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The Itch that won't Quit: Decoding Canine Atopic Dermatitis

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Abstract:

Canine atopic dermatitis (CAD) is a chronic, pruritic, and inflammatory skin disorder characterized by a complex interaction between genetic predisposition, environmental allergens, and immune dysregulation. A defective skin barrier facilitates allergen penetration, triggering a T-helper 2 (Th2)-dominated immune response and IgE-mediated hypersensitivity. Clinically, CAD manifests as persistent itching, erythema, and recurrent secondary infections, significantly compromising the quality of life of affected dogs and their owners. The condition also imposes notable emotional and financial burdens. Recent advances in understanding the immunopathogenesis of CAD have led to the development of targeted therapies such as oclacitinib and lokivetmab, in addition to conventional treatments like glucocorticoids and cyclosporine. Effective management requires a multimodal and individualized approach that integrates allergen avoidance, pharmacotherapy, skin barrier repair, and long-term maintenance. This article provides an overview of the etiology, impact, immunopathology, and management of CAD, highlighting the need for improved epidemiological data and holistic care strategies.

Keywords: Dogs, Atopy, Dermatitis, Lokivetmab, CAD

Introduction:

Canine atopic dermatitis (CAD) is one of the most common allergic skin diseases encountered in veterinary practice and represents a significant clinical and welfare concern. It is a chronic, relapsing condition characterized by pruritus and inflammation resulting from an abnormal immune response to environmental allergens such as dust mites,

pollens, molds, and dander. The pathogenesis of CAD is multifactorial, involving genetic susceptibility, epidermal barrier dysfunction, and immune dysregulation. Although the reported prevalence ranges from 3% to 15%, the true incidence remains uncertain due to variations in diagnostic criteria, geographic differences, and underreporting of mild or atypical cases. In

addition to its clinical manifestations, CAD has a profound impact on the quality of life of both affected dogs and their owners, often leading to behavioral changes, sleep disturbances, and financial strain due to long-term treatment requirements. Advances in veterinary dermatology have improved our understanding of the underlying immunological mechanisms

What is CAD?

Canine atopic dermatitis is a persistent allergic skin disorder resulting from an atypical immune reaction to environmental allergens. These allergens may consist of dust mites, pollen, moulds, and even dander from humans. Similar to hay fever in humans, dogs that are affected are often genetically predisposed and typically exhibit symptoms at an early age. Canine atopic dermatitis (CAD) is a complex pruritic condition, where both genetic and environmental elements significantly contribute to its development and underlying mechanisms. Characteristics of CAD include skin barrier dysfunction and an abnormal immune response. The estimated prevalence of CAD ranges from 3% to 15%. However, according to the American College of Veterinary Dermatology (ACVD) task force on atopic dermatitis (AD), these figures are not founded on dependable epidemiological data, leading the ACVD task force to determine that the true incidence and prevalence of CAD within the canine population remains poorly understood. Why do dogs get so itchy? The reason is the integrity of the skin barrier gets compromised compared to healthy individuals, facilitating the

and have facilitated the development of targeted therapeutic options. However, due to the chronic and complex nature of the disease, effective management requires a comprehensive and individualized approach. This article aims to provide an overview of CAD, including its causes, impact, immunopathogenesis, and current management strategies.

easy entry of allergens. This situation provokes an overactive immune response, which results in inflammation and severe itching (pruritus). The cycle of itching and scratching rapidly exacerbates the condition, frequently leading to secondary infections caused by bacteria or yeast. While numerous studies offer insights into the prevalence of CAD, the findings are affected by factors such as geographical locations, methodologies of surveys, population selection, types of veterinary practices, and the diagnostic criteria employed for CAD and other skin disorders. Research indicates that dogs residing indoors exhibit a greater incidence of developing CAD in comparison to those living in rural settings, cohabiting with other animals, or being exercised in forested regions. Typically, the emergence of clinical symptoms associated with CAD occurs between the ages of 4 months and 3 years. Nevertheless, the age at which these symptoms manifest can differ among various breeds, leading to variations in the prevalence reported for each breed, particularly if a breed is predominantly found in a certain geographic location. Sex-related predispositions for CAD

have not been reported, but studies have shown higher numbers in either sex. The prevalence of CAD also depends on the representation of specific breeds in geographical areas where studies are conducted. Multiple studies report that Golden Retrievers, Labrador Retrievers, West Highland Terriers, German Shepherds, and French Bulldogs are at an increased risk of developing CAD. Despite all the studies, it should be noted that true prevalence and incidence of CAD is hard to determine due to the complex development, presentation, and management of the disease. Numerous cases of CAD are handled

Impact of CAD:

As discussed above CAD is a significant malady of the pet population. Veterinarians rely on clinical signs and behaviour of the animal when assessing the effect of a disease on the wellbeing of pets. Diseases of pets can affect quality of life of the pets as well as that of their owners. Since 2010, several questionnaires have been developed for skin diseases in small animals, and some of these also assess owner quality of life. Some questionnaires have been validated, and assessing quality of life in therapy studies is becoming more common. Studies have revealed that the owners of dogs with CAD reported the disease affected their own quality of life, and a majority of owners felt the disease affected their pet's quality of life. Those effects included changes or interruptions in mood, family life, leisure activities, and sleep. Some owners were also concerned with expenses and

by veterinarians without a definitive diagnosis, including mild forms of CAD that are treated symptomatically, as well as specific clinical manifestations like chronic otitis, which clinicians may not recognize as CAD, thereby impacting incidence reporting. Moreover, the impact of various environmental risk factors on disease progression influences the reported prevalence. Given the multitude of factors that can influence the diagnosis and presentation of CAD, there is a pressing need for comprehensive epidemiological studies to assess the prevalence and incidence of canine atopic dermatitis.

the burden of treatment.

The management of CAD necessitates continuous oversight, which involves a long-term financial obligation from pet owners. This requirement may pose a challenge and could potentially limit access to care in certain situations. Nevertheless, considering the disease's prevalence, the treatment and management of CAD could represent a substantial revenue stream for the veterinary sector. However, data regarding the financial implications of CAD for patients, pet owners, and the veterinary industry remains scarce. The integration of quality-of-life metrics is contributing to a better understanding and treatment of CAD. There is a pressing need for targeted research focusing on the financial, behavioral, and emotional effects of CAD on pets and their owners.

Immunopathology:

Canine atopic dermatitis (CAD) is a chronic inflammatory skin condition with a genetic predisposition, characterized by a multifaceted immunopathology that includes dysfunction of the skin barrier and dysregulation of the immune system. Deficiencies in the epidermal barrier allow environmental allergens to penetrate, which are then processed by antigen-presenting cells, such as Langerhans cells, and presented to naïve T lymphocytes. This interaction leads to a polarization towards a T-helper 2 (Th2)–dominant immune response. This response is marked by an increased production of cytokines, including interleukin (IL)-4, IL-5, IL-13, and IL-31, which facilitate IgE class switching, eosinophil activation, and the sensation of pruritus. Allergen-specific IgE attaches to high-affinity receptors on mast cells and basophils;

Management of CAD:

The management of canine atopic dermatitis (CAD) relies on a comprehensive and individualized strategy designed to alleviate pruritus, manage inflammation, and restore the integrity of the skin barrier. The initial phase of management involves the identification and avoidance of allergens, as well as the maintenance of skin hydration through topical treatments like emollients and medicated shampoos. Pharmacological treatment aims to control pruritus and immune dysregulation, with oclacitinib, a Janus kinase (JAK1) inhibitor, and lokivetmab, a monoclonal antibody that targets interleukin-31 (IL-31), being commonly utilized

upon subsequent exposure to allergens, the cross-linking of IgE initiates mast cell degranulation and the release of histamine and other pro-inflammatory mediators, resulting in erythema, edema, and severe itching. As the condition advances, the immune response becomes increasingly intricate, involving Th1, Th17, and regulatory T-cell pathways, which contribute to chronic inflammation and skin remodeling. Furthermore, cytokines such as IL-33 and various chemokines enhance the inflammatory cascade by attracting immune cells to the skin. In summary, CAD is a multifactorial immunological disorder primarily driven by a Th2-skewed, IgE-mediated hypersensitivity reaction, leading to ongoing immune dysregulation.

for their swift and effective antipruritic effects (Fig.1). Traditional treatments, including glucocorticoids and cyclosporine, continue to hold significance, especially in chronic or severe instances, although their application may be restricted due to potential adverse effects. Moreover, allergen-specific immunotherapy (ASIT) stands out as the sole disease-modifying intervention capable of changing the trajectory of CAD by fostering immune tolerance. Effective management also necessitates the prompt recognition and treatment of secondary bacterial and *Malassezia* infections, which can worsen clinical symptoms. Recent strategies underscore

the necessity of long-term maintenance therapy, integrating both systemic and topical treatments to reduce flare-ups and enhance the quality of life.

In summary, the effective management of CAD

demands a holistic approach that addresses both the fundamental immunopathogenesis and the environmental factors involved.

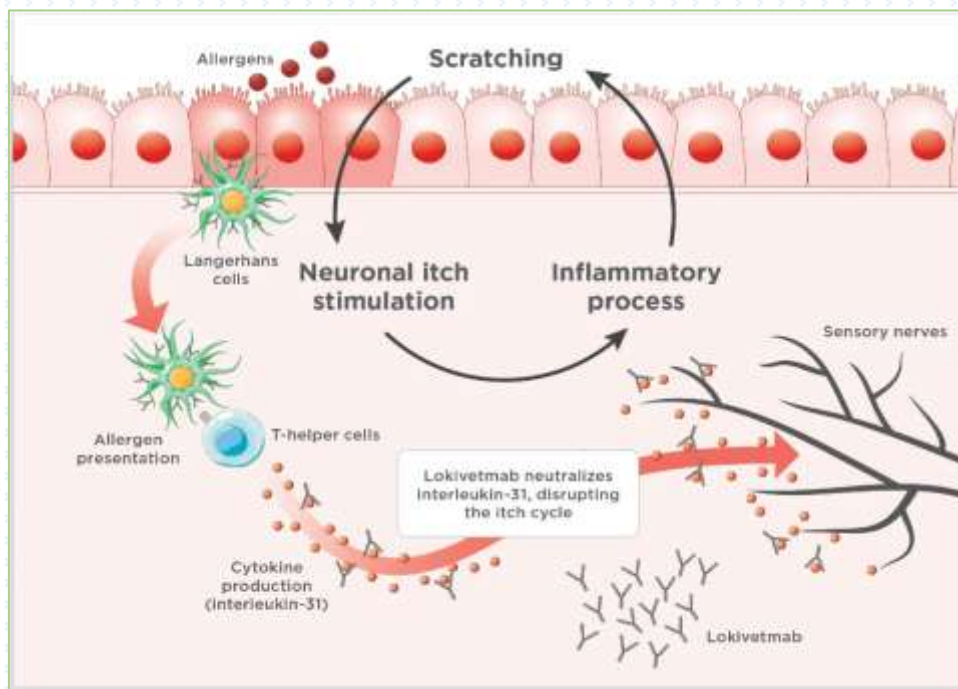


Fig 1: The role of lokivetmab in stopping the itch cycle. Overexpression of canine interleukin-31 (IL-31) has been implicated in the pathophysiology of pruritus in dogs with atopic dermatitis. By neutralizing IL-31, lokivetmab inhibits pruritus and reduces inflammatory skin lesions. Illustration adapted from: Cytopoint interrupts the itch cycle. Zoetis United Kingdom. Accessed November 20, 2023. <https://www.zoetis.co.uk/products/dogs/cytopoint/moa-itch-cycle.aspx>.

Conclusion:

Canine atopic dermatitis is a complex, chronic disease that significantly impacts both affected dogs and their owners. Its multifactorial pathogenesis involves genetic predisposition, skin barrier dysfunction, and immune dysregulation, resulting in persistent pruritus and inflammation. Although advances in understanding and treatment have improved disease management, there is no definitive cure.

Effective control relies on a multimodal and individualized approach that addresses both underlying causes and clinical manifestations. Greater awareness, improved diagnostic strategies, and further research into epidemiology and long-term outcomes are essential to enhance disease management and overall quality of life.

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