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Is "milk crust" a transient form of golden retriever ichthyosis?

Anja Roethig*, Kirsti J. M. Schildt†, Monika M. Welle‡, Brett E. Wildermuth§, Reto Neiger* and Nina Thom*

*Clinic for Small Animal Internal Medicine, Justus-Liebig-Universität, Frankfurter Straße 126, 35392, Giessen, Germany
†Animagi Aurinkolahti, Solvikinkatu 13, 00990, Helsinki, Finland
‡Institute of Animal Pathology, Vetsuisse Faculty, University of Bern, Länggasstraße 122, PO Box 8466, 3001, Bern, Switzerland
§Tierdermatologie Wildermuth, Borsigstraße 7, 65205, Wiesbaden, Germany

Correspondence: Anja Roethig, Klinik für Kleintiere, Justus-Liebig-Universität, Frankfurter Straße 126, 35392 Giessen, Germany. E-mail: anja.roethig@vetmed.uni-giessen.de

Background – A recessive inherited form of lamellar ichthyosis is well recognized in golden retrievers. In this breed, young puppies demonstrate a self-limiting scaling disorder which is commonly recognized by breeders, who use the term "milk crust" to describe this syndrome.

Hypothesis/Objectives – To determine whether "milk crust" is a new keratinization disorder or a self-limiting form of golden retriever ichthyosis.

Animals – A total of 179 golden retriever dogs (21 dams and 158 puppies) were examined.

Methods – Dermatological examination and assessment of the patatin-like phospholipase-1 (*PNPLA1*) genotype by PCR testing of buccal mucosal swabs. Skin biopsies from one affected puppy were evaluated for histopathological abnormalities.

Results – Forty-five of 158 (28%) puppies exhibited scaling at 8 weeks of age; 113 of 158 (72%) were dermatologically normal. Of 144 analysed samples, 40 of 144 (28%) puppies demonstrated a homozygous mutation of the *PNPLA1* genotype [of which, 36 of 40 (90%) had signs of scaling], 77 of 144 (53%) demonstrated a heterozygous mutation and 27 of 144 (19%) were a normal wild-type. In six of 17 (35%) dams, a homozygous mutation of the *PNPLA1* genotype was found, eight of 17 (47%) demonstrated a heterozygous mutation and three of 17 (18%) were normal wild-type. Dams with a homozygous mutation were clinically unaffected. A 1 year follow-up revealed that 23 of 28 (82%) puppies affected with this syndrome failed to develop typical signs of ichthyosis. In five of 28 (18%) dogs there was persistence of mild scaling.

Conclusions and clinical importance – We hypothesize that the clinical syndrome termed "milk crust" could represent a transient form of golden retriever ichthyosis. Remission is not fully linked to *PNPLA1* genotype, suggesting that unknown factors may contribute to the clinical disease.

Introduction

The skin forms a protective barrier through the complex process of cornification, desquamation and formation of an intercellular lipid layer.[1,2] Primary cornification disorders, such as ichthyosis, arise from abnormalities in this process.[3] In human medicine, ichthyosis represents a group of scaling disorders with different phenotypes, including syndromic and nonsyndromic forms.[4] The heterogeneity and understanding of the pathogenesis of ichthyosis in human medicine has resulted in multiple classification systems for this disease.[5,6] In veterinary medicine, nonsyndromic cornification disorders in several breeds of dogs are predominantly recognized. Light microscopy has permitted further classification of canine ichthyosis into epidermolytic and nonepidermolytic forms.[3]

A cornification disorder has been reported in the golden retriever breed.[7,8] Affected dogs demonstrated evidence of clinical scaling and hyperpigmentation of variable severity, predominantly affecting the axilla, thoracic and inguinal regions. The large, loosely adherent scales varied from white to grey in colour.[7,9] This nonpruritic disorder reportedly predisposes affected individuals to secondary bacterial infection. Clinical signs typically occur prior to 1 year of age in 76–85% of affected dogs.[7,9] Histopathological abnormalities of ichthyosis in the golden retriever are characterized by a diffuse lamellar orthokeratotic hyperkeratosis, in which the corneocytes are arranged as compact, often desquamating layers. Epidermal hyperplasia and dermal inflammation are lacking.[7–9] The mode of inheritance is reportedly autosomal recessive and an insertion–deletion mutation in the patatin-like phospholipase-1 (*PNPLA1*) gene is typical in dogs affected with golden retriever ichthyosis.[7–10] The PNPLA1 protein is

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expressed in the upper epidermis and is thought to play a role in glycerophospholipid synthesis or remodelling, which is essential for the normal lipid barrier function of the skin.[10] A disruption of the lipid barrier leads to inappropriate desquamation of corneocytes, resulting in the clinical signs of scaling.[10]

A gene test (Antagene, Limonest, France) is available to screen golden retrievers for the mutation in the *PNPLA1* gene;[11] in Switzerland, the prevalence of heterozygous and homozygous carriers of the gene mutation is reportedly 50 and 25%, respectively.[12] It is the impression of veterinarians and golden retriever breeders that the number of clinically affected dogs is much lower in the German golden retriever population.

Golden retriever breeders recognize a scaling disorder in young puppies referred to as "Milchschorf", which translates into English as "milk crust". Affected puppies demonstrate scaling of the lateral and ventral thorax, axillae, ventral abdomen and inguinal regions. Very rarely, the dorsum is also mildly affected. Scales vary in size, are white and either loosely adherent to the skin surface or already detached and trapped in the hair coat. The scaling ranges in severity from mild (Figure 1) to severe (Figure 2). This syndrome usually resolves between 4 and 6 months of age, with no clinical recurrence in adult dogs. Among golden retriever breeders this is considered to be a well-known, self-limiting skin condition of minimal significance.

The aim of this prospective study was to determine whether the syndrome termed "milk crust" represents a new keratinization disorder or is a self-limiting, transient form of golden retriever ichthyosis.

Materials and methods

The study was performed from December 2012 to July 2014. The German retriever club (Deutscher Retriever Club e.V) and individual breeders were contacted, and puppies of 8 weeks of age were enrolled in the study. The entire litter (dam and puppies) was included whether puppies were affected or unaffected. The dam and all littermates underwent a dermatological examination when the puppies were 8 weeks of age. Examinations were performed by veterinarians or one of three breed wardens, who are experienced golden retriever breeders, well aware of the syndrome of "milk crust" and familiar with the normal appearance of the skin and hair coat of this breed. They received detailed examination instructions and training from the authors prior to their participation in the study. A buccal mucosal swab to obtain DNA was collected from all dogs with a sterile cytobrush (DOC® cytobrush; Gardening srl, Genova, Italy). Dogs had no access to food and water for 30 min before sampling. The inside of the cheek was brushed by firmly rotating the brush for at least 20 s. A gene test for the *PNPLA1* mutation was performed as previously described.[11]

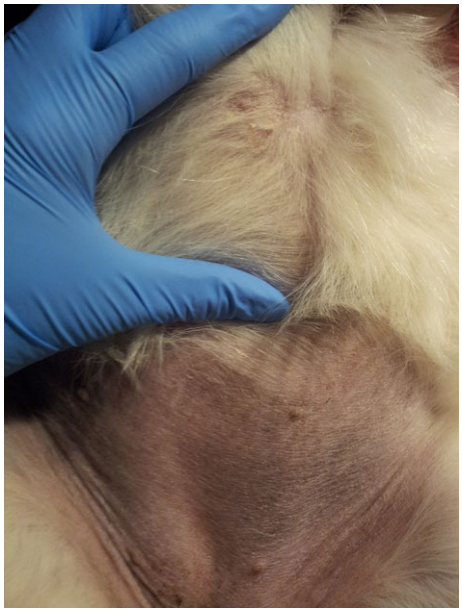

Figure 1. Mild scaling of the sternal and thoracic region of an affected 8-week-old puppy.

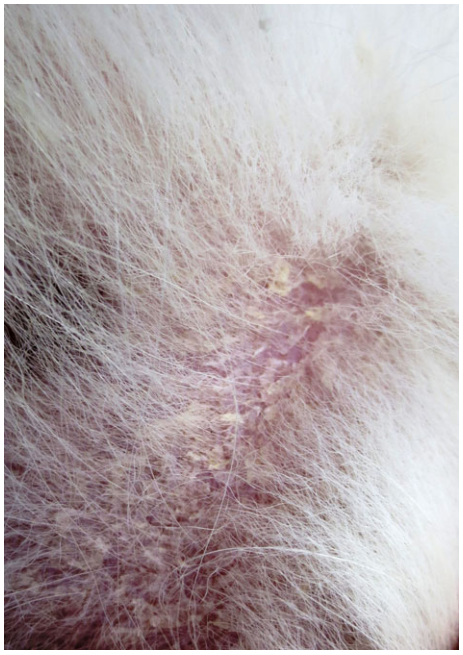

Figure 2. Severe scale of the ventral abdominal region of an affected 8-week-old puppy.

Skin biopsies were collected from one affected puppy at 4 months of age and were submitted for histopathological evaluation at the owner's request. Three skin biopsies were collected (flank, ventral abdomen and shoulder) using local anaesthesia and a skin biopsy punch.

A telephone follow-up was conducted by the first author 9–16 months later to document the presence or absence of scaling in all dogs tested. Statistical analysis of the data was performed by chi-square test. Data were considered significant at $P \leq 0.05$.

Results

Twenty-two litters with 158 puppies and 21 dams were enrolled in this study. Of the 158 8-week-old puppies, 45 (28%) exhibited scaling affecting the axilla and thoracic/abdominal/inguinal area and 113 (72%) were unaffected. None of the 21 adult dogs demonstrated any scaling. One dam had two litters included. From the 22 litters studied, 12 litters had affected puppies; 10 litters had no affected puppies.

Fourteen puppies, including nine with signs of scaling (one complete litter with 7 scaly puppies), and four dams were excluded from genetic analysis. Reason for exclusion was either because no DNA could be extracted (n = 8 puppies, n = 3 dams) or because a cross-contami-

nation of samples occurred (n = 6 puppies, n = 1 dam). A homozygous mutation, heterozygous mutation or normal wild-type *PNPLA1* gene was demonstrated in 40 of 144 (28%), 77 of 144 (53%) and 27 of 144 (19%) of puppies, respectively. Six of the adult dogs (35%) demonstrated a homozygous mutation of the *PNPLA1* gene, 47% (eight of 17) had a heterozygous mutation and 18% (three of 17) were normal wild-type (Table 1). In 90% (36 of 40) of the puppies with a homozygous mutation for the *PNPLA1* gene, there was clinical evidence of scaling. Four puppies with a homozygous mutation for the *PNPLA1* gene were unaffected. All puppies with a heterozygous mutation or normal wild-type gene status were dermatologically normal. All dams with a homozygous mutation were dermatologically unaffected. Statistical analysis detected a significant association between dogs with a homozygous mutation of the *PNPLA1* genotype and dogs affected with the "milk crust" phenotype (P = 0.003).

Histological evaluation of the skin biopsies (Figures 3 and 4) collected from the affected puppy with a homozygous mutation of the *PNPLA1* genotype revealed an epidermis of normal thickness with moderate laminar orthokeratotic hyperkeratosis. Scattered keratinocytes in the granular cell layer had prominent clear membrane-bound cytoplasmic vacuoles. The dermis and the adnexal structures were unremarkable. The morphological diagnosis was a diffuse moderate laminar orthokeratotic hyperkeratosis. The genotype, histopathological abnormalities and phenotype of this one affected puppy were consistent with the description for typical ichthyosis of the golden retriever. During the following 12 months, scaling decreased, and at 1 year of age the residual scaling affecting the axillae and stifle regions was very mild and not apparent to the owners.

Telephone follow-up data was available for 28 of 36 (78%) of the initially affected puppies. No clinical evidence

Table 1. Genotype and phenotype of the dam and the corresponding litter

Genotype of dam	Phenotype of dam	Genotype of puppies	Phenotype of puppies at 8 weeks	Phenotype of puppies at ~1 year	Inbreeding coefficient
Homozygous mutated	Normal	8 heterozygous	8 normal	7 normal*	1.56
Homozygous mutated	Normal	1 heterozygous, 1 homozygous mutated	1 normal, 1 scaly	1 normal †	1.56
Homozygous mutated	Normal	2 heterozygous, 2 homozygous mutated	2 normal, 2 scaly	2 normal, 2 normal	3.12
Heterozygous	Normal	6 heterozygous, 3 homozygous mutated	6 normal, 3 scaly	6 normal, 3 normal	0
Normal wild-type	Normal	11 normal wild-type	11 normal	11 normal	0
Heterozygous	Normal	5 heterozygous, 2 homozygous mutated	5 normal, 2 scaly	3 normal, * 2 normal	0
Heterozygous	Normal	1 heterozygous, 3 homozygous mutated	1 normal, 3 scaly	1 normal, 1 scaly, 2 normal	0.78
Homozygous mutated	Normal	9 homozygous mutated	9 scaly	9 no data*	0
Heterozygous ‡	Normal	4 normal, 5 heterozygous	9 normal	9 normal	1.56
Normal wild-type	Normal	4 normal wild-type	4 normal	3 normal*	0
Heterozygous	Normal	1 normal wild-type, 4 heterozygous, 2 homozygous mutated	1 normal, 4 normal, 2 normal	No data*	3.12
Heterozygous	Normal	1 normal wild-type, 2 heterozygous, 4 homozygous mutated	1 normal, 2 normal, 4 scaly	1 normal, 1 normal,* 4 normal	0.78
Homozygous mutated	Normal	2 heterozygous, 5 homozygous mutated	2 normal, 5 scaly	2 normal, 1 scaly, 4 normal	0.78
Normal wild-type	Normal	10 heterozygous	10 normal	8 normal,*	0
Homozygous mutated	Normal	3 heterozygous, 4 homozygous mutated	3 normal, 4 scaly	2 normal,* 1 scaly, 3 normal	0
Heterozygous§	Normal	5 heterozygous, 1 homozygous mutated	5 normal, 1 scaly	5 normal, 1 normal	0
Heterozygous	Normal	4 normal wild-type, 2 heterozygous	6 normal	No data*	0
Heterozygous	Normal	2 normal wild-type, 3 heterozygous	5 normal	No data*	6.25
Heterozygous‡	Normal	3 heterozygous, 4 homozygous mutated	3 normal, 2 scaly, 2 normal	3, 1 scaly, 2 normal*	0
No data¶	Normal	13 heterozygous	13 normal	No data*	0
No data¶	Normal	2 heterozygous	2 normal	No data*	0

The inbreeding coefficient is calculated for four generations based on Wright's formula.[14,15] Data of all puppies excluded from the genetical analysis and the dam that had a litter of seven scaly puppies, as given above, are not shown.

*No further data available either because breeders declined follow-up or owners were not available.

†The dog died before the end of the study and therefore no telephone follow-up was available. This dog was excluded from further analysis.

‡The dam had two litters that were included in the study.

§This dam was excluded from statistical analysis due to suspected cross-contamination of DNA sample.

¶No DNA could be extracted from this sample; therefore, no data were available.

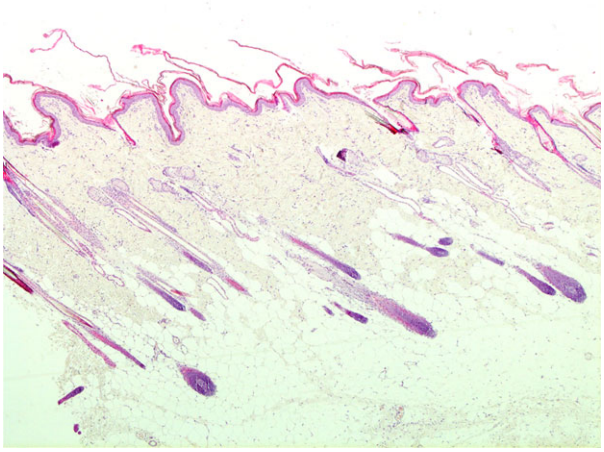

Figure 3. Haired skin of a 16-week-old affected golden retriever puppy with "milk crust". Moderate hyperkeratosis; note the normal epidermis (i.e. no hyperplasia) and no dermal inflammation. Haematoxylin and eosin, ×10 magnification.

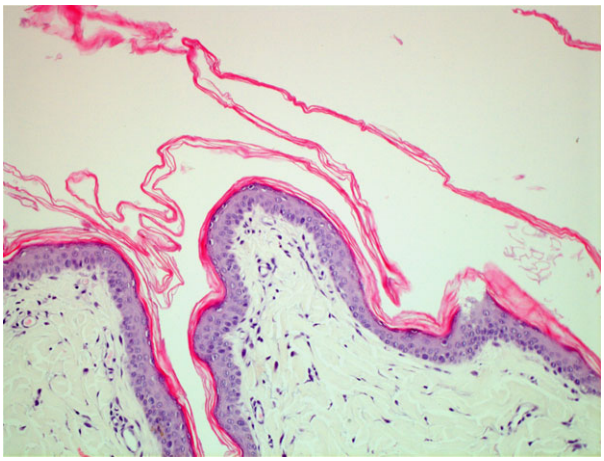

Figure 4. Haired skin of an 16-week-old affected golden retriever puppy with "milk crust". Stratum corneum with moderate laminar orthokeratotic hyperkeratosis and scattered vacuolated keratinocytes. Haematoxylin and eosin, ×40 magnification.

of scaling was reported in 23 of 28 (82%) dogs, while in five of 28 (18%) dogs, scaling had persisted. No inflammatory changes, including erythema, alopecia, greasy hair coat or pruritus were reported.

Discussion

The term "milk crust" is the colloquial name assigned by breeders of golden retrievers to describe a syndrome of self-limiting scaling affecting young puppies, with a prevalence estimated by German breeders of up to 30%. Interestingly, the scaling resolves in most affected puppies (82%) before 1 year of age, irrespective of the degree of scaling evident at 8 weeks of age.

An insertion–deletion mutation in the *PNPLA1* gene is typical in dogs affected with golden retriever ichthyosis.[10] All the affected golden retriever puppies in this study demonstrated a *PNPLA1* homozygous genotype. Our hypothesis, therefore, is that this transient scaling disorder may represent an early manifestation of golden retriever ichthyosis. In 90% of the puppies with a homozygous mutation, scaling was evident at 8 weeks of age. Four puppies with the homozygous mutation, however, had no demonstrated evidence of scale. Retrospectively, we cannot exclude the possibility that mild scaling might have been overlooked in the clinical examination. Alternative explanations for these dogs being asymptomatic include the *PNPLA1* mutation being associated with subclinical disease or that the syndrome "milk crust" is only linked partly to the *PNPLA1* gene mutation.

A homozygous mutation of the *PNPLA1* gene was demonstrated in 35% of adult dogs in this study. No adult dog with the homozygous mutation demonstrated any clinical evidence of scaling, consistent with the observation that ichthyosis manifests clinically in puppyhood and often becomes subclinical in adult dogs.[13] The prevalence of *PNPLA1* mutation in this cohort of dogs is similar to that reported in a recent study from Switzerland, where a prevalence of 50% heterozygous and 25% homozygous carriers was demonstrated.[12]

A single gene mutation in human ichthyosis can cause several disease phenotypes with varying clinical symptoms.[4,5] This has also recently been described in golden retriever ichthyosis, where only 69% of adult dogs affected with the homozygous mutation were clinically affected with scale.[13] The genotype appears to correlate well with the clinical phenotype at a young age but not in adult dogs. No adult dog with the homozygous mutation for the *PNPLA1* gene had scaling at the time of examination in the present study. Only two dams were reported to have had a transient scaling in puppyhood that resolved without recurrence. It appears that the *PNPLA1* genotype cannot reliably predict whether a golden retriever affected with the homozygous mutation will have overt signs of ichthyosis as an adult. Nevertheless, the genotype may be useful to assess the potential carrier status of dogs used for breeding.[3] Given the high prevalence of this mutation in the golden retriever population it would, however, be impractical to exclude all dogs affected with either a heterozygous or a homozygous mutation.[13]

Early studies suggested an autosomal recessive mechanism of inheritance for golden retriever ichthyosis, and this has been confirmed in more recent reports.[7–10] Incomplete penetrance or additional genes may play a role in this disease. Humans affected with autosomal recessive retention ichthyosis can have a *PNPLA1* mutation of the catalytic patatin domain of the protein. Affected individuals are born as collodion babies and later develop generalized severe ichthyosis.[10] In golden retriever ichthyosis, the *PNPLA1* mutation is located in the C-terminal region of the protein presumed to be the lipid-binding site. The mutation may alter protein activity, but the exact nature of the dysfunction is unknown.[10] The variation in the clinical manifestation of ichthyosis in humans and dogs affected with a *PNPLA1* mutation could be explained by the different location of the mutation and altered protein function.

There are several limitations to the design of this study. Firstly, a 1 year telephone follow-up was performed to assess the presence of clinical lesions, which is less optimal than a dermatological examination. This relied on the ability of an owner to interpret the presence of clinical lesions. Secondly, while the clinical onset of ichthyosis in

most dogs occurs prior to 1 year of age, adult onset has been described.[7,9] In this light, our follow-up period of 12 months may have been too short to exclude the recurrence of ichthyosis in some homozygous dogs. Thirdly, while the histopathological lesions sampled from one puppy were consistent with those described for golden retriever ichthyosis, there are significant limitations in having sampled only one affected dog.

In conclusion, we propose that the syndrome colloquially described as "milk crust" by golden retriever breeders is a cornification disorder affecting golden retriever puppies that may represent a transient form of golden retriever ichthyosis. In the present study, the majority of dogs with a homozygous mutation of the *PNLA1* gene demonstrated clinical signs in early puppyhood, but only 25% of these dogs had persistent scale during the first 12 months of life. A gene test for the *PNPLA1* mutation could assist in the detection of carriers and may be used for genetic counselling, but exclusion of all dogs affected with the heterozygous and homozygous mutation from a breeding programme is impractical. Further studies are required to confirm an inter-relationship between this disease and golden retriever ichthyosis.

Acknowledgements

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Résumé

Contexte – Une forme héréditaire récessive d'ichtyose lamellaire est bien reconnue chez le golden retriever. Dans cette race, les jeunes chiots présentent un squamosis de résolution spontanée généralement reconnue par les éleveurs qui utilisent le terme de "croutes de lait" pour décrire ce syndrome.

Hypothèses/Objectifs – Déterminer si les « croûtes de lait » sont une nouvelle anomalie de la kératinisation ou une forme à résolution spontanée de l'ichtyose du golden retriever.

Sujets – Un total de 179 golden retrievers (21mères et 158 chiots) a été examiné.

Méthodes – Un examen dermatologique et une évaluation du génotype de PNPLA1 (patatin-like phospholipase-1) par PCR d'écouvillons buccaux. Des biopsies cutanées d'un chiot atteint ont été évaluées par histopathologie.

Résultats – Quarante-cinq des 158 (8%) des chiots présentaient du squamosis à l'âge de 8 semaines ; 113 des 158 (72%) étaient dermatologiquement normaux. Sur les 144 échantillons analysés, 40 es 144 (28%) des chiots présentaient une mutation homozygote du génotype PNPLA1[pour lesquels, 36 sur 40 (90%) avaient des signent de squamosis], 77 sur 144 (53%) présentaient une mutation hétérozygote et 27 sur 144 (19%) avaient un génotype sauvage normal. Pour six sur 17 (35%) des mères, une mutation homozygote de PNPLA1 a été trouvée, huit sur 17 (47%) présentaient une mutation hétérozygote et trois sur 17 (18%) étaient de type sauvage normal. Les mères avec une mutation homozygote étaient cliniquement indemnes. Un suivi d'un an a révélé que 23 des 28 chiots atteints (82%) de ce syndrome ne présentaient pas de lésions typiques de l'ichtyose. Pour cinq des 28 (18%) chiens, il persistait un squamosis modéré.

Conclusions et importance clinique – Nous supposons que le terme de « croûte de lait » pourrait représenter une forme transitoire de l'ichtyose du golden retriever. Une rémission n'est pas totalement liée au génotype PNPLA1, suggérant que des facteurs inconnus contribuent à l'expression clinique de la maladie.

Resumen

Introducción – se ha reconocido una forma de ictiosis lamelar hereditaria recesiva en perros de raza Golden Retriever. En esta raza, los cachorros presentan una enfermedad descamativa autolimitante que es comúnmente reconocida por los criadores que utilizan el término ´´costra lechosa´´ para describir este síndrome.

Hipótesis/Objetivos – determinar si la enfermedad ´´costra lechosa´´ es un nuevo defecto de queratinización o una enfermedad autolimitante de la forma de ictiosis del Golden Retriever.

Animales – un total de 179 perros de raza Golden Retriever (21 hembras y 158 cachorros) fueron examinados.

Métodos – se realizó examen dermatológico y evaluación del genotipo de la proteína similar a patatina fosfolipasa-1 (PNPLA1) mediante análisis por PCR de hisopos de la mucosa bucal. Biopsias de piel de un cachorro afectado fueron evaluadas para las anormalidades histopatológicas.

Resultados – 45 de 158 (28 %) de los cachorros presentaron descamación a las ocho semanas de edad; 113 178 (72 por ciento) fueron dermatológicamente normales. De 144 muestras analizadas, 40 de 144 (28%) de cachorros demostraron una mutación homocigótica del genotipo PNPLA1 [de los cuales 36 de 40 (90%) tenían signos de descamación], 77 de 144 (53%) demostraron una mutación heterocigótica y 27 de 144 (19%) presentaron fenotipo normal. En seis de las 17 hembras (35%) había una mutación homocigótica del genotipo PNPLA1, 8 de 17 (57%) demostraron una mutación heterocigótica y tres de 17 (18%) presentaron fenotipo normal. Las hembras con una mutación homocigótica no presentan signos clínicos. Tras un año de seguimiento se observó que 23 de 28 (82%) de los cachorros afectados con este síndrome no presentan signos clínicos de ictiosis. En cinco de los 28 (18%) de perros hubo descamación ligera persistente.

Conclusiones e importancia clínica – nuestra hipótesis es que el síndrome clínico conocido como ´´costra lechosa´´ puede representar una forma transitoria de la ictiosis del Golden Retriever. La remisión no está asociada completamente con el genotipo de PNPLA1, lo cual sugiere que hay factores desconocidos que pueden contribuir a la enfermedad clínica.

Zusammenfassung

Hintergrund – Beim Golden Retriever ist eine rezessive vererbte Form einer lamellären Ichthyose gut bekannt. Bei dieser Rasse zeigen junge Welpen eine selbstlimitierende Schuppenbildung, die häufig von Züchtern erkannt wird, die dafür den Ausdruck „Milchkruste" verwenden, um dieses Syndrom zu beschreiben.

Hypothese/Ziele – Das Ziel dieser Studie war es herauszufinden, ob „Milchkruste" eine neue Keratinisierungsstörung darstellt oder ob es sich um eine selbst-limitierende Form der Ichthyose des Golden Retrievers handelt.

Tiere – Insgesamt wurden 179 Golden Retriever (21 Hündinnen und 158 Welpen) untersucht.

Methoden – Es wurde eine dermatologische Untersuchung durchgeführt und der Genotyp der Patatin-like Phospholipase-1 (PNPLA1) mittels PCR Test aus einem Abstrich der Backenschleimhaut bestimmt. Hautbiopsien eines betroffenen Welpen wurden im Hinblick auf histopathologische Veränderungen untersucht.

Ergebnisse – Fünfundvierzig von 158 (28%) Welpen zeigten Schuppenbildung im Alter von 8 Wochen; 113 von 158 (72%) waren dermatologisch normal. Von 144 analysierten Proben, zeigten 40 von 144 (28%) der Welpen eine homozygote Mutation des PNPLA1 Genotyps [von denen 36 von 40 (90%) Anzeichen von Schuppenbildung hatten], 77 von 144 (53%) hatten eine heterozygote Mutation und 27 von 144 (19%) entsprachen dem normalen Wildtyp. Mutterhündinnen mit einer homozygoten Mutation waren klinisch nicht betroffen. Ein Follow-Up nach 1 Jahr zeigte, dass 23 von 28 (82%) der Welpen, die von diesem Syndrom betroffen waren, keine Anzeichen von typischer Ichthyose zeigten. Bei fünf der 28 (18%) Hunde blieb eine milde Schuppenbildung erhalten.

Schlussfolgerungen und klinische Bedeutung – Wir stellen die Hypothese auf, dass das klinische Syndrom, welches als „Milchkruste" bezeichnet wird, eine vorübergehende Form der Golden Retriever Ichthyose darstellt. Eine Remission kann nicht zur Gänze mit dem PNPLA1 Genotyp in Verbindung gebracht werden, was auf unbekannte Faktoren schließen lässt, die zur klinischen Krankheit beitragen.

要約

背景 — 葉状魚鱗癬の劣性遺伝形式はゴールデンレトリーバーにおいてよく認識されている。この犬種において、若い子犬はこの症候群を説明するのに"乳痂"という用語を使う、ブリーダーによってよく認められる自己限定性鱗屑性疾患を示す。

仮説/目的 — "乳痂"が新しい角化性疾患あるいは自己限定型のゴールデンレトリーバー魚鱗癬なのか決定すること。

供与動物 — 全部で179頭のゴールデンレトリーバー(21頭の母犬と158頭の子犬)を検査した。

方法 — 皮膚科学検査および頬粘膜スワブのPCR検査によるpatatin-like phospholipase-1(PNPLA)遺伝型の評価。1頭の罹患した子犬からの皮膚生検の病理組織学的な異常を評価した。

結果 ― 158頭中45頭(28%)の子犬が生後8週間で鱗屑を示し、158頭中113頭(72%)が皮膚科学的に正常であった。解析された144のサンプルの中で、144頭中40頭(28%)の子犬がPNPLA1遺伝型のホモ接合の変異を示しており[その中で、40頭中36頭(90%)は鱗屑の症状を示していた]、144頭中77頭(53%)がヘテロ接合の変異を示し、144頭中27頭(19%)が正常な野生型であった。17頭中6頭(35%)の母犬において、PNPLA1遺伝型のホモ接合の変異が発見され、17頭中の8頭(47%)がヘテロ接合の変異を示し、17頭中3頭(18%)が正常な野生型であった。ホモ接合の変異を示す母犬は臨床的に無症状であった。1年の追跡で、この疾患に罹患した28頭中23頭(82%)の子犬に魚鱗癬の典型的な症状は発生しなかった。28頭中5頭(18%)のイヌでは、軽度の鱗屑が持続していた。
結論および臨床的な重要性 ― 筆者らは"乳痂"と呼ばれていた臨床的な症候群はゴールデンレトリーバー魚鱗癬の一過性の形態を示す可能性があると仮説した。寛解はPNPLA1遺伝型と完全には関連しておらず、知られていない因子が臨床的な疾患に関係している可能性を示唆している。

摘要
背景 ― 众所周知,金毛巡回犬隐性遗传层状鱼鳞病。这个品种的年轻幼犬出现自限性脱屑病时,经常能被繁殖者识别出来,他们用"奶痂"来描述这种综合征。
假设/目的 ― 确定"奶痂"是种新的角化病,还是金毛巡回犬自限性鱼鳞病。
动物 ― 179只金毛巡回犬(21只繁殖母犬以及158只幼犬)参与试验。
方法 ― 皮肤病学检查以及取口腔黏膜拭子,通过PCR实验评估马铃薯糖蛋白样磷脂酶-1(PNPLA1)基因型。一只患病幼犬的皮肤活检,组织病理评估为异常。
结果 ― 158只中的45只(28%)幼犬在八周龄时出现皮屑;158只中的113只(72%)皮肤正常。144份分析样本,144只中的40只(28%)幼犬,为纯合子PNPLA1基因型突变[40只中的36只(90%)有皮屑症状],144只中的77只(53%)杂合子突变,144只中的27只(19%)为正常野生型。17只中的6只(35%)繁殖母犬为纯合子PNPLA1基因型突变,17只中的8只(47%)为杂合子突变,17只中的3只(18%)为正常野生型。纯合子突变的繁殖母犬没有临床症状。1年的追访显示,28只中的23只(82%)患病幼犬没有继续出现典型的鱼鳞病症状。28只中的5只(18%)仍持续轻度脱屑。
总结与临床意义 ― 我们假设"奶痂"是一过性金毛巡回犬鱼鳞病的临床症状。症状的缓解与PNPLA1基因型没有完全关联,这暗示该临床表现源于未知因素。