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Authors

Soltero-Rivera, Maria
Quinones, Marilucy Pilar Del Toro
Arzi, Boaz
et al.

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Importance of early diagnosis, multimodal treatment, and a multidisciplinary approach for oral eosinophilic lesions in cats: a retrospective study of 38 cases (1997–2022)

Maria Soltero-Rivera, DVM, Dipl AVDC^{1*}; Marilucy Pilar Del Toro Quinones, BS¹;
Boaz Arzi, DVM, DAVDC, DEVDC, FF-AVDC-OMFS^{1,2}; Natalia Vapniarsky, DVM, PhD, Dipl ACVP^{2,3}

¹Department of Surgical and Radiological Sciences, School of Veterinary Medicine, University of California-Davis, Davis, CA

²Veterinary Institute for Regenerative Cures, School of Veterinary Medicine, University of California-Davis, Davis, CA

³Department of Pathology, Microbiology, and Immunology, School of Veterinary Medicine, University of California-Davis, Davis, CA

*Corresponding author: Dr. Soltero-Rivera (msoltero@ucdavis.edu).

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OBJECTIVE

This study aimed to characterize the clinical and histopathologic features of oral eosinophilic lesions in cats.

ANIMALS

38 client-owned cats.

METHODS

The medical records database was searched for cats diagnosed with histologically confirmed eosinophilic oral lesions from 1997 to 2022. Information such as medical history, lifestyle factors, clinical presentation, and radiographic and histopathologic features was included for 38 client-owned cats. Response to treatment and long-term follow-up was also recorded.

RESULTS

The most affected site was the tongue, with approximately half of the affected cats showing signs of oral discomfort and difficulty eating or breathing. Ulcerative lesions were common, with two-thirds of patients showing more than 1 site affected. Histological samples had a classic appearance, whereas some had an atypical appearance characterized by degenerate collagen clusters associated with multinucleated giant cells. A significant association between lesion location, clinical signs, and prognosis was also found, with patients with palatal lesions being more likely to show respiratory signs and less likely to respond to treatment. Finally, treatment response was observed in most cases within 2 months of commencing therapy combining antimicrobial, and immunosuppressive treatment.

CLINICAL RELEVANCE

The results of this study demonstrate the importance of early diagnosis and treatment of cases of oral eosinophilic lesions in cats. Additionally, it emphasizes the need for a multimodal approach to treatment which should include antibacterial therapy. Of no less importance is that other systems may be affected in these patients, warranting a multidisciplinary approach to their management.

Keywords: oral medicine, feline, dentistry, eosinophilic stomatitis, eosinophilic granuloma complex

Eosinophilic granuloma complex (EGC) refers to varying disease manifestations characterized by the infiltration of eosinophils into the skin and/or oral tissues, leading to raised, often ulcerated lesions.¹ The cause of EGC in dogs and cats remains unknown and the clinical appearance of these may vary.² Suspected causes include ectoparasites,^{3,4} environmental allergens, bacterial infections,⁵ and autoimmunity,^{6,7} yet these studies have mostly focused on the lip ulcer manifestation. Feline herpesvirus-1 (FHV-1) has also

been associated with EGC.^{8–10} Finally, pythiosis, a potentially fatal but noncontagious disease caused by the fungus *Pythium insidiosum*, though rarely described in the cat, has been reported to cause a severe multifocal coalescing eosinophilic granulomatous inflammation in the oral cavity.¹¹ Taken together, the data available suggest an allergic reaction as the most likely cause of this disease, although individual genetic variation may also play a role in supporting the need for further studies.¹²

In a study¹³ evaluating the frequency of oral cavity lesions in cats in Portugal, EGC (n = 33; 11.1%) was third on this list featuring the most common histopathologic diagnosis. Clinically, oral lesions tend to manifest as well-demarcated areas of proliferation or ulceration in the tongue, buccal mucosa, gingiva, lip, and palate. Cases may have a multifocal presentation. Literature¹⁴ reports that feline oral EGC may be clinically recognized by the appearance of white to yellow pinpoint areas on the surface of proliferative or ulcerated lesions due to mineralization of its collagen and eosinophil-derived proteins. The clinical presentation of the disease in the oral cavity may lead to oral pain, decrease of appetite, and difficulty eating, drinking, and/or breathing thus affecting their quality of life.

Although lesions can be screened via cytology,¹⁵ histopathology is needed to confirm the diagnosis of eosinophilic disease and rule out other differential diagnoses of similar clinical appearance to these lesions such as food allergy,¹⁶ squamous cell carcinoma, feline chronic gingivostomatitis, or other granulomatous, immune-mediated, and autoimmune diseases.¹⁷ EGC lesions are histopathologically confirmed via the presence of a large number of eosinophils. The term “granuloma” has been historically used to describe the presence of accumulated material from eosinophil degranulation surrounded by macrophages, giant cells, and lymphoplasmacytic inflammation in chronic cases.¹⁴ Ulcerated lesions show hyperplasia of the bordering epithelium as is characteristically seen with lip lesions also known as “rodent ulcers.”¹⁴ Previous literature¹⁸ reports flame figures, small foci that contain intact collagen fibers surrounded by degranulated eosinophils as a histopathological characteristic of EGC lesions. Secondary bacterial infections may also be present when the lesions are ulcerated,⁵ and culture and sensitivity have been recommended if rod-shaped bacteria are seen or if antimicrobial resistance is suspected.¹⁹

Current multimodal therapeutic approach includes hypoallergenic diet trial,¹⁶ ectoparasites treatment,²⁰ systemic steroids¹⁹ or other immunosuppressants,^{21,22} antimicrobials,⁵ and surgical excision²³ in some cases. However, the efficacy of these therapeutic approaches has been inconsistent and is usually transient.

Characterizing the manifestation of oral eosinophilic lesions in cats is essential for accurately diagnosing, treating, and managing this condition thereby improving affected cats' quality of life. The purpose of this retrospective case series is to set a foundation for the clinicopathological features of oral eosinophilic disease in cats and assess if there are correlations between clinical, lifestyle, or histopathologic features with response to treatment and overall prognosis. We hypothesize that the prognosis for cats with oral eosinophilic lesions may vary depending on the location of the lesion and the severity of clinical signs. The results of this study may also aid in progressing to identify alternative treatment options with a more prolonged response and higher success rate.

Methods

Case selection

Medical records from the Dentistry and Oral Surgery Service at the William R. Pritchard Veterinary Medical Teaching Hospital of the University of California-Davis ranging from 1997 to 2022 were reviewed. A total of 38 client-owned cats, with biopsy-confirmed oral eosinophilic disease (ie, oral granuloma, cheilitis, granuloma oral cavity, stomatitis, glossitis, indolent ulcer) and complete medical records were included in the study.

Data collection

The following data were collected for each cat: (1) signalment, (2) medical history, (3) environmental factors, (4) clinical signs at presentation, (5) physical examination findings, (6) CBC results, (7) findings from anesthetized oral evaluation including dental charting and intraoral dental radiography, and (8) treatment as well as corresponding response. The environmental factors were the type of diet, parasite prevention regimen, whether they lived indoors or outdoors, and if they lived with other feline companions. Oral clinical signs were categorized as follows: asymptomatic (usually attributed to an incidental finding) versus symptomatic (oral pain, bleeding, hypersalivation, halitosis, difficulty eating). Concurrent clinical signs were also noted as follows: gastrointestinal (weight loss, vomiting, diarrhea, hyporexia, anorexia, nausea, gagging), skin (pruritus, alopecia), and respiratory (nasal discharge, sneezing, reverse sneezing, cough, wheezing). Lesion location refers to the following regions in the oral cavity: alveolar mucosa, buccal mucosa, gingiva, tongue, palate, lip, and pharyngeal. Lesion type (ulcerative vs proliferative) was also recorded. Concurrent skin lesions on the pelvic limbs and abdomen were also noted. The following treatments were considered: periodontal treatment under anesthesia, surgical debulking (of a mass-like lesion), tooth extraction, antimicrobial (including topicals such as chlorhexidine), immunosuppressive (ie, steroids, cyclosporine), antihistamine, antiparasitic, hypoallergenic diet, and stem cell treatment. Rounds of treatment were noted, and response was characterized as complete, partial, or absent. Complete and partial responses were further classified as transient or permanent.

Histological evaluations

Histopathological records of biopsies that included “eosinophilic inflammation” were reexamined by a board-certified pathologist (NV) and board-certified dentist (MS-R). The samples were graded for the presence of erosion, ulceration, status of the epithelium, presence of eosinophilic granulomas, scattered eosinophils, collagen degeneration, mineralization of the granulomas, presence of multinucleated giant cells, and presence of additional inflammatory cell infiltrates such as mast cells, lymphocytes, and plasma cells. The grading scheme applied is summarized elsewhere (**Supplementary Table S1**).

Statistical analysis

Descriptive statistics were used to describe patient demographics (ie, age, weight, sex, breed), oral eosinophilic lesions (ie, location, type), lifestyle/environmental factors, presence of concurrent diseases, clinical signs at presentation, treatment, and response.

Fisher's exact test was used to evaluate the association between clinical signs and lesion location; clinical signs and lesion type; gross result and lesion location; and gross result and lesion type. Odds ratios were also calculated for all these comparisons. Logistic regression analysis was performed to evaluate the association between concurrent diseases (ie, periodontal disease (PD), tooth resorption, endodontal disease, stomatitis, neoplasia, lymphadenomegaly, oronasal fistula, and skin disease), and oral eosinophilic lesions. Estimated proportion and 95% confidence interval were calculated for concurrent diseases. *P* values were considered significant when $< .05$, and 95% confidence intervals were reached. All analysis was carried out in R statistical software (R Core Team. R: a language and environment for statistical computing. R Foundation for Statistical Computing; 2022: <http://www.R-project.org/>).

Results

Signalment and presenting complaint

Medical records of 38 cats met the inclusion criteria with a total of 73 affected sites. Purebred cats accounted for 32% ($n = 12$) of the population. Patient age at the time of diagnosis ranged from 7 months to 17 years of age (mean = 7.8 years). Weight ranged from 3 kg to 7.7 kg (mean = 4.9 kg). Of those diagnosed with eosinophilic lesions, 24 (63%) of 38 were male and 14 (37%) of 38 were female, all of which ($n = 38$) were castrated or spayed.

Patients were referred for evaluation of ulcerative, proliferative, or both, localized to multifocal lesions some of which were also described to be erythematous with white to yellow deposits on the surface. The mean duration of clinical signs before presentation was 24 months (0.25 to 108 months). Of the 38 cats, 11 (29%) were asymptomatic while the remaining 27 (71%) exhibited some type or combination of oral, gastrointestinal, skin, or respiratory symptoms. Of the 27 symptomatic patients, a total of 20 (74%) showed oral clinical signs. Of the 20 cats that displayed oral clinical signs, 7 exhibited oral pain, 5 had impaired function, and 4 patients experienced both oral pain and impaired function likely due to the eosinophilic lesion(s).

Concurrent gastrointestinal signs were seen in 12 (44%) patients, 10 (37%) patients showed skin-related signs or lesions, and 9 (33%) showed respiratory signs. Five patients displayed clinical signs consistent with lower airway disease (ie, coughing, wheezing) while the remaining 4 patients displayed clinical signs related to upper airway disease (ie, sneezing, runny nose). Taken together, 15 (39%) cats experienced a combination of clinical signs. Twelve (31.6%) cats had peripheral eosinophilia

($> 1,500/\mu\text{L}$) confirmed by hematology results (ie, CBC). The presence of peripheral eosinophilia on complete blood counts of patients with oral clinical signs was only weakly positively correlated ($P = .086$) to the presence of oral eosinophilic lesions with an odds ratio of 2.81 (95% CI, 0.86 to 15.5).

Anesthetized evaluation

All patients were presented for evaluation of ulcerative and/or proliferative lesions in the oral cavity with 17 (44.7%) cats presenting ulcerative lesions and 11 (29%) presenting with proliferative lesions while a total of 10 (26.3%) cats had both proliferative and ulcerative lesions (**Figure 1**). The frequency of lesions by location is summarized (**Figure 2**). Patients could have 1 or more affected sites. As such, 36.8% ($n = 14$) only had 1 affected site, 39.5% (15) had 2 affected sites, 18.4% (3) had 3 affected sites, and 5.3% (2) had 4 affected sites. It is important to note that there could be multiple lesions in 1 affected site.

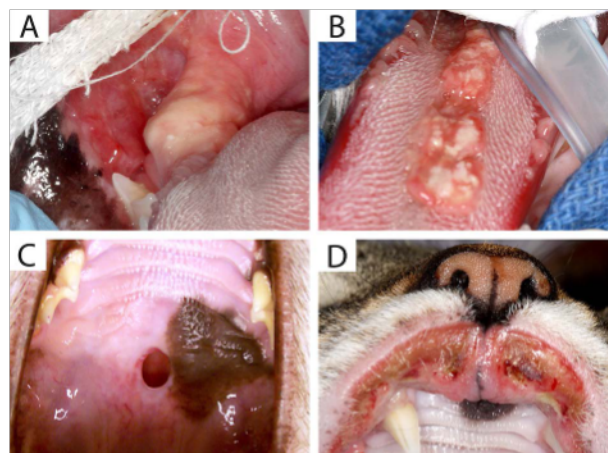


Figure 1—Clinical presentation of eosinophilic granuloma lesion in a cat. A—Ulcerated buccal mucosa and thickened tan-colored palatoglossal fold in an 8-month-old female spayed (FS) domestic shorthair. B—Proliferative tongue lesion with white to tan areas on the surface in a 12-year-old male castrated domestic shorthair. C—Nonhealing palatal defect in a 7-year-old FS Egyptian mau. D—Ulcerated lip lesion with some light brown to red crusting in a 15-year-old FS domestic shorthair.

There was a statistically significant association between palatal lesions and the presence of respiratory signs ($P = .04$). Logistic regression analysis showed that patients with palatal lesions are 5.65 (0.88 to 41.2) more likely to show respiratory signs as compared to other locations. Oronasal fistulas were identified in 3 patients with palatal lesions. The rest of the patients did not undergo diagnostic workup for nasal disease at the time of diagnosis. A weakly positive correlation was found between pharyngeal lesions and oral ($P = .086$) as well as respiratory signs ($P = .108$). Fisher's exact test was statistically insignificant for other outcomes evaluated in relation to lesion location and lesion type as well as for clinical signs when evaluated in relation to lesion type.

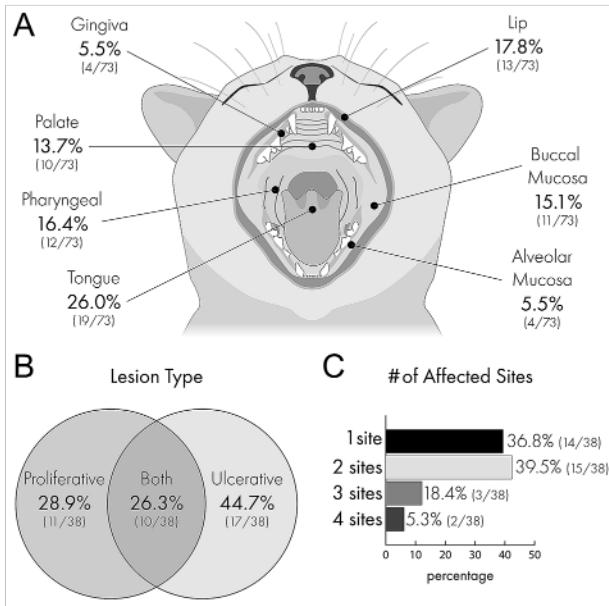


Figure 2—Visual representation of the clinical presentation of eosinophilic lesion(s). A—Percentage of lesions found per location. B—Percentage of cases with lesions characterized as ulcerative, proliferative, or both. C—Percentage of sites affected per case.

Concurrent diseases and associations

Pertinent medical history for the patients in our population included: 55% (n = 21) had a history of skin disease (ie, alopecia, environmental allergies, ectoparasite infestation, etc). Seventy-nine percent (n = 30) of patients had concurrent PD. Fifty percent of cases (n = 19) exhibited tooth resorption. Forty-seven percent (n = 18) of cats had concurrent tooth resorption and PD. Thirty-four percent (n = 13) of all cases had endodontal disease, of which 35% (12) had concurrently reported PD. Mandibular lymphadenomegaly was noted in 37% (n = 14) of cases. Statistical analysis revealed that the odds of having an oronasal fistula are positively correlated with the presence of eosinophilic lesions (estimated proportion 0.79; 95% CI, 0.017 to 0.214). As previously mentioned, 3 patients with eosinophilic lesions on the palate had concurrent oronasal fistulas. When evaluating the frequency of neoplasia in our cohort, the odds of having oral neoplasia are not correlated to the presence of eosinophilic oral lesions (estimated proportion 0; 95% CI, 0, 0.093). Concurrent stomatitis was reported in 26% of cases.²⁴

Lifestyle and environmental factors

In terms of lifestyle, of the 25 patients who addressed their household environment, 22 (88%) lived in multicat households with all (n = 28) residing indoors while 16 (57%) patients also had outdoor access.

Histopathologic findings

Thirty-eight patients with a total of 42 slides underwent histopathological evaluation for eosinophilic lesions. All biopsies were either incisional

or excisional and all underwent H&E staining. Ten samples were obtained via excisional biopsies and 29 via incisional biopsies, and for 3 samples, this information was unavailable. The classic features included subepithelial eosinophilic granulomas composed of an amorphous granular central core surrounded by variable degranulated eosinophils. The lamina propria was additionally infiltrated by numerous scattered eosinophils. The overlying epithelium was either intact, eroded, or ulcerated. In cases with ulceration or erosion, neutrophilic presence was more prominent. Eosinophilic granulomas often formed linear aggregates parallel to the ulcerated surface, and in these cases, reactive fibroblasts and capillaries lined by reactive endothelial cells were frequently observed underneath. Likewise in classic cases, the collagen fibers heavily infiltrated and separated by eosinophils had hyper eosinophilic appearance (degenerate collagen; **Figure 3**).

However, 8 cases evaluated histologically lacked some classic hallmarks. For instance, degenerate collagen was sometimes present without associated intact or degranulated eosinophils (eosinophilic granulomas). These degenerate collagen clusters were instead associated with multinucleated giant cells. Five out of 8 histologically atypical cases were affecting the palatoglossal folds. Four were ulcerated, and 1 had a combination of ulcerative and proliferative changes. One atypical case affected the buccal mucosa and was proliferative. Another was ulcerative and located on the soft palate. One located on the lip was described as proliferative. Interestingly, only 20 samples had classic eosinophilic granulomas present. Cases without eosinophilic granulomas had scattered eosinophilic inflammation with or without degenerate collagen fibers. If not ulcerated, the epithelium was frequently hyperplastic. Lymphoplasmacytic infiltration was another factor that was considered atypical. This infiltrate was substantial and more dominant than the eosinophilic component in 16 cases. Out of these, only 1 sample had eosinophilic granulomas, while others had minimal to moderate eosinophilic infiltration. One case initially diagnosed with eosinophilic inflammation contained many Mott cells (plasma cells) that were most likely misdiagnosed for eosinophils. This case was thus removed from this study (**Figure 4**).

Treatment, response, and follow-up

Treatments are summarized (**Table 1**). Systemic antimicrobials used included amoxicillin with clavulanic acid, clindamycin, and amoxicillin, and the topical antimicrobial used was chlorhexidine mouthwash. Immunosuppressives prescribed included prednisone or prednisolone (n = 15) and cyclosporine (5).

Of the 38 patients evaluated for treatment, 89% (n = 34) received a combination of therapies. One patient received no treatment. Among the patients, 42% (n = 16) needed a second round of treatment, and 18% (7) required a third round of treatment before a response was observed. For the lesions that

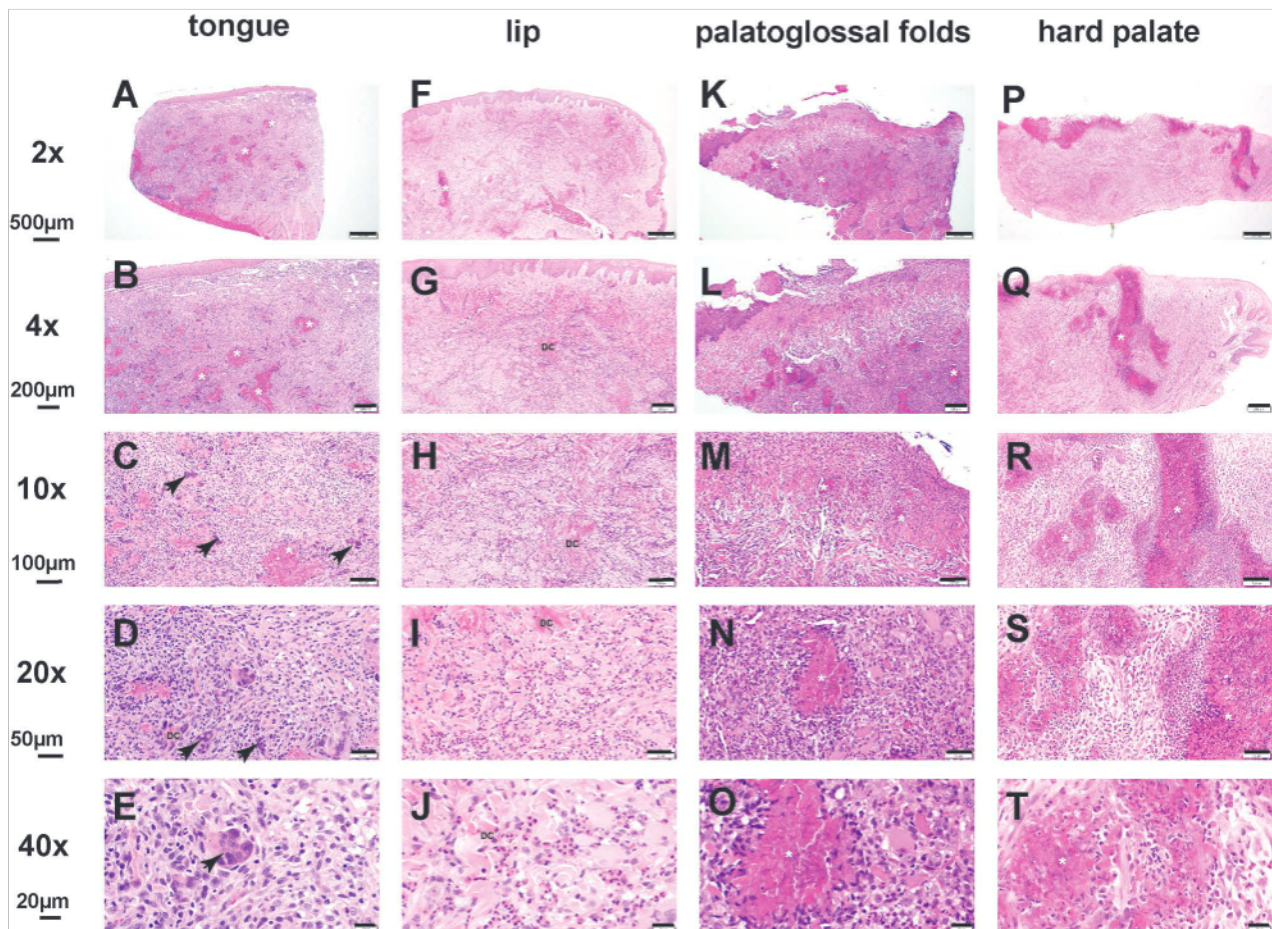


Figure 3—Classic histomorphology of eosinophilic lesions of the tongue (A to E), lips (F to J), palatoglossal folds (K to O), and hard palate (P to T). A and B—Note multiple eosinophilic granulomas (white *) in the lamina propria of the tongue. The epithelium is intact. C and D—Multiple multinucleated giant cells (black arrowheads) are associated with degraded collagen fibers. E—A large multinucleated giant cell and other inflammatory cells such as lymphocytes, plasma cells, and occasional neutrophils infiltrate the lamina propria. F to H—A giant eosinophilic granuloma (white *; F) and multiple degenerate collagen foci (G and H). Epithelia are intact. I and J—Note myriads of scattered eosinophils. K and L—More eosinophilic granulomas (white *) and ulcerated epithelium are shown. M to O—Eosinophilic granulomas have granular strongly eosinophilic cores formed by degenerate and degranulated eosinophils rimmed by lymphocytes and macrophages. P and Q—The eosinophilic granulomas are arranged linearly parallel to the ulcerated epithelium. They are “pushed” out toward the surface by a reparative response underneath. R to T—More eosinophilic granulomas are highlighted.

required multiple rounds of therapy, 37% (n = 14) had persistent disease, and 5% (2) had recurrent disease. The 8 patients that underwent surgical debulking had proliferative lesions. Five of these patients had multiple sites affected.

Five patients were reported to have stomatitis with lymphoplasmacytic and eosinophilic inflammation. Three of these patients were treated with full-mouth tooth extractions, and of these 1 had a complete resolution, 1 had partial improvement, and 1 had no response. Two patients were treated with partial mouth tooth extractions, and of those 1 had a full response, and 1 had no response. One additional patient with kidney disease was noted to have uremic ulcers on the lip commissures.

Follow-up was obtained in 28 patients and varied between 3 weeks and 61 months (mean = 14 months). Twelve patients were lost to follow-up

on treatment and response. Taken together of the 28 patients with a known response to treatment and follow-up, 22 had resolution of their lesions and/or in clinical signs and 6 did not. When evaluating the resolution of lesions alone, 9 patients had complete resolution of lesions, 8 patients had mild improvement of their lesions, and 11 patients had no change of their lesions to treatment. When evaluating response of clinical signs alone, a complete resolution of clinical signs was noted in 12 patients, while 7 patients showed a partial response, and 9 patients showed no response in clinical signs to treatment.

Of the patients that showed a response to treatment, 9 showed a response to antimicrobial treatment, 7 responded to antimicrobial treatment in combination with immunosuppressive medication, 2 responded to marginal excision, and 3 responded

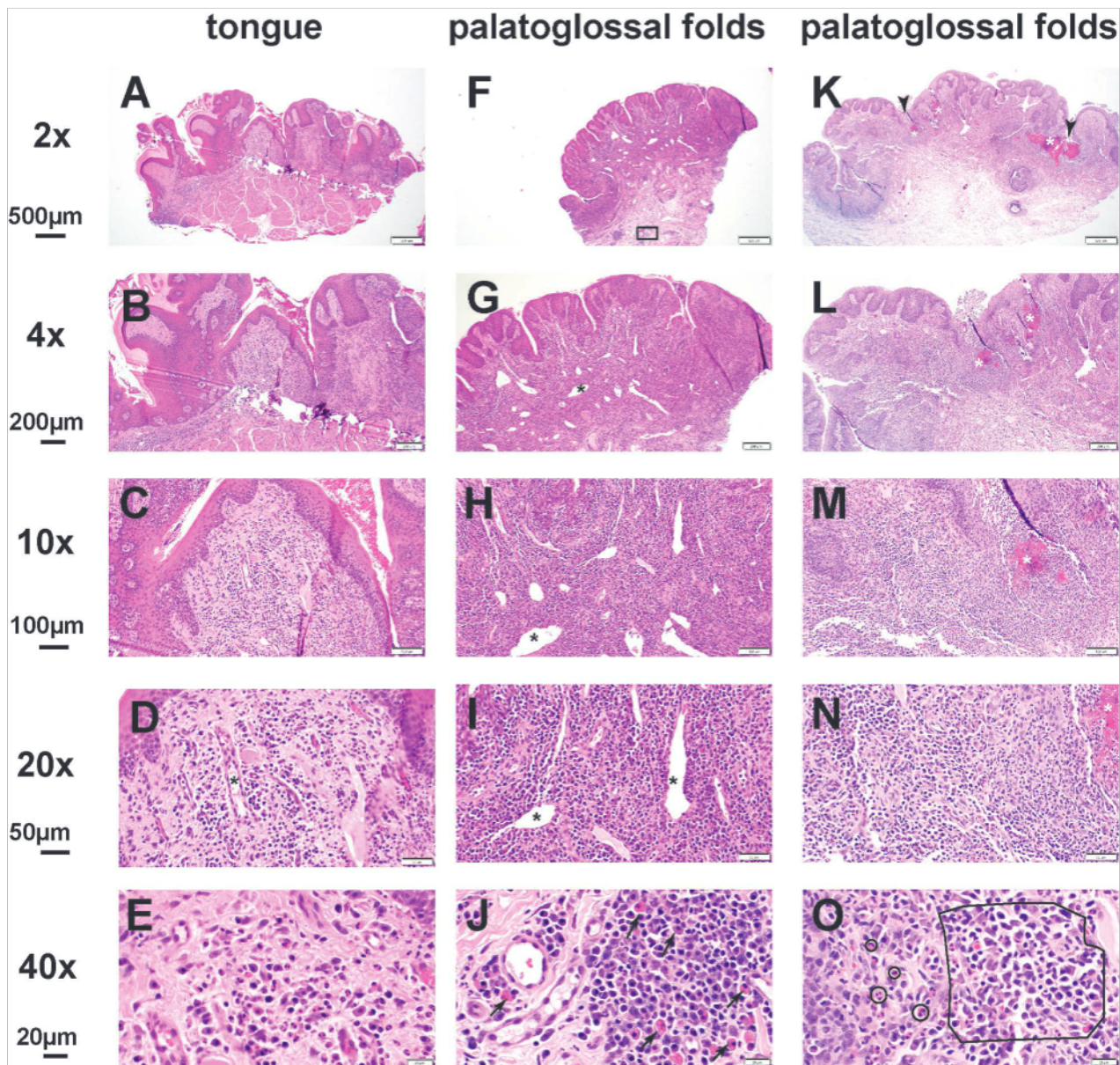


Figure 4—Atypical presentations of oral eosinophilic lesions in the tongue (A to E) and 2 cases of palatoglossal folds (F to J) and (K to O). A to E—The epithelium is hyperplastic and thrown into multiple folds. The lamina propria is expanded by primarily lymphoplasmacytic infiltrate with fewer eosinophils and occasional neutrophils. No eosinophilic granulomas are present. Note dilated lymphatic vessels in D lined by reactive endothelium (black *). F to J—Similar to the tongue lesion with a predominant population of lymphocytes and plasma cells infiltrating and expanding lamina propria. The lymphatics are dilated (black *). This case was misdiagnosed for eosinophilic infiltration due to numerous Mott cells (black arrow) shown in J. The area in J is a high magnification of that enclosed in a black rectangle in F. K to O—A case of predominant lymphoplasmacytic infiltration and eosinophilic granulomas (white *). Scattered eosinophils (black circles) are also observed in a background of severe lymphoplasmacytic inflammation (large black rectangle).

to marginal excision in combination with antimicrobial therapy. The average time to respond to treatment was 2 months (0.3 to 17 months). An odds ratio of < 1 ($P = .03$) was noted when evaluating the correlation between palatal lesions and complete resolution of disease suggesting that a successful treatment outcome is less likely to occur with a lesion on the palate. No correlation between histological type (ie, classic vs atypical)

and treatment outcome was found ($P = .55$) in our population.

Three patients were euthanized due to decreased quality of life resulting from this disease or side effects related to treatment, and these patients had eosinophilic lesions located on the palate, lip, tongue, and pharynx. One patient had only 1 site affected, 1 had 2 affected sites, and the other patient had 3 affected sites.

Table 1—Summary of treatments prescribed to patients with oral eosinophilic lesions.

Treatment modality	Response rate (n)
Periodontal treatment	68% (25)
Surgical debulking	22% (8)
Tooth extractions	51% (19)
Systemic antimicrobials	73% (27)
Topical antimicrobial	46% (17)
Immunosuppressives	53% (20)
Antihistamine	3% (1)
Antiparasitics	35% (13)
Hypoallergenic diet	27% (10)

Discussion

Oral eosinophilic lesions in cats can be a challenge to treat and may negatively impact a patient's quality of life. This retrospective study aimed to establish a foundation for the clinical and histopathologic features of this disease in the oral cavity. Our study found the tongue to be the most affected site followed by the lip and pharyngeal regions with nearly half of the lesions having an ulcerative appearance grossly. We also found a significant association between lesion location and prognosis with patients with palatal lesions exhibiting respiratory clinical signs more commonly and having a lower likelihood of responding to treatment. Histopathologically, the appearance of these lesions varies with some cases showing subepithelial eosinophilic granulomas composed of an amorphous granular central core surrounded by variable degranulated eosinophils, although others were atypical in that degenerate collagen was present in the absence of intact or degranulated eosinophils. In addition, symptomatic patients may require more than 1 course of treatment, which tends to be multimodal and include antimicrobials along with immunosuppression with a response seen approximately 2 months after initiating treatment.

We noted that lingual eosinophilic lesions were more prevalent in cats. This is in contrast to the report² in dogs where eosinophilic lesions were most commonly found in the palate (65.4%) followed by the tongue (26.9%). Ulcerative lesions were more commonly seen in our cohort however, approximately a quarter of our patients had both ulcerative and proliferative lesions. Additionally, 63% of our patients had multiple sites affected with possibly more than 1 lesion per site. This ulceration and multifocal nature of this disease may negatively impact the quality of life of affected patients. Lingual lesions, especially those that are proliferative, can certainly grow enough to impact a patient's ability to eat and drink, and approximately 74% of the patients had evidence of oral pain or impaired function on presentation. However, in our study patients exhibiting palatal lesions had a statistically significant effect on the patient's quality of life beyond the pain and impaired function and were more likely to present respiratory signs. We noted that 30% (3/10) of patients with palatal lesions had evidence of communication between the nasal and oral cavities, and

the statistical analysis for this study revealed higher odds of having an oronasal fistula in patients with eosinophilic lesions. Bone infiltration and destruction by eosinophilic disease have been previously reported in a dog.^{25,26} If there is no clear oronasal communication, respiratory signs may still indicate the possibility of eosinophilic disease. However, it is essential to consider other potential conditions such as infection (viral), lymphoplasmacytic rhinitis, or neoplasia as well, as they cannot be definitively ruled out. Taken together, these data highlight the importance of early diagnosis and treatment of eosinophilic lesions, especially palatal lesions, to prevent progression to the development of an oronasal communication and of concurrent evaluation of the airways in those cases where the clinical appearance of the lesion and the patient's medical history fail to explain the clinical signs.

The presence of peripheral eosinophilia, noted in one-third of our population, was only weakly positively correlated with oral clinical signs. Although this association was weak, it does remind clinicians of the importance of performing an anesthetized oral examination in patients presenting both of these concerns. The mandibular lymphadenomegaly noted in nearly 40% of cases is likely reactive lymphadenopathy as has been previously reported in cases of eosinophilic skin disease.¹⁹ Slightly over a third of the population in this cohort had a history of skin disease (ie, alopecia, environmental allergies, ectoparasite infestation, etc) as compared to a 15% prevalence rate in the normal population.²⁷ Gastrointestinal signs were noted in approximately 40% of our population, which appears to be consistent with the prevalence of these clinical signs in feline patients with chronic enteropathies without drawing any major conclusions.²⁸ Consequently, and considering that respiratory signs may also be seen, these patients may require a multidisciplinary approach for the diagnosis and management of their comorbidities, although this could also be specific to the population evaluated in our institution. In terms of concurrent oral diseases, the prevalence of both PD (n = 25) as well as tooth resorption (26) was like that of the general patient population. Thus, periodontal treatment, extraction of affected teeth, and continued home care are recommended to decrease the bacterial burden in the oral cavity of cats with eosinophilic oral lesions.

Histopathologically, several similarities were observed between cases. Specifically, although the word "eosinophilic" was often used in the morphologic diagnosis of the cases selected for this study, approximately half of the cases did not exhibit the classic eosinophilic granulomas and/or degenerated collagen often also referred to as "flame figures." The location and clinical characteristics of atypical cases varied; however, 63% of these were in the region of the palatoglossal folds. Similar to our study, previous histopathologic studies¹⁸ of EGC of the skin have found a lack of correlation between the histopathological features of the EGC and the clinical aspects of the disease and vice versa.

Cases with significant dominance of lymphoplasmacytic infiltrates with minimal eosinophilic involvement and no other features of EGC may present a separate entity. Alternatively, these could be cases of feline chronic gingivostomatitis with eosinophilic components. In certain instances, distinguishing between eosinophilic granulomas and degenerated collagen, especially when degenerated collagen fibers were not associated with eosinophilic aggregation, was not straightforward. Similarly, for the atypical cases and those described as having concurrent stomatitis, further studies should evaluate if the presence of eosinophils is of prognostic significance.^{29,30} Alternatively, different appearances of lesions may represent various stages in the disease continuum and various responses to treatment. Thus, longitudinal studies with repeat biopsies in the same patient over time would be necessary to elucidate the reason for the histological differences observed among cases in this study. To avoid misdiagnosis of Mott cells for eosinophils, examining the section under higher magnification is recommended. Alternatively, eosinophil peroxidase monoclonal antibody or Luna stain can be used to differentiate eosinophils from Mott cells.^{29,31}

We noted that 79% of the patients responded to treatment in this cohort. A response to treatment was defined as resolution or improvement of the lesion(s) or clinical signs at presentation. Patients with proliferative lesions, especially those with pharyngeal and lingual lesions, were treated via marginal excision due to mass effect caused by these having an impact of the patient's ability to eat and breathe comfortably. Most patients that responded to therapy (19/22; 86%) received antimicrobial and/or immunosuppressive treatment. A response was noted after approximately 2 months of therapy. This is consistent with findings in dogs for which the combination of antimicrobial and immunosuppressive treatment was correlated to the resolution of disease.² Palatal lesions were significantly less likely to respond to treatment. This is contrary to dogs in which palatal lesions had a more favorable prognosis.²

This retrospective case study aimed to establish a foundation for the clinical and histopathological manifestations of this understudied disease. Like all retrospective studies, the limitations of this study are attributed to incomplete records, loss of follow-up, and a small sample size. There were also a lower number of cases that recurred than expected, and thus, it is possible that recurrence may have been incorrectly characterized as persistent disease if the patient was not seen during the time of remission. Nonetheless, important information regarding the clinical presentation, histologic variation seen in these cases, as well as management and prognosis for these cases was derived from this cohort. Lingual lesions were most abundant, and histology did not correlate with the clinical appearance. A significant association between lesion location and prognosis was found in patients with palatal lesions having concurrent respiratory signs. These patients are

less likely to respond to treatment. Finally, we found that a combination of antimicrobial with and without immunosuppression led to a treatment response in most of the population within 2 months after the start of therapy. Further studies evaluating individual variations in affected patients, including genetic-wide association studies as well as single-cell sequencing of the eosinophils and spatial genomics, could shed some light on the etiology of this disease.

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Disclosures

The work described in this manuscript involved the use of nonexperimental (owned or unowned) animals. Established internationally recognized high standards ("best practice") of veterinary clinical care for the individual patient were always followed and/or this work involved the use of cadavers. Ethical approval from a committee was therefore not specifically required for publication.

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Supplementary Materials

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