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September 2021

MULTIMODAL TREATMENT OF ATOPIC DERMATITIS

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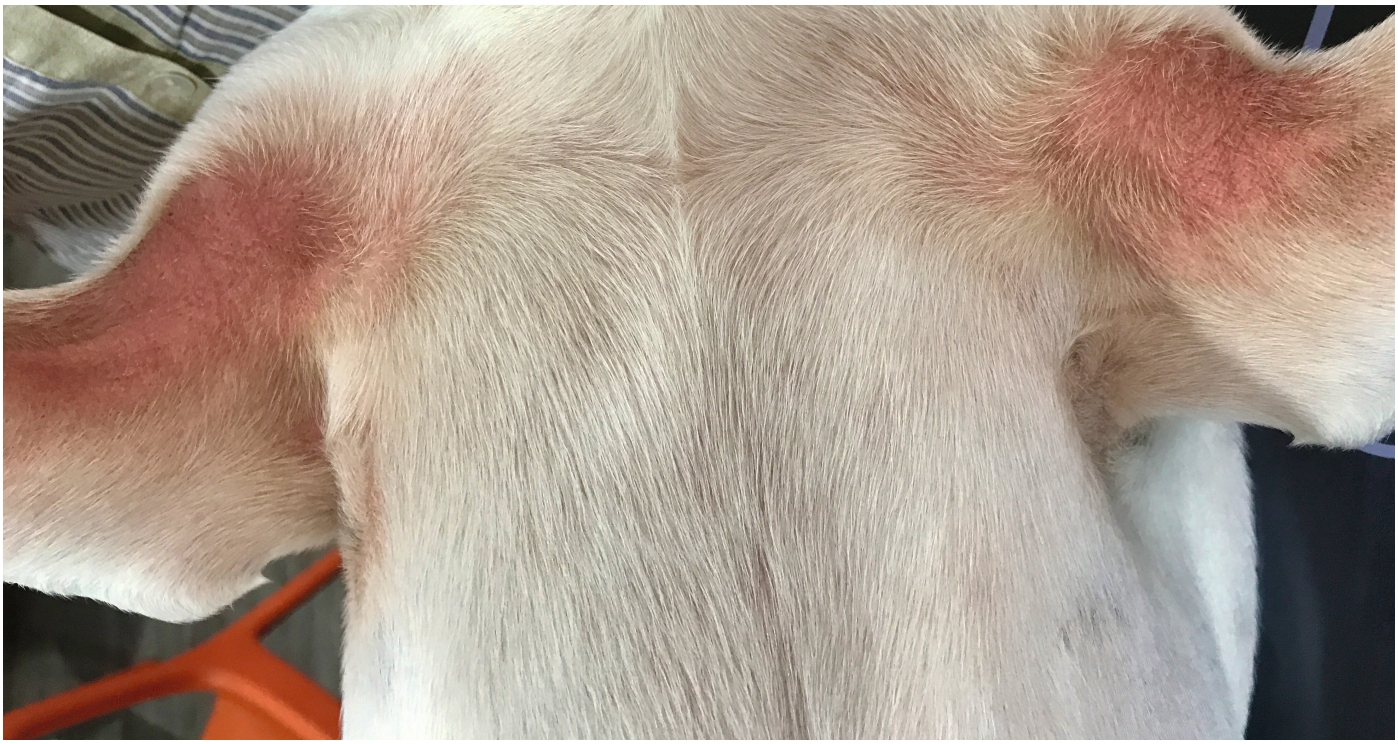

Figure 1: Erythema in axillae in atopic dermatitis

Source: Dr Carmen Lorente

Atopic dermatitis (AD) is an IgE-mediated allergic skin disease to environmental allergens. Several factors play a role in its development, primarily the alteration of the immune response, the alteration of the skin barrier (genetic factors) and the environment.
The clinical presentation of AD is pruritus and its associated lesions. Its genetic condition determines its chronicity and the need for life long treatment.

Previous considerations to atopic dermatitis treatment

1. **Diagnosis of the disease** - ruling out other pruritic conditions, including food allergy.
2. Year round **flea control program** - the bite of fleas can trigger an allergic dermatitis (Flea allergic dermatitis - FAD) and can complicate atopic disease.
3. It is a **chronic disease** that needs life long **treatment of the animal** on an annual or seasonal basis, depending on presentation.

A frequent mistake is to stop the treatment once the animal is free of clinical signs, which leads to reactivation of the inflammatory process. Once inflammation exceeds the itching threshold, the animal begins to scratch and the clinical signs return.

REACTIVE AND PROACTIVE THERAPY

"Reactive therapy" represents the treatment of active disease aimed at controlling pruritus and lesions. It is a rescue treatment based on systemic anti-inflammatory/antipruritic drugs with rapid action and high efficacy, together with frequent topical therapy.

Once the clinical picture is controlled and stable for a few weeks, the so-called **"proactive therapy"**, aimed at avoiding the reactivation of the inflammatory process, would be established. During this treatment phase, the goal is to keep the animal free of clinical signs using the minimum effective dose. In proactive therapy, antiinflammatory/antipruritic treatment, topical treatment and allergen-specific immunotherapy (ASIT) can be used.

MULTIMODAL TAILORED TREATMENT

Treatment should be multimodal and include:

1. Strict annual flea control program
2. Treatment of pruritus with anti-inflammatory/ antipruritic drugs (systemic and topical)
3. Restructuring and hydration of the skin: nutrition and topical treatment
4. Control of secondary infections
5. Allergen-specific immunotherapy (ASIT) or "allergy vaccine"

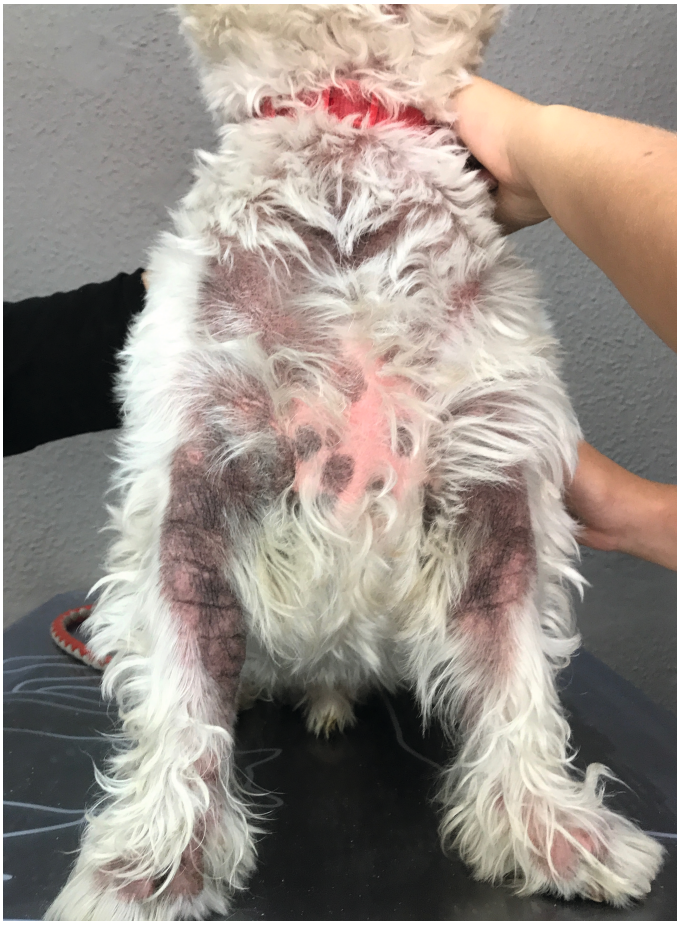

Figure 2: Chronic atopic dermatitis with active inflammation. Reactive therapy is required. Source: Dr Carmen Lorente

1. FLEA CONTROL

Atopic animals are more prone to developing other allergies. Contact with fleas can trigger the allergic process. It is crucial to carry out effective preventive treatment on an annual basis.

2. ANTI-INFLAMMATORY/ANTIPRURITIC TREATMENT

Control of inflammation and pruritus is essential to keep the atopic animal free from the clinical signs of the disease. Drugs with proven efficacy in the treatment of atopic dermatitis are:

Glucocorticoids are anti-inflammatory and immunosuppressive drugs (according to the dose) that have high efficacy and rapid effect in controlling skin inflammation, pruritus and associated lesions. They can be used in dogs and cats.
For atopic dermatitis treatment, low anti-inflammatory doses of oral corticosteroids are enough. Do not use high doses or delayed effect glucocorticoids as they are not more effective but increase the risk of side effects.
The dosage of glucocorticoids depends on their potency. Commonly used are prednisolone and prednisone. Rarely, oral triamcinolone or oral dexamethasone are used. Dexamethasone is ten times more potent than prednisolone/prednisone, so its dose is ten times lower. Side effects of glucocorticoids are proportional to drug potency, dosage and duration of administration.

REACTIVE / PROACTIVE TREATMENT IN DOGS WITH ATOPIC DERMATITIS

DRUG	REACTIVE THERAPY				PROACTIVE THERAPY	
	Mild pruritus /mild lesions		Severe inflammation, pododermatitis, interdigital cysts.			
	Dose	Duration	Dose	Duration	Dose	Duration
Prednisolone/ prednisone	0.5 mg/kg q24h	3-5 days then gradually taper to proactive doses.	1 mg/kg q24h	Until control of lesions, then taper to proactive doses.	0.25 mg q48h	Year round if it is annual. In case of seasonal allergy during the clinical signs season.
Dexamethasone	0.05 mg/kg q24h	3-5 days	0.1 mg/kg q24h		0.025 mg/kg q48h	
Oclacitinib	0.4-0.6 mg/kg q12	14 days	0.4-0.6 mg/kg q12	14 days	0.4-0.6 mg/kg q24h	
Lokivetmab	1-2 mg/kg	Every 4 weeks	Not applicable		1-2 mg/kg usually monthly.	
Cyclosporin	5 mg/kg q24h. No quick effect. It must be started with other drugs to be maintained later as a proactive therapy.				5 mg/kg q24h 1 month then alternate days -> 2 days / week.	Year round
ASIT					1 ml monthly	Life long
Schampoo-therapy	Every other day or as frequent as possible				Weekly	

REACTIVE / PROACTIVE TREATMENT IN CATS WITH ATOPIC DERMATITIS						
DRUG	REACTIVE THERAPY				PROACTIVE THERAPY	
	Mild pruritus /mild lesions		EGC lesions			
	Dose	Duration	Dose	Duration	Dose	Duration
Prednisolone/ prednisone	1 mg/kg q24h	4-7 days, then taper to proactive dose	1 mg/kg q12h	To lesion heal, then taper to proactive dose.	0.25-0.5mg/kg q48h	Year round if it is annual. In case of seasonal allergy during the clinical signs season.
Dexamethasone	0.1 mg/kg q24h		0.1mg/kg q12h		0.025-0.05 mg/kg q48h	
Oclacitinib no registered	1-1.3 mg/kg q12h	15-30 days, then taper to proactive dose.			0.8-1 mg/kg q12-24h	
Cyclosporin	7 mg/kg q24h. No quick effect. It must be started with other drugs to be maintained later as a proactive therapy.				7 mg/kg q24h one month then alternate days -> 2 days / week.	
ASIT					1 ml monthly	For life

Oclacitinib (Apoquel®) is an inhibitor of IL-31, the main cytokine involved in the mechanism of pruritus, by binding and blocking its receptor Janus kinase. Oclacitinib reduces inflammation and pruritus. Its effect is fast and last a maximum of 24 hours.

It is not licensed for use in cats, but there is good scientific evidence of its efficacy at a dose of 1 mg/kg every 12 or 24 hours. Its off-label use needs close monitoring of these animals.

Lokivetmab (Cytopoint®) is a caninized anti-L31 monoclonal antibody (MAb) that specifically binds to and neutralizes IL31. It is administered subcutaneously at a dose of 1-2 mg/kg and lasts for an average of 4 weeks. It has a rapid anti-pruritic effect, generally within 8 hours of its administration. As it is a species-specific MAb, it can only be used in dogs.

Cyclosporin (CsA) is an immunomodulatory, anti-pruritic, and anti-inflammatory drug. It has no immediate effect and may take up to a month to effectively control atopic dermatitis. Its most frequent side effects are gastrointestinal disorders that are normally temporary. The administration of the capsules frozen usually avoid these effects.

It is registered for cats and dogs. It is administered daily until effect, usually one month, and subsequently, the administration schedule is prolonged (alternate days -> 3-2 days per week).

Others

Today, it is known that histamine has no principal role as a mediator of pruritus in animals with atopic dermatitis. Scientific evidence shows that the efficacy of antihistamines for the treatment of AD is nil to moderate, being even less as monotherapy.

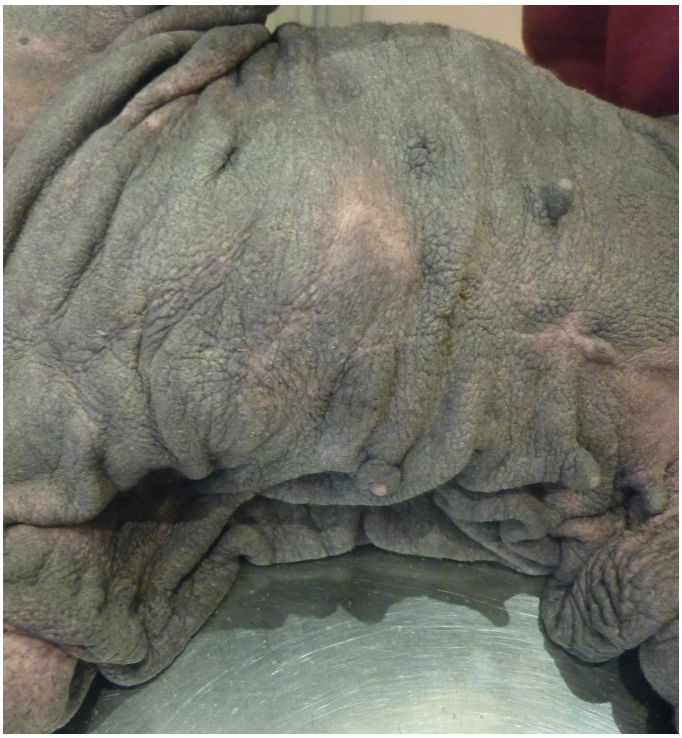

Figure 3: Chronic atopic dermatitis with severe acanthosis. Topical therapy is needed to restructure the skin. Source: Dr Carmen Lorente

Topical treatment

Atopic dermatitis clinical picture appears differently in each animal. Individuality makes each individual have areas (ears, paws, axilla, abdomen, neck, inguinal region...) where inflammation and pruritus are more intense and flare easier. Topical treatment complements systemic treatment to control the most sensitive areas and is very useful as reactive and proactive therapy.

Glucocorticoids and topical tacrolimus are effective in controlling localised puritus. The recommended glucocorticoid is hydrocortisone aceponate, as it is metabolised in the skin and has no systemic effects. Other glucocorticoids can contribute to the development of iatrogenic Cushing and skin atrophy.

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3. RESTRUCTURING AND HYDRATION OF THE SKIN

Changes in the skin and the cutaneous barrier have been demonstrated in atopic animals. They are due to genetic factors associated with disease and to the inflammation. Skin changes favour the multiplication of infectious agents (bacteria and yeasts), the penetration of allergens, pruritus and predispose to the development of more skin lesions.

Topical treatment focused on restoring the skin physiology and function is crucial in atopic animals.

Shampoo therapy removes allergens deposited on the skin or hair, as well as scabs, cellular debris, secretions and bacterial agents; it helps skin restructuring and hydration and has a calming, anti-inflammatory and antipruritic effect.

In addition to baths, there are products in the form of foams, creams or spot-ons with restructuring properties.

A complete and balanced diet with nutritional complexes adapted to atopic disease is also necessary.

4. SECONDARY INFECTIONS CONTROL

Secondary bacterial (pyoderma) or Malassezia infections are very common in atopic animals. Skin infection causes puritus and increases inflammation. Puritus due to infection is not controlled with antipruritic drugs.

In any atopic animal with active lesions, the possible existence of an infectious component must be evaluated and, if necessary, treated.

5. ALLERGEN-SPECIFIC IMMUNOTHERAPY (ASIT)

It is the only treatment that can reverse this incurable disease. It is a long-term treatment whose objective is to "educate" the immune system not to overreact to environmental allergens. Its use is recommended in all animals diagnosed with atopic dermatitis.

ASIT does not have an immediate effect, as "education" of the immune system takes time, and should be joined to the antipruritic treatment until maximal effect. Some animals can have an excellent response in 4-6 months, but the maximum response to ASIT can take 1-2 years in other cases. A recent study describes an improvement in the clinical picture in a mean time of 4.7 months. 58% of dogs were maintained exclusively with ASIT, without the need for additional medication, in less than ten months of the start of treatment.

It should be used together with antipruritic treatment until possible to reduce or suspend antipruritic treatment (better efficacy after one year of treatment).

Recommended lectures:

- Fischer NM and Müller RS. Allergen Specific Immunotherapy in Canine Atopic Dermatitis: an Update. Current Dermatology Reports. 2019; 8: 297–302.
- Mueller RS et al. Treatment of the feline atopic syndrome – a systematic review. Vet Derm. 2021, 32(1): 43-48.
- Olivry T et al. Treatment of canine atopic dermatitis: 2010 clinical practice guidelines from the International Task Force on Canine Atopic Dermatitis. Vet Derm. 2010; 21(3):233-48.
- Olivry T et al. Treatment of canine atopic dermatitis: 2015 updated guidelines from the International Committee on Allergic Diseases of Animals (ICADA). BMC Veterinary Research. 2015; 11(1):210.
- Olivry T, Banovic F. Treatment of canine atopic dermatitis: time to revise our strategy? Vet Derm. 2019; 30 (2): 87-90.
- Ramió-Lluc et al. Allergen-specific immunotherapy in dogs with atopic dermatitis: is owner compliance the main success-limiting factor? Vet Rec. 2020; 187(12): 493.
- Tamamoto-Mochizuki C et al. Proactive maintenance therapy of canine atopic dermatitis with the anti-IL-31 lokivetmab. Can a monoclonal antibody blocking a single cytokine prevent allergy flares? Vet Derm. 2019; 30: 98-e26.

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