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Clinicopathological Features, Risk Factors and Predispositions, and Response to Treatment of Eosinophilic Oral Disease in 24 Dogs (2000-2016)

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Abstract

The objectives of this study were to retrospectively describe clinicopathological features of eosinophilic oral disease in dogs, to identify possible risk factors or predispositions to the condition, and to report overall treatment response. Canine medical records from a veterinary teaching hospital and private referral practice over a 17-year period were reviewed for a diagnosis of eosinophilic oral disease. Twenty-four dogs with 26 lesions met the inclusion criteria. Patient mean age and body weight were 6.8 (3.8) years and 13.4 kg, respectively. Fifteen breeds were represented including Cavalier King Charles spaniel (16.7%), Labrador retriever (12.5%), and West Highland white terrier (12.5%). Eosinophilic lesions were found in the palate (65.4%), tongue (26.9%), and other oral locations (7.7%). Median follow-up time was 5 months. Analysis revealed statistically significant associations between lesion location and body weight (palatal and tongue lesions were more likely in smaller dogs, whereas lesions in the other category [lip or mucosa] were more likely in larger dogs). There was a correlation in lesion location and resolution (all dogs with palatal lesions became asymptomatic at their last recheck), and resolution and the use of antibiotics plus prednisone (greater likelihood of resolution without the use of this combination). Seventy percent of asymptomatic dogs resolved without medication or with allergen therapy alone, suggesting that asymptomatic dogs may respond well to conservative management. No associations were found between lesion location and breed, signalment and response to therapy, lesion resolution and the use of glucocorticoids, or significance of peripheral eosinophilia.

Keywords

eosinophilic disease, eosinophilic granuloma, eosinophilic granuloma complex, eosinophilic stomatitis, eosinophilic palatitis, oral, dog, canine, veterinary dentistry

Introduction

Eosinophilic granuloma complex is a general term used to encompass a variety of cutaneous, mucocutaneous, and oral cavity lesions in the dog and cat.[1,2] When referenced in dogs, the disease is typically called eosinophilic stomatitis or eosinophilic granuloma.[3,4] There is unfortunately no formalization of these terms which are used interchangeably in the literature, regardless of the appearance or location of the lesions. These conditions are considered to be rare in the dog and are typically described as nodules or plaques on the soft palate or vegetative masses on the tongue. Less frequently, lesions are reported on the ventral abdomen, prepuce, digits, flanks, cheeks, external ear canal, nasal plane, and trachea.[3] There appears to be no age or sex predilection, although the disease has been reported more commonly in dogs less than 3 years of age.[2,3] Studies indicate a possible genetic component in Siberian huskies, greyhounds, and Cavalier King Charles spaniels.[3,5]

The objectives of the present study were to retrospectively describe clinicopathological features of eosinophilic oral disease in dogs, to identify possible risk factors or predispositions to the condition, and to report overall response to treatment. Analyses of individual lesions and locations were performed to determine whether the various lesions responded differently to

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medical management and whether certain lesions were more commonly found in specific breeds. It was hoped that this retrospective analysis can help provide insight into a disorder that is seen in clinical practice but not well represented or described with consistency within the current literature.

Materials and Methods

Medical records from Ryan Veterinary Hospital of the University of Pennsylvania and Red Bank Veterinary Hospital were searched for dogs that had a diagnosis of eosinophilic oral disease over a 17-year period (2000-2016). All records were reviewed for a confirmed diagnosis via histopathology. A complete medical record with at least one follow-up examination and biopsy confirmation was required for dogs to be included in the study. Twenty-four dogs with a total of 26 lesions met the inclusion criteria.

The following data were assessed: breed, gender, neuter status, age, weight, lesion location, history of allergic symptoms, clinical signs at the time of presentation, presence of peripheral eosinophilia, histopathological report and diagnosis, and treatment and response to treatment. Lesion locations were grouped into 3 categories: tongue (including sublingual), palate (combining both hard and soft palate), and other (encompassing lesions on the labial and buccal mucosa and lip).

The clinical signs of individual dogs at initial presentation were compared with those at the final recheck examination. Improvement was defined in 2 ways and assigned a score of 0, 1, or 2. The first scoring system for improvement was based on clinical symptoms combined with the degree of lesion resolution at the final recheck examination (CS/LR = clinical symptoms/lesion resolution). The second scoring system was based on clinical symptoms combined with whether or not the dog was off medication at its final recheck examination (CS/M = clinical symptoms/medications). The physical presence of a lesion did not factor into this category.

The scores for the CS/LR were defined as follows:

- 0: Little to no improvement in the lesions or clinical signs; the lesions were still present or had progressed, and the dog had similar or worsened clinical signs.
- 1: Moderate improvement in the lesions and/or clinical signs; the lesions were still present but stable (in cases with multiple lesions, at least one lesion was still detectable), or the dog was symptomatic but stable.
- 2: Complete resolution of the lesions and clinical signs; all lesions had resolved, and the dog was asymptomatic.

The scores for the CS/M were defined as follows:

- 0: The dog was symptomatic and on medication.
- 1: The dog was asymptomatic but still on medication.
- 2: The dog was asymptomatic and no longer on medication.

The treatments performed were categorized as follows:

- Oral prednisone.
- Topical therapy (including bacitracin zinc/neomycin sulfate/polymyxin B sulfate ophthalmic ointment, silver sulfadiazine cream, mupirocin ointment, antiseptic wipes, and antibacterial or anti-inflammatory gel).
- Antibiotics (amoxicillin, amoxicillin trihydrate/clavulanate potassium, enrofloxacin, clindamycin, doxycycline, cefpodoxime, and tetracycline).
- Allergic treatment (flea prevention, novel protein or hypoallergenic diet, and antihistamines).
- Excisional biopsy or laser excision.
- Other (oral antiviral, vitamin E, allergy shots, antiparasitic treatment, and change in food bowl).

When looking at extended medical management of dogs, allergic treatments and antiparasitic treatment were not taken into consideration.

The clinical signs were categorized as follows:

- Asymptomatic or incidental finding.
- Oral signs (reluctance to open mouth, jaw quivering, chattering, difficulty chewing or swallowing, pruritus or pawing at face, dropping food, oral bleeding, halitosis, nasal congestion, sneezing, or coughing).
- Gastrointestinal signs (weight loss, lip smacking/nausea, vomiting, not eating or drinking, decreased appetite, change in food or toy preference).
- Other (lethargy, decreased grooming).

Descriptive statistics were calculated. Normally distributed continuous variables were reported as a mean (standard deviation [SD]), while those that were not normally distributed were reported as a median and range. Categorical data were expressed as frequencies and proportions. The Fisher exact test was used to identify associations between categorical variables. The Wilcoxon rank-sum test was used to identify associations between categorical variables and non-normally distributed continuous variables. The Student t test was used to identify associations between categorical variables and normally distributed continuous variables. All tests were 2-tailed, and a $P < .05$ was considered statistically significant. STATA 13 was used to perform statistical analysis.

Results

Medical record evaluation revealed 36 dogs with eosinophilic oral disease, of which 24 met the criteria for inclusion in this study. The most common reasons for exclusion from the study were a lack of histopathology or incomplete medical records.

The mean age of the dogs at the time of diagnosis or biopsy was 6.8 (3.8) years. There was a median follow-up time of 5 months (range: 0.5-115 months). The median body weight was 13.4 kg (range: 3.8-73 kg). There were 13 (54.2%) male (10 neutered and 2 intact) and 11 (45.8%) female dogs (10 spayed and 1 intact). Fifteen dog breeds were represented including Cavalier King Charles spaniel (n = 4; 16.7%), Labrador retriever (n = 3; 12.5%), West Highland white terrier

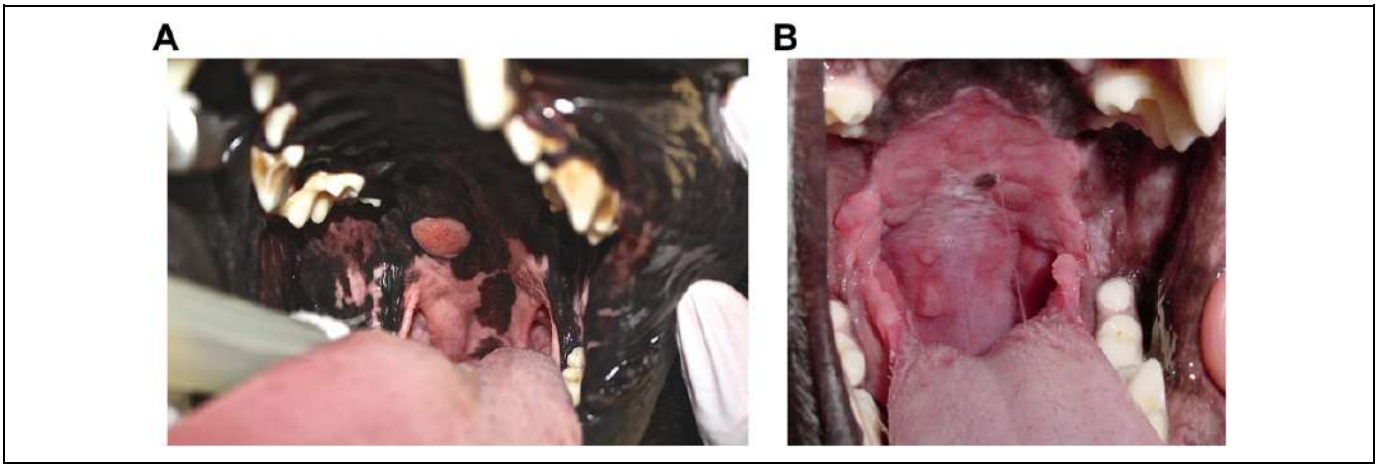

Figure 1. (A) Solitary eosinophilic granuloma on the soft palate of a Labrador retriever. (B) Diffuse eosinophilic palatitis of the soft palate in a whippet.

(n = 3; 12.5%), pug (n = 2; 8.3%), German shepherd (n = 2; 8.3%), and 1 of each of the following: Doberman pinscher, Great Dane, greyhound, Havanese, mixed breed, Portuguese water dog, Pekingese, Staffordshire bull terrier, shih tzu, and whippet. All patients in this study were pure breed dogs except for one mixed breed.

Eosinophilic lesions were found in the following locations: palate (n = 17; 65.4%) (Figure 1), tongue (n = 7; 26.9%), and other location (n = 2; 7.7%). Two dogs had lesions in multiple locations. Ten dogs presented for the lesion and were asymptomatic at presentation, 13 dogs presented for oral signs, 8 dogs had gastrointestinal signs, and 2 dogs were categorized as other. Blood test results prior to initiation of treatment were available in 22 dogs. Of these, 3 showed peripheral eosinophilia. Patient records showed 7 (29.2%) dogs that either had a history of allergies or were diagnosed with allergies at the time of presentation. Seven (29.2%) dogs appeared to have lesions that waxed and waned. One tongue lesion, 5 palatal lesions, and 1 lesion listed as other were reported to wax and wane.

The signalment of the dogs and lesion locations are summarized in Table 1. The only statistically significant ($P = .0367$) correlation noted was between lesion location and body weight. Lesions in the other category (lip or mucosa) were significantly more likely found in dogs with a median body weight of 52.1 kg, whereas lesions on the tongue or palate were significantly more likely present in dogs with a median body weight of 11.4 kg. Despite all 4 Cavalier King Charles spaniels having palatal lesions, no statistically significant association was noted between dog breed and lesion location.

Lesion resolution took place in 83.3% (n = 5) of dogs with tongue lesions, in 64.7% (n = 11) of dogs with palatal lesions, and in 50% (n = 1) of dogs with lesions listed as other. One hundred percent of dogs with lesions on the palate were asymptomatic at the time of their final follow-up examination, but none of the lesion locations showed a significant association between outcome and location when either improvement scale was used. Also, there was no association between the presence of single or multiple lesions and their tendency to wax and wane.

Twelve (50%) dogs were treated with a single therapy, and 12 (50%) dogs were treated with multimodal therapy. For all treatments combined, 11 (45.8%) dogs were treated with prednisone, 7 (29.2%) dogs with topical therapy, 4 (16.7%) with amoxicillin trihydrate/clavulanate potassium, 7 (29.2%) dogs with other antibiotics, 9 (37.5%) dogs with allergic treatments, 5 (20.8%) dogs with excisional biopsy or laser excision, and 10 (41.7%) dogs had other treatments.

Seventeen (71.4%) dogs showed complete resolution of the lesions and clinical signs (CS/LR score of 2) at the final recheck examination. Sixteen (66.7%) dogs were asymptomatic and no longer on medication at the final recheck examination (CS/M score of 2), while 7 (29.2%) dogs were asymptomatic but still on medication (CS/M score of 1). One (4.2%) dog was clinically symptomatic and on medication at the final recheck examination (CS/M score of 0). Combined CS/M scores of 1 and 0 indicated that 8 (33.3%) dogs were still on medication at the time of the last recheck examination. These dogs were considered to be in need of extended medical management. Table 2 provides a description of each dog and its response to treatment.

Because of the frequent use of prednisone or antibiotics as a treatment modality, the Fisher exact test was performed to determine whether either influenced the clinical outcome. There was no statistical significance with regard to lesion resolution (CS/LR) noted when comparing dogs on prednisone without antibiotics ($P = .341$) or dogs on antibiotics without prednisone ($P = .597$). Six dogs were on both prednisone and an antibiotic, while 18 dogs were not on this combination. When comparing dogs with CS/LR scores of 2 (complete resolution of clinical signs and lesions), 33.3% (n = 2) were on both prednisone and antibiotics compared to 83.3% (n = 15) that were not on this combination. This was shown to be statistically significant ($P = .038$). Twenty-nine percent (n = 7) of the dogs had a history of allergies (including presumed or verified diagnoses). Treatment for these dogs included

Table 1. Signalment, Lesion Location, and Presence of Concurrent Disease in 24 Dogs With Eosinophilic Oral Disease.

Dog	Breed	Age at Biopsy (year)	Weight (kg)	Lesion Location	Concurrent Disease
1	PUGS	6.6	7.8	Hard palate	
2	PEKS	11.7	9.6	Soft palate	
3	SHIZ	10.3	9.4	Sublingual	
4	LABR	10.2	25.7	Soft palate	
5	PUGS	7.4	11.4	Soft palate	
6	WHWT	14.4	10.2	Tongue	
7	GERM	4.1	30.6	Soft palate	
8	LABR	2.3	49.8	Lip	Eosinophilic bronchopneumopathy
9	CKCS	7	7.6	Hard palate	
10	LABR	11.3	30.8	Tongue	
11	DOBE	3.9	32.8	Tongue, sublingual	
12	GERM	7.6	33.3	Soft palate	
13	STBU	7.8	26	Tongue	
14	CKCS	4.8	15.3	Soft palate	
15	WHIP	2.5	11.4	Soft palate	
16	WHWT	0.7	7.7	Hard palate	
17	CKCS	7.1	8.2	Soft palate	
18	MIXB	3.1	40	Soft palate	
19	WHWT	12.4	9.3	Soft palate	
20	CKCS	3.5	3.8	Soft palate	
21	POWD	5.3	25.1	Soft palate	
22	GREY	11.3	54.4	Soft palate, buccal mucosa	
23	GRDA	2.2	73	Sublingual	
24	HAVE	5.3	6.2	Soft palate	

Abbreviations: CKCS, Cavalier King Charles spaniel; DOBE, Doberman pinscher; GERM, German shepherd; GRDA, Great Dane; GREY, greyhound; HAVE, Havanese; LABR, Labrador retriever; MIXB, mixed breed; PEKS, Pekingese; POWD, Portuguese water dog; PUGS, pug; SHIZ, shih tzu; STBU, Staffordshire bull terrier; WHIP, whippet; WHWT, West Highland white terrier.

Table 2. Treatment Performed and Outcome Scores Calculated in 24 Dogs With Eosinophilic Oral Disease.[a,b]

Dog	Treatment	CS/LR score	CS/M score
1	Hypoallergenic prescription diet and antihistamines	2	2
2	Excisional biopsy	2	2
3	Prednisone and cefpodoxime proxetil	2	1
4	Tetracycline, prednisone, vitamin E, clindamycin, flea prevention, diphenhydramine, loratadine	1	2
5	None	1	2
6	Amoxicillin trihydrate/clavulanate potassium	2	2
7	Prednisone	2	2
8	Prednisone	2	1
9	Amoxicillin trihydrate/clavulanate potassium, clindamycin	2	2
10	1-tetradecanol complex, oral chlorhexidine gel, oral zinc ascorbate gel, clindamycin	2	2
11	Excisional biopsy, carprofen, prednisone	2	2
12	Excisional biopsy	2	2
13	Clindamycin, amoxicillin trihydrate/clavulanate potassium, carprofen, prednisone	0	0
14	Prednisone, doxycycline, tramadol, famotidine, cetirizine, chlorhexidine oral gel, hypoallergenic prescription diet	1	1
15	Prednisone, hypoallergenic prescription diet	2	1
16	Prednisone, amoxicillin trihydrate/clavulanate potassium, chlorhexidine oral rinse	1	1
17	Carprofen, tramadol, chlorhexidine oral gel, zinc ascorbate oral gel, topical chlorhexidine pads, flea prevention, fluconazole, pyriproxyfen spray, nitenpyram, fipronil/cyphenothrin	2	2
18	Prednisone	1	1
19	Antihistamine, chlorhexidine shampoo, vitamin E	2	2
20	None	2	2
21	Increased flea prevention	2	2
22	Excisional biopsy, changed to glass bowls, carprofen, chlorhexidine oral gel	1	1
23	Excisional biopsy, silver sulfadiazine cream, mupirocin ointment, tramadol, amoxicillin, enrofloxacin, famotidine, prednisone, flea prevention, hypoallergenic (grain-free) diet, allergy shots	2	2
24	Antihistamine	2	2

[a] CS/LR score = Clinical symptoms/lesion resolution at the final recheck examination; 0: Little to no improvement in the lesions or clinical signs; 1: Moderate improvement in the lesions and/or clinical signs; 2: Complete resolution of the lesions and clinical signs.

[b] CS/M score = Clinical symptoms/medications at the final recheck examination; 0: The dog was symptomatic and on medication; 1: The dog was asymptomatic but still on medication; 2: The dog was asymptomatic and no longer on medication.

antihistamines, allergy injections, and prednisone. Of those dogs, 100% (n = 7) had a CS/LR score of 2 (resolution of both clinical signs and lesion) at the final recheck examination, which was determined not to be statistically significant. Of the dogs with a history of allergies, 42.9% (n = 3) had lesions that tended to wax or wane.

Discussion

Eosinophilic granuloma refers to conditions affecting the lip/labial mucosa, hard/soft palate, tongue/sublingual mucosa, and skin that are characterized histopathologically by the presence of an eosinophilic infiltrate. With the exception of a few case reports and review articles, this condition is scarcely documented in the veterinary literature. Determining whether there are predisposing factors to the disease or overall outcome of affected dogs is important in educating our clients and treating patients.

Type 1 cell-mediated hypersensitivity reaction appears to play a role in the pathogenesis.[1] This theory is supported by the predominance of eosinophils in these lesions as well as their positive response to glucocorticoid therapy.[1,5,6] The impetus for such hypersensitivity reactions may be inhaled or ingested allergens including seasonal allergens (pollens and molds),[5] insects (fleas or mosquitoes),[7] food, or exposure to irritants (fungi and bacteria).[5,7-9] One case report describes a hereditary etiology in a greyhound litter. Multiple puppies were affected, and the eosinophilic lesions on the caudal palate were severe enough to cause an oronasal fistula.[10] At least one dog in a study of 6 Siberian huskies with eosinophilic lesions on the ventrolateral aspect of the tongue had a dam with similar lesions.[1]

Typical histopathological characteristics of the condition include a predominantly eosinophilic inflammatory infiltrate with varying numbers of mast cells, histiocytes, and lymphocytes.[1,3,5,8,11] Depending on the severity of the lesion, epidermal hyperplasia, erosions, ulcerations, and variable amounts of spongiosis and necrosis may be present.[6,9,12,13] The so-called "flame figures," collagen fibers surrounded by degranulated eosinophils, are a commonly described finding but are not unique to this condition.[2,3,5,9] The histopathological appearance can vary but is consistent within the location of the lesion and its chronicity and severity.[6] Mineralization can occasionally be noted and was present in a lesion of one dog in the present study.

Eosinophilic granules have been histologically observed in the tongue papillae of mice, rats, guinea pigs, hamsters, and dogs.[14] The granules are believed to be involved in papillary cell differentiation. Despite the presence of these granules, the current study did not find the tongue to be more predisposed to eosinophilic lesions compared to other areas of the mouth. Histopathology of tongue lesion biopsies containing eosinophils should be interpreted in light of the normal presence of granules.

The majority of eosinophilic lesions in practice are treated on the basis of clinical presentation without histopathological confirmation of the disease or diagnosis of an underlying cause. Conventional therapy consists of a combination of symptomatic treatment and control of the suspected cause such as parasitic, infectious, or allergic agents. Therapeutic drugs may include glucocorticoids, antihistamines, or other hyposensitization therapies.[15] Other methods of treatment yielding varying results include CO_2 laser therapy, surgical incision or dish curettage, megestrol acetate, cyclosporine, long-acting injectable glucocorticoids, intralesional injections of glucocorticoids, radiation therapy, and injectable gold.[8,11,16] It has been recommended that any method implemented should be continued for 3 to 6 weeks prior to switching to another method.[17]

If immunosuppressive therapy is chosen as treatment, it is important to attempt identification of an underlying or predisposing cause.[8] In particular, the risk of using glucocorticoids must be weighed against the benefits gained. Immunosuppressive treatments are not generally considered cures and may carry undesirable side effects with symptoms recurring once therapy is interrupted or discontinued.[15] Alternatively, while some lesions may regress spontaneously without treatment, systemic glucocorticoid therapy has been shown to hasten the regression.[1] Combining medications, such as administering a low dose of prednisone together with an antihistamine, can balance achieving clinical improvement while minimizing the risk of immunosuppression.[11]

The current study had 15 breeds represented, with Cavalier King Charles spaniels (n = 4), Labrador retrievers (n = 3), and West Highland white terriers (n = 3) most commonly represented. The condition has previously been reported more commonly in Cavalier King Charles spaniels (in which case the lesions were commonly referred to as eosinophilic stomatitis or canine eosinophilic granuloma),[5] Siberian huskies,[1,2,5] and Alaskan malamutes with sporadic cases reported in Labrador retrievers,[5] English setters, German shepherds, and greyhounds.[3,10] Interestingly, there were no Siberian huskies affected in the present study. There were 2 Siberian huskies found in the initial data search, but they were excluded due to lack of complete medical records. To the authors' knowledge, this condition has not previously been reported in the Doberman pinscher, Portuguese water dog, whippet, or Great Dane; one of each of these was represented in the present study. Also, with the exception of one dog, all others in this study were purebred. Statistical limitations did not allow us to compare these results to the general population. Further studies with a larger case load as well as comparing affected dogs with the overall population of dogs presented within the study period are needed to determine whether there is a predisposition of this disease to purebred dogs.

There was no sex predilection found in the present study (54.2% male and 45.8% female dogs). Twenty of the dogs were neutered. The mean age at the time of biopsy or diagnosis was 6.8 years, which is older than the previously reported number (younger than 3 years of age).[2] Only 3 of 22 dogs in the present study showed peripheral eosinophilia on pretreatment blood work, which is consistent with results of other authors but contradicting the findings of a study that found the eosinophilic lesions to be predominantly present in younger, male Siberian huskies of which 21% had peripheral eosinophilia.[2,18]

The typical presentation of eosinophilic disease in dogs involves only one body system, but there have been reports

of multiple systems involved in Cavalier King Charles spaniels.[5] One of the Labrador retrievers in the present study had lesions in multiple organ systems. The lesions of dog #9 were pulmonary and oral. The multiple lesions in 4 other dogs were all oral. Two of the 5 dogs with multiple lesions had only one of their lesions biopsied. It should be emphasized that only the lesions with histopathological confirmation of eosinophilic oral disease were included in the statistical analysis.

There was no statistically significant association between the location of lesions and breed of the dogs in the present study. However, analysis revealed a statistical significance between lesion location and body weight. Dogs with a median weight of 52.1 kg were significantly more likely to have lesions on their lip or mucosa than dogs with a median weight of 11.4 kg. Although all 4 Cavalier King Charles spaniels in this study had lesions on their palate, this was not found to be statistically significant, which may be due to the low sample size. These Cavalier King Charles spaniels, however, all fell within the body weight parameter significantly correlated with palatal lesions. The lesion location/body weight correlation is further supported by 2 case reports of Cavalier King Charles spaniels where the lesions were located to the palate.[1,19]

Nine (90%) of 10 dogs that were asymptomatic at their initial presentation had lesions on the palate (2 on the hard palate and 7 on the soft palate). All of the dogs with palatal lesions ($n = 17$) were asymptomatic and no longer on medications at the final recheck examination (CS/M score of 2). However, it is impossible to conclude with certainty via medical record review how many of these lesions could be observed in the awake dog. Instead, it is possible that all of these asymptomatic dogs still had some detectable lesions present which could not be observed on conscious oral examination.

Previously published literature generally reports eosinophilic disease to be highly glucocorticoid responsive, occasionally resulting in complete lesion regression and no need for further therapy.[1-3,5] Some lesions may undergo spontaneous remission, while others are chronically or seasonally recurrent.[2] The retrospective data regarding therapeutic management of affected dogs were difficult to interpret for the present study because 50% of the dogs were placed on multiple treatments at the same time, making it nearly impossible to judge which individual or combination treatment was ultimately successful. It was also not possible to make conclusions regarding the use of antibiotics for treatment of the condition other than in combination with prednisone as previously noted. The authors were interested in analyzing the use of antibiotics and lesion response since a recent study in cats suggested that the use of amoxicillin trihydrate–clavulanate potassium as monotherapy can be used to treat eosinophilic lesions.[20] However, most dogs in the present study that were given antibiotics appeared to have received them because of concurrent dental or dermatologic issues, rather than as targeted therapy for their eosinophilic oral disease.

Regarding overall clinical improvement, 70.8% (CS/LR score of 2) of dogs had complete resolution, 25% (CS/LR score of 1) had moderate improvement, and only 4.2% (CS/LR score of 0) had little to no improvement. There were 40% of dogs that required continued medical management after the final recheck examination due to continued clinical signs and presence of lesions. No particular treatment option or lesion location correlated significantly with improving outcome. However, when comparing dogs that were not on prednisone and antibiotics, there was a significantly greater likelihood of lesion resolution compared to dogs on both medications (33.3% vs 83.3%). This result may be biased by the subpopulation being treated. It could be that dogs with more severe lesions were more likely to receive multimodal therapy, while dogs with milder lesions were more likely to be monitored. Dogs with less severe lesions may be more likely to experience spontaneous remission of their lesions, not necessitating medications, thus creating a bias in the statistical analysis. Due to subjectivity in lesion descriptions when interpreting medical records retrospectively, the severity of lesions was not a compared data point in this study, and so this potential bias cannot be quantified.

Four (40%) of the 10 dogs that presented asymptomatically resolved without medications (this included dogs with excisional biopsies). An additional 3 dogs were treated only with allergic treatment (allergy therapy and/or flea control). Therefore, 70% of asymptomatic dogs resolved without medications or with allergen therapy. Lesions of only 2 (14%) of 14 dogs presenting with clinical signs associated with eosinophilic disease resolved in a similar fashion. One resolved with excisional biopsy, and the other received flea prevention. Given these results, it does not appear that asymptomatic dogs necessarily require treatment.

One of the goals of the present study was to examine whether a diagnosis of allergies influenced the therapeutic outcome. The hypothesis was that a diagnosis of allergies could allow treatment of the underlying cause, thus improving clinical resolution of the eosinophilic oral disease. All 7 dogs with a history of allergies had complete resolution (CS/LR = 2) at the time of the final recheck examination. Four (66.7%) of the 7 dogs with a history of allergies were treated with prednisone (either alone or in combination with other treatments). Although treatment with prednisone appeared to be correlated with clinical resolution within the population of allergic dogs, it was not statistically significant when compared to dogs without an allergic diagnosis.

Although every effort was made to group and analyze data objectively and accurately, there are always challenges when gathering information for a retrospective study. For example, they include an inability to take into account if the eosinophilic lesion was currently in a wax/wane state at the final recheck examination. This could falsely elevate the improvement category. When analyzing waxing and waning features of the lesions, it was noted that some dogs had multiple lesions with only one tending to show this attribute. In dogs with multiple similarly appearing lesions in different areas of the mouth or body, each lesion was not always biopsied. It was noted during data analysis that some lesions had initial cytologic diagnoses of eosinophilic oral disease that were not supported by subsequent histopathological examination. Only lesions with histopathological confirmation of eosinophilic disease in biopsy samples were included in the analysis. With a larger sample size, it is possible that these lesions may carry a different outcome.

Treatment choices also challenged the analysis. Multiple medications were used, often concurrently. Medications were sometimes changed between the initial presentation and the final recheck examination, and occasionally without the recommended 3- to 6-week interval in between therapies. Combined with the condition's potential to spontaneously resolve, the authors of the present study were not able to derive a particular significance for any single type of therapy. A positive response to treatment may have also been falsely elevated by the location of the lesions. Most dogs were not sedated for their final recheck examination. Not observing a lesion in a caudal oral position does not rule out a more subtle change that may have been noticed under sedation. The severity of the lesion may have also influenced the likelihood of a positive treatment outcome. However, the variation in details between medical records did not allow the authors to objectively categorize the severity of the lesions. Finally, the retrospective format and the strict guidelines applied for admission of dogs to the present study limited the overall population available for statistical analysis. Only 24 of the initially identified 36 dogs met the inclusion criteria, and not all lesions present in the 24 dogs met the study criteria. Even with these limitations, however, the current study likely has the largest population of dogs with eosinophilic oral disease analyzed to date.

Eosinophilic oral disease is a condition that is not uncommonly recognized in practice. However, apart from a few case reports in dogs, it is sparsely documented in the veterinary literature, and most therapeutic decisions are made on the basis of personal and anecdotal experience. Results of the present study challenge breed predispositions previously reported, suggest that treatment is not always necessary in asymptomatic dogs, present a statistical significance between lesion location and body weight, present a correlation between resolution of clinical signs and palatal location of the lesion at the final recheck examination, demonstrate that dogs had a significantly greater likelihood of resolution without the combined use of prednisone and antibiotics, and did not show a significant correlation between lesion resolution and the use of prednisone.

This study is meant as a starting point for future research into eosinophilic oral disease in dogs. Further investigation into treatment options is warranted. Routine biopsy of all lesions and careful selection of single versus multimodal therapies will create accurate future data points. Determining whether there are predisposing factors to the disease and variables affecting clinical outcome is important in educating dog owners and treating veterinary patients. This study is presented in the hope that larger analyses can be performed which may aid in determining the best treatment options for dogs with eosinophilic oral disease.

Declaration of Conflicting Interests

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