be treated at the same time the elimination diet trial is instituted. Because some of these patients are severely pruritic, anti-inflammatory therapy is necessary. Symptomatic therapy must be discontinued for the last 2 to 3 weeks of the diet trial to assess effectively the response to the elimination diet.

The prognosis of CFAR is very good if the offending allergen is identified and as long as patient and owner compliance is guaranteed. Occasional recurrences of the skin problems may occur because some patients may become sensitive to the new protein after 2 to 3 years. Whether animals can become tolerant to a food allergen after an extended period of avoidance, as reported in people, has not been proven, but natural hyposensitization seems to be rare.

**Zinc-responsive dermatosis**

Zinc is an important mineral for many critical biologic functions, such as cellular metabolism, which is crucial for the maintenance of a healthy coat and skin. Zinc deficiency is rare but has been reported in various species,
including dogs, goats, sheep, alpacas, llamas, and horses.\textsuperscript{37-44} Goats, South American camelids, and Nordic breed dogs, such as Siberian Huskies and Alaskan Malamutes, seem to be affected more commonly.\textsuperscript{36,37,39-41}

Zinc-responsive dermatosis has been divided in two syndromes: syndrome I is considered to be a hereditary zinc deficiency resulting in decreased capability of absorbing zinc from the intestines seen in the Nordic breed dogs and probably in goats.\textsuperscript{40,45} Skin lesions develop despite sufficient dietary zinc and most commonly appear in young-adult dogs.\textsuperscript{35} Syndrome II occurs in puppies of fast-growing breeds, such as Great Dane, Doberman Pinscher, German Shepherd, or Labrador Retriever, or in young-adult animals fed a zinc-deficient diet.\textsuperscript{46}

Early skin lesions demonstrate erythema, followed by alopecia and crusting around the muzzle, eyes, and ears. (Figure 4). Hyperkeratosis may also develop in areas such as the anus, vulva, prepuce, scrotum, and footpads. In goats, llamas, and alpacas, the hyperkeratosis tends to be more severe, hard, and dry, affecting mainly the dorsum, legs, udder, face, and ears (Figure 5).\textsuperscript{36,40,43} Pruritus may also develop, especially after the development of secondary pyoderma.

In either syndrome, serum or hair zinc levels may be abnormal. Alpacas and llamas, in general, have lower serum zinc concentrations than do sheep and goats, with no obvious difference between animals with or without skin lesions, which makes proper interpretation of serum test results difficult.\textsuperscript{36,43}

Diagnosis is made by the assessment of a complete history, physical examination, and skin biopsy specimens. The characteristic histologic finding in dogs is a marked diffuse and epidermal/follicular parakeratosis, whereas in goats and alpacas/llamas, a mixed (parakeratotic and orthokeratotic) epidermal and follicular hyperkeratosis is usually present.\textsuperscript{36,40,43} Superficial perivascular dermatitis can be found in all species.

Zinc supplementation in animals with syndrome II usually results in a good response and resolution of the skin lesions within 2 to 6 weeks. Most common preparations for the treatment of zinc-responsive dermatosis are elemental zinc (2 to 3 mg/kg/d), zinc sulfate (10 mg/kg/d), zinc gluconate (5 mg/kg/d), or zinc methionine (1.7 mg/kg/d).\textsuperscript{36,39} In patients with lack of response to oral zinc supplementation, intravenous injection with sterile zinc sulfate (10 to 15 mg/kg) has been effective.\textsuperscript{47} Zinc supplementation for patients with syndrome I is typically lifelong.
Vitamin A-responsive dermatosis and vitamin A deficiency

Deficiency, as well as excessive supplementation of vitamin A, has been associated with skin lesions, such as poor coat quality, alopecia, seborrhea, crusting, increased susceptibility of secondary pyoderma, *Malassezia* dermatitis, and poor wound healing in dogs, horses, caged birds, and reptiles.36,48,49 Vitamin A-responsive dermatosis in dogs is a rare condition characterized by an abnormality of cornification that occurs in adult dogs, predominantly Cocker Spaniels, but also in Labrador Retrievers and miniature Schnauzers.36,50 Owing to the breed-specific occurrence, a hereditary etiology is suspected, but the mode of inheritance is not known. The skin lesions typically present as multifocal areas of alopecia, erythematous plaques, scaling, crusting, follicular plugging with frond-like keratinous debris mainly localized on the ventral and lateral chest (Figure 6), and ceruminous otitis. Analysis of skin biopsy specimens combined with vitamin A supplementation is routinely used to confirm the diagnosis of a vitamin A-responsive dermatosis.50 The histopathologic hallmark of vitamin A-responsive dermatosis is orthokeratotic epidermal and predominantly follicular hyperkeratosis. Therapy consists of oral supplementation of 10,000 IU of vitamin A (retinol), once daily with food. A response and clinical resolution to therapy should be seen within 3 to 8 weeks. Treatment must be continued and is lifelong for most patients.

Vitamin A deficiency in captive reptiles and caged birds, especially parrots, is common when nutritional requirements are not met. Seeds are commonly deficient in vitamin A, and so birds fed seeds exclusively often develop a deficiency resulting in hyperkeratotic skin, white plaques in the oral mucosa, rhinitis, and blepharitis (Figure 7).51 In reptiles, especially in box turtles, vitamin A deficiency is characterized by periocular edema, conjunctivitis, squamous metaplasia, hyperkeratosis of the skin and mouth parts, and aural abscesses (Figure 8).49,52 Therapy consists of a diet change (adding carrots and cod liver oil), and intramuscular injections of vitamin A (2000 IU/kg in reptiles and 5000 to 20,000 IU/kg in birds).49

Vitamin C deficiency

Almost all mammals, except humans and guinea pigs, produce L-ascorbic acid.53 Vitamin C deficiency is a common problem in guinea pigs that are fed a commercial diet deficient in vitamin C.

Fig. 6 Vitamin A-responsive dermatosis: marked ventral hyperkeratosis and seborrhea on the ventrum of an American Cocker Spaniel. (Photo courtesy of C. Sousa.)

Fig. 7 Vitamin A deficiency: nostril distortion and rhinolith due to squamous metaplasia in an African gray parrot. (Photo courtesy of S. Divers.)

Fig. 8 Vitamin A deficiency: conjunctivitis due to squamous metaplasia in a box turtle. (Photo courtesy of S. Divers.)
rabbit chow or outdated commercial guinea pig chow as the sole diet.\textsuperscript{54} Guinea pigs are incapable of endogenous synthesis of vitamin C because they are unable to produce the enzyme L-gulono-\(\gamma\)-lactone oxidase, which is necessary to convert glucose to ascorbic acid.\textsuperscript{55} For this reason guinea pigs have an absolute dietary daily requirement of 10 mg/kg, rising to 30 mg/kg in pregnancy.\textsuperscript{56} Skin lesions associated with vitamin C deficiency are cutaneous petechiae, ecchymoses, hematomas, ulcerations, generalized seborrhea, and poor coat quality (Figure 9).\textsuperscript{54,56} Treatment of vitamin C deficiency consists of correcting the diet and the administration of subcutaneous injections of vitamin C (50 to 100 mg daily) until clinical manifestations resolve, followed by daily oral supplementation.\textsuperscript{56,57}

Although vitamin C deficiency is rare in reptiles, it has been associated with gingival bleeding and spontaneous skin ruptures in snakes, especially boas and pythons.\textsuperscript{49}

Fig. 9  Vitamin C deficiency: ulcerative foot pad lesions and poor coat quality in a guinea pig. (Photo courtesy of S. Divers.)

Surgical repair and oral or subcutaneous daily supplementation of 10 to 20 mg/kg has been used successfully to manage this condition.

Vitamin C deficiency has also been reported in growing calves, aged 2 to 10 weeks, fed a diet low in vitamin C content.\textsuperscript{58} Skin lesions range from nonpruritic seborrhea, crusting, alopecia, easy hair epilation, erythema, petechiae, and ecchymoses, starting on the head and limbs (Figure 10).\textsuperscript{59}

**Fatty acid deficiency**

Dogs and cats are unable to synthesize linoleic acid; thus, a dietary source is essential in both species. In addition, cats exhibit low \(\delta\)-6 desaturase activity and cannot meet their physiologic requirement for arachidonic acid through biotransformation from linoleic acid.\textsuperscript{60} Consequently, linoleic acid and arachidonic acid both are considered essential nutrients for cats.\textsuperscript{61} Fatty acid deficiency has become rare due to the use of commercially available high-quality pet diets; however, commercial dry food that has been poorly preserved or a home-cooked diet could potentially result in fatty acid deficiency. Oxidation of fat during storage, especially at higher temperatures, is a great concern because the essential fatty acids are destroyed when fat becomes rancid. Animals may also develop fatty acid deficiency in association with intestinal malabsorption, pancreatic disease, and chronic hepatic disease.

Clinical signs may not be obvious for several months and usually start with mild scaling and loss of luster of the hair coat. Over time the degree of seborrhea increases (Figure 11) and the skin becomes more greasy and thickened, followed by secondary skin infections and pruritus.\textsuperscript{36}

Specific testing methods to diagnose a fatty acid deficiency are not available, and so a diagnosis must be made according to the response to treatment. Therapy in

Fig. 10  Vitamin C deficiency: generalized multifocal areas of erythema and alopecia in a calf.

Fig. 11  Fatty acid deficiency: dry seborrhea with a dull hair coat in a dog.
such patients consists of switching the diet to a food with a high fatty acid content or by adding an essential fatty acid supplement composed of ω-6, ω-3, and vitamin E. Resolution of mild skin lesions should be observed during a period of 3 to 8 weeks but may take up to 6 months in severe cases.

References


