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DIAGNOSIS OF CANINE ATOPIC DERMATITIS (INCLUDING FOOD ALLERGY)

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1. Introduction

Canine Atopic Dermatitis (CAD) is the most frequent canine dermatosis. It has been defined as a “genetically predisposed inflammatory and pruritic allergic skin disease with characteristic clinical features associated with IgE antibodies most commonly directed against environmental allergens”. The revised nomenclature for veterinary allergy also takes into account dogs with clinical signs of atopic dermatitis but no demonstrable allergen-specific IgE: the term atopic-like dermatitis (ALD) was coined to describe this group of dogs.

In veterinary dermatology, cutaneous adverse food reaction (CAFR) and CAD have been historically considered as two different conditions. In fact, CAFR includes both immune-mediated and non immune-mediated food intolerances and may be associated with a wide range of clinical signs such as gastro-intestinal disturbances, urticaria, angioedema, and signs mimicking those of atopic dermatitis. This latter point has led the International Task Force on Canine Atopic Dermatitis to suggest that some cases of CAFR may trigger flares of atopic dermatitis. The clinical signs of CAD may thus be associated with sensitization to environmental (CAD *sensu stricto*), food allergens (CAFR with clinical signs of CAD: Food-Induced Atopic Dermatitis: FIAD) or with ALD. The presentation will consequently describe the clinical features and diagnostic methods of dogs affected by CAD from whatever cause.

2. Clinical signs of CAD

Signalement of CAD dogs:

The definition of CAD suggests strong breed and/or familial predispositions. Reliable evaluation of breed predispositions for veterinary diseases is complicated by the fact that the population at risk is often unknown. Several studies have, however, addressed the question of breed predisposition for CAD. Some studies only mentioned the most frequently represented breeds while some others have been based on a comparison between atopic dogs and the hospital or insurance population. The former do not present any statistical analysis and the latter may be biased by the absence or the underrepresentation of healthy dogs. One single study is based on a large population of insured dogs but contains another potential bias: the authors did not make the diagnosis of CAD themselves but referred to the diagnosis of general practitioners, who may have used variable inclusion criteria. To further complicate the analysis, predisposed breeds may vary by geographical areas. One single study is based on the comparison of a population of atopic dog and a validated population of healthy dogs. This study was however limited to Switzerland. Some breeds such as WHWT, boxers, Bulldogs are, however, mentioned in virtually all these studies. Some others such as German shepherd

dogs, golden retrievers or Labrador retrievers seem to be predisposed for CAD only in some geographical regions.

Reports of sex predisposition in CAD dogs are inconsistent. Some studies reported predisposition for male, female or for neither sex. We have recently studied a large population of 843 CAD dogs and no sex predilection was detected when the whole population was taken into account. However, some sex predispositions were detected in some breed such as golden or Labrador retrievers (more female) or Boxer (more male). The typical age at onset of CAD is reported to be between 6 months and 3 years. We have however recently shown that about 78% of CAD present with clinical signs before three years of age. It does mean that every fifth CAD dog develops the first clinical signs later in life.

History of CAD dogs:

Information regarding the history of the affected dog should be recorded carefully. Some important questions have already been mentioned (age at onset, breed, familial predisposition) but some others such as seasonality, presence of pruritus sine material at onset, efficacy of previous treatment, should be asked before any clinical examination. Clinical signs of CAD may be seasonal or not but seasonality is often present at onset (42-75%). Approximately 80% of dogs with seasonal signs are symptomatic in spring or summer while the others exhibit signs in winter or autumn. It should be mentioned that some dogs with non seasonal disease do exhibit worsening of clinical signs during one specific season.

Pruritus must be present and its absence rules out the diagnosis CAD. In fact, some CAD dogs do exhibit initially "pruritus sine material", namely pruritus with no skin changes. This feature was recorded in 61% of affected dogs in our recent study. As well, 43% of CAD dogs presented first with an episode of otitis externa. CAD dogs are often treated with glucocorticoids and responses to such therapy should be evaluated carefully. In the same study, we have shown that 78% of CAD dogs responded adequately to such treatment. In the first stages of the disease, the pruritus responds well and readily to the administration of reduced amount of glucocorticoid (i.e. 0.3-0.5mg/kg Prednisolone daily). In chronic cases however, the development of secondary bacterial or yeast infections corresponds usually to a poorer responses to such treatment.

Last but not least, we have also showed that 82% of atopic spend most of their time indoor. It suggests that prolonged exposure to house dust mites may trigger or worsen CAD clinical signs.

Clinical signs of CAD:

Although very frequent, CAD may be difficult to diagnose owing to the lack of pathognomonic signs and the protean clinical picture. Erythema and pruritus are however virtually always present and often represent the first clinical signs.

However, mild pruritus may remain unrecognized by the owner and the veterinarian may sometimes rely on indirect proofs of pruritus such as the presence of excoriations or saliva-coloured hairs.

Most of the signs are actually due to self-trauma and/or secondary infections. In fact, small erythematous papules, which are considered the primary lesion of CAD, are rarely observed in CAD dogs. The practitioner will usually observe the consequences of the inflammation and pruritus, namely excoriations and self-induced alopecia and/or the signs of the secondary bacterial infection (papules, pustules, crusts, erosions) and/or the symptoms of secondary yeast dermatitis (epidermal hyperplasia, hyperpigmentation, lichenification). Recurrent or chronic skin or ear infections are very frequently observed in CAD: In our study, bacterial infections were observed in 66% of the patients while malassezia dermatitis and otitis externa were present in 33% and 50% of all affected dogs, respectively.

Most of these signs are however not specific at all and the distribution of these lesions is consequently more helpful. The most often affected areas are the pinnae (58%), the axillae (62%), the abdomen (66%), the front (79%) and hind feet (75%), the lips (42%) and the perineal area (43%). Unfortunately, all these areas are rarely simultaneously affected in the same individual, except in chronic cases.

Dermatological (pyotraumatic dermatitis, interdigital fistulae) and non dermatological signs are sometimes associated with CAD and their presence should reinforce the suspicion. Spring/summer conjunctivitis, for example, is presented in approximately 20% of CAD dogs while gastro-intestinal signs (soft stools, diarrhea, vomiting) are recognized in 26% of FIAD dogs.

Clinical signs of FIAD dogs differ very slightly from those of classical, environment-induced AD. In fact, in our study, statistically significant differences were only uncovered for gastro-intestinal signs, seasonality, cortico-sensible pruritus and pruritus sine material (less frequent in FIAD dogs). As well, more FIAD dogs have the first clinical signs early in life (less than one year) or, on the contrary, rather late (more than 6 years of age).

3. Diagnosis of CAD:

CAD is a diagnosis of exclusion:

The diagnosis of CAD is based on the history (age at onset, seasonality, pruritus without skin lesions at onset, familial or breed predisposition, previous response to glucocorticoids), the development of the disease (seasonality, “wax and wane” character, development of secondary skin infections) and the lesional pattern. A diagnosis of CAD should however never be made, as long as resembling diseases such as fleas, ectoparasites (especially but not only sarcoptic mange) and primary skin infections (bacterial and fungal) have not been ruled out. Depending on the clinical presentation and the age of the affected dog, some other differentials such as demodicosis, dermatophytosis, cheyletiellosis, cutaneous lymphoma etc... should be properly ruled out. It should also be mentioned that the histological aspect of allergic skin is usually not specific and that this test is consequently not adequate to make the diagnosis. It may be indicated, however, to perform skin biopsies in some instances, to rule out some differentials such as cutaneous lymphoma, for example. As well, allergy testing (serological evaluation of allergen-specific IgE and intradermal skin testing) are not

regarded as criteria for the diagnosis of CAD. This is because numerous healthy dogs are sensitized to environmental allergens and are consequently positive (poor specificity of this criterion) and ALD and some FIAD dogs are deemed negative. These tests should consequently be only carried out to identify the offending allergens (i.e. to choose the allergens for allergen-specific immune therapy: desensitization). In the same way, in order to identify FIAD dogs, a 8-week elimination diet and a subsequent challenge with the previous food should be carried out in all dogs with clinical signs of CAD. It has recently been shown that 90% of the dogs with food allergy improve within 8 weeks. It could consequently be necessary to continue the diet in some dogs.

Criteria do not replace thorough work-up:

	Use	Reliability
Set 1:	• Use for clinical studies and adapt required criteria based on the goal of the study.	• 5 criteria:
1. Age at onset <3 years	• If higher specificity is required, 6 criteria should be fulfilled (e.g., drug trials with potential side effects)	Sens. 85.4 %
2. Mostly indoor	• If higher sensitivity is required, 5 criteria should be fulfilled (e.g., epidemiological studies)	Spec. 79.1 %
3. Corticosteroid-responsive pruritus		
4. Chronic or recurrent yeast infections		• 6 criteria:
5. Affected front feet		Sens. 58.2 %
6. Affected ear pinnae		Spec. 88.5 %
7. Non-affected ear margins		
8. Non-affected dorso-lumbar area		
Set 2:	• Use to evaluate the probability of the diagnosis of canine AD	• 5 criteria:
1. Age at onset < 3 years	• 5 criteria should be fulfilled	Sens. 77.2 %
2. Mostly indoor	• Do not use alone for diagnosis of canine AD, and rule out resembling diseases	Spec. 83 %
3. "Alesional" pruritus at onset		• 6 criteria:
4. Affected front feet		Sens. 42 %
5. Affected ear pinnae		Spec. 93.7 %
6. Non-affected ear margins		
7. Non-affected dorso-lumbar area		

Several sets of criteria have been proposed for the diagnosis of CAD. These criteria are however mainly used for clinical trial to increase homogeneity of the recruited dogs. We have recently performed a

study, in which 1800 pruritic dogs were included by experienced dermatologists throughout the world. One of the goals of the study was to identify criteria for the diagnosis of CAD. The best identified set of criteria has been associated with a sensitivity and specificity of about 80%, when 5 out of 8 criteria are fulfilled (see table). It does mean that using these sole criteria would lead the practionner to make a wrong diagnosis in every fifth dog. These data confirm that ruling out resembling diseases should always be a compulsory prerequisite for the diagnosis of CAD.

The place of "allergy tests" in CAD work-up:

As mentioned above, allergen-specific IgE tests cannot be regarded as "allergy tests", because negative results may be found in some atopic dogs and positive results are often found in healthy individuals. These tests are only useful to identify the allergens potentially involved in the allergic reaction in CAD dogs. In this regard, it is however impossible to compare skin tests (Intradermal tests) and blood tests (IgE serology) or to determine whether one allergen provider or one lab is better than the others! In fact outcomes of allergen-specific immunotherapy based on serology or skin were similar in one study. It is important to mention that these tests are only useful for the determination of environmental allergens but are not reliable for food allergens. For this diagnosis, a

study has shown that patch testing is better than skin tests or food allergen-specific IgE serology. As well, some promising results have been obtained using lymphocyte stimulation or basophil degranulation. It is however important that the former tests are difficult to carry out in daily practice and that the latter could only be made in specialized labs. Recently, a western-blot based test has been proposed in several European countries. This test is marketed for the choice of diet for ED and not for the diagnosis of food allergy. The accuracy of this test for the latter indication is still under evaluation.

4. Conclusions

The diagnosis of CAD is one of the most difficult diagnoses in veterinary dermatology. It is because no pathognomonic signs are known and because of the etiological and phenotypical variability of the disease. For this reason, only a thorough work-up can guarantee a proper diagnosis. It should be kept in mind that no diagnostic test or sets of criteria can effectively replace this thorough work-up!

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