

Alterations in circulating concentrations of IL-17, IL-31 and total IgE in dogs with atopic dermatitis

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Background – The pathogenesis of canine atopic dermatitis (AD) is complex. Dysregulation of the cutaneous immune system is considered to be an important part of the allergic response. Exploration of association of interleukin-17 (IL-17), IL-31, IgE and leukogram attributes with canine AD could provide novel insights into its immunopathology.

Hypothesis/Objectives – To investigate possible associations of IL-17, IL-31, IgE and leukogram attributes of canine AD.

Animals – 17 dogs diagnosed with AD and six healthy dogs.

Methods and materials – Circulating concentrations of IL-17, IL-31 and total IgE from sera samples were determined using commercial canine-specific quantitative immunoassay kits. Complete blood cell counts were analysed by an automated haematology analyser. Statistical differences between the two groups were determined using an unpaired *t*-test. The degree of relationship between the IL-17, IL-31, IgE, total leukocyte count (TLC) values and clinical signs scores (Canine Atopic Dermatitis Lesion Index and pruritus Visual Analog Scale pVAS) was determined by Pearson's *r* correlation statistic.

Results – Dogs with AD had significantly ($P < 0.0001$) higher circulating concentrations of IL-17, IL-31 and total IgE compared with healthy dogs. Dogs with AD also had significantly higher TLC ($P < 0.0002$), absolute neutrophils ($P < 0.0001$) and absolute eosinophils ($P < 0.0001$) counts, and percentage of neutrophils ($P < 0.03$) and eosinophils ($P < 0.0001$) compared with healthy controls. A significant positive correlation ($r^2 = 0.396$; $P < 0.007$) between the pVAS and IL-31 was observed in dogs with AD.

Conclusions and clinical importance – Marked elevation in circulating IL-17, IL-31 and total IgE along with the abnormalities in leukogram may be associated with canine AD and could be possible targets in the therapeutic management of canine AD.

Introduction

Canine atopic dermatitis (AD) is a common skin disease with a complex pathogenesis. It has been reported that interleukin-31 (IL-31) is a potent pruritogenic cytokine that plays a key role in pruritic skin conditions in humans and animals.^{1,2} In one study the administration of anti-IL-31

receptor antibody was reported to significantly alleviate pruritus in human patients with AD.³ In addition to cytokines produced from Th1 and Th2 cells, IL-17, produced from Th17 cells, has been reported to have proinflammatory properties.⁴ Interleukin-17 stimulates the production of IL-6 and IL-8 in human keratinocytes and results in increased T-cell migration to the skin.⁵ The association of IL-17 with canine AD has not been investigated.

The study of the possible association of IL-17 with IL-31 and immunoglobulin-E (IgE) may provide insights into canine AD. It also may identify new therapeutic targets for the management of canine AD. Inflammatory cells are known to be involved in the pathogenesis of canine AD. Concurrent investigation of changes in leukograms alongside proinflammatory cytokines may reveal helpful information. The goals of this study were to evaluate circulating concentrations of IL-17, IL-31 and IgE, and leukograms in dogs with clinical AD.

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Conflicts of Interest: No conflicts of interest have been declared.

Methods and materials

Ethical approval

The study was conducted in accordance with ethical standards of the Institutional Animal Ethics Committee of UP Pandit Deen Dayal Upadhyaya Pashu-Chikitsa Vigyan Vishwavidyalaya Evam Go Anusandhan Sansthan (DUVASU), Mathura (UP), India.

Inclusion and exclusion criteria of dogs

Dogs were client-owned dogs and presented to Kothari Hospital of College of Veterinary Science and Animal Husbandry, DUVASU, Mathura, and fulfilled five of eight published criteria for a diagnosis of AD.⁶ In addition, dogs were free from flea infestations, none had any skin lesion in the dorso-lumbar area and all had a history of receiving regular flea preventative with fipronil and s-methoprene at monthly intervals. Skin scrapings did not detect *Demodex* or *Sarcoptes* mites. There also was no response to treatment for mite infestations using amitraz, ivermectin or doramectin. None of the dogs had received glucocorticoids, ciclosporin, oclacitinib, lokivetmab, antihistamines, essential fatty acids or ear products containing glucocorticoids during the last 30 days before the clinical examination. None of the enrolled dogs were receiving allergen-specific immunotherapy.

All of the dogs were screened for bacterial pyoderma or yeast overgrowth by cytological examination of skin impression smears. The dogs confirmed to have pyoderma and or yeast overgrowth infections were not included. At the time of the first clinical examination, a Canine Atopic Dermatitis Lesion Index (CADLI)⁷ and pruritus Visual Analog Scale (pVAS) based on owner-derived data,⁸ were recorded for each atopic dog.

Apparently healthy dogs were recruited from dogs presented for routine annual vaccination or wellness examinations. These dogs were free of skin lesions, parasites, bacterial and yeast skin infections and haemo-parasites, as determined by routine diagnostic methods which also included routine analysis of complete blood count and serum biochemistry.

Collection of blood samples

Approximately 5 mL of blood was collected from each dog before the start of any therapy. Two millilitres of blood were collected for routine haematological examination. The remaining 3 mL of blood was transferred into vials containing a clot activator and used for harvesting serum. Harvested serum samples were transferred into cryovials and kept at -20°C until use for evaluation of cytokines and total IgE concentration.

Assessment of cytokines and total IgE

Circulating concentrations of canine IL-17, IL-31 and total IgE were estimated using commercial quantitative immunoassay ELISA kits that were reported to be canine-specific (E0208Ca-IgE, E0007Ca-IL-17, E0191Ca-IL-31, Bioassay Technology Laboratory; Shanghai, China) following the procedures as described by the manufacturer. The circulating IL-17 and IL-31 concentrations were expressed as ng/L and total IgE concentration was expressed as $\mu\text{g/mL}$. The manufacturer reported the same inter and intra assay reproducibility coefficients of $<8\%$ and $<10\%$ for IL-17, IL-31 and IgE.

Haematological examination

Complete blood cell counts of dogs with AD and the healthy group were analysed by an automated haematology Analyser (BC-2800 Vet Haematology Analyser, Mindray Electronic Co. Ltd; Shenzhen, China).

Statistical analysis

Normality of data distribution was tested using the Shapiro–Wilk test. The data were found to be distributed normally. Statistical differences between the two groups were evaluated using the unpaired *t*-test on GraphPad Prism 8 (San Diego, CA, USA). Moreover, to determine the degree of relationship between the IL-17, IL-31, IgE and total leukocyte count (TLC) values, and clinical signs scores (CADLI

and pVAS), Pearson's *r*-correlation statistic was used. Data are presented as mean $\pm$ standard error ($\pm\text{SE}$); *P*-values < 0.05 were considered statistically significant.

Results

Seventeen dogs ranging in age from one to four years of age met the inclusion criteria for canine AD. Six apparently healthy dogs were included in the study. Data on circulating concentrations of IL-31, IL-17 and total IgE in dogs with AD, and healthy control groups are summarized in Figures 1 and 2. Circulating concentrations of IL-17 and IL-31 were found to be significantly ($P < 0.0001$) elevated in dogs with AD compared to the healthy dogs (Figure 1 and Table 1). Serum concentrations of total IgE also were found to be significantly ($P < 0.0001$) elevated in dogs with AD compared to that in the healthy dog group (Figure 2 and Table 1).

The CADLI and pVAS scores (mean $\pm$ SE) in dogs with AD were calculated to be 22.18 ± 1.37 and 6.47 ± 0.26 , respectively. A significant positive correlation ($r^2 = 0.396$; $P < 0.007$) between IL-31 concentrations and pVAS was present in dogs with AD (Table 2), whereas significant correlation between other parameters was not found (Table 2). Significant alterations in leukogram values were observed between the dogs with AD and healthy controls (Table 1). Data analysis revealed that the dogs with AD had significantly higher TLC ($P < 0.0002$), absolute neutrophil counts ($P < 0.0001$), absolute eosinophil counts ($P < 0.0001$), neutrophils percentage ($P < 0.03$) and eosinophils percentage ($P < 0.0001$) compared to healthy dogs.

Discussion

In the present study, an elevated circulating total IgE concentration in dogs with AD suggests the possible association of type-1 hypersensitivity with canine AD. Mast cells, upon activation, produce or downregulate secretion of various cytokines, chemokines and arachidonic acid derivatives.⁹ Our observation of significant elevation in total circulating IgE concentration in dogs with AD is similar to

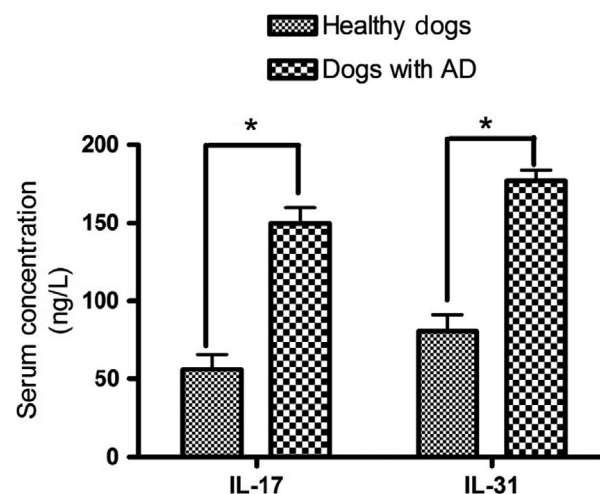


Figure 1. Circulatory concentrations of pro-inflammatory cytokines of dogs with atopic dermatitis ($n = 17$) and healthy dogs ($n = 6$).

*Significantly higher ($P < 0.0001$) than the healthy dogs. Data presented are mean $\pm$ SE.

that observed in clinically affected atopic human patients.^{10,11} Contrary to our findings, no significant difference between the total serum IgE concentrations of dogs with AD and healthy ones has been reported.¹² Although IgE is considered a component in AD, some studies have shown that AD is not always IgE-mediated.^{13,14} Higher production of IgE could be due to percutaneous absorption of allergens into the body resulting in degranulation of mast cells and excessive production of histamine.¹⁵

An elevated circulating concentration of IL-17 in dogs with AD was observed in the present study and this may

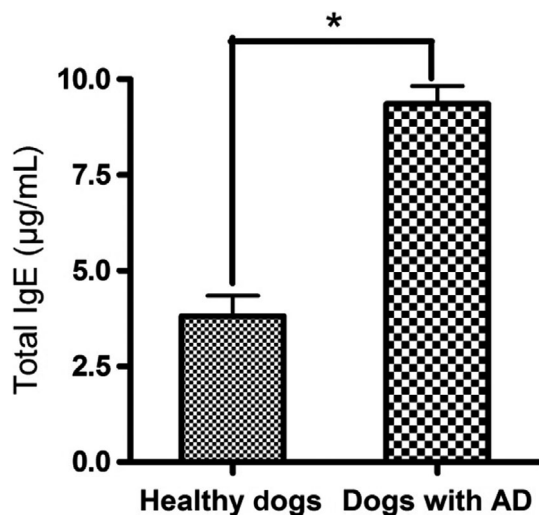


Figure 2. Circulatory total IgE concentration in dogs with atopic dermatitis (n = 17) and healthy dogs (n = 6).

*Significant ($P < 0.0001$) higher than the healthy dogs. Data presented are mean $\pm$ SE.

support the possible association of IL-17 with AD in dogs. A previous study reported that the production of IL-17A in the peripheral blood mononuclear cells of dogs was associated with adverse food reaction (AFR).¹⁶ It was suggested that the possible association of IL-17 with concurrent bacterial infection was because IL-17 was not correlated with clinical improvement but rather with the bacterial count.¹⁷ However, in our study, none of the dogs with AD was suffering from concurrent microbial infection. The best-known function of IL-17 is protection against bacterial and fungal infections. Even though we found higher concentrations of IL-17 in dogs with AD than in healthy dogs, the lack of correlation between this interleukin and clinical scores (CADLI and pVAS) leads us to speculate that IL-17 may have a role in the initiation of AD in dogs, rather than in its progression. In line with our observations, an elevated concentration of IL-17 in acute AD lesions and increased percentage of Th17 cells in the peripheral blood and skin tissues of human patients with AD and psoriasis have been reported.^{18,19} The differences between our data in dogs with AD and human patients or dogs with AFR¹⁶ could be due to different inclusion criteria or different population included in the present study. Therefore, further studies are required to explore the possible association of IL-17 with the pathogenesis of canine AD.

Interleukin-31 and its receptor are considered to play key roles in pruritic skin conditions of humans.¹ Marked elevation in IL-31 in pruritic versus nonpruritic human skin conditions and correlation of serum IL-31 concentrations with the severity of disease in adult humans and children with AD has been documented.²⁰ Similarly, a positive correlation between the severity of canine AD and circulating

Table 1. Comparative immunological and haematological values for healthy dogs and dogs with atopic dermatitis (AD)

Parameters	Healthy control dogs (n = 6)	Dogs with AD (n = 17)	Reference range	P-values
Interleukin-17 (ng/L)	56.27 $\pm$ 9.62	149.93 $\pm$ 10.22	–	< 0.0001
Interleukin-31 (ng/L)	80.78 $\pm$ 10.49	177.14 $\pm$ 6.79	–	< 0.0001
Total IgE (µg/mL)	3.81 $\pm$ 0.54	9.35 $\pm$ 0.47	–	< 0.0001
Total leukocytes count ($10^3/\mu\text{L}$)	13.56 $\pm$ 0.72	25.41 $\pm$ 1.52	5.0–14.1	< 0.0002
Neutrophils ($10^3/\mu\text{L}$)	7.75 $\pm$ 0.49	17.31 $\pm$ 1.1	2.9–12.0	< 0.0001
Lymphocytes ($10^3/\mu\text{L}$)	4.36 $\pm$ 0.51	7.57 $\pm$ 0.98	0.4–2.9	0.0738
Monocytes ($10^3/\mu\text{L}$)	0.71 $\pm$ 0.06	1.18 $\pm$ 0.13	0.1–1.4	0.0609
Eosinophils ($10^3/\mu\text{L}$)	0.48 $\pm$ 0.06	3.11 $\pm$ 0.25	0–1.3	< 0.0001
Neutrophils (%)	58.7 $\pm$ 3.4	65.8 $\pm$ 1.3	58–85	< 0.03
Lymphocytes (%)	32.0 $\pm$ 2.7	29.1 $\pm$ 2.5	8–21	< 0.5368
Monocytes (%)	5.3 $\pm$ 0.61	4.91 $\pm$ 0.37	2–10	0.5980
Eosinophils (%)	3.38 $\pm$ 0.25	11.73 $\pm$ 0.97	0–9	< 0.0001
Red blood cell count ($10^6/\mu\text{L}$)	7.87 $\pm$ 0.39	7.57 $\pm$ 0.41	4.95–7.87	$P = 0.6866$
Platelets ($10^3/\mu\text{L}$)	272 $\pm$ 44	233 $\pm$ 20	211–621	0.3775

Data presented are mean $\pm$ SE. Values in bold were significantly higher than the healthy dogs (i.e. $P < 0.05$).

Table 2. The degree of relationship (R^2) between two cytokines, total IgE, total leukocyte count with clinical signs scores [Canine Atopic Dermatitis Lesion Index (CADLI) and pruritus Visual Analog Scale (pVAS)] of dogs with atopic dermatitis

Parameter	CADLI			pVAS		
	Correlation	R^2	P-value	Correlation	R^2	P-value
Interleukin-31	0.122	0.015	0.642	0.629	0.396	0.007
Interleukin-17	0.430	0.185	0.085	0.430	0.185	0.085
Total IgE	0.067	0.004	0.798	0.346	0.120	0.174
Total leukocytes count	0.356	0.126	0.161	0.302	0.091	0.238

Significant positive correlation between the parameter and clinical signs score, i.e. $P < 0.05$.

IL-31 concentrations has been reported.¹⁷ The administration of canine IL-31 to dogs resulted in a significant increase in pruritic behaviour.² Therefore, IL-31 seems to play a crucial role in inducing pruritus and may be dysregulated in dogs with AD.² Our finding of elevated circulating IL-31 concentration in dogs with AD supports the potential association of IL-31 with canine AD. It also adds support to the observation of IL-31-mediated AD development in dogs.²

A significant positive correlation between the pVAS and IL-31 concentrations observed in the present study supports a role for IL-31 in canine AD. Estimation of serum IL-31 concentration is considered more informative than the quantification of IL-31 mRNA gene expression because one study failed to detect IL-31 mRNA in the skin of dogs with AD.²¹ Our observation of an elevated serum IL-31 concentration in dogs with AD is in agreement with a previous report.²¹ Moreover, another study also demonstrated a significant upregulation of the IL-31 cytokine gene in acute canine AD skin lesions.²²

The dogs with AD in the present study revealed significant alterations in leukograms with significant elevations in TLC, absolute neutrophil and eosinophil counts, and percentage of neutrophils and eosinophils. Environmental antigens stimulate peripheral blood mononuclear cells. Therefore, the possibility of the antigen-induced inflammatory response in dogs with AD cannot be ruled out. Elevated values of leukogram attributes in dogs with AD suggest the possible association of AD with the marked inflammatory process. Our observations on altered leukograms support previous reports of significant elevation in neutrophils, eosinophils and TLC in dogs with AD.^{23,24} Elevation in TLC could be due to the cellular and humoral immune response in allergic dermatitis and/or toxins released from tissue damage following inflammation.¹³ Significantly elevated eosinophils count and percentage observed in atopic dogs might be attributed to the hypersensitivity reaction which incites release of eosinophils in blood circulation. The atopic dogs participated in the present study were client-owned; therefore, it was not possible to keep all the participating dogs in similar environmental conditions. Furthermore, the numbers of atopic dogs participated in the study are small; hence, studies on a large number of dogs suffering from clinical AD or experimentally induced AD are needed to elucidate the association of IL-17 in the development or pathogenesis of canine AD.

It can be concluded that dogs with AD manifest inflammatory response along with eosinophilia. Marked elevation in circulating IL-17 along with IL-31, IgE and altered leukogram attributes may be associated with canine AD. Therefore, IL-17 along with IL-31 can be considered as the potential targets in the therapeutic management of canine AD.

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Résumé

Contexte – La pathogénie de la dermatite atopique canine (AD) est complexe. La dysrégulation du système immunitaire cutané est considéré comme une part importante de la réponse allergique. L'exploration de l'association d'interleukines 17 (IL-17), IL-31, IgE et les particularités du leucogramme avec l'AD canine pourrait fournir de nouveaux renseignements d'immunopathologie.

Hypothèses/Objectifs – Etudier les associations possibles d'IL-17, IL-31, IgE et particularités du leucogramme de l'AD canine.

Sujets – Dix sept chiens diagnostiqués avec AD et six chiens sains.

Matériel et méthode – Les concentrations circulantes d'IL-17, IL-31 et IgE totaux sériques ont été déterminées à l'aide de kits immunologiques quantitatifs spécifiques canins. Les numérations formules ont été analysées par un analyseur automatique d'hématologie. Les différences statistiques entre les deux groupes ont été déterminées à l'aide d'un t-test non-pairé. Le degré de relation entre les valeurs de IL-17, IL-31, IgE, TLC (total leucocyte count) et les scores cliniques (Canine Atopic Dermatitis Lesion Index and pruritus Visual Analog Scale pVAS) a été déterminé par statistique de corrélation de Pearson r .

Résultats – Les chiens avec AD avaient significativement ($P < 0.0001$) des concentrations circulantes plus élevées de IL-17, IL-31 et IgE totaux comparé aux chiens sains. Les chiens avec AD avaient aussi des comptages significativement plus élevés de TLC ($P < 0.0002$), neutrophiles absolus ($P < 0.0001$), et éosinophiles absolus ($P < 0.0001$) et un pourcentage de neutrophiles ($P < 0.03$) et d'éosinophiles ($P < 0.0001$) comparé aux contrôles sains. Une corrélation significative positive ($r^2 = 0.396$; $P < 0.007$) entre pVAS et IL-31 a été observée chez les chiens avec AD.

Conclusions et importance clinique – L'élévation marquée d'IL-17, IL-31 et IgE totaux parmi les anomalies de leucogramme peut être associé à l'AD canine et pourrait être une cible possible dans la gestion thérapeutique de l'AD canine.

Resumen

Introducción – la patogenia de la dermatitis atópica canina (EA) es compleja. La disregulación del sistema inmunitario cutáneo se considera una parte importante de la respuesta alérgica. La exploración de la asociación de la interleuquina-17 (IL-17), la IL-31, la IgE y el los patrones del leucograma con AD canina podría proporcionar nuevos avances sobre su inmunopatología.

Hipótesis/Objetivos – investigar posibles asociaciones de IL-17, IL-31, IgE y los patrones del leucograma durante la AD canina.

Animales – 17 perros diagnosticados con AD y seis perros sanos.

Métodos y materiales – las concentraciones circulantes de IL-17, IL-31 e IgE total de muestras de sueros se determinaron utilizando kits de inmunoensayos cuantitativos comerciales específicos para perros. Los recuentos completos de células sanguíneas se analizaron mediante un analizador de hematología automatizado. Las diferencias estadísticas entre los dos grupos se determinaron mediante una prueba t no pareada. El grado de relación entre los valores de IL-17, IL-31, IgE, y recuento total de leucocitos (TLC) y los valores de signos clínicos (índice de lesión de dermatitis atópica canina y de Escala análoga visual de prurito (pVAS)) se determinó mediante la correlación estadística r de Pearson.

Resultados – los perros con AD tuvieron concentraciones circulantes significativamente más altas ($P < 0.0001$) de IL-17, IL-31 e IgE total en comparación con los perros sanos. Los perros con AD también tuvieron un TLC significativamente mayor ($P < 0.0002$), recuento de neutrófilos absolutos ($P < 0.0001$) y eosinófilos absolutos ($P < 0.0001$) y porcentaje de neutrófilos ($P < 0.03$) y eosinófilos ($P < 0.0001$) en comparación con los controles sanos. Se observó una correlación positiva significativa ($r^2 = 0.396$; $P < 0.007$) entre el pVAS y la IL-31 en perros con AD.

Conclusiones e importancia clínica – la elevación marcada en la IL-17 circulante, la IL-31 y la IgE total, junto con anomalías en el leucograma, pueden asociarse con la AD canina y podrían ser posibles objetivos en el manejo terapéutico de la enfermedad.

Zusammenfassung

Hintergrund – Die Pathogenese der atopischen Dermatitis (AD) des Hundes ist vielfältig. Eine Dysregulierung des kutanen Immunsystems wird als wichtiger Regulator der allergischen Antwort verstanden. Die Untersuchung des Zusammenhangs von Interleukin-17 (IL-17), IL-31, IgE und Eigenschaften des Leukogramms im Zusammenhang mit caniner AD könnte neue Erkenntnisse in ihre Immunpathologie bringen.

Hypothese/Ziele – Eine Untersuchung der möglichen Zusammenhänge von IL-17, IL-31, IgE und des Leukogramms mit canner AD.

Tiere – 17 Hunde, die mit AD diagnostiziert waren und sechs gesunde Hunde.

Methoden und Materialien – Es wurden die zirkulierenden Konzentrationen von IL-17, IL-31 und Gesamt IgE in Sera Proben mittels kommerziellen Hunde-spezifischen quantitativen Immunassay Kits bestimmt. Ein Gesamtblutbild wurde mittels automatischen Hämatologie Analyser bestimmt. Statistische

Unterschiede zwischen den beiden Gruppen wurden mittels ungepaarten *t*-Test bestimmt. Das Ausmaß des Zusammenhangs zwischen IL-17, IL-31, IgE Gesamt Leukozytenzahlen (TLC) Werten und den Werten der klinischen Zeichen (Canine Atopic Dermatitis Lesion Index und Pruritus Visual Analog Scale (pVAS) wurde mittels Pearson's Korrelationsstatistik bestimmt.

Ergebnisse – Hunde mit AD zeigten signifikant ($P < 0,0001$) höhere zirkulierende Konzentrationen von IL-17, IL-31 und Gesamt IgE im Vergleich zu den gesunden Hunden. Hunde mit AD hatten auch signifikant höhere TLC ($P < 0,0002$) Werte, absolute Neutrophilen- ($P < 0,0001$) und absolute Eosinophilenzahl ($P < 0,0001$) im Vergleich zu den gesunden Kontrollen. Eine signifikante positive Korrelation ($r^2 = 0,396$; $P < 0,007$) zwischen den pVAS und IL-31 wurde bei den Hunden mit AD beobachtet.

Schlussfolgerungen und klinische Bedeutung – Eine deutliche Erhöhung der zirkulierenden IL-17, IL-31 und Gesamt IgE gemeinsam mit den Veränderungen im Leukogramm könnten mit der AD des Hundes im Zusammenhang stehen und möglicherweise Ziele für ein therapeutisches Management der AD des Hundes darstellen.

要約

背景 – 犬アトピー性皮膚炎(AD)の病因は複雑である。皮膚免疫系の調節不全は、アレルギー反応の重要な要素の一つと考えられている。犬ADとのインターロイキン-17(IL-17)、IL-31、IgE、および白血球像の特性との関連性に対する探求は、その免疫病理学に新たな洞察を提供することができる。

仮説/目的 – 本研究の目的は、犬ADのIL-17、IL-31、IgEおよび白血球像の特性との関連性の可能性を調査することである。

被験動物 – ADと診断された犬17頭および健康犬6頭。

材料および方法 – 血清サンプルからのIL-17、IL-31および総IgEの循環濃度は、市販の犬特異的定量的免疫アッセイキットを用いて決定した。全血球数を自動血液分析装置によって分析した。2群間の統計的差異は、対応のない検定を用いて決定した。IL-17、IL-31、IgE、総白血球数(TLC)値、および臨床徴候スコア(犬のアトピー性皮膚炎病変指数と掻痒性ビジュアルアナログスケールpVAS)の間の関連性の程度は、ピアソンのr相関統計によって決定した。

結果 – AD犬は、健康犬と比較して、IL-17、IL-31、および総IgEの血中濃度が有意に高かった($P < 0,0001$)。AD犬は、健康コントロール群と比較して有意に高いTLC($P < 0,0002$)、絶対好中球数($P < 0,0001$)および絶対好酸球数($P < 0,0001$)、ならびに好中球の割合($P < 0,03$)および好酸球の割合($P < 0,0001$)を有した。pVASおよびIL-31との間に有意な正の相関($r^2 = 0,396$; $P < 0,007$)がAD犬において観察された。

結論と臨床的重要性 – 白血球像の異常に伴う循環IL-17、IL-31および総IgEの著しい上昇は、犬ADに関連している可能性があり、犬ADの治療管理における可能性のある標的となりうる。

摘要

背景 – 犬异位性皮膚炎(AD)の发病机制复杂,皮肤免疫系统失调被认为是过敏反应的重要组成部分。白细胞介素-17(IL-17)、IL-31、IgE和白细胞血象与犬AD间关系的研究,可以为其免疫病理学研究提供新思路。

假设/目标 – 探讨IL-17、IL-31、IgE和白细胞血象与犬AD的可能相关性。

动物 – 17只确诊为AD的犬和6只健康犬。

方法和材料 – 使用市面上犬特异性定量免疫分析试剂盒,测定血清样品中IL-17、IL-31和总IgE的循环浓度。通过自动血液分析仪分析全血白细胞计数。两组之间的统计学差异采用非配对t检验确定。通过Pearson's相关统计量确定IL-17、IL-31、IgE、总白细胞计数(TLC)值和临床体征评分(犬异位性皮肤炎病変指数和搔痒评分pVAS)之间的相关程度。

结果 – 与健康犬相比,AD患犬的IL-17、IL-31和总IgE的循环浓度明显较高($P < 0,0001$)。同样的,AD组的TLC($P < 0,0002$)、绝对中性粒细胞计数($P < 0,0001$)、绝对嗜酸性粒细胞计数($P < 0,0001$)、中性粒细胞百分比($P < 0,03$)和嗜酸性粒细胞百分比($P < 0,0001$)均显著高于健康对照组。在AD患犬中观察到pVAS和IL-31之间存在显著正相关性($r^2 = 0,396$; $P < 0,007$)。

结论和临床价值 – IL-17、IL-31和总IgE循环浓度的显著升高,以及白细胞血象中的异常可能与犬AD相关,并且可能成为治疗犬AD的靶点。

Resumo

Contexto – A patogênese da dermatite atópica (DA) canina é complexa. A desregulação do sistema imune cutâneo é considerada uma parte importante da resposta alérgica. A exploração da associação da interleucina-17 (IL-17), IL-31, IgE e leucograma atribuídos à DA canina pode trazer novos conhecimentos sobre a sua imunopatogenia.

Hipótese/Objetivos – Investigar as possíveis associações entre IL-17, IL-31, IgE e leucograma atribuídos à DA canina.

Animais – Dezessete cães diagnosticados com DA e seis cães saudáveis.

Métodos e materiais – As concentrações circulantes de IL-17, IL-31 e IgE total das amostras de soro foram determinadas utilizando um kit de imunoensaio quantitativo específico canino. As contagens de células sanguíneas foram determinadas utilizando um analisador hematológico automatizado. As diferenças estatísticas entre os dois grupos foram determinadas utilizando um teste-t não pareado. O grau de correlação entre IL-17, IL-31, IgE, contagem total de leucócitos (CTL) e escores de sinais clínicos [(Indicador

de lesão de dermatite atópica canina - *Canine Atopic Dermatitis Lesion Index* e escala visual analógica de prurido - *pruritus Visual Analog Scale* (pVAS)] foi determinado por correlação estatística de Pearson.

Resultados – Cães com DA apresentaram concentrações séricas de IL-17, IL-31 e IgE total significativamente mais altas ($P < 0.0001$) comparado a cães normais. Cães com DA também apresentaram significativamente mais altas a CTL ($P < 0.0002$) e a contagem absoluta de neutrófilos ($P < 0.0001$) e de eosinófilos ($P < 0.0001$), bem como a porcentagem de neutrófilos ($P < 0.03$) e de eosinófilos ($P < 0.0001$) comparado aos controles saudáveis. Uma correlação positiva significativa ($r^2 = 0.396$; $P < 0.007$) entre pVAS e IL-31 foi observada nos cães com DA.

Conclusões e importância clínica – Uma elevação importante nos níveis séricos de IL-17, IL-31 e IgE total juntamente a alterações no leucograma podem estar associadas com a DA canina e podem ser possíveis alvos no manejo terapêutico da DA canina.