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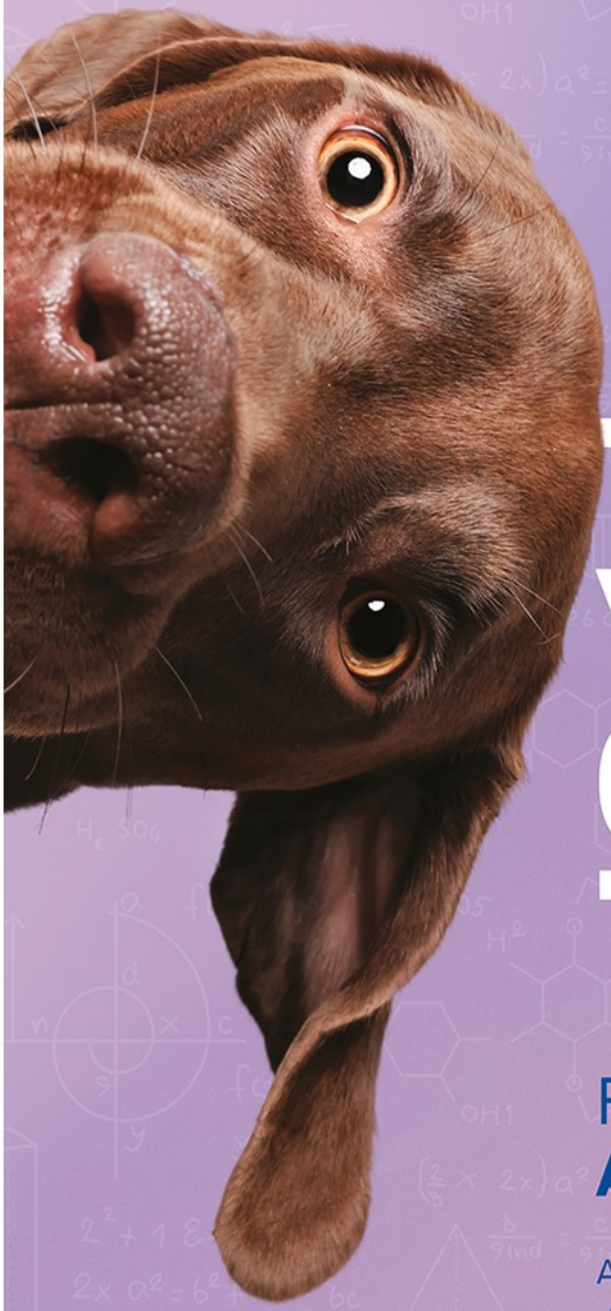

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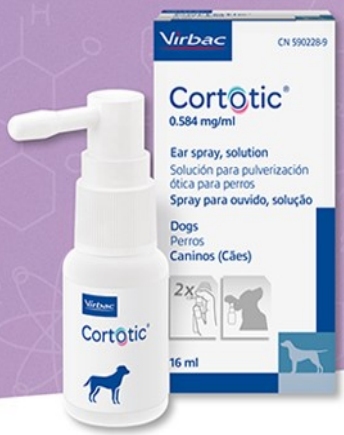

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Serum concentrations of IL-31 in dogs with nonpruritic mast cell tumours or lymphoma

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Background – The aim of this study was to compare serum interleukin (IL)-31 concentrations in dogs with lymphoma and mast cell tumours (MCT) without pruritus to those of healthy dogs.

Hypothesis/Objectives – To determine if IL-31 plays a role in tumour pathogenesis and if IL-31 could be a biological marker for disease progression.

Animals – Forty-eight healthy dogs and 36 dogs with neoplasia [multicentric lymphoma (14), MCT (15) and cutaneous lymphoma (7)] were included in the study.

Methods and materials – Dogs with neoplasia were assigned to three different groups. Group 1 consisted of patients with multicentric lymphoma, which were diagnosed by cytological, histopathological and clonality investigations. Thoracic radiographs, ultrasound examination of the abdominal cavity, and fine-needle aspirates from liver and spleen were used to determine the lymphoma stage Patients with cutaneous lymphoma, diagnosed by cytological and histopathological findings, were included in Group 2. Patients with MCT, diagnosed by cytological and histopathological findings, were included in Group 3. Serum was frozen at –80°C before measuring the concentration of IL-31 via a Simoa ultra-sensitive, fully automated two-step immunoassay.

Results – Serum concentrations of IL-31, regardless of the disease and its staging, were within the normal range in all patients; there was no difference between any of the different tumour groups and healthy dogs.

Conclusions and clinical importance – IL-31 is not likely to be involved in the pathogenesis of canine MCT or lymphoma without pruritus.

Introduction

In human medicine, the role of interleukin (IL)-31 in the pathogenesis of pruritus as well as of neoplastic diseases has been studied extensively.[1–9] IL-31 belongs to the IL-6 cytokine family and is secreted primarily by activated CD4+ T-helper cells. IL-31 acts via a heterodimeric IL-31 receptor (IL-31R) and the oncostatin receptor (OSMR).[10–12] It can be secreted by monocytes, macrophages and immature dendritic cells in response to irradiation or hydrogen peroxide (H_2O_2).[9] In dogs, IL-31 can be secreted by T cells after allergen exposure or exposure to bacterial antigens.[1,13] IL-31 was found to activate the Janus kinase-signal transducer and activator of transcription proteins pathway as well as the mitogen-activated protein kinase pathway in canine cells.[1]

In human medicine, an increase in the serum concentration of IL-31 has been detected in diseases such as asthma,[14,15] inflammatory bowel disease[16,17] and atopic dermatitis (AD).[18–20] Elevated IL-31 serum concentrations also have been reported in patients with neoplastic diseases.[2–4,7,10,21–23] The role of IL-31 in patients with cutaneous lymphoma is unclear.[24] A reduction in IL-31 serum concentrations was reported to be associated with successful treatment of pruritus in patients with cutaneous lymphoma.[25] In another study,[5] IL-31 serum concentrations of lymphoma patients did not correlate with pruritus severity. It was found that IL-31 was produced by T-cell lymphoma cells and that serum concentrations correlated with pruritus in patients with cutaneous T-cell lymphoma (CTCL), and not the stage of the disease, suggesting that IL-31 does not play an important role in the pathogenesis of patients with CTCL.[6] By contrast, IL-31 did not correlate with pruritus in the early stages of cutaneous T-cell

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lymphoma and did seem to be involved in pathogenesis of the disease in another study.[5] Based on work with human tumour cell cultures and mice,[10] IL-31 can inhibit angiogenesis, tumour growth and metastasis. Reduced serum concentrations of IL-31 are associated with a poor prognosis in mice with MC38 tumour-murine colorectal carcinoma.[10]

Serum concentrations of IL-31 are elevated in dogs with AD and use of the monoclonal anti-IL-31-antibody, lokivetmab, decreases pruritus in atopic dogs.[26] To the best of the authors' knowledge there is no information about the role of IL-31 in dogs with neoplastic disease. It is conceivable that IL-31 plays a role in paraneoplastic pruritus, tumour pathogenesis and possibly as a biological marker for disease progression. The aim of the present study was to evaluate the serum IL-31 concentration in dogs with lymphoma and mast cell tumour (MCT) without pruritus.

Methods and Materials

Study patients

The study protocol was approved by the Ethics Committee of the Faculty of Veterinary Medicine/LMU Munich, Germany under the number 130-25-06-2018. Patients with confirmed multicentric lymphoma, epitheliotropic and nonepitheliotropic cutaneous lymphoma and MCT presented to the Oncology Service at the Centre for Clinical Veterinary Medicine, LMU Munich, Germany (n = 33), or referred to the Zoovetservis clinic, Kyiv, Ukraine (n = 3), were included in the study and assigned to separate groups. Inclusion criteria were a confirmed diagnosis of lymphoma or mast cell tumour in a dog lacking pruritus. In all dogs, cytological investigation was conducted and was diagnostic. Exclusion criteria were treatments with glucocorticoids, immunosuppressants or chemotherapy in the two months before presentation. Group 1 consisted of patients with multicentric lymphoma at the time of the first presentation or relapse. Histopathological and clonality investigations, thoracic radiographs, an ultrasound examination of the abdominal cavity, and fine-needle aspirates from the liver and spleen were conducted as indicated (Table 1). Group 2 consisted of patients with epitheliotropic and nonepitheliotropic cutaneous lymphoma (Table 2). Patients with cutaneous MCT at the time of the first presentation or recurrence were included in Group 3 (Table 2). Thoracic radiographs, abdominal ultrasound and fine-needle aspirates from the liver and spleen excluded distant metastases. Serum concentrations of IL-31 in 48 healthy dogs were used as normal controls.

IL-31 evaluation

Blood was collected in serum separator tubes from all included dogs. Tubes were centrifuged, and serum was frozen at –80°C before measuring the concentration of IL-31. A Simoa ultra-sensitive, fully automated two-step immunoassay (Quanterix; Lexington, MA, USA) was used to quantify canine IL-31 (cIL-31) in canine serum. Serum samples were diluted 1:4 in Simoa Sample Diluent before being incubated with caninized anti-cIL-31-coated Simoa paramagnetic capture beads and biotinylated mouse anti-cIL-31 detector antibodies for 35 min. Beads then were washed in Simoa Bead Wash Buffer and resuspended in streptavidin-β-galactosidase (SβG; Quanterix) for 5 min. Beads were washed again and resorufin β-D-galactopyranoside (RGP; Quanterix) substrate solution was added, and then the sample was transferred to the Simoa Disc array. The fluorescent signal (574 nm) was detected on an HD-1 instrument (Quanterix) Sample concentrations of cIL-31 were extrapolated from an eight point standard curve (12–50,000 fg/mL) determined to be in the linear range of quantitation during assay validation. To confirm performance of the assay from run to run, high (20 pg/mL), medium (2 pg/mL) and low (0.2 pg/mL) quality control standards were included in each assay run and needed to be within 20% of intended concentrations, with the percentage coefficient of variance (%CV) within 20%, for the assay run and results to be accepted.

Statistics

The concentrations of serum IL-31 measured in the different groups were compared with the values of healthy control dogs with a Kruskal–Wallis test and Dunn post test; $P < 0.05$ was considered significant.

Results

Study patients

Signalment, diagnostic proceedings and results of IL-31 concentrations of included patients are presented in Tables 1–3. In Group 1 (multicentric lymphoma) staging was carried out in 13 of 14 patients, and stage IV lymphoma was observed in 12 of these according to the WHO staging system.

Seven dogs had cutaneous lymphoma(Group 1). In three patients with the nonepitheliotropic form of lymphoma, cytological examination for diagnosis was performed. In two of those patients, lymph nodes also were affected, whereas only skin lesions were observed in one patient. None of the dogs included showed pruritus.

All 15 dogs with MCT(Group 3) were staged: in three patients, metastases to the lymph nodes were observed; in 10 patients, one solitary tumour (0.9 to 4.5 cm diameter) was observed; and in three patients multiple tumours were present. Different tumour localizations were present including potentially unfavourable regions such as the lips, vulva, perineum and nasal cavity.

IL-31 evaluation

Blood was taken from 14 patients with a multicentric lymphoma, from 15 patients with a MCT, and from seven patients with the cutaneous form of lymphoma (three of those with the epitheliotropic and four with the nonepitheliotropic form); no dog showed pruritus. The concentration of IL-31 of the patients in the three groups was compared to the serum IL-31 concentration in 48 healthy control dogs (Table 3). There was no significant difference between the serum concentrations of IL-31 in healthy dogs, dogs with mast cell tumours and dogs with multicentric or cutaneous lymphoma. For comparison, the reported level of IL-31 in the Simoa assay averaged 0.531 pg/mL for normal dogs and 13.541 pg/mL for atopic dogs.[13,27]

Discussion

In this study, serum IL-31 concentrations in dogs with nonpruritic multicentric lymphoma, MCT and cutaneous lymphoma were all within the normal range.[27]

Cytokines and their influence on processes of proliferation, angiogenesis and carcinogenesis have been the subject of numerous studies in oncology,[8–10,22] sometimes with contrasting results. Most of the research has evaluated human patients with epitheliotropic lymphoma and pruritus.[7,8,24,25] An elevated serum IL-31 concentration was found in patients with pruritic epitheliotropic lymphoma in comparison with clinically healthy people.[6] Other studies have reported that IL-31 does not correlate with pruritus in early stage cutaneous T-cell lymphoma.[5] IL-31 serum concentrations were significantly higher in one study in

Table 1. Individual data for dogs with multicentric lymphoma (Group 1) and cutaneous lymphoma (Group 2)

Diagnosis	Tumour location	Radiographic examination	Ultrasound abdomen	Histological examination	Breed	Age (years)	Sex
Multicentric lymphoma	Multiple lymph nodes	Enlarged sternal and mediastinal lymph nodes	Splenic involvement	+	Mixed breed	9	F
Multicentric lymphoma	Multiple lymph nodes	No abnormalities	Splenic involvement	+	Mixed breed	5	FC
Multicentric lymphoma	Multiple lymph nodes	Enlarged mediastinal lymph nodes	Splenic involvement	+	American bulldog	8	M
Multicentric lymphoma	Multiple lymph nodes	No abnormalities	Splenic involvement	+	Labrador retriever	11	MC
Multicentric lymphoma	Multiple lymph nodes	No abnormalities	No abnormalities	–	Labrador retriever	11	MC
Multicentric lymphoma	Multiple lymph nodes	No abnormalities	Splenic involvement	+	Giant schnauzer	9	FC
Multicentric lymphoma	Multiple lymph nodes	Possible lung infiltration	Splenic involvement, enlarged abdominal lymph nodes	+	Puli	11	F
Multicentric lymphoma	Multiple lymph nodes	Not done	Splenic involvement	+	German shepherd dog	4	MC
Multicentric lymphoma	Multiple lymph nodes	Possible lung infiltration and enlarged sternal lymph nodes	Splenic involvement, enlarged abdominal lymph nodes	–	Basset hound	10	FC
Multicentric lymphoma	Multiple lymph nodes	Possible enlargement of trachea-bronchial lymph nodes	No abnormalities	–	Pinscher	9	FC
Multicentric lymphoma	Multiple lymph nodes	Not done	Not done	–	German shepherd dog	7	FC
Multicentric lymphoma	Multiple lymph nodes		Not done	–	Mixed breed	5	M
Multicentric lymphoma	Multiple lymph nodes	Possible enlargement of sternal and trachea-bronchial lymph nodes	Splenic and liverinvolvement	+	Hovawart	7	FC
Multicentric lymphoma	Multiple lymph nodes	No abnormalities	Splenic and liver involvement	–	Viszla	14	M
Cutaneous nonepitheliotropic lymphoma	Three cutaneous masses (≤2.1 cm), multicentric lymphoma in remission	Not done	Not done	–	Jack Russell terrier	9	F
Cutaneous nonepitheliotropic lymphoma	Subcutaneous mass (1.1 cm)	Not done	No abnormalities	–	Mixed breed	6	F
Cutaneous nonepitheliotropic lymphoma	Anal cutaneous mass and multicentric lymphoma in remission	Not done	Not done	–	Golden retriever	6	F
Cutaneous nonepitheliotropic lymphoma	Cutaneous mass on the ventral neck (10 x 7 cm)	Not done	Not done	+	Mixed breed	4	F
Cutaneous epitheliotropic lymphoma	Multiple cutaneous plugs	Not done	Not done	+	Airedale terrier	9	M
Cutaneous epitheliotropic lymphoma	Cutaneous mass on the lip and the spinal area (1 cm each)	Not done	Not done	+	Boxer	13	FC
Cutaneous epitheliotropic lymphoma	Multiple cutaneous plugs	Not done	Not done	+	English cocker spaniel	11	FC

F, female; FC, female castrated; M, male; MC, male castrated.

CTCL patients than in the control group, indicating a possible role for this cytokine in the pathogenesis of cutaneous T-cell lymphoma.[5] Another study found no correlation between IL-31 expression and the development of pruritus, nor between IL-31 concentrations and the severity of disease.

In veterinary medicine, the role of IL-31 has been investigated only in canine AD. IL-31 serum concentrations

Table 2. Individual data for dogs with mast cell tumours (Group 3)

Tumour mass location	Radiographic examination	Ultrasound abdomen	Histological examination	Breed	Age (years)	Sex
Tarsus (2.1 cm)	No abnormalities	No abnormalities	Not done	English bulldog	7	FC
Nose (1.5 x 0.7 cm)	No abnormalities	No abnormalities	Low grade	Mixed breed	9	M
Three masses: two in area of shoulder, one in area of ribs(1–3 cm) and cervical lymph node metastasis	No abnormalities	No abnormalities	Low grade	Mixed breed	7	F
Right popliteal area (1.8 x 2.9 cm)	No abnormalities	No abnormalities	High grade	Labrador retriever	9	F
Nasal cavity with metastasis in mandibular lymph nodes	No abnormalities, CT	Not done	High grade	Australian shepherd dog	11	FC
Right axilla (4 x 4 cm)	No abnormalities	No abnormalities	Not done	Irish terrier	10	FC
on the lateral chest (0.9 cm)	Not done	No abnormalities	Not done	Mixed breed	8	M
Right lip (1.2 cm & 0.6 cm)	No abnormalities	No abnormalities	Low grade	Dachshund	9	M
Cutaneous mass in ventral tail area(2 x 1.5 cm)	No abnormalities	No abnormalities	Low grade	Pug	11	FC
Tail base (4 x 2 cm)	No abnormalities, CT	Not done	Low grade	Irish terrier	11	FC
Vulvar area (4 x 3 cm) and flank (3.5 cm)	No abnormalities	No abnormalities	Not done	Irish setter	8	F
Shoulder (4.8 x 7 cm) and cervical lymph node metastasis	No abnormalities	No abnormalities	Not done	Labrador retriever	9	M
Head (2.5 x 1 cm)	No abnormalities	No abnormalities	Low grade	Rhodesian ridgeback	8	MC
Lip (2.5 cm) with bilateral mandibular involvement	no abnormalities		Not done	Shar pei	10	M
Ten small masses (0.5–1.2 cm)	Not done	Not done	Not done	Mixed breed	11	F

MCT, mast cell tumour; F, female; FC, female castrated; M, male; MC, male castrated.

were significantly higher in atopic than in healthy dogs.[1,13,27] The role of IL-31 in the development of canine neoplastic diseases has not yet been studied. The group of patients with multicentric lymphoma was homogeneous, dogs had stage 3–4 lymphoma according to WHO criteria. However, all dogs had IL-31 serum concentrations within the normal range, suggesting that IL-31 is not involved in the pathogenesis of canine multicentric lymphoma.

Increased serum concentration of IL-31 in human patients with pruritus and MCT has been described; the increase correlated with disease progression. Other studies confirmed elevated concentrations of IL-31 in the skin[3] and serum[28] of patients with mastocytosis, which were associated with disease severity.[28] IL-31 concentration was significantly higher in human patients with progressive disease than in patients without progression.[28] Reduction of pruritus was described in a dog with pruritic mastocytosis after using lokivetmab, a monoclonal antibody against canine IL-31.[29] In humans, mast cells were described as a source of IL-31[30] as well as the target of IL-31 exposure in people with pruritus,[8] similar to what was described in patients with carcinoma of the endometrium.[2] In our study, dogs with MCT had one or more tumours of various sizes without distant metastases, three dogs had metastases in regional lymph nodes and one patient had mastocytosis. None of those patients, regardless of the severity of the mast cell tumour, showed an increase in IL-31 serum concentration, suggesting that this cytokine is not involved in the pathogenesis of cutaneous MCT.

None of the dogs had pruritus reported by their owner. Possibly, IL-31 only plays a role in the pathogenesis of neoplastic diseases associated with pruritus. Alternatively, IL-31 concentrations should be measured directly in the affected skin rather than the serum.

This study had several limitations. First, there was no direct control group of healthy dogs included in the study. However, the normal range of IL-31 in healthy dogs was determined in the same laboratory with the same assay.[27] Second, only a limited number of patients was included. Finally, dogs with various tumour stages were evaluated and possibly IL-31 only plays a role in some subsets of those neoplasias. Prospective studies of different subsets and various stages of neoplastic diseases with larger numbers of patients may shed more light on the role of IL-31 in canine tumour pathogenesis.

Based on this study, it seems unlikely that IL-31 is involved in the pathogenesis of canine MCT or lymphoma without pruritus. It would be interesting to assess serum IL-31 concentrations in pruritic patients with epitheliotropic lymphoma and to establish whether there is a correlation between the severity of pruritus and the IL-31 concentration in those dogs, or to evaluate IL-31 concentration directly in the skin of dogs with cutaneous lymphoma.

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Résumé

Contexte – Le but de cette étude est de comparer les concentrations d'interleukine (IL)-31 sériques chez les chiens avec lymphome et mastocytome (MCT) sans prurit à celles de chiens sains.

Hypothèses/Objectifs – Déterminer si l'IL-31 joue un rôle dans la pathogénie des tumeurs et si l'IL-31 pourrait être un marqueur biologique de la progression de la maladie.

Sujets – Quarante-huit chiens sains et 36 chiens avec néoplasie [lymphome multicentrique (14), MCT (15) et lymphome cutané (7)] ont été inclus dans l'étude.

Matériels et méthodes – Les chiens avec néoplasie ont été répartis dans trois groupes différents. Le groupe 1 regroupait les patients avec lymphome multicentrique, diagnostiqués par cytologie, histopathologie et test de clonalité. Les radiographies thoraciques, échographies de la cavité abdominale et ponctions à l'aiguille fine du foie et de la rate ont été utilisées pour déterminer le grade du lymphome. Les patients avec lymphome cutané, diagnostiqués par cytologie et histopathologie ont été inclus dans le groupe 2. Les patients avec MCT, diagnostiqués par cytologie et histopathologie ont été inclus dans le groupe 3. Le serum a été congelé à -80°C avant mesure de la concentration d'IL-31 par immunomarquage automatique en deux temps Simoa ultra-sensible.

Résultats – Les concentrations sériques d'IL-31, quelque soit la maladie et son grade, étaient dans les valeurs usuelles pour tous les patients ; il n'y avait pas de différence significative entre les différents groupes de tumeurs et les chiens sains.

Conclusions et importance clinique – L'IL-31 ne semble pas impliqué dans la pathogénie des MCT ou des lymphomes canins sans prurit.

RESUMEN

Introducción – el objetivo de este estudio fue comparar las concentraciones séricas de interleuquina (IL) -31 en perros con linfoma y mastocitomas (MCT) sin prurito con los de perros sanos.

Hipótesis/Objetivos – determinar si IL-31 juega un papel en la patogénesis tumoral y si IL-31 podría ser un marcador biológico para evaluar la progresión de la enfermedad.

Animales – se incluyeron en el estudio cuarenta y ocho perros sanos y 36 perros con neoplasia [linfoma multicéntrico (14), MCT (15) y linfoma cutáneo (7)].

Métodos y materiales – los perros con neoplasia se asignaron a tres grupos diferentes. El grupo 1 consistió en pacientes con linfoma multicéntrico, que fueron diagnosticados por investigaciones citológicas, histopatológicas y de clonalidad. Las radiografías torácicas, el examen de ultrasonido de la cavidad abdominal y los aspirados con aguja fina del hígado y el bazo se utilizaron para determinar la fase del linfoma. Los pacientes con linfoma cutáneo, diagnosticados por hallazgos citológicos e histopatológicos, se incluyeron en el Grupo 2. Los pacientes con MCT, diagnosticados por los hallazgos citológicos e histopatológicos se incluyeron en el Grupo 3. El suero se congeló a –80 ° C antes de medir la concentración de IL-31 mediante un inmunoensayo Simoa ultrasensible, totalmente automatizado en dos pasos.

Resultados – las concentraciones séricas de IL-31, independientemente de la enfermedad y su estadificación, estuvieron dentro del rango normal en todos los pacientes; no hubo diferencia entre ninguno de los diferentes grupos tumorales y perros sanos.

Conclusiones e importancia clínica – no es probable que IL-31 esté involucrada en la patogénesis de MCT canino o linfoma sin prurito.

Zusammenfassung

Hintergrund – Das Ziel dieser Studie war ein Vergleich von Serum Interleukin (IL)-31 Konzentrationen bei Hunden mit Lymphomen und Mastzelltumoren (MCT) ohne Juckreiz mit jenen von gesunden Hunden.

Hypothese/Ziele – Das Ziel war es festzustellen, ob IL-31 bei der Pathogenese von Tumoren eine Rolle spielt und ob IL-31 ein biologischer Marker für den Fortschritt der Erkrankung sein könnte.

Tiere – Achtundvierzig gesunde Hunde und 35 Hunde mit Neoplasien [multizentrisches Lymphom (14), MCT (15) und kutane Lymphome (7)] wurde in die Studie inkludiert.

Methoden und Materialien – Die Hunde mit Neoplasien wurden in drei verschiedene Gruppen eingeteilt. Gruppe 1 bestand aus Patienten mit multizentrischen Lymphomen, die mittels zytologischer, histopathologischer und mit Hilfe von Klonalitätsuntersuchungen diagnostiziert worden waren. Röntgen des Thorax, Ultraschalluntersuchung des Abdomens und Feinnadelaspirate der Leber und der Milz wurden angewendet, um den Grad der Lymphome zu bestimmen. Patienten mit kutanen Lymphomen, die mittels zytologischer und histopathologischer Befunde diagnostiziert worden waren, kamen in Gruppe 2. Patienten mit MCT, welche mittels zytologischer und histopathologischer Befunde diagnostiziert worden waren, kamen in Gruppe 3. Sera wurden bei -80° C eingefroren, bevor die Konzentrationen von IL-31 mittels Simoa Ultrasensiblem, vollautomatischem Zwei-Schritt Immunassay gemessen wurden.

Ergebnisse – Die Serumkonzentrationen von IL-31, egal bei welcher Krankheit und ihrem Grad, waren bei allen Patienten innerhalb des Normalbereichs; es bestand kein Unterschied zwischen den verschiedenen Tumorgruppen und den gesunden Hunden.

Schlussfolgerungen und klinische Bedeutung – Es ist unwahrscheinlich, dass IL-31 bei der Pathogenese der caninen MCT oder bei Lymphomen ohne Juckreiz eine Rolle spielt.

要約

背景 – 本研究の目的は、掻痒のないリンパ腫およびマスト細胞腫瘍（MCT）を有する犬の血清インターロイキン（IL）-31濃度を、健常犬と比較することであった。

仮説/目的 – IL-31が腫瘍の病因に役割を果たすかどうか、そしてIL-31が疾患の進行の生物学的マーカーになるかどうかを判断する。

供試動物 – 48頭の健常犬および36頭の腫瘍を有する犬[多中心性リンパ腫（14）、MCT（15）、皮膚型リンパ腫（7）]を研究に包含した。

材料と方法 – 腫瘍を有する犬を3つの異なるグループに割り当てた。グループ1は、細胞学的、組織病理学的およびクローナリティ検査によって診断された多中心型リンパ腫の犬で構成された。グループ2は、細胞学的および組織病理学的所見により診断され、胸部レントゲン写真、腹部超音波検査、および肝臓および脾臓の穿刺吸引液を使用して皮膚型リンパ腫の病期を判定した皮膚リンパ腫の犬を包含した。グループ3は、細胞学的および組織病理学的所見によりMCTと診断された犬を包含した。Simoa超高感度完全自動化2段階イムノアッセイ法によるIL-31濃度を測定する前に、血清を–80°Cで凍結した。

結果 – IL-31血清濃度は、疾患とその病期に関係なく、すべての患者で正常範囲内であった。異なる腫瘍群と健常犬の間に相違はなかった。

結論と臨床的重要性 – IL-31は、掻痒のないMCTまたはリンパ腫の病因に関与している可能性は低い。

摘要

背景 — 本研究的目的是比较无瘙痒的淋巴瘤和肥大细胞瘤(MCT)患犬与健康犬的血清白介素(IL)-31浓度。

假设/目的 — 确定IL-31是否在肿瘤发病机制中发挥作用，以及IL-31是否可作为疾病发生的生物学标志物。

动物 — 48只健康犬和36只肿瘤犬[多中心淋巴瘤(14)、MCT(15)和皮肤淋巴瘤(7)]被纳入研究。

方法和材料 — 将患瘤犬分配至三个不同组。第1组为多中心淋巴瘤患犬，经细胞学、组织病理学和克隆检查确诊。经细胞学和组织病理学结果确诊的皮肤淋巴瘤病患，纳入第2组，胸部x线片、腹腔超声检查、肝脾细针穿刺确定淋巴瘤分期。经细胞学和组织病理学结果确诊的MCT病患，纳入第3组。在通过Simoa超灵敏、全自动两步免疫测定法测定IL-31浓度前，将血清在-80°C下冷冻。

结果 — 所有病患的血清IL-31浓度均在正常范围内，与疾病及其分期无关；任何不同肿瘤组和健康犬之间均无差异。

结论和临床重要性 — IL-31不可能参与犬MCT或淋巴瘤（无瘙痒）的发病机制。

Resumo

Contexto – O objetivo deste estudo foi comparar as concentrações séricas de interleucina (IL) -31 em cães com linfoma e mastocitoma (MCT) sem prurido com as de cães saudáveis.

Hipótese/Objetivos – Determinar se a IL-31 desempenha um papel na patogênese tumoral e se a IL-31 pode ser um marcador biológico para a progressão da doença.

Animais – Quarenta e oito cães saudáveis e 36 cães com neoplasia [linfoma multicêntrico (14), MCT (15) e linfoma cutâneo (7)] foram incluídos no estudo.

Métodos e materiais – Os cães com neoplasia foram divididos em três grupos diferentes. O Grupo 1 consistiu de pacientes com linfoma multicêntrico, que foram diagnosticados por investigação citológica, histopatológica e de clonalidade. Radiografias torácicas, ultrassom abdominal e aspiração por agulha fina de fígado e baço foram utilizados para determinar o estágio do linfoma. Pacientes com linfoma cutâneo, diagnosticados por achados citológicos e histopatológicos, foram incluídos no Grupo 2. Pacientes com MCT, diagnosticados por os achados citológicos e histopatológicos foram incluídos no Grupo 3. O soro foi congelado a –80 ° C antes da concentração de IL-31 ser mensurada por meio de um imunoensaio Simoa ultrasensível, totalmente automatizado em duas etapas.

Resultados – As concentrações séricas de IL-31, independentemente da doença e do estadiamento, estavam dentro da normalidade em todos os pacientes; não houve diferença entre qualquer um dos diferentes grupos de tumor e cães saudáveis.

Conclusões e importância clínica – É improvável que a IL-31 esteja envolvida na patogênese do MCT canino ou linfoma sem prurido.

