Symmetrical Lupoid Onychodystrophy in Dogs: A Retrospective Analysis of 18 Cases (1989-1993)

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A unique, symmetrical onychodystrophy is described in 18 dogs. A rather sudden onset of onychomadesis is followed by chronic onychodystrophy affecting all claws. Pain and lameness are recognized in half of the patients, but the dogs are healthy otherwise. Histopathologically, this disorder is characterized by hydropic and lichenoid interface dermatitis. Nine dogs were treated with a commercial, fatty-acid supplement and had good-to-excellent responses. Due to the clinicopathological characteristics of this disorder, the authors propose the name "symmetrical lupoid onychodystrophy. "

Introduction

Claw disorders of the dog are the focus of very few publications in veterinary medicine. (Ref 1-8) This paucity of published information is, in part, due to the fact that claw disorders rarely are encountered as the sole manifestation of dermatologic disease in dogs. (Ref 8) In addition, the definitive diagnosis of claw disease often requires the surgical amputation of the third phalanx of an affected digit, so that the claw bed can be examined histologically. (Ref 8) Many owners, understandably, are hesitant to have this done to their pets.

In a recently published retrospective study of 196 cases of canine claw disorders, (ref 8), seven dogs had an apparently previously unreported symmetrical onychodystrophy with histopathological findings resembling those of lupus erythematosus. The purpose of this paper is to detail the clinicopathological features of this unique lupoid onychodystrophy in 18 dogs diagnosed at the College of Veterinary Medicine (CVM) at Cornell University.

Materials and Methods

From January 1989 to February 1993, lupoid onychodystrophy was diagnosed in 18 dogs at the CVM. Diagnosis was based on clinical and biopsy findings in all cases. Ten cases were examined at the CVM, and eight cases were diagnosed based upon claw biopsies submitted to the diagnostic

laboratory by private practitioners. A retrospective analysis of these 18 cases was conducted by reviewing the medical records of the 10 cases seen at the CVM and sending a questionnaire to each veterinarian who had submitted biopsies on the other eight cases. In both situations, patient records were scrutinized for many parameters including age, breed, sex, age of onset of clinical signs, duration of disease, nutrition, previous and concurrent illnesses, clinical appearance of the diseased claws, previous and concurrent therapies, and laboratory examinations performed. An attempt was made to contact the owners of all 18 dogs for a current status report.

Biopsies from 16 dogs were reviewed. All specimens were fixed in 10% neutral buffered formalin. Cut tissues were decalcified in 50% formic acid solution buffered with 5% sodium citrate. Decalcified specimens then were embedded in paraffin, sectioned at 6 µ and stained with hematoxylin and eosin (H&E) stain and Grocott-Gomori methenamine silver nitrate stain. For two of the dogs examined at the CVM (case nos. 12, 16), biopsies had been submitted to other laboratories, and slides were not available for review.

All biopsy specimens (of the distal portion of the third phalanx and associated claw) received at the CVM were sectioned at 4 µ and processed for direct immunofluorescence testing. (Ref 9) Sections were deparaffinized and treated with 0. 1% trypsin and 0. 1% calcium chloride (pH 7.8) for 1 hr at 37° C. Rabbit anticanine immunoglobulin G (IgG), immunoglobulin A (IgA), immunoglobutin M (IgM), complement factor 3 (C3), and polyvalent immunoglobulin (1g) were used. (Footnote a) After incubation with these reagents at a standard concentration of 50 µg antibody per ml, sections were washed and incubated with fluorescein labeled goat-antirabbit immunoglobulins. For negative controls, nonimmune rabbit serum was substituted for the primary antibody. Normal plasma cells in the inflammatory infiltrate served as positive controls. Sections were examined with a Leitz-Ortholux fluorescence microscope at a wave length of 490 to 520 nm.

Fifteen digits also were obtained from 15 different dogs to be used as controls for direct immunofluorescence testing. Ten of the 15 dogs had been submitted to the necropsy service at the CVM in 1993. These dogs included six males and four females of various breeds, ranging in age from one to 15 years. None of these dogs had dermatologic disease at the time of necropsy. The other five were selected from cases diagnosed as having infectious claw diseases which were submitted to the surgical pathology service in 1992 and

1993. These five cases included three males and two females of various breeds, ranging in age from five to seven years.

Results
The following breeds were represented: German shepherd dog (n=4), boxer (n=2), greyhound (n=2), Doberman pinscher (n= 1), rottweiler (n= 1), bearded collie (n=l), Weimaraner (n=l), Drahthaar (n=l), Irish setter (n=l), Great Dane (n= 1), and mixed-breed dog (n=3) [Table I]. German shepherd dogs may be predisposed as they accounted for 22.2% of the cases, but only 4% of the CVM hospital population (relative risk of 5.6). The dogs varied from three to eight years of age and included 12 females and six males. The claw disorder had been present for one to eight months prior to biopsy. All dogs were being fed a completely nutritious, commercial dog food and had received no drugs or vaccinations within four weeks of the onset of claw disease.

All dogs were presented for claw disease and were healthy otherwise. Typically, owners first noticed a single, abnormal claw on two or more paws. However, within a short period of time (two to nine weeks), every claw on all four paws was affected. In half of the cases, the condition was painful, being associated with varying degrees of lameness and discomfort on palpation. The other half of the dogs seemed to be unaware of their disease.

The initial clinical sign usually was a separation at the claw bed and sloughing (i.e., onychomadesis) of one or more claws. Particularly observant owners reported a "brown line" or "bruising" at the claw bed prior to sloughing. Such changes probably represented subungual hemorrhage. After claws had been sloughed, regrowth was characterized by short, misshapen, dry, soft, brittle, often crumbly, and discolored claws. In four dogs there was malodorous, hemorrhagicopurulent discharge from the claw bed, presumably due to secondary bacterial paronychia.

Hemograms, urinalyses, and serum chemistry panels were normal in all 18 dogs. Antinuclear antibody (ANA) tests (ref 9) were positive at a low titer (1:20) in only two (case nos. 11, 17) of 12 dogs examined. Bacterial cultures and sensitivities were performed on samples from five dogs and grew various combinations of Escherichia coli (E. coli), Corynebacterium sp., Bacillus sp., Streptococcus sp., Enterococcus sp., and Staphylococcus intermedius sensitive to various antibiotics. Fungal cultures also were

performed on samples from five dogs and were either negative (n=3) or grew Cladosporium sp. (n= 1) or Aspergillus sp. (n= 1).

Table 1. Clinical and Therapeutical Data in 18 Dogs With Lupoid Onychodystrophy

Case	Breed	Age (yr)	Sex	Duration of Disease (mos)	Therapy	Follow Up (mos)
1	Boxer	3	F	3	DVM Derm Caps	36
2	Mixed-breed	7	F	4	Unknown	0
3	Mixed-breed	3.5	M	2	Unknown	0
4	Doberman pinscher	4.5	F	5	Unknown	0
5	Boxer	2	FS	6	Unknown	0
6	German shepherd	7	F	3	Prednisone	13
7	Mixed-breed	8	F	6	DVM Derm Caps	15
8	Rottweiler	3	M	2	DVM Derm Caps	9
9	German shepherd	7	F	1	DVM Derm Caps	11
10	Greyhound	6	MC	6	DVM Derm Caps	4
11	Greyhound	6	MC	2	DMV Derm Caps	24
12	German shepherd	4.5	FS	6	None	24
13	Bearded collie	7	FS	3	DVM Derm Caps	18
14	Weimaraner	4.5	M	4	DVM Derm Caps	18
15	Drahthaar	4	FS	4	Prednisone	18
16	German shepherd	8	MC	8	None	18
17	Irish setter	6	FS	4	Vitamin E	36
18	Great Dane	7.5	F	3	DVM Derm Caps	5

F = female; M = male; FS = spayed female; MC = castrated male

All dogs had received similar previous therapies including removal of loose claws, daily paw soaks in chlorhexidine or povidone-iodine solutions, and at

least one of the following oral antibiotics: amoxicillin, amoxicillin clavulanate, chloramphenicol, erythromycin, enrofloxacin, cephalexin, lincomycin, and sulfadimethoxineormetoprim. Three dogs were treated with oral griseofulvin. Little or no beneficial response was seen with any treatment.

The most prominent histopathological lesions were distributed along the dorsal aspect of the claw, most consistently along the coronary band, and they frequently extended over the dorsal ridge and lateral walls, sometimes in a discontinuous fashion. Involvement of the ventral aspect of the claw was less frequent and always less severe than that seen dorsally. The most consistently and most severely affected area was the dermoepidermal interface. A list of the histologic findings with their respective incidence and severity appears in Table 2.

Table 2. Histopathological Findings in Claw Biopsies from 16 Dogs with Symmetrical Lupoid Oychodystrophy

Tissue	Abnormality	Number/% of cases	Grade*
Epidermis	Apoptosis of basal cells	15/93.8	1-2
	Lymphocytic exocytosis	15/93.8	1-3
	Hydropic degeneration of basal cells	13/81.2	1-3
	Spongiosis	11/68.8	1-3
	Erythrocytic exocytosis	9/56.2	1-3
	Neutrophilic exocytosis	9/56.2	1-2
	Squamatization of basilar layer	7/43.8	2-3
	Ulceration	7/43.8	1-4
	Intracorneal microabscesses	6/37.5	1-4
	Atrophy	6/37.5	1-2
Dermis	Lymphocytes	15/93.8	1-3
	Plasma cells	14/87.5	1-4
	Lichenoid infiltrate	14/87.5	1-3
	Pigmentary incontinence	11/68.8	1-4
	Edema	11/68.8	1-2
	Hemorrhage	9/56.2	1-3
	Mucinosis	8/50	1-3
	Fibroplasia	8/50	1-3

	Macrophages	8/50	1-2
	Neutrophils	7/43	1-4
	Vasodilatation	6/37.5	1-2
	Eosinophils	1/6.2	2
	Civatte body	1/6.2	1
Bone	Osteolysis	8/50	1-3
	Osteogenesis	4/25	1-2
	Osteomyelitis	1/6.2	3

* 1 = Mild; 2 = Moderate; 3 = Marked; 4 = Severe

Epidermal ulceration and intracorneal pustules were present in less than half of the cases. Ulcerations always were dorsal and most of the time distal, with granulation tissue proliferating over the exposed dermis. There was mild-to-moderate neutrophilic exocytosis at the margins of the ulcers. In three cases, intraepidermal neutrophils were present without any ulceration or pustule in the plane of the section.

The most frequent and consistent changes were mild-to-marked lymphocytic exocytosis in the lower third of the epidermis, mild-to-moderate apoptosis of basal epidermal cells, and mild-to-marked hydropic degeneration of basal epidermal cells . In every case, at least two of these three changes were present simultaneously.Less frequently, these were associated with mild-to-marked spongiosis and mild-to-marked erythrocytic exocytosis. Occasionally, an apoptotic keratinocyte was present above the basal cell layer. In slightly more than half of the cases there was mild-to- moderate atrophy of the epidermis over the areas of dermal inflammation or areas of basal hydropic degeneration, or both, characterized by a thinning of all epidermal layers and sometimes absence of the basal layer with direct contact of cells from the stratum spinosurn to the basement membrane zone (i.e., squarnatization).

The dermal changes were inflammatory, ranging in chronicity from edema and hemorrhage to early fibrosis. In most cases, there was a mild-to-severe, mixed interface, inflammatory infiltrate forming a band parallel to the basement membrane zone (i.e., a lichenoid pattern) with occasional deeper, perivascular, cellular aggregates. In one case, no lichenoid pattern was discernable, and a few perivascular aggregates of inflammatory cells were present. In another case, dermal inflammatory cells were absent, and the changes consisted mainly of hydropic degeneration of the basal epidermal

layer with mild, petechial hemorrhages in the underlying dermis. Components of the inflammatory infiltrate were primarily lymphocytes and plasma cells present in mild-to-marked and mild-to-severe numbers, respectively. Lymphocytes were more numerous in the superficial dermis, and plasma cells were more abundant deeper in the band, sometimes concentrated around blood vessels. Macrophages rarely were found, except as distinctly visible subepidermal melanophages when their cytoplasms were packed with phagocytized melanin. Pigmentary incontinence commonly was present, and the severity ranged from mild to severe. The severity did not correlate well with that of basal cell hydropic degeneration, lichenoid inflammatory infiltrate. or dermal fibroplasia. A mild-to-severe neutrophilic component was added to the inflammatory infiltrate in some cases, usually in conjunction with epidermal ulceration and intraepidermal microabscesses.

Mild-to-moderate edema, frequently associated with mucinosis, was present in most cases, as were mild-to-marked multifocal hemorrhages. Mild-to-marked fibroplasia was found in the deep dermis, often in close association with the periosteum and occasionally extended superficially to blend with the lichenoid inflammatory infiltrate. Vasculitis was not a feature of the disease. In less than half of the cases, mild-to-moderately dilated capillaries were present within the superficial dermis.

The bone forming the ungual crest usually was normal. In a few cases there were features indicative of active, osteoclastic osteolysis at the margins of the bone, as well as irregular bands of periosteal proliferation distally and occasional osseous metaplasia of the deep dermis around the coronary band at the base of the claw fold.

The pathology reports on the biopsies from the two dogs (case nos. 12, 16) sent to other laboratories were consistent with the described findings.

The incidence, intensity, and patterns of fluorescence in the specimens processed for direct immunofluorescence testing were comparable between affected claws and those from control animals. Antibodies against IgG and polyvalent Ig were present focally in the intercellular spaces of involved epidermis in five of 16 (3 1.2%) affected claws and five of 15 (33.3%) controls. In addition, the same antibodies were present in a fine, fibrillar linear band at the dermoepidermal junction in five of 16 (31.2%) affected claws and three of 15 (20.0%) controls. These linear bands of immunofluorescence always were distant from the site of inflammation,

restricted to portions of the claw fold, and did not have the granularity of the typical lupus band. (Ref 9, 10) These bands are artifacts referred to as fibrillar pseudobands. (Ref 9, 10)

Twelve of the 18 dogs received treatment after biopsy results were reported [Table 1]. Nine of the 12 received a commercial omega-3/omega-6 fatty-acid product (Footnote b) according to the manufacturer's recommendations (I capsule per 9.1 kg body weight q 24 hrs). All nine of these dogs showed a good-to-excellent response to therapy, with clinical improvement visible within three to four months and maximum improvement achieved within one year. In two dogs (case nos. 13, 14), treatment was stopped, the claw disease relapsed, and remission was achieved a second time with the fatty-acid supplement.

Three other dogs were treated with prednisone (2.2 mg/kg body weight q 24 hrs for 10 days, then alternate-morning therapy) or vitamin E (400 mg q 12 hrs) by mouth. Responses were as described for the fatty-acid supplement. Two dogs (case nos. 12, 16) received no treatment and continued to have claw disease 1.5 and two years, respectively, following biopsy diagnosis. Four dogs were lost to follow-up.

Discussion

The claw disorder described herein apparently has been recognized only recently. (Ref 8) It seems highly unlikely that this onychodystrophy is a "new disease." Rather, its recent recognition probably is attributable to the increasing interest in claw diseases and the increasing willingness of veterinarians and owners to submit the type of biopsy (i.e., partial amputation) which is required to permit a diagnosis. This disorder probably is one of potentially several disorders that are buried in the frustrating group often referred to as "idiopathic onychodystrophy." (Ref 1, 2, 6-8)

The suggestive clinical feature of the onychodystrophy reported here is the rather sudden onset of symmetrical claw disease, characterized initially by onychomadesis and subsequently by onychodystrophy (i.e., onychorrhexis, onychomalacia, onycholysis) in a patient that typically is healthy otherwise. Pain and lameness are problems in half of the cases. The major differential diagnoses include immune-mediated diseases (i.e., pemphigus, lupus erythematosus, vasculitis), endocrinopathies, and keratinization abnormalities. (Ref 8)

Histopathologically, this claw disorder may be characterized as a hydropic and lichenoid interface dermatitis. (Ref 11-13) This type of inflammatory response usually is associated with various uncommon-to-rare dermatoses of presumed immune-mediated origin. From a histopathological perspective, this claw disorder most closely resembles lupus erythematosus. (Ref 11-13) However, the focal thickening and smudging of the basement membrane zone that often are seen with lupus erythernatosus were not seen in these cases. Furthermore, direct immunofluorescence testing revealed the absence of immunoglobulin or complement, or both, deposited in a granular pattern along the basement membrane zone of lesional tissue. (Ref 9, 10, 12, 15)

Direct immunofluorescence testing revealed the deposition of IgG in two anatomical sites. One of these sites was within the intercellular spaces of involved claw epidermis. As this IgG deposition was focal, associated with spongiosis, and was not accompanied by the histopathoiogical changes of pemphigus (i.e., acantholysis), it must be considered as nondiagnostic and as resulting from the percolation of immunoglobulins through an edematous epidermis, as has been described for numerous dermatoses. (Ref 9-10, 12, 14-15)

The other site of IgG deposition was at the dermoepidermal junction in nonlesional tissue. This deposition occurred as fibrillar pseudobands. (Ref 9-10) Fibrillar pseudobands occur in skin as an ill-defined, faint glow of fluorescence at the dermoepidermal junction where the dermis is pressed against the dermoepidermal junction so that the auto fluorescence and nonspecific fluorescence of elastic tissue and other components mimic a lupus band. The nondiagnostic nature of the direct immunofluorescence test findings is confirmed further, of course, by the finding of identical patterns and frequencies of IgG deposition in claws from normal dogs and those with infectious claw bed disease.

The question of whether or not to treat this unique onychodystrophy depends upon the discomfort of the patient and the personal preference of the owner. It would appear that the disorder is unlikely to resolve spontaneously, due to the following observations:

- Dogs were affected for up to eight months prior to diagnosis
- Two untreated dogs (that were asymptomatic, and owners declined therapy) continued to have abnormal claws for over two years

- Two dogs rapidly relapsed after treatment was stopped following clinical resolution.

Because of the histological resemblance of this onychodystrophy to lupus erythematosus, and the authors' successful experience treating mild-to-moderate cases of canine discoid lupus erythernatosus with an omega-3/omega- 6 fatty-acid supplement, the majority of the dogs were treated in this manner, with good-to-excellent clinical responses and no adverse reactions. The authors were reluctant to begin with more aggressive chemotherapy (such as large doses of glucocorticoids, azathloprine, or chlorambucil) because of the localized nature of the disease and the good health of the patients.

The etiology of this condition is unknown. The authors could not incriminate diet, prior drug exposure, nor prior disease. Also, there was no clinical evidence that the disorder was infectious or contagious, and no description of a similar onychodystrophy could be found in humans. Although nail involvement does occur in humans with lupus erythernatosus (discoid or systemic), dermatomyositis, erythema multiforme, and lichen planus-diseases which also are characterized by hydropic and lichenoid interface dermatitis of the nail bed-the clinicopathological features of the conditions are not consistent with those seen in these dogs. (Ref 16-17)

The authors propose the name "symmetrical lupoid onychodystrophy" for this newly recognized, canine claw disorder. The name embodies the clinical and histopathological "essence" of this disease as it currently is understood. The key clinical features are symmetrical and dystrophic and are restricted to the claws. The key histopathological features resemble those of lupus erythematosus. "Lupoid" is an adjective used in human medicine which is derived from "lupus," and the suffix, "-oid," meaning like that condition. Precedence certainly exists for using such an adjective in veterinary dermatology, such as in the newly described genodermatosis of German shorthaired pointers, "hereditary lupoid dermatosis."" wherein the "lupoid" also refers to the histopathological resemblance to lupus erythematosus.

Footnotes

- Organon Teknika. Cappel Laboratories, Malvern, PA
- DVM Derm Caps. DVM Pharmaceuticals. Miami. FL

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