

Canine Perianal Fistulas

Clinical Presentation, Pathogenesis, and Management



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KEYWORDS

- Canine • Perianal fistula • Anal furunculosis • German shepherd dog
- Immune-mediated • Cyclosporin A

KEY POINTS

- Canine perianal fistulas are painful ulcers or sinus tracts that spontaneously occur in the skin around the anus and can be debilitating for affected dogs.
- Middle-aged German shepherd dogs are most commonly affected and may have a genetic susceptibility, but other purebred and mixed-breed dogs also develop perianal fistulas.
- Although anatomic factors were once believed to contribute to development, an immune-mediated pathogenesis is now recognized.
- Over the years, there has been a paradigm shift from surgical management to long-term medical management of canine perianal fistulas.
- Immunomodulatory medications, in particular cyclosporin A with or without ketoconazole, are most commonly used for management of canine perianal fistulas.

INTRODUCTION

Perianal fistulas, also known as anal furunculosis, are painful sinus tracts or ulcers that spontaneously occur in the skin around the anus (**Fig. 1**). German shepherd dogs are predisposed to developing perianal fistulas, but other purebred and mixed-breed dogs also are affected. Although development of perianal fistulas was once believed related to anatomic conformation, the condition is now recognized as immune mediated, although the pathogenesis has not been fully delineated. Likewise, although surgical intervention and correction of anatomic factors were once the mainstays of therapy, medical management is the current standard of care for dogs with perianal fistulas. This condition can be debilitating for affected dogs and can result in

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Fig. 1. Multiple sinus tracts around the anus in a 7-year-old intact male German shepherd dog.

euthanasia if not effectively managed. Rapid and accurate diagnosis and aggressive medical therapy are key to successful management of canine perianal fistulas. This article reviews current knowledge regarding the clinical presentation, pathogenesis, and medical management of perianal fistulas.

CLINICAL PRESENTATION

Dogs with perianal fistulas may present with a single or multiple sinus tracts or ulcers in the skin around the anus. In some cases, ulcers may be large and deep or crateriform. Despite widespread use of the term, *perianal fistula*, in the veterinary medical literature, the cutaneous sinus tracts do not generally communicate with the rectal lumen (as is the case for humans with fistulizing Crohn's disease).¹ Due to the location and discomfort on examination, dog owners may not be aware of the lesions but may present their dog to the veterinarian due to associated clinical signs, such as licking around the anus, tenesmus, hematochezia, or mucopurulent discharge (**Fig. 2**).^{2,3} An association between perianal fistulas and colitis has been demonstrated, and some affected dogs also may have a history of soft or mucoid stools, diarrhea, and increased frequency of defecation.^{2,3}

German shepherd dogs are most commonly affected (reported to comprise more than 80% of the patient population⁴), but several other breeds, including the beagle, border collie, Australian shepherd, Irish setter, Chesapeake Bay retriever, Leonberger, Staffordshire bull terrier, and mixed-breed dogs, have also been reported to develop perianal fistulas.³⁻¹⁰ The author has also diagnosed perianal fistulas in an American Staffordshire terrier (**Fig. 3**), a Brittany spaniel, a soft-coated wheaten terrier, and mixed-breed dogs.

Perianal fistulas are typically adult onset. The age of onset can vary widely, from young adult to geriatric, although middle-aged dogs are most commonly affected.^{4,5,11} A definitive gender predisposition has not been demonstrated, although



Fig. 2. Perianal ulcer with mucopurulent exudate in an 8-year-old intact male German shepherd dog. This dog also presented with severe tenesmus.

an increased risk in intact male German shepherd dogs compared with neutered male German shepherd dogs has been suggested.¹²

DIAGNOSIS

Perianal fistulas are visually distinct and, in most cases, are diagnosed based on clinical presentation alone, especially in a German shepherd dog. An ulcerated perianal neoplasm (perianal adenoma or adenocarcinoma) and mucocutaneous lupus

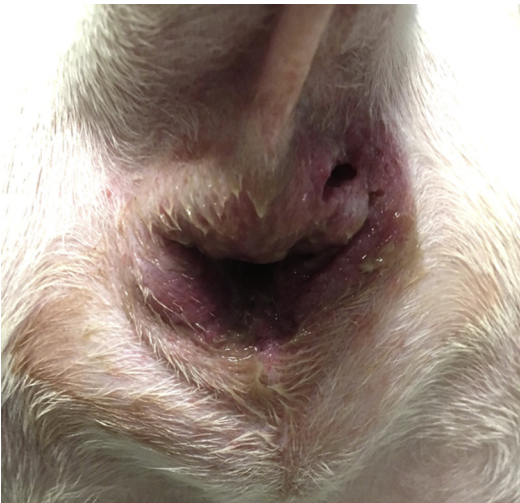


Fig. 3. Multiple perianal ulcers and sinus tracts in 6-year-old castrated male American Staffordshire terrier dog. This dog also had a history of chronic diarrhea and inflammatory bowel disease (colitis and proctitis) confirmed via endoscopic biopsies.

erythematosus (MCLE) are the primary rule-outs, but other conditions resulting in perianal draining tracts also should be considered. For example, glandular tissue left behind after an anal saccullectomy can result in chronic perianal draining tracts that can be misdiagnosed as perianal fistulas. German shepherd dogs are also predisposed to MCLE, and anal or perianal lesions are common in this condition.¹³ Perianal fistulas generally are clinically differentiated from MCLE. Perianal fistulas are typically sharply demarcated sinus tracts or crateriform ulcers, whereas MCLE is associated with more confluent erosions, ulcers, erythema, and crusts.¹³ For more information about canine MCLE, see Frane Banovic's article, "[Canine Cutaneous Lupus Erythematosus Newly Discovered Variants](#)," in this issue.

Histopathology is rarely performed for diagnosis of canine perianal fistulas but can be considered in cases of unusual clinical presentation or in an uncommonly affected breed (such as a small breed dog). In humans with perianal fistulas due to Crohn's disease, malignant transformation can occur and, although not well documented in dogs with perianal fistulas, could be a reason to prioritize histopathology in patients with chronic disease.¹⁴

Histopathologic features of canine perianal fistulas include periadnexal inflammation with or without furunculosis, pronounced hidradenitis, periadnexal fibrosis, ulceration, and formation of epithelial-lined sinus tracts within the dermis.^{4,5} Inflammatory infiltrates, composed of neutrophils, lymphocytes, plasma cells, and macrophages, may be noted within sinus tracts.⁴ Deeper lesions also may be associated with pyogranulomatous cellulitis and lymphoid follicles.⁵ If clinical differentiation of perianal fistulas from MCLE is difficult, skin biopsies for histopathology may be helpful. MCLE is characterized by a lymphocyte-rich interface dermatitis with evidence of basal cell damage.¹³ Colonic biopsies from dogs with perianal fistulas may demonstrate histopathologic evidence of colitis; 1 study found histopathologic changes consistent with a diagnosis of colitis in 9 of 18 dogs with perianal fistulas.³

In addition to close examination of the perianal skin, the physical examination for dogs suspected of having perianal fistulas should include a rectal examination. Sedation may be required to accomplish this and is dependent on patient comfort level. All patients should be assessed for anal strictures, the anal sacs should be carefully palpated, and expression of the anal sacs should be attempted. Abnormalities of the anal sacs, including impaction, difficult expression, or rupture, may occur in patients with perianal fistulas and are usually secondary to inflammation and fibrosis in the region of the anal sac ducts.^{15,16} The author has encountered perianal fistulas and a concurrent apocrine gland adenocarcinoma of the anal sac in the same patient (a middle-aged German shepherd dog). This patient presented with a mildly enlarged, firm, and nonexpressible anal sac that did not markedly change despite resolution of the perianal fistulas with medical therapy.

PATHOGENESIS

The predisposition to development of perianal fistulas in German shepherd dogs was initially believed related to anatomic conformation. Several conformational features were speculated to contribute to the development of perianal fistulas, including low tail carriage encouraging fecal retention and an increased density of perianal apocrine sweat glands.^{5,11} The low tail carriage was believed to produce a warm, humid environment, leading to chronic inflammation and secondary infection of perianal and anal glands with fecal flora.¹¹ The occurrence of perianal fistulas in other dog breeds without low tail carriage, as well as the lack of a clinical response to antimicrobial therapy alone, led investigators to question this anatomic conformation theory.⁵

Gradually, a probable immune-mediated pathogenesis for canine perianal fistulas emerged. An early study investigating the immunologic status of dogs with perianal fistulas demonstrated a blunted lymphocyte proliferation response following stimulation with phytomitogens in 9 of 33 dogs with active disease. After lesion resolution, the lymphocyte proliferation response normalized in 4 of 9 dogs. Based on this result, the investigators suggested that the suppression of the lymphocyte proliferation response may be an acquired abnormality secondary to perianal fistulas.¹⁷ More recent work has demonstrated that perianal fistulas likely develop as a consequence of local T-cell-mediated inflammation. This is supported by studies demonstrating perivascular aggregates of CD3⁺ T lymphocytes within lesional skin of dogs with perianal fistulas¹⁸ as well as increased expression of T-cell-associated, in particular type 1 helper T-cell-associated cytokine mRNA in lesional skin of affected dogs compared with controls.⁶ A decrease in expression of interleukin (IL)-2 in lesional skin after cyclosporin A therapy has also been demonstrated.⁸ Abnormal macrophage activation by type 1 helper T cells has also been suggested to play a role in the development of perianal fistulas. One study found increased expression of matrix metalloproteinase (MMP)-9 and MMP-13 mRNA in lesional skin from dogs with perianal fistulas compared with controls. MMP-9 and MMP-13 are produced by activated macrophages and are involved in the early stages of wound healing, primarily by degradation of the extracellular matrix. The investigators of this study proposed that impaired wound healing, in particular failure to initiate wound repair, may play a role in the persistence of ulcers and sinus tracts.⁷ Similarly, up-regulation of MMPs may play a role in the pathogenesis of human fistulizing Crohn's disease, which is proposed to be a correlate of canine perianal fistulas.¹⁹

A dysfunctional immune response to microbes in the anal and perianal regions also has been proposed to contribute to the pathogenesis of canine perianal fistulas. One culture-based study performed in 1988 from tissue samples collected at the time of surgical fistula excision showed that *Escherichia coli*, *Staphylococcus* sp, β -hemolytic streptococci, and *Proteus mirabilis* were isolated most frequently. The investigators concluded that the bacterial isolates likely represented contaminants and that microbial infection did not play a primary role in the development of perianal fistulas.⁵ In 2008, House and colleagues²⁰ investigated mRNA expression and function of several pattern recognition receptors in vitro using monocyte/macrophages derived from the blood of dogs with perianal fistulas. They found evidence of a decreased response in the NOD2 pattern recognition receptor of macrophage/monocytes derived from dogs with perianal fistulas after stimulation with microbial pathogen-associated molecular patterns compared with controls. This result suggests a possible innate immunodeficiency in dogs with perianal fistulas. Dogs with perianal fistulas were also shown to have increased antistaphylococcal IgG compared with normal dogs²¹ and a dysregulated T-cell-mediated response to cutaneous or fecal microbial antigens in dogs with perianal fistulas has been proposed.⁸

Since these studies were performed in the late 1990s and early 2000s, there has been an increasing focus in the medical community on characterization of microbial populations (the microbiome) via non-culture-based methods and on the complex interplay between shifts in microbial populations and the promotion of disease. Shifts in the cutaneous and/or intestinal microbiome have been proposed to contribute to the development of hidradenitis suppurativa (also proposed as a human correlate of canine perianal fistulas), although this link has not been well established.²² Intestinal dysbiosis has been well described in association with inflammatory bowel disease in humans,²³ and manipulation of the intestinal microbial flora via fecal transplantation may be effective at ameliorating the clinical signs of Crohn's disease and ulcerative colitis in humans.²⁴ To explore the role that cutaneous and intestinal microbial populations may play in canine perianal fistulas, the author and colleagues have completed a

longitudinal evaluation of the cutaneous and rectal microbiome in German shepherd dogs with perianal fistulas, both prior to and while receiving immunomodulatory therapy with cyclosporin A and ketoconazole (the study was funded by an internal grant from the Penn Vet Center for Host-Microbial Interactions, Philadelphia, Pennsylvania). Clinically normal German shepherd dogs were sampled as a control population; data analysis currently is in progress.

An adverse food reaction has been reported for some dogs with perianal fistulas. One study of adverse food reactions in dogs with dermatologic signs reported a significant association between perianal fistulas and adverse food reaction, but only 4 dogs with perianal fistulas were included and all were German shepherd dogs.²⁵ Three studies reported a positive clinical response to a novel protein diet in dogs with perianal fistulas; in 1 study, a fish and potato diet was fed long term after surgical excision of sinus tracts and bilateral anal saccullectomy.⁹ In the second study, dogs were fed an exclusive venison and potato or fish and potato diet but also received metronidazole initially as well as topical tacrolimus 0.1% ointment and a tapering course of oral prednisone for 16 weeks.²⁶ In the third study, dogs were fed a commercially available lamb and rice or vegetarian diet but concurrently received a tapering course of oral prednisone at an initial immunosuppressive dose.² Although the author regularly recommends an elimination diet trial using a prescription novel protein or hydrolyzed protein diet as part of the diagnostic work-up for dogs with perianal fistulas, it is unclear from the available literature how many dogs may achieve long-term disease remission with dietary control alone.

GENETIC BASIS

The strong association of perianal fistulas with the German shepherd breed suggests a genetic susceptibility. A few studies have explored potential genetic risk factors for the disease in German shepherd dogs. An association between the class II MHC allele DLA-DRB1*00101 and increased risk of development of perianal fistulas has been found in populations of German shepherd dogs from the United Kingdom and Finland. Dogs homozygous for the DLA-DRB1*00101 allele may develop perianal fistulas earlier in life (at <8 years of age).^{12,27} Class II molecules of the major histocompatibility complex (MHC) are involved in antigen presentation and T-cell activation; thus, an association with an MHC allele further supports a T-cell-mediated pathogenesis for this disease.^{12,27} A genome-wide association study of 21 affected German shepherd dogs and 25 unaffected German shepherd dogs, followed by genotyping of potentially associated single nucleotide polymorphisms in cohorts of affected and unaffected German shepherd dogs in the United Kingdom and Finland, found a potential association with the *ADAMTS16* and *CTNND2* gene regions.²⁸ The *CTNND2* gene region also has been associated with human Crohn's disease and ulcerative colitis, suggesting a potential shared pathogenesis for human inflammatory bowel disease and canine perianal fistulas.²⁸ Another study investigated genes encoding for several pattern recognition receptors in German shepherd dogs with perianal fistulas. This study failed to identify any single nucleotide polymorphisms in genes encoding for pattern recognition receptors associated with perianal fistulas but did show restricted pattern recognition receptor genotypes in German shepherd dogs (both affected and unaffected) versus other dog breeds. The restricted pattern recognition receptor genotypes in German shepherd dogs may influence innate immune function in this breed.²⁹

HUMAN CORRELATES

Two human conditions, hidradenitis suppurativa and fistulizing Crohn's disease, have been proposed as correlates of canine perianal fistulas.^{5,10} Like perianal fistulas in

dogs, both of these conditions are painful and debilitating and can have a negative impact on quality of life of patients.^{19,22,30} Management of both of these conditions is challenging; no universally effective therapy has been identified and relapses are common.^{14,19,22,30}

Hidradenitis suppurativa is associated with nodules, abscesses, sinus tracts, and scarring, primarily in intertriginous regions (axilla, groin, perianal region, and mammary region).²² Hidradenitis suppurativa was initially proposed as a potential correlate of canine perianal fistulas because of similar histopathologic features, including furunculosis, hidradenitis, and formation of epithelial-lined sinus tracts.^{5,22} The pathogenesis of hidradenitis suppurativa has not been fully elucidated, but it is likely an immune-mediated condition with a genetic susceptibility. Alterations in cutaneous or intestinal microbiota may play a role in the pathogenesis. Risk factors include obesity, smoking, metabolic syndrome, hormonal influences, and diabetes mellitus; an association with inflammatory bowel disease has also been suggested.^{22,31} Medical management of hidradenitis suppurativa involves use of topical or systemic antimicrobials (potentially helpful for anti-inflammatory and/or immunomodulatory properties more so than direct targeting of microbes), retinoids, systemic or intralesional corticosteroids, and cytokine-directed therapies (inhibitors of tumor necrosis factor [TNF] or IL-1).³⁰

Perianal manifestations of Crohn's disease are common, estimated to affect 25% to 33% of Crohn's disease patients.^{14,19,32} Perianal fistulas are more common in patients with colonic or rectal disease and may be simple (a fistulous tract with a single external opening) or complex (multiple fistulous tracts, perianal abscesses, or anal/rectal stricture).^{14,19} Unlike the typical disease in dogs, these are true fistulas that communicate with the intestinal lumen. The pathogenesis of perianal fistulas in Crohn's disease is not fully understood but has been shown to involve epithelial-to-mesenchymal transition and up-regulation of MMPs and proinflammatory cytokines. Genetic susceptibility, as well as alterations in the cutaneous and/or intestinal microbiota, may play a role in development of perianal fistulas in humans.^{14,19} Like canine perianal fistulas, there has been a shift in management of fistulizing Crohn's disease from primarily surgical intervention to incorporation of medical therapies.³² Successful management of fistulizing Crohn's disease usually necessitates multimodal surgical and medical approaches. To date, the most efficacious medical therapies are cytokine-directed therapies (inhibitors of TNF or IL-12/IL-23), intrafistula mesenchymal stem cell injections, and adjunctive antimicrobials (although antimicrobials alone are not effective for resolution of fistulas).^{1,14,19,32}

Both hidradenitis suppurativa and fistulizing Crohn's disease share clinical features with canine perianal fistulas. Similarities in the pathogenesis of hidradenitis suppurativa and Crohn's disease have been demonstrated, in particular infiltration of diseased tissue by type 17 T helper cells.³³ Future studies should focus on better characterization of the underlying etiology of these 3 conditions and may help direct the development of future therapies, such as antibodies targeting specific cytokines, for perianal fistulas in dogs.

SURGICAL MANAGEMENT

A comprehensive review of surgical management of canine perianal fistulas is beyond the scope of this article. With the increasing recognition of an immune-mediated pathogenesis for the disease, there was a corresponding shift in standard-of-care from surgical intervention to medical management. Several surgical procedures have been described, including en bloc surgical excision (usually performed together with bilateral anal saccullectomy) followed by surgical reconstruction, laser excision, cryosurgery, and amputation at the tail base.^{9,15,16,34-37} One study reported good control

of perianal fistulas using a combination of immunomodulatory therapy with prednisone and azathioprine or cyclosporin A with or without ketoconazole followed by surgical excision of remaining sinus tracts, bilateral anal sacculectomy, and cryptectomy.³⁵ Another study reported a complete response (lack of visible sinus tracts or ulcers) in 29 of 33 dogs after en bloc surgical resection of perianal fistulas, bilateral anal sacculectomy, and diet change to a fish and potato diet. Six of these 29 dogs continued to exhibit clinical signs, such as perianal licking, tenesmus, diarrhea, or constipation.⁹ Potential complications of surgical repair of perianal fistulas include dehiscence, lesion recurrence (reported in more than 50% of dogs in one study³⁴), likely related to the failure to control the underlying immune-mediated inflammation, fecal incontinence, and anal stricture.^{16,34}

MEDICAL MANAGEMENT

Mesenchymal Stem Cell Injections

Injections of mesenchymal stem cells, administered directly into fistulas, have been shown effective for humans with fistulizing Crohn's disease.¹ Mesenchymal stem cells have immunomodulatory activity, such as decreasing proliferation and activation of T lymphocytes and dendritic cells and increasing production of T-regulatory cells.^{10,19} The efficacy of mesenchymal stem cell injections for canine perianal fistulas has been reported for a small number of dogs by Ferrer and colleagues.¹⁰ Six dogs with perianal fistulas that had failed therapy with cyclosporin A at standard dosing for a minimum of 6 months of administration were enrolled in an open-label trial and received a single injection of human embryonic stem cell-derived mesenchymal stem cells within perianal lesions. The dogs were followed for 6 months postinjection; all dogs had resolution of sinus tracts or ulcers by 3 months after injection of stem cells. Two dogs had recurrence of perianal fistulas by 6 months postinjection.¹⁰ Although mesenchymal stem cell injections are a promising treatment option for canine perianal fistulas, additional controlled studies are needed to apply these results to larger populations of affected dogs as well as to determine the optimal frequency of injections.

Antimicrobials

Antimicrobials alone do not seem effective for management of perianal fistulas in dogs. In the author's experience, many dogs are treated with antimicrobials at the time of onset of clinical signs of perianal fistulas but continue to experience disease progression. A few studies have reported use of metronidazole in combination with other therapies (azathioprine, tacrolimus ointment, prednisone, and novel protein diet) for treatment of dogs with perianal fistulas.^{26,38} In addition to activity against anaerobic bacteria and protozoa, metronidazole may also have anti-inflammatory activity, including promotion of T-regulatory cell differentiation.³⁹ This anti-inflammatory activity may aid in treatment of immune-mediated diseases, but the efficacy of metronidazole alone for treatment of perianal fistulas is unknown at this time.

Immunomodulatory Agents

Several immunomodulatory agents have been reported as treatments for canine perianal fistulas, including oral prednisone (at initial immunosuppressive doses), azathioprine, cyclosporin A (alone or in combination with ketoconazole), topical tacrolimus, and mycophenolate mofetil.^{2,35,38,40-51} The best evidence of efficacy is for calcineurin inhibitors (cyclosporin A and tacrolimus); these are discussed later. In 1 study of German shepherd dogs with perianal fistulas treated with a tapering course of oral

prednisone (at an initial immunosuppressive dose of 2 mg/kg/d) and a commercially available novel protein diet for up to 16 weeks, complete lesion resolution was noted in 9 of 27 dogs (33.3%).² Due to the need for ongoing administration of immunomodulatory agents for management, as well as the risk of side effects with long-term administration of corticosteroids, the author does not typically use corticosteroids for management of canine perianal fistulas. In another study by Harkin and colleagues,⁴⁰ 14 dogs with perianal fistulas were treated with azathioprine alone. After 16 weeks of therapy, 8 of 14 dogs (57%) achieved complete resolution of lesions. To the author's knowledge, there is only a single report of the use of mycophenolate mofetil for the management of perianal fistulas in the veterinary literature; this dog was treated for 4 weeks without improvement in lesions.⁵¹

Calcineurin Inhibitors (Cyclosporin A and Tacrolimus)

Cyclosporin A and tacrolimus are immunomodulatory agents that work by binding to the intracellular protein cyclophilin-1, which inhibits calcineurin. This inhibition of calcineurin prevents the dephosphorylation of nuclear factor of activated T cells and subsequent production of proinflammatory cytokines, such as IL-2. Decreased production of IL-2 leads to decreased growth and activation of T lymphocytes.⁵²

Several studies have supported the efficacy of cyclosporin A for treatment of canine perianal fistulas, including randomized and controlled clinical trials. In a randomized clinical trial comparing cyclosporin A with a placebo in German shepherd dogs with perianal fistulas, complete lesion resolution was reported in 17 of 20 dogs (85%) receiving cyclosporin A after 16 weeks of treatment. Mean total surface area and depth of lesions improved by 78% and 62%, respectively, after 4 weeks of therapy in dogs receiving cyclosporin A.⁴¹

Cyclosporin A doses investigated for treatment of canine perianal fistulas vary widely—from 1.5 mg/kg every 24 hours to 10 mg/kg every 12 hours.^{42–46} In general, higher doses were associated with improved outcome,⁴⁶ but all dogs were not treated with the same formulation of cyclosporin A (some received nonmodified cyclosporin A)⁴² and cyclosporin A was administered with food in some cases.⁴³ Modified or microemulsified formulations of cyclosporin A have superior bioavailability in dogs and should be used preferentially in all cases. Bioavailability of cyclosporin A in dogs is also reduced by the presence of food and it is best administered on an empty stomach (ie, 2 hours prior to or after a meal).⁵²

The cost of cyclosporin A, particularly at higher doses or for larger dogs, may be prohibitive. Administration of cyclosporin A with ketoconazole can inhibit metabolism of cyclosporin A by hepatic cytochrome P450 microenzymes as well as improve bioavailability via inhibition of intestinal P-glycoprotein (thus decreasing transport of cyclosporin A to the intestinal lumen). Coadministration of the 2 drugs can improve cyclosporin A bioavailability by 75% or more, depending on the ketoconazole dose, and allow cyclosporin A dose reduction.^{47,52} The combination of cyclosporin A (at doses of 1 mg/kg/d to 5.5 mg/kg/d) and ketoconazole (at doses of 5.1 mg/kg/d to 11 mg/kg/d) was shown effective in clinical trials with complete lesion resolution in 93% of dogs in 16 weeks,⁴⁸ 100% of dogs in 3 to 10 weeks,⁴⁹ and 67% of dogs with a mean time to resolution of 13.9 weeks.⁴⁷

The author regularly uses the combination of cyclosporin A at initial doses of 2 mg/kg/d to 4 mg/kg/d and ketoconazole at initial doses of 5 mg/kg/d to 10 mg/kg/d for treating perianal fistulas in dogs. Relapses can occur when immunomodulatory therapy is discontinued.^{41,43,45–49} For this reason, after complete resolution of lesions (which generally requires 8–12 weeks of therapy), the author slowly tapers cyclosporin A and ketoconazole to the lowest effective dosing and dose

frequency. The author does not routinely perform cyclosporin A blood level monitoring in these patients because cyclosporin A blood levels do not correlate well with clinical response.⁴⁶

Tacrolimus 0.1% ointment has also been shown effective for treatment of canine perianal fistulas, although randomized controlled clinical trials have not been performed.^{26,50} In 1 report of 10 dogs treated with tacrolimus, 0.1% ointment applied to the perianal skin twice daily for 16 weeks, 5 dogs achieved complete resolution of lesions. Tacrolimus is more appropriate for topical application than cyclosporin A because of its smaller molecular weight, leading to improved absorption through the epidermis.²⁶ Because of the discomfort that may be associated with application, the author most commonly recommends topical tacrolimus ointment for dogs with mild lesions or for dogs with more severe lesions after complete or partial resolution with oral cyclosporin A (most often in combination with ketoconazole). Some dogs may be transitioned to topical tacrolimus ointment alone for maintenance to prevent relapses of perianal fistulas (**Fig. 4**).

Other Considerations for Medical Management

Dogs with active perianal fistulas can be painful, particularly on defecation.^{2,3} Stool softeners should be considered, and, in some cases, enemas may be necessary to ease tenesmus. Analgesia should be prioritized for dogs with active lesions but the potential for constipation with use of some analgesics, such as opioid agonists,⁵³ should be considered when formulating a pain management plan. Some dogs with perianal fistulas are euthanized due to unremitting disease, development of complications such as anal stricture, or expense of long-term management.⁴³ For these reasons, early diagnosis and aggressive medical management of canine perianal fistulas are



Fig. 4. Complete resolution of perianal sinus tracts in the 7-year-old German shepherd dog pictured in **Fig. 1**. This dog was treated with oral cyclosporin A and ketoconazole to the point of lesion resolution, then transitioned to topical tacrolimus 0.1% ointment. Clinical remission has been maintained for more than 12 months with application of tacrolimus ointment.

key. In the author's experience, management of patients with chronic lesions can be more challenging and these patients can be more refractory to medical therapy. Future studies should focus on better characterizing the genetics and immunopathogenesis of this disease, assessing quality of life of affected dogs and their owners (see Chiara Noli's article, "Assessing Quality of Life for Pets with Dermatologic Disease and their Owners," in this issue), and developing targeted medical therapies.

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