Canine Atopic Dermatitis

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Abstract

Canine Atopic Dermatitis is a genetically predisposed, inflammatory and pruritic skin disease with characteristic clinical features associated with IgE antibodies directed against environmental allergens. Primary dermatological signs include pruritis, lesions at ventral, face, feet and axilla, otitis externa, erythema of inner ear flap and erythema of paws. Signs due to secondary disease include pyoderma, malassezia and chronic skin changes such as seborrhea, hair loss, hyperpigmentation and lichenification. Diagnosis is based on clinical criteria, intradermal test and elevated IgE. Treatment of atopic dermatitis includes avoidance of flare factors, treatment of secondary infection, topical tacrolimus, topical and oral glucocorticoids, cyclosporine and allergen specific immunotherapy.

Keywords: Atopic dermatitis; canine; intradermal test; pruritus; tacrolimus

Introduction

Canine Atopic Dermatitis (CAD) is a complex and multifactorial disease involving immune dysregulation, allergic sensitization, cutaneous barrier defects, microbial colonization and environmental factors. CAD is defined as an 'Inherited predisposition to development of IgE antibodies to environmental allergens resulting in disease'. ACVD task forces define 'Canine Atopic Dermatitis is a genetically predisposed, inflammatory and pruritic skin disease with characteristic clinical features most commonly (but not necessarily) associated with IgE antibodies directed against environmental allergens'. Atopy from greek word meaning strange disease is a term that has long been applied to describe three conditions namely allergic asthma, hay fever and atopic dermatitis, which have number of features in common viz a familiar pattern, association with environmental allergens, involvement of IgE in the pathogenesis and a possible predisposition to other allergic diseases.

Pathogenesis

The pathogenesis of canine AD is not fully understood. Whereas the traditional dogma stressed the importance of IgE-mediated early and late-phase hypersensitivity reactions to airborne allergens. The current theory on the pathogenesis of canine AD can be summarized as follows: In the acute phase of the disease, putative epidermal barrier defects are thought to facilitate contact of environmental (and possibly microbial) allergens with epidermal immune cells. Epidermal antigen-presenting cells capture allergens with allergen specific IgE, and then migrate to the dermis and regional lymph nodes. Microbial products and immune cell-derived inflammatory mediators activate keratinocytes, which in turn, release more chemokines and cytokines. Immunoglobulin E-coated dermal mast cells release histamine, proteases, chemokines and cytokines following contact with allergens. There is an early influx of granulocytes (neutrophils and eosinophils), allergen-specific T-lymphocytes and dermal dendritic cells. Eosinophils degranulate and release proteins that induce dermal and epidermal damage. Type-2 helper T lymphocytes release cytokines promoting IgE synthesis and eosinophil survival. Microbes, self-trauma and neuromediators might also contribute to persistent inflammation in chronic skin lesions. There is a continuous cycle of chemokine release that leads to influx and activation of leukocytes and the release of additional pro-inflammatory mediators. The failure to down regulate pro-inflammatory mechanisms is followed by self-perpetuating cutaneous inflammation.

Genetic background

Canine atopic dermatitis is very common with upto
10 per cent of dogs affected worldwide. There are number of widely recognized breed associations suggesting that atopic dermatitis is a genetically mediated familial condition. In Labrador and Golden retriever crosses the heritability is 0.47, meaning that nearly 50 per cent of risk of developing atopic dermatitis can be accounted for by their genotype.

**Breed predisposition**

There are number of reports citing increased incidences in various breeds. It has been found that non-descript in our population are also susceptible for the disease. However breeds with increased incidence include West Highland Terriers, Dalmatian, Golden retriever, Boxer, Lhasa Apso, Labrador retrievers, Irish setter and Non Descript dogs.

Historical and clinical criteria consistent with a diagnosis of canine atopic dermatitis

- Onset of signs under three years of age
- Dog living mostly indoors
- Glucocorticoid-responsive pruritus
- Pruritus before skin lesions
- Affected front feet and concave (ie inner) surface of the ear pinnae
- Non-affected ear margins (affected ear margins most consistent with *Sarcoptes*)
- Non-affected dorsolumbar area (affected dorsolumbar area most consistent with flea allergic dermatitis)

**Clinical signs**

Primary dermatological signs includes pruritis, lesions at ventral, face (Fig1 and 2), feet and axilla (Fig 3 and 4), otitis externa, erythema of inner ear flap and erythema of paws. Signs due to secondary disease include pyoderma, malassezia and chronic skin changes such as seborrhea, hair loss, hyperpigmentation and lichenification. Distribution of lesions include all flexural and friction areas.

Pruritis is the hallmark of the disease and majority of clinical signs are due to self trauma in response to pruritis. Primary skin lesions were rarely recorded in atopic dogs. Face rubbing and foot licking were predominantly observed. The lesions were most often found in less protected areas of body such as ventral abdomen, face, foot and axilla. In more than 50% of cases allergic otitis externa, with the inflammation affecting the inner ear flap and ventral canal alone.

**Secondary diseases**

Recurrent pyoderma is seen in some 40-60% of cases primarily due to self trauma, seborrhea leading on to colonization of bacteria, adherence of bacteria to skin of atopy affected dogs and impaired cell mediated immunity. Atopic dogs with secondary pyoderma respond to antibiotic and immunotherapy.

In some cases, there is proliferation of staphylococci on the surface which contributes to pathogenesis of disease, either by production of endotoxin or possibly also through the
production of anti staphylococci IgE. This condition has been termed as Fig. 3: Lesion in foot
Fig. 4: Lesion in axilla (hyperpigmentation) “bacterial over growth”.

Inflamed skin of atopic dogs favours growth of yeast which contributes to both the level of pruritis and inflammation (possibly via Malassezia specific IgE). Chronic skin changes in atopic dogs include seborrhoea, hair loss, generalized erythema, hyper pigmentation and lichenification.

Affected sites and clinical features that are more likely seen in certain breeds with atopic dermatitis
• Dalmatian: Lips and/or pruritus without lesions
• French bulldog: Axillae, eyelids and flexor surfaces
• German shepherd: Elbows, hind limbs and thorax, seborrhoea, generalised disease and/or pruritus without lesions
• Boxer: Urticaria and otitis
• Labrador retriever: dry skin

Suspected environmental factors that may be associated with development of canine atopic dermatitis:

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<tr>
<th>Risk of developing atopic dermatitis</th>
<th>Environmental factor</th>
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<td>Increased</td>
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<td>High human</td>
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<td>Population density</td>
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<td>Increased average annual rainfall</td>
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<td>Adoption at age of 8-12 weeks</td>
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<td>Regular bathing of young healthy dogs</td>
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<td>Walking in forests</td>
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<td>Feeding non-commercial foods to lactating bitches</td>
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<td>Season of birth</td>
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<td>Home environment</td>
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Diagnosis
The clinical signs are fairly characteristic and many merit of tentative diagnosis on their own. However, it is important to rule out other disease process such as parasitic disease, food allergy and contact allergy which have similar clinical signs. It has been proposed to use certain diagnostic criteria (as in atopic dermatitis in man). A definitive diagnosis requires at least 3 of the following major criteria.

- Pruritus
- Typical morphology and distribution
- Chronically relapsing course
- Family history or breed predisposition
- In addition, the diagnosis requires at least 3 of the following major criteria
  - Onset less than 3 years of age
  - Facial erythema and cheilitis
  - Bilateral conjunctivitis
  - Superficial pyoderma
  - Hyperhydrosis
  - Immediate skin test reactivity to inhalants
  - Elevated allergic specific IgG
  - Elevated allergic specific IgE

Intradermal Skin test
Most dermatologist favours the use of allergic extracts from Greer Laboratories, USA and some from Hal and Artu Laboratories, Netherlands. However, in developing countries such as India, allergic extracts used in human are being used. Various workers have agreed that home dust mites are usually of greatest significance in atopic dogs.

The dog is restrained in lateral recumbency and an area on lateral chest is clipped. Restraining is done with the help of xylazine, 0.05 ml allergen is injected intradermally, together with positive (1:100000 w/v of histamine phosphate) and a negative control of allergen diluents. Skin tests are evaluated after 15 minutes. Measurement of wheal diameter, when a positive and negative controls. It is important to remember that a positive test is merely an indication that patient has IgE antibodies to that allergen. Normal non atopic dogs can also show positive results. Hence the results of skin test should be done in relaxation to clinical signs. Further there are false positive and false negative skin tests.

Key recommendations from the 2010 ICADA guidelines for treatment of Atopic Dermatitis

Treatment of acute flares of atopic dermatitis
- Avoidance of flare factors:
  - Regular flea control
  - Evaluation of the role of food allergens
- Identification and avoidance of environmental factors (eg, temperature, humidity, irritants and allergens)
- Identification and treatment of secondary staphylococcal and Malassezia infections
- Bathing with emollient and anti-pruritic shampoos
Topical glucocorticoids (e.g., hydrocortisone aceponate or triamcinolone)
Oral glucocorticoids

**Treatment of chronic atopic dermatitis**
- Avoidance of flare factors:
  - Regular flea control
  - Evaluation of the role of food allergens
  - Identification and avoidance of environmental factors (e.g., temperature, humidity, irritants, and allergens)
- Identification and treatment of secondary staphylococcal and *Malassezia* infections
- Bathing with emollient and anti-pruritic shampoos
- Dietary supplementation with essential fatty acids or feeding essential fatty acid enriched diets
- Topical glucocorticoids (e.g., Hydrocortisone aceponate or Triamcinolone)
- Topical tacrolimus
- Oral glucocorticoids
- Oral cyclosporin
- Allergen-specific immunotherapy:

To prevent future flares associated with allergen exposure, *ie* to induce tolerance to environmental allergens

**Management and therapeutics**

Allergen-specific immunotherapy (allergy shots)
Hyposensitization (also called desensitization or allergy vaccination) involves subcutaneous injection of relevant allergens at intervals and in increasing concentrations (induction period), until target maintenance dose is reached. This dose is administration on a regular basis as needed by the patient.

The success rate of this therapy varies between 50% and 80% in most studies. Improvement is not expected for first few months of therapy. Allergy shots should be administered for a minimum of 1 year before treatment is considered ineffective and discontinued.

**Allergens**
The allergens extracts need to be selected carefully with consideration of previous history and likely allergen exposure. The Veterinary surgeon who formulates the allergen extracts needs to consider factors such as local allergen distribution and pollination times. The general practitioner is advised to contact veterinary dermatologists or medical allergists for advice at the outset.

- Aqueous allergens are used most commonly and require small doses but frequent administration Emudion allergens (allergens in propylene glycol, glycerine or mineral oil) are slowly absorbed and require the least number of injections.
- Alum-precipitated allergens are an intermediate form only rarely used in USA or Australia, but used commonly in Europe.

**Schedule**
Immunotherapy schedules vary greatly among practicing allergists. Typically, subcutaneous injections are given every other day to once weekly. Maintenance doses are reached after 1-4 months with the various regimens. Typical maintenance therapy uses 1 ml of extract subcutaneously every 1-3 weeks. Owners may be educated to give the injections and also need to be aware of possible side effects, particularly anaphylactic shock.

**Monitoring**
Monitoring atopic patients on immunotherapy is essential and regular phone contacts or revisits are recommended, if the patient deteriorates on therapy diagnosis and (if needed) treatment of possible secondary bacterial or yeast infections are very important.

**Response**
A significant improvement on immunotherapy is not expected until several weeks to months into therapy. Owners tend to get frustrated in this initial period and often need to be encouraged to continue therapy despite an apparent lack of response. To avoid owner frustration, concurrent symptomatic therapy is frequently necessary. The patient should always show mild residual pruritis to allow judgement of vaccine efficacy. If patient’s pruritis disappears completely, symptomatic therapy should be decreased until either mild pruritis is present again or patient is exclusively maintained with allergen-specific immunotherapy.

**Remission and relapse**
Once a patient is in remission on allergy shots only, the frequency of injection may be decreased slowly until mild pruritis recurs or injections are given every 2 months for a whole year without any recurrence of clinical signs. At
that time, owners may decide to continue therapy indefinitely or try to discontinue allergy shots. A small number of dogs will stay in long-term remission after some years of immunotherapy, but relapses are also possible.

**Decreasing the allergen load**
Decreasing the amount of allergen the patient is exposed to has been attempted in human and veterinary medicine and has been particularly effective in humans sensitive to house dust mites. Unfortunately, clients may invest a lot of effort and money with no apparent result. However, some patients may benefit from measures described below.

Typically, patients allergic to indoors antigens such as housedust mites have symptoms perennially are worse during periods of prolonged indoor confinement and better if taken on camping trips or being boarded kennels or hospitals. A decrease in house dust mite allergens may be achieved with various methods. Vacuuming frequently typically worsens the situation as antigens are too small to be kept in the vacuum bag and are dispersed through air. However, those vacuum cleaners with HEPA or electro statically charged microfilters perform well. The major reservoirs for house dust mites are carpets, upholstered furniture and mattresses and pillows. Plastic encasings for mattresses and pillows are available and may be particularly useful if the animal sleeps on or in close proximity to these. Removing carpets and replacing with wooden floors boards, tiles or linoleum oil greatly reduce the number of housedust mites. There is evidence that environmental flea control measures such as insect growth regulators or sodium borate applied to carpets may reduce the number of housedust mites.

Patients allergic to pollen allergens often present with a history of deterioration during and after walks or at certain times of the year. A dog may be rinsed or hosed with water after walks. In colder climates or seasons, this can be limited to just the distal limbs.

**Symptomatic therapy**
Most dogs and cats will receive glucocorticoids, antihistamines, fatty acid supplementation or a combination there of. In refractory patients, newer and/or more expensive drugs may be considered.

**Systemic therapy**
Glucocorticoids: at anti-inflammatory doses, glucocorticoids are the most effective drugs for atopic dermatitis. Prednisone and triamcinolone are most commonly used. Some animals may not respond well to these or show excessive adverse effects such as PU/PD or polyphagia and may benefit from alternative drugs.

Alternate day to every third day therapy is preferred to daily administration; however, some dogs are controlled better on a very small dose of daily glucocorticoid rather than a fairly high dose of alternate day administration. Atopic patients on glucocorticoid therapy may initially respond well to low doses, but may become increasingly refractory with time. Severe calcinosis cutis has been seen in dogs on 0.2mg/kg of prednisone every other day for few weeks to months. Although this is not common, it emphasis that there is no safe dose of glucocorticoids. Oral administration is preferred as dose adjustments are achieved more easily and quickly.

A sparing effect of antihistamines and fatty acid supplementation has been reported in various studies, even in patients where these antihistamines and fatty acids had not improved the condition at all on their own. Tapering a glucocorticoids to the lowest possible dose to maintain the pruritis at a very low level and then adding antihistamines or fatty acids will often result in a significantly reduced glucocorticoid requirement and should always be encouraged. If the patient shows no sign of pruritis, the dose of the glucocorticoid is decreased until mild pruritis is present. This allows tailoring of the dose to the minimum required by that particular patient at any given time as these requirements may vary from week to week and season to season.

**References**